

Edited:

RABBITV1 - SEND 3.1 for CBER Proof of Concept Study for a Vaccine

Anonymized Final Study Report

Items removed or substituted:

Study identifiers

Test Facility and Site identifiers

Test Article identifiers and descriptions

Lab specific Software names

Signature pages and names

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## **GLP COMPLIANCE STATEMENT OF THE STUDY DIRECTOR**

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### **Phases conducted at TEST Facility**

The study was performed in compliance with standard operating procedures and the following principles of Good Laboratory Practice\*:

\* With the following deviations:

- there were no analyses of the vaccine formulations prepared during the study. However, the test item was reconstituted following an established procedure provided by the Sponsor, the whole formulation amount contained in the syringes was administered to the animals and the amount of adjuvant placed in the new sterile stoppered vials was weighed. Therefore, this deviation to GLP was not considered to have an impact on the global GLP status of the study,
- on Day 57, a new reagent was used to determine the Creatine Kinase (CK) because the previous one was not available anymore, but it was not yet validated. Data are presented as "indicative values". This GLP deviation was not considered to have an impact on the global GLP status of the study nor on the data interpretation, since all groups including controls were impacted in a similar way, no test item-related effects were seen on this parameter during the treatment period and the validation preliminary results with the new reagent obtained after completion of the study confirmed it was conformed.

### **Phase conducted at test site**

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Study completion date: *27 March 2013*

## **STATEMENT OF QUALITY ASSURANCE UNIT**

| Type of inspection                  | Dates                   |                                |                        |
|-------------------------------------|-------------------------|--------------------------------|------------------------|
|                                     | Inspection              | Reported to the Study Director | Reported to Management |
| Study plan                          | 03 August 2018          | 03 August 2018                 | 03 August 2018         |
| Study plan amendment No. 1          | 17 August 2018          | 17 August 2018                 | 17 August 2018         |
| Treatment                           | 03 September 2018       | 03 September 2018              | 03 September 2018      |
| Blood sampling                      | 19 September 2018       | 25 September 2018              | 25 September 2018      |
| Study plan amendment No. 2          | 09 October 2018         | 09 October 2018                | 09 October 2018        |
| Study plan amendment No. 3          | 26 October 2018         | 26 October 2018                | 26 October 2018        |
| Study plan amendment No. 4          | 20 November 2018        | 20 November 2018               | 20 November 2018       |
| Tabulated data                      | 11 to 14 December 2018  | 14 December 2018               | 14 December 2018       |
| Tabulated data<br>(immunology data) | 07 and 12 December 2018 | 12 December 2018               | 12 December 2018       |
| Report (study report)               | 19 to 21 December 2018  | 27 December 2018               | 27 December 2018       |
| Report (pathology report)           | 27 December 2018        | 27 December 2018               | 27 December 2018       |
| Study plan amendment No. 5          | 17 January 2019         | 17 January 2019                | 17 January 2019        |
| Final check<br>(pathology report)   | 14 March 2019           | 14 March 2019                  | 14 March 2019          |
| Final check<br>(immunology report)  | 14 March 2019           | 14 March 2019                  | 14 March 2019          |
| Final check (study report)          | 14 March 2019           | 14 March 2019                  | 14 March 2019          |

In addition, process and facility based inspections are carried out according to the annual quality assurance program.

The inspections were performed in compliance with Quality Assurance Unit procedures and the principles of Good Laboratory Practices.

The final report is considered to constitute an accurate and complete reflection of the study raw data.

**STATEMENT OF QUALITY ASSURANCE UNIT (continued)**

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**Inspections performed at Principal Investigator (PI) test site**

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Date: *26 March 2019*

## **SUMMARY**

The objective of the study was to evaluate the local tolerance and systemic toxicity of the test items, in the New Zealand White (NZW) rabbit, following three intramuscular injections, two weeks apart. Any delayed onset toxicity and/or the reversibility of any finding observed on completion of the treatment period was evaluated during a 4-week observation period.

A total of 60 (30 males and 30 females) NZW rabbits were allocated to 3 groups and received either the test items, or the control item (NaCl 0.9%), by intramuscular (IM) route (approximately 0.75 mL/injection) on Days 1, 15 and 29, according to the following table:

| Group | Treatment           | Nominal dose level | Nominal dose level | Number of animals      |
|-------|---------------------|--------------------|--------------------|------------------------|
|       |                     | (mg)               |                    |                        |
| 1     | Control (NaCl 0.9%) | 0                  | 0                  | 10 males<br>10 females |
| 2     | SENDVACC10          | 12.5               | 15                 | 10 males<br>10 females |
| 3     | SENDVACC99          | 12.5               | 45                 | 10 males<br>10 females |

The animals were observed every day for morbidity, mortality, clinical signs and local reactions at the injection site. Body weights were recorded at pre-test, on the day and on the day after each injection, and then every 3 or 4 days. Food consumption was recorded at pre-test and then daily throughout the study. Rectal temperature was recorded at pre-test, before each injection and then 3, 6 and 24 hours after each injection. An ophthalmological examination was conducted at pre-test, 2 days after the first injection (on Day 3) and on the days of necropsies (on Days 31 and 57). Blood samples were collected for the evaluation of hematology, blood biochemistry, C-Reactive Protein (CRP) and coagulation parameters at pre-test, 2 days after the first injection (on Day 3) and on the days of necropsies (on Days 31 or 32 and 57). Serum samples were collected for immunogenicity evaluation at pre-test and on the days of necropsies (on Days 31 and 57).

The first five animals/sex (principal animals) were euthanized 2 days after the last injection (on Day 31) and the last five animals/sex (recovery animals) were euthanized 4 weeks after the last injection (on Day 57). A full macroscopic *post-mortem* examination was performed, designated organs were weighed and a full list of tissue specimens was preserved. A microscopic examination was performed on the preserved tissues from all animals.

There were no unscheduled deaths and no adverse clinical signs observed during the study. At the injection sites, hematomas were observed in all groups including controls with a slight increase in incidence and severity in animals given SENDVACC99 as compared to controls; an effect of the adjuvanted test item treatment could not be excluded, but was considered non-adverse. There were no changes in rectal temperature and no observations at the ophthalmological examination.

There was a transient minimal mean body weight loss in both test item-treated groups after the first (females) and second (both sexes) injections, which had not impacted the terminal mean body weight of the animals. The changes in body weight gain were associated with minimally lower mean food consumption over the same periods.

Adjuvanted test items may have induced minimally increased mean white blood cell counts (SENDVACC10 females), including neutrophils, monocytes (SENDVACC10 females) and large unstained cells (both vaccines and sexes) noted after the third administration. Adjuvanted test items induced an increase in fibrinogen and CRP levels, as well as a decrease in albumin/globulin ratio. These changes were considered as non-adverse, reversible and related to the pharmacology activity of the adjuvanted vaccines. They correlated with inflammation seen at the histopathological examination. Other changes in clinical pathology parameters (*i.e.* cholesterol) were considered of no biological significance.

At necropsy, both test items induced an increase in absolute and relative (to body and brain) weights of the spleen correlating with lymphoid hyperplasia at histopathological examination. There was partial recovery in males, and complete recovery in females.

At the macroscopic examination, reversible gelatinous abdominal adipose tissue, correlating with edema at microscopic examination, was present in females treated with both test items while enlarged right inguinal lymph nodes, correlating with lymphoid hyperplasia at microscopic examination, were present in males given SENDVACC99

At the histopathological examination, observations for both vaccines consisted of lymphoid hyperplasia and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue (on the right side only). These changes showed partial recovery by the end of the 4-week recovery period. These histopathological findings were considered as non-adverse and related to the pharmacology activity of the adjuvanted vaccines.

Finally, the immunogenicity evaluation showed very high levels of specific IgG at the end of the treatment and recovery periods in all animals treated with the vaccines.

## **Conclusion**

The three intramuscular administrations of SENDVACC10 and SENDVACC99 in the New Zealand White rabbit, two weeks apart, at the anticipated human dose, were both locally and systemically well tolerated. Both adjuvanted test items induced non-adverse transient minimal mean body weight loss associated with minimal reduction in mean food consumption shortly after the first two administrations. Other adjuvanted vaccines-related effects included reversible increase in mean fibrinogen and CRP concentrations, reversible decrease in mean albumin/globulin ratio, as well as potentially short minimal to slight hematomas at the injection sites and reversible increase in some white blood cell subpopulations. Adjuvanted test items induced lymphoid hyperplasia and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue. These histopathological findings showed partial recovery at the end of the 4-week observation period.

These changes were considered non-adverse and generally consistent with the pharmacology activity of adjuvanted vaccines.

The immunogenicity assay confirmed the exposure of all vaccinated rabbits to the adjuvanted vaccines.

## **1. INTRODUCTION**

### **1.1 OBJECTIVE**

The objective of the study was to evaluate the local tolerance and systemic toxicity of SENDVACC10 and SENDVACC99, in the New Zealand White (NZW) rabbit, following three intramuscular injections, two weeks apart. Any delayed onset toxicity and/or the reversibility of any finding observed on completion of the treatment period was evaluated during a 4-week observation period.

The rabbit was chosen because it is a non-rodent species accepted by Regulatory Authorities for this type of toxicology studies with vaccines. The NZW strain was selected since background data from previous studies are available. Moreover, the intramuscular administration of influenza vaccine in rabbit induces specific immune response to the vaccine antigen, and adjuvant effect was previously demonstrated in this species.

The intramuscular route was selected since it is the intended route of administration in humans.

The dose levels were selected by the Sponsor and correspond to the anticipated human dose of vaccines to be administered in human.

### **1.2 REGULATORY COMPLIANCE**

The study design was based on the following guidelines:

- . WHO guidelines on nonclinical evaluation of vaccines, Annex 1. WHO Technical Report Series, 2005; 927: 31-63,
- . WHO guidelines on the nonclinical evaluation of vaccine adjuvants and adjuvanted vaccines, WHO

Expert Committee on Biological Standardization, sixty-fourth meeting, WHO, 21-25 October 2013.

### **1.3 IN-HOUSE ETHICS REVIEW**

### **1.4 CONFIDENTIALITY**

The information in this document and any future information supplied contain trade secrets and commercial information that are privileged or confidential and may not be disclosed unless such disclosure is required by laws or regulations. In all eventualities, persons to whom the information is disclosed must be informed that the information is privileged or confidential and may not be disclosed by themselves.

## **2. MATERIALS AND METHODS**

### **2.1 TEST AND CONTROL ITEMS AND ADJUVANTS**

#### **2.1.1 Identifications**

##### **2.1.1.1 Test item 1**

**Name:** SENDVACC10

**Synonyms:**

*All denominations correspond to the same test item.*

**Batch No.:** 1

**Description:**

**Containers:**

**Storage condition:**

**Specific requirements  
(handling conditions):**

**Purity:**

**Concentration:**

**Correction factor:**

**Date of receipt:**

**Expiry date:**

Data relating to the characterization of the test item 1 were provided by the Sponsor and are documented in certificates of analysis and compliance (see [Appendix 1](#)).

2.1.1.2 Test item 2

**Name:** SENDVACC99

**Synonyms:**

*All denominations correspond to the same test item.*

**Batch No.:** 2

**Description:**

**Containers:**

**Storage condition:**

**Specific requirements  
(handling conditions):**

**Purity:**

**Concentration:**

-

**Correction factor:**

**Date of receipt:**

**Expiry date:**

Data relating to the characterization of the test item 2 were provided by the Sponsor and are documented in a certificate of analysis (see [Appendix 1](#)).

### 2.1.1.3 Adjuvant

**Name:** XYZ

**Synonyms:**

*All denominations correspond to the same adjuvant.*

**Batch No.:** 3

**Description:**

**Containers:**

**Storage conditions:**

**Specific requirements  
(handling conditions):**

**Purity:**

**Nominal concentration:**

**Measured concentration:**

**Correction factor:**

**Date of receipt:**

**Expiry date:**

Data relating to the characterization of the adjuvant were provided by the Sponsor and are documented in a certificate of analysis (see [Appendix 1](#)), a certificate of stability ([Appendix 2](#)) and in an e-mail dated.

### 2.1.1.4 Control item

The control item for administration to the control group (control dose formulation) was selected by the Sponsor, based on previous experimental work and/or preliminary study(ies).

**Name:** NaCl 0.9%

**Batch Nos.:**

**Storage condition:**

**Expiry dates:**

2.1.2 Dose formulation preparation for group 1 (control item)

**Type of formulation  
(visual observation):** Ready-to-use solution

**Preparation procedure:**

**Delivery condition:** At room temperature

2.1.3 Dose formulation preparation for groups 2 and 3

**Type of formulation  
(visual observation):** Emulsion

**Preparation procedure:**

(a)

(b)

(c)

(d)

**Delivery condition:** At room temperature.

## 2.1.4 Chemical analysis of the dose formulations

## 2.2 TEST SYSTEM

### 2.2.1 Animals

Number: 64 rabbits (32 males and 32 females) were received on 06 and 14 August 2018.

Strain and sanitary status: New Zealand White, INRA, A1077, Specific Pathogen Free.

Breeder:

Age/Weight: at the beginning of the treatment period, the animals were approximately 14 weeks old. The males had a mean body weight of 2781 g (range: 2540 g to 2980 g) and the females had a mean body weight of 2948 g (range: 2685 g to 3225 g).

Receipt: upon arrival at Citoxlab France, the animals were given a clinical examination to ensure that they were in good condition.

Acclimation: the animals were acclimated to the study conditions for a period of 14 days before the beginning of the treatment period. Two supernumerary animals/sex were allocated to the study and acclimated, in order to permit the selection and/or replacement of individuals.

Allocation to groups: during the acclimation period, the required number of animals (30 males and 30 females) were allocated to the groups, according to a computerized stratification procedure based on the last body weight recorded by the breeder, to ensure comparatively similar mean body weight of the groups.

Identification: the animals were individually identified by an ear tattoo at the breeder's facility. After allocation to groups, each animal received a unique identity number.

### 2.2.2 Environmental conditions

On arrival, the animals were housed in a secured unit.

The animal room conditions were set as follows (see § Study plan adherence):

- . temperature :  $18 \pm 3^{\circ}\text{C}$ ,
- . relative humidity :  $50 \pm 20\%$ ,
- . light/dark cycle : 16 h/8 h,
- . ventilation : 5 to 15 cycles/hour of filtered, non-recycled air.

The corresponding instrumentation and equipment are checked and calibrated at regular intervals. The temperature and relative humidity are recorded continuously (recording devices equipped with alarm systems).

### 2.2.3 Housing

The animals were individually housed in noryl cages (Tecniplast, 4200 cm<sup>2</sup>).

The cages were suspended in batteries over trays with absorbent paper and were placed in numerical order on the racks.

Each cage contained a platform and one toy (dumbbell) and hay (batch No. 5467149) was distributed regularly for the environmental enrichment of the animals. Music was also put on for the same purpose.

### 2.2.4 Food and water

All animals had free access to pelleted "type 110 C" diet batch Nos 17326, 18053 and 18101 (SAFE, Augy, France), and tap water (filtered with a 0.22 µm filter) contained in bottles. The food and water were distributed regularly.

During periods of fasting, food was removed but the animals were not deprived of water.

The diet formulae are presented in [Appendix 3](#).

### 2.2.5 Contaminant analyses

The batches of diet were analyzed by the Suppliers for composition and contaminant levels.

Bacterial and chemical analyses of water are performed regularly by external laboratories. These analyses include the detection of possible contaminants (pesticides and heavy metals). No contaminants were present in the diet or drinking water at levels which could have been expected to interfere with or prejudice the outcome of the study.

## 2.3 TREATMENT

### 2.3.1 Treatment groups

The treatment groups for the present study are detailed in the following table:

| Group | Treatment                | Nominal dose level of adjuvant (mg/dose) | Nominal dose level <sup>(1)</sup> | Number, sex and identity of animals                              |
|-------|--------------------------|--|-----------------------------------|--|
| 1     | Control item (NaCl 0.9%) | 0  | 0                                 | 10 males:<br>N30641 to N30650<br>10 females:<br>N30711 to N30720 |
| 2     | SENDVACC10 <sup>)</sup>  | 12.5                                     | 15                                | 10 males<br>N30651 to N30660<br>10 females:<br>N30721 to N30730  |
| 3     | SENDVACC99 <sup>)</sup>  | 12.5                                     | 45                                | 10 males<br>N30661 to N30670<br>10 females:<br>N30731 to N30740  |

### 2.3.2 Administration schedule

The dose formulations were administered by the intramuscular route on three occasions at 2-week intervals (on Days 1, 15 and 29).

At the end of the treatment period, the first five animals/sex (principal animals) were euthanized 2 days after the last injection (on Day 31), while the last five animals/sex (recovery animals) were euthanized after a 4-week observation period after the last injection (on Day 57).

For scheduling convenience, two sets of animals were stagger-started.

### 2.3.3 Administration

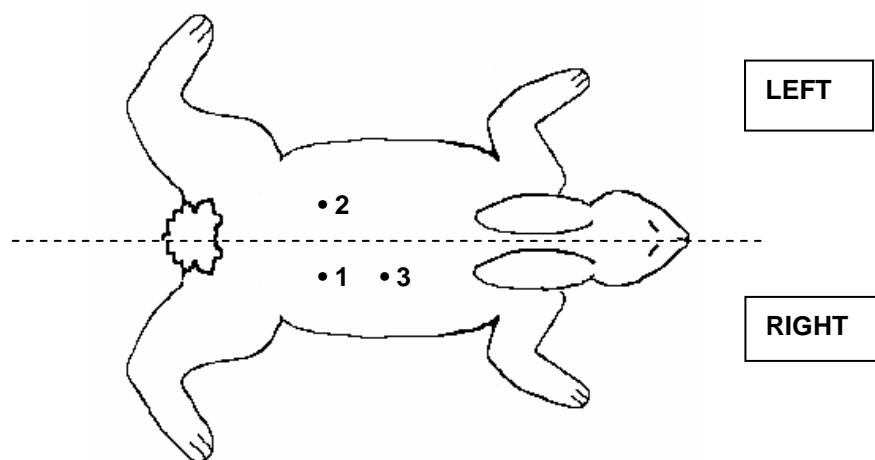
The dose formulations were administered using a pre-filled syringe (x + vaccine) fitted with a fine needle (see details in [§ Description of injection sites](#)). The syringe and needle were changed between each animal. The injection site was disinfected with 70% alcohol prior to injection.

The last two steps of the formulation preparation [see steps c) and d) in [§ Dose formulation preparation for groups 2 and 3](#)] was performed next to the animal room just before the treatment and the formulations were then delivered to the study room at room temperature (one pre-filled syringe per animal). The formulations were manually gently shaken before injection to each animal. The whole volume of one pre-filled syringe, which was approximately 0.75 mL, was administered to each animal each time. The control animals (group 1) were given 0.75 mL/injection of the control item.

The test items were administered to the animals within 10 minutes after reconstitution.

### 2.3.4 Description of injection sites

Three injection sites were used and each injection was performed in the dorsal muscles.



The injection site was clipped free of hair very carefully at least 24 hours before the administration. Clipping was repeated thereafter whenever necessary to allow the evaluation of local effects. Only animals with healthy intact skin were used. Any site showing damage or irritation as a result of shaving was not used. Prior to the injections, the animal was positioned with the hindlimbs under the abdomen. Both iliac crests were identified with the fingers by palpation as well as the spinous process of the last lumbar vertebra (between both iliac crests).

Injections [using a limiting device on the 25G (16 mm) needle to ensure 12 mm depth of injection (see § Study plan adherence), oriented with an angle of approximately 30° external] were performed as follows:

- . Day 1 at injection site 1: right side, 2 cm from the vertebra column, 5 cm from the basis of the template towards the cranial part,
- . Day 15 at injection site 2: left side, 2 cm from the vertebra column, 5 cm from the basis of the template towards the cranial part,
- . Day 29 at injection site 3: right side, 2 cm from the vertebra column, 9 cm from the basis of the template towards the cranial part.

## 2.4 CLINICAL EXAMINATIONS

### 2.4.1 Morbidity and mortality

Each animal was checked for mortality and morbidity once a day during the acclimation period and twice a day during the treatment and observation periods, including weekends. Attention was paid to humane endpoints.

### 2.4.2 Clinical signs

Each animal was observed at least once a day for the recording of clinical signs. On days of treatment, clinical signs were recorded once before administration, and once after administration, at approximately the same time on each day of treatment.

A detailed physical examination was performed once pre-test in males (see § Study plan adherence) then weekly during the treatment and recovery periods.

### 2.4.3 Local reactions

Local reactions at the injection sites were evaluated daily from the day of the first administration (see § Study plan adherence). On the days of treatment, this was performed before and 3 hours after the administration (at the time of the first body temperature measurement after treatment).

The following scoring scale was used:

#### Erythema and edema:

- . 0: no observation,
- . 1: very slight (barely perceptible),
- . 2: well-defined,
- . 3: moderate to severe,
- . 4: severe erythema (beet redness) to slight eschar formation (injuries in depth) or severe edema (raised more than one millimeter).

#### Hematoma and induration:

- . 0: no hematoma/induration,
- . 1: area  $\leq 1 \text{ cm}^2$ ,
- . 2: area  $> 1 \text{ cm}^2$  and  $\leq 2 \text{ cm}^2$ ,
- . 3: area  $> 2 \text{ cm}^2$  and  $\leq 3 \text{ cm}^2$ ,
- . 4: area  $> 3 \text{ cm}^2$ .

Any other lesions were also recorded (see § Study plan adherence).

#### 2.4.4 Body weight

The body weight of each animal was recorded twice during the acclimation period (including once before group allocation), then on each day of treatment (before treatment), on the day after each treatment day (24 hours  $\pm$  1 hour after treatment) (see [§ Study plan adherence](#)) and every 3 or 4 days between each injection and after the last injection until the end of the study.

#### 2.4.5 Food consumption

The quantity of food consumed by the animals was recorded daily from 5 days before the beginning of the treatment period and then throughout the study (see [§ Study plan adherence](#)).

Food consumption was calculated per animal and per day. Any evidence of spillage was documented.

#### 2.4.6 Rectal temperature

The rectal temperature of each animal was recorded (before any blood collection) as follows:

- . on four occasions before the first treatment, at approximately the same time of the day,
- . on the days of treatment: before treatment, 3 hours ( $\pm$  30 minutes), 6 hours ( $\pm$  30 minutes) and 24 hours ( $\pm$  1 hour) after treatment (see [§ Study plan adherence](#)).

This examination was carried out using a digital thermometer, which was inserted in the rectum.

#### 2.4.7 Ophthalmology

Ophthalmological examinations were performed on all animals:

- . once before the beginning of the treatment period,
- . on Day 3,
- . before euthanasia (Day 31 for principal animals or Day 57 for recovery animals).

The pupils of the animals were dilated with tropicamide (Mydriaticum®, Laboratoires Théa, Clermont-Ferrand, France). After assessment of the corneal reflex (at instillation of the tropicamide), the appendages, optic media and fundus were examined by indirect ophthalmoscopy (Omega 500, Heine, Herrsching, Germany). A slit-lamp biomicroscope (Portable slit-lamp SL-17, Kowa, Japan) was used to investigate the anterior segment and the lens.

### 2.5 SCHEDULE OF BLOOD SAMPLING

| Study days   | Parameter    | Target total blood volume (mL)/occasion | Animals/sex/group                   |
|--|--------------|---|-------------------------------------|
| Pretest  | H/C/B/CRP/Ig | 4.6                                     | All animals                         |
| Day 3 (48 hours post-dose of Day 1)                  | H/C/B/CRP    | 2.6                                     | All animals                         |
| Day 31   | H/C/CRP/Ig   | 3.9                                     | All animals                         |
| Day 31   | B            | 0.7                                     | All principal males and all females |
| Day 32 (see <a href="#">§ Study plan adherence</a> ) | B            | 0.7                                     | All recovery males                  |
| Day 57   | H/C/B/CRP/Ig | 4.6                                     | All recovery animals                |

H: Hematology; C: Coagulation; B: Biochemistry; Ig: Immunogenicity; CRP: C-Reactive Protein.

## **2.6 IMMUNOGENICITY**

### **2.6.1 Blood collection**

Blood samples for the specific immune response to the vaccine were taken from each animal as indicated in the [§ Schedule of blood sampling](#).

Fasting was not required but generally performed because of the other laboratory investigations performed).

Blood (approximately 2 mL) was collected from the auricular artery into a plain tube (with clot activator). The blood was allowed to clot for 30 to 60 minutes maximum at room temperature (see [§ Study plan adherence](#)), and was centrifuged [approximately at + 4°C 3000g (pre-treatment) or 1800g (Days 31 and 57), for 10 minutes]. The serum was aliquoted into two cryotubes of 250 µL (aliquots 1 and 2) and a third one with the remaining volume when applicable (aliquot 3), and stored at -80°C.

Aliquot 2 was sent to the Principal investigator (see [§ Shipments](#)). Aliquots 1 and 3 were kept as backup aliquots. They are retained until acceptance of the final report by the Sponsor. Remaining aliquots will then be disposed of.

### **2.6.2 ELISA assay**

The determination of specific antibodies was performed by the Principal Investigator at the test site using a validated ELISA method to measure immunoglobulins (IgG). Details concerning the conduct of the delegated phase and results are presented in [Appendix 12](#).

## **2.7 CLINICAL PATHOLOGY**

### **2.7.1 Blood collection**

Prior to blood sampling, the animals were deprived of food for an overnight period of at least 14 hours (see [§ Study plan adherence](#)).

Blood samples were taken from the auricular artery and collected into tubes containing the appropriate anticoagulant (see following pages).

### **2.7.2 Hematology**

#### **2.7.2.1 Peripheral blood**

Blood was collected into BD Microtainer® (K2EDTA) tubes. The following parameters were determined for all concerned animals (see [§ Schedule of blood sampling](#)) using the ADVIA 120 Hematology analyzer (Siemens):

| Parameter                | Method                 | Unit |
|--------------------------|------------------------|------|
| Erythrocytes (RBC)       | Laser morphometry      | T/L  |
| Mean cell volume (MCV)   | Laser morphometry      | fL   |
| Packed cell volume (PCV) | Calculated             | L/L  |
| Hemoglobin (HB)          | Colorimetric (Drabkin) | g/dL |

(continued)

| Parameter  | Method                                     | Unit      |
|--|--|-----------|
| Mean cell hemoglobin concentration (MCHC)          | Calculated                                 | g/dL      |
| Mean cell hemoglobin (MCH)                         | Calculated                                 | pg        |
| Thrombocytes (PLT)                                 | Laser morphometry                          | G/L       |
| Leucocytes (WBC)                                   | Peroxidase cytochemistry/laser morphometry | G/L       |
| Differential white cell count with cell morphology | Peroxidase cytochemistry/laser morphometry |           |
| . neutrophils (N)                                  |  | G/L       |
| . eosinophils (E)                                  |  | G/L       |
| . basophils (B)                                    |  | G/L       |
| . lymphocytes (L)                                  |  | G/L       |
| . large unstained cells (LUC)                      |  | G/L       |
| . monocytes (M)                                    |  | G/L       |
| Reticulocytes (RTC)                                | Oxazine cytochemistry/laser morphometry    | % and T/L |

A blood smear stained with May Grünwald Giemsa for possible determination of the differential white cell count (with cell morphology) was prepared for each animal. As some blood samples were not accepted by the ADVIA 120 Analyzer, a microscopic examination was performed on the blood smears of these animals. Then all the smears were archived.

A blood (stained with blue cresyl) smear for possible determination of the reticulocyte count was prepared for each animal. As all the blood samples were successfully analyzed by the ADVIA 120 the blood smears were archived without further investigation.

#### 2.7.2.2 Bone marrow

Two bone marrow smears were prepared from the sternum (at necropsy) of all animals at each euthanasia (Days 31 and 57). The bone marrow smears were stained with May Grünwald Giemsa.

As no abnormalities requiring a bone marrow differential cell count were observed during the hematological or histopathological investigations, the smears were archived without further investigations.

### 2.7.3 Coagulation

Blood was collected into sodium citrate tubes (plasma was separated within 90 minutes of blood collection; see [§ Study plan adherence](#)). The following parameters were determined for all concerned animals (see [§ Schedule of blood sampling](#)) using the ACL Top 550 CTS blood coagulation analyzer (Werfen):

| Parameter                                    | Method                                  | Unit |
|--|---|------|
| Prothrombin time (PT)                        | Chrono-Turbidimetry with thromboplastin | s    |
| Fibrinogen (FIB)                             | Chrono-Turbidimetry with thromboplastin | g/L  |
| Activated partial thromboplastin time (APTT) | Chrono-Turbidimetry /with ellagic acid  | s    |

### 2.7.4 Blood biochemistry

Blood was collected into lithium heparin tubes (plasma was separated within 90 minutes of blood collection, see [§ Study plan adherence](#)). The following parameters were determined for all concerned animals (see [§ Schedule of blood sampling](#)) using the ADVIA 1800 blood biochemistry analyser (Siemens):

| Parameter                    | Method  | Unit                     |
|------------------------------|---|--------------------------|
| Sodium ( $\text{Na}^+$ )     | Indirect potentiometry                        | mmol/L                   |
| Potassium ( $\text{K}^+$ )   | Indirect potentiometry                        | mmol/L                   |
| Chloride ( $\text{Cl}^-$ )   | Indirect potentiometry                        | mmol/L                   |
| Calcium ( $\text{Ca}^{++}$ ) | Colorimetry with ortho-cresol-phthaleine      | mmol/L                   |
| Inorganic phosphorus (PHOS)  | Colorimetry with phosphomolybdate             | mmol/L                   |
| Glucose (GLUC)               | Colorimetry with hexokinase                   | mmol/L                   |
| Urea (UREA)                  | Colorimetry with urease                       | mmol/L                   |
| Creatinine (CREAT)           | Colorimetry with creatininase                 | $\mu\text{mol}/\text{L}$ |
| Total bilirubin (TOT.BIL)    | Colorimetry with vanadate oxydation           | $\mu\text{mol}/\text{L}$ |
| Total cholesterol (CHOL)     | Colorimetry with cholesterol esterase/oxydase | mmol/L                   |
| Triglycerides (TRIG)         | Colorimetry (Trinder reaction)                | mmol/L                   |

(continued))

| Parameter                               | Method   | Unit |
|---|--|------|
| Alkaline phosphatase (ALP)              | Diethanolamine assay   | U/L  |
| Alanine aminotransferase (ALAT)         | Modified International Federation of Clinical Chemistry method | U/L  |
| Aspartate aminotransferase (ASAT)       | Modified International Federation of Clinical Chemistry method | U/L  |
| Creatine kinase (CK)                    | Standard German Society for Clinical Chemistry (DGKC) method   | U/L  |
| Creatine kinase (CK-L) (non GLP) Day 57 | Modified International Federation of Clinical Chemistry method | U/L  |
| Gamma-glutamyl transferase (GGT)        | Modified International Federation of Clinical Chemistry method | U/L  |
| Lactate dehydrogenase (LDH)             | Colorimetry with pyruvate/NADH                                 | U/L  |
| Total proteins (PROT)                   | Colorimetric (Biuret)  | g/L  |
| Albumin (ALB)                           | Colorimetry with bromocresol green                             | g/L  |
| Albumin/globulin ratio (A/G)            | Calculated   |      |
| Globulin (GLOB)                         | Calculated   | g/L  |

## 2.8 C-REACTIVE PROTEIN LEVELS

Blood samples were taken at approximately the same time in the morning, after recording of the rectal temperature (whenever applicable), from the auricular artery of each unanesthetized animal (see § Schedule of blood sampling) (see § Study plan adherence).

Blood (approximately 0.5 mL) was collected into a plain tube. The blood was allowed to clot for 30 to 60 minutes maximum at room temperature (see § Study plan adherence) and was centrifuged (approximately at +4°C and 3000g for 10 minutes).

The serum was aliquoted into three microtubes of 50 µL and stored at -20°C (see § Study plan adherence) until analysis using a validated ELISA method. Two aliquots were used for CRP testing. The third aliquot is kept as backup sample at -20°C until finalization of the report and then will be destroyed.

## 2.9 PATHOLOGY

### 2.9.1 Euthanasia

Two days (Day 31) or 28 days (Day 57) after the last administration, all animals were euthanized by an intravenous injection of sodium pentobarbital after at least 14 hours fasting followed by exsanguination.

### 2.9.2 Organ weights

The body weight of each animal was recorded before scheduled euthanasia (Day 31 or 57). The organs specified in the Tissue Procedure Table were weighed wet as soon as possible after dissection. The ratio of organ weight to body weight (recorded immediately before euthanasia) as well as the ratio of organ weight to brain weight was calculated.

### 2.9.3 Macroscopic *post-mortem* examination

A complete macroscopic *post-mortem* examination was performed on all animals. This included examination of the external surfaces, all orifices, the cranial cavity, the external surfaces of the brain, the thoracic, abdominal and pelvic cavities with their associated organs and tissues and the neck with its associated organs and tissues.

### 2.9.4 Preservation of tissues

For all animals, the tissues specified in the Tissue Procedure Table were preserved in 10% buffered formalin (except for the eyes with optic nerves, the testes and epididymides, which were fixed in Modified Davidson's Fixative) (see § Study plan adherence).

Two bone marrow smears (see § Bone marrow) were prepared from the sternum of all animals at each euthanasia (Day 31 or 57).

A particular attention was paid to the collection of the injection sites.

### 2.9.5 Preparation of histological slides

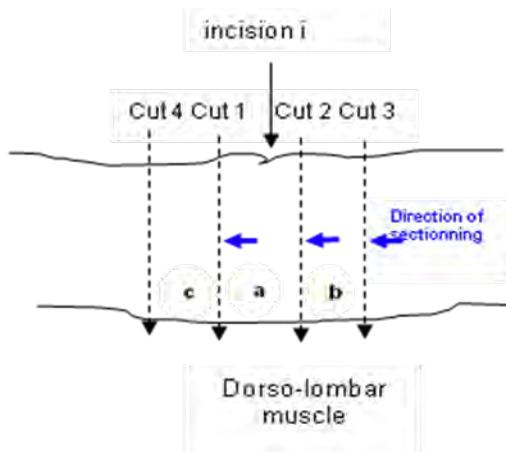
#### 2.9.5.1 Injection sites

The tissues were fixed and then three pieces of approximately 5 mm of muscle were prepared. A first piece (a) was obtained by cutting the muscle 2.5 mm on both sides of the superficial incision i (cut 1 and cut 2, see Figure). A second piece (b) was obtained by cutting the muscle 5 mm beside cut 2 (cut 3, see Figure). Finally, a third piece (c) was obtained by cutting the muscle 5 mm beside cut 1 (cut 4, see Figure).

The excised pieces were numbered (a: between cut 1 and 2; b: between cut 2 and 3; c: between cut 1 and 4), examined for gross macroscopic changes and processed for microscopic examination.

The thickness of each piece was adjusted to match the cassette (approximately 3 to 4 mm). The pieces were embedded in paraffin wax in order to start the sectioning of blocks at the level of the cuts 3, 2, and 1, respectively (see direction of the cuts on the [figure](#)).

From each paraffin blocks a, b and c, one section was performed. The 5 µm sections were stained with hematoxylin-eosin.



#### 2.9.5.2 All other tissues

All other tissues required for microscopic examination were embedded in paraffin wax, sectioned at a thickness of approximately four microns and stained with hematoxylin eosin.

#### 2.9.6 Microscopic examination

A microscopic examination was performed on all the tissues listed in the Tissue Procedure Table for all animals by Dr. Roger Alison, BVSc, MRCVS, DECVP, Citoxlab France.

The slides were examined at his address or on site. When he examined them at his address, the slides were shipped to him (see [§ Shipments](#)) and at the end of microscopic examination, all slides were sent to the peer-review Pathologist.

Peer review was performed by sponsor's pathologist, to confirm that findings recorded by the study Pathologist were consistent and accurate. The study plan and amendments were sent to the peer review Pathologist. The address for the slides shipment for the pathology peer review is specified in [§ Shipments](#). After completion of the pathology peer review, all tissue slides returned for archiving. The original peer review statement was sent to and archived at the Test Facility; it is presented in [Appendix 17](#).

### TISSUE PROCEDURE TABLE

| Organs  | Organ weights | Preservation of tissues | Microscopic examination |
|---|---------------|-------------------------|-------------------------|
| <b>Macroscopic lesions</b>  |               | X                       | X                       |
| Adrenals  | X             | X                       | X                       |
| Aorta   |               | X                       | X                       |
| Brain (including medulla/pons cerebellar and cerebral cortex)   | X             | X                       | X                       |
| Cecum   |               | X                       | X                       |
| Colon   |               | X                       | X                       |
| Diaphragm   |               | X                       | X                       |
| Draining lymph nodes [sacral, inguinal ( <i>i.e.</i> sub-iliac) and iliac ( <i>i.e.</i> medial iliac)] <sup>a,b</sup> |               | X                       | X                       |
| Duodenum  |               | X                       | X                       |
| Epididymides  | X             | X                       | X                       |
| Esophagus   |               | X                       | X                       |
| Eyes  |               | X                       | X                       |
| Femoral bone with articulation  |               | X                       | X                       |
| Gall bladder  |               | X                       | X                       |
| Gut-Associated Lymphoid Tissue (GALT)   |               | X                       | X                       |
| Harderian glands  |               | X                       | X                       |
| Heart   | X             | X                       | X                       |
| Ileum   |               | X                       | X                       |
| Injection sites (muscle of the dorso-lumbar region)   |               | X                       | X                       |
| Jejunum   |               | X                       | X                       |
| Kidneys   | X             | X                       | X                       |
| Lacrimal glands   |               | X                       | X                       |
| Larynx  |               | X                       | X                       |
| Liver   | X             | X                       | X                       |
| Lungs (including mainstem bronchi)  | X             | X                       | X                       |
| Lymph nodes that do not drain the injection sites (mandibular and mesenteric)   |               | X                       | X                       |
| Mammary gland area  |               | X                       | X                       |
| Nasal cavity (nasal oropharyngeal cavity and nasal tissue including bones, hard palate and nasopharyngeal duct)       |               | X                       | X                       |
| Optic nerves  |               | X                       | X                       |
| Ovaries   | X             | X                       | X                       |
| Oviducts  |               | X                       | X                       |
| Pancreas  |               | X                       | X                       |
| Pituitary gland   | X             | X                       | X                       |
| Prostate <sup>c</sup>   | X             | X                       | X                       |
| Rectum  |               | X                       | X                       |
| Salivary glands (parotid, sublingual and mandibular)  |               | X                       | X                       |
| Seminal vesicles <sup>c</sup>   | X             | X                       | X                       |
| Sciatic nerves  |               | X                       | X                       |
| Skeletal muscle ( <i>biceps femoris</i> )   |               | X                       | X                       |
| Skin overlying injection sites  |               | X                       | X                       |
| Skin and subcutis (untreated)   |               | X                       | X                       |
| Spinal cord (cervical, thoracic and lumbar)   |               | X                       | X                       |

a: draining lymph nodes were preserved when possible (lymph nodes might be hidden by fat in rabbits).

b: right and left lymph nodes were identified and preserved separately, when applicable.

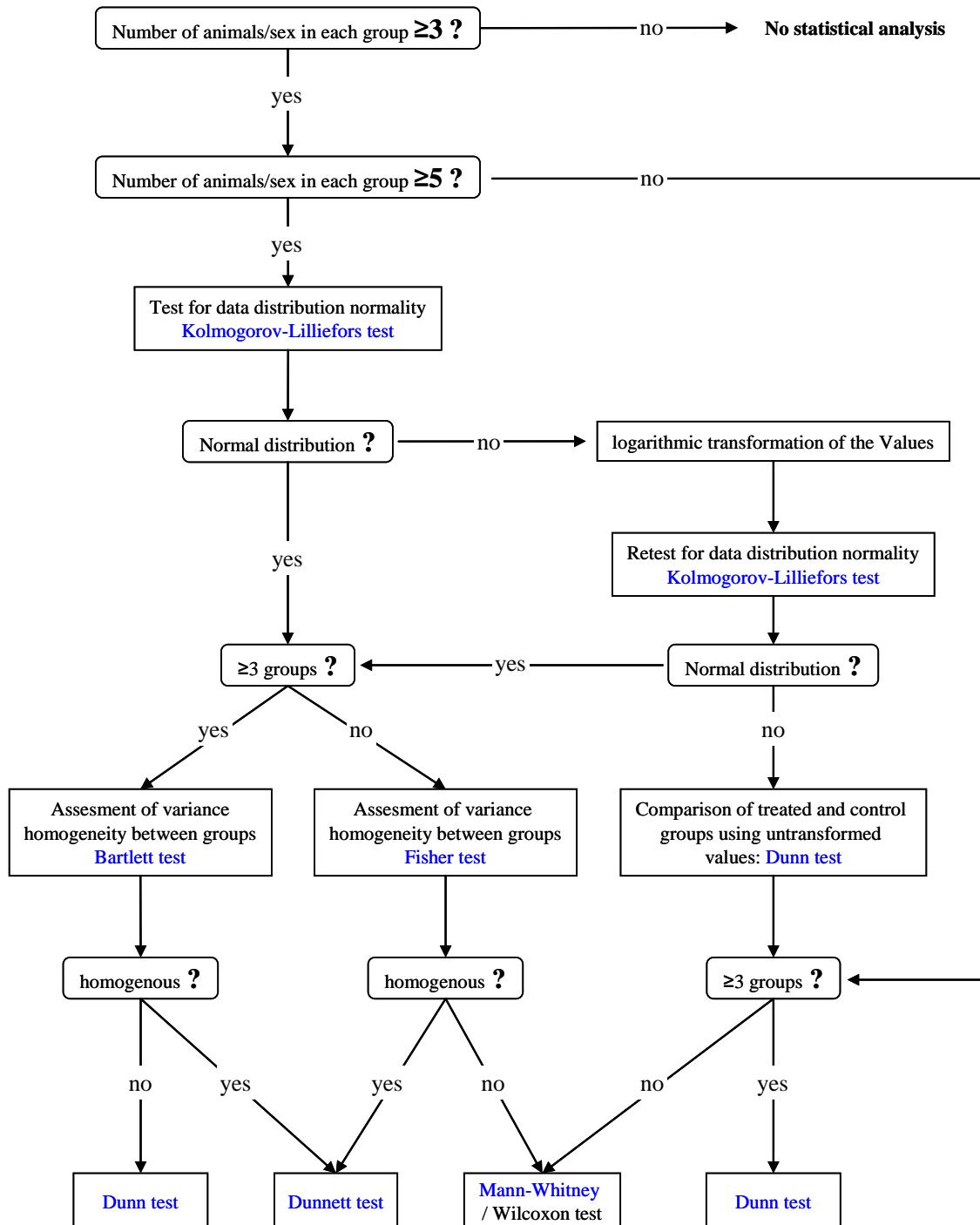
c: prostate and seminal vesicles were weighed together.

**TISSUE PROCEDURE TABLE (continued)**

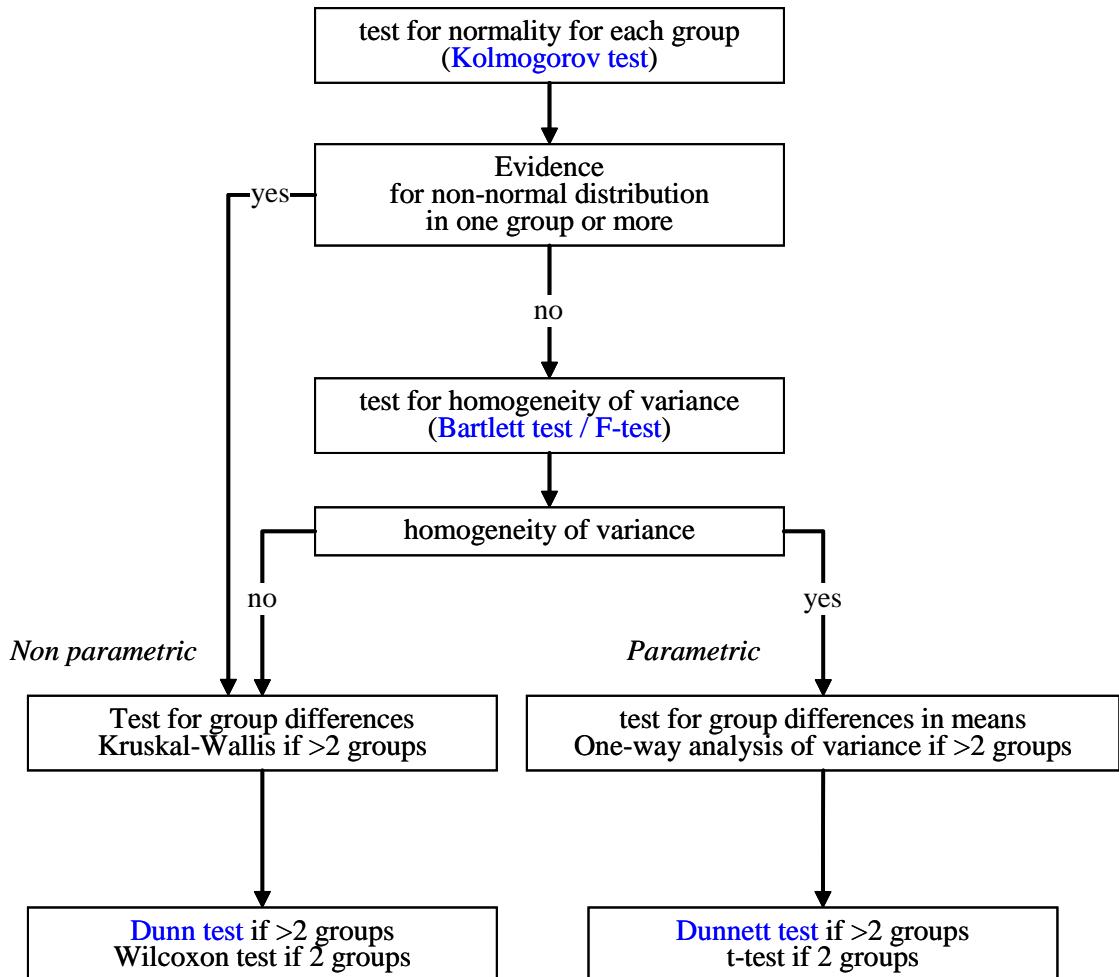
| Organs                     | Organ weights | Preservation of tissues | Microscopic examination |
|----------------------------|---------------|-------------------------|-------------------------|
| Spleen                     | X             | X                       | X                       |
| Sternum with bone marrow   |               | X                       | X                       |
| Stomach                    |               | X                       | X                       |
| Testes                     | X             | X                       | X                       |
| Thymus                     | X             | X                       | X                       |
| Thyroids with parathyroids | X             | X                       | X                       |
| Tongue                     |               | X                       | X                       |
| Trachea                    |               | X                       | X                       |
| Ureters                    |               | X                       | X                       |
| Urinary bladder            |               | X                       | X                       |
| Uterus (horns and cervix)  | X             | X                       | X                       |
| Vagina                     |               | X                       | X                       |

## 2.10 STATISTICAL ANALYSIS

software was used to perform the statistical analysis of body weight, food consumption, rectal temperature, CRP levels, hematology, coagulation and blood biochemistry data according to the following sequence:



PathData software was used to perform the statistical analysis of organ weight data (level of significance: 0.05 or 0.01) according to the following sequence:



## **2.11 COMPUTER SYSTEMS**

The computer systems used in the study are detailed in the following table:

Software

**Shipment Table**

| Type<br>of shipped material                                 | Material as<br>described<br>under §  | Shipment schedule<br>and conditions   | Address<br>including<br>addressee |
|---|--|---|-----------------------------------|
| <b>Serum for<br/>immunogenicity<br/>testing (aliquot 2)</b> | <b>§ Immunogenicity</b>  | During Week 44, 2018<br>(within one week after the<br>last blood sampling)<br>One consignment, frozen on<br>dry ice |                                   |
| <b>Histological slides</b>                                  | <b>§ Preparation of<br/>histological slides;</b><br><b>§ Microscopic<br/>examination</b> | During Weeks 41 and 43,<br>2018<br>Two consignments, at room<br>temperature   |                                   |
| <b>Histological slides</b>                                  | <b>§ Microscopic<br/>examination (peer<br/>review)</b>                                   | During Week 48, 2018 ;<br>during Week 47, 2018  |                                   |

All shipments were done by an express service specialized in sample shipment (with tracking system). All serum samples were kept at -80°C until dispatch.

## 2.13 ARCHIVING

### 2.13.1 Phases conducted

The following study materials are retained in the archives for 5 years after the signature of the study report by the Study Director:

- . study plan and amendments,
- . raw data generated at Citoxlab France,
- . correspondence,
- . final report and any amendments,
- . tissues in preservative, blocks and histological slides,
- . hematological slides,
- . any documents received from the peer reviewer,
- . samples of the test items (one sample per receipt of each batch is retained and can refer to several studies in the same project).

The total duration of archiving (depending on regulations) is the responsibility of the Sponsor.

Deep frozen specimens are retained until acceptance of the final report by the Sponsor. Samples will then be disposed of.

## 2.13.2 Phase conducted at test site

The archiving of study materials is described in [Appendix 12](#).

## 2.14 CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

| Procedure  | Date                          | Study day           |
|--|-------------------------------|---------------------|
| <b>Study plan approved by:</b>   |                               |                     |
| . Study Director   | 03 August 2018                |                     |
| . Sponsor Representative   | 20 August 2018                |                     |
| <b>Experimental starting date</b><br>(first day of acclimation period) | 06 August 2018                | -14                 |
| <b>Males</b>   |                               |                     |
| . First day of acclimation period                                      | 06 August 2018                | -14                 |
| . Randomization and weighing   | 06 August 2018                | -14                 |
| . Hematology, blood biochemistry,<br>CRP and immunogenicity            | 08 and 09 August 2018         | -12 and -11         |
| . Rectal temperature   | 09, 10, 13 and 16 August 2018 | -11, -10, -7 and -4 |
| . Ophthalmology  | 16 August 2018                | -4                  |
| <b>First injection (site 1)</b>  | 20 August 2018                | 1                   |
| <b>Week 1</b>  |                               |                     |
| . Rectal temperature   | 20 and 21 August 2018         | 1 and 2             |
| . Hematology, blood biochemistry and CRP                               | 22 August 2018                | 3                   |
| . Ophthalmology  | 22 August 2018                | 3                   |
| <b>Second injection (site 2)</b>                                       | 03 September 2018             | 15                  |
| <b>Week 3</b>  |                               |                     |
| . Rectal temperature   | 03 and 04 September 2018      | 15 and 16           |
| <b>Third injection (site 3)</b>  | 17 September 2018             | 29                  |
| <b>Week 5</b>  |                               |                     |
| . Rectal temperature   | 17 and 18 September 2018      | 29 and 30           |
| . Hematology, blood biochemistry, CRP<br>and immunogenicity            | 19 September 2018             | 31                  |
| . Ophthalmology  | 19 September 2018             | 31                  |
| . Blood biochemistry (recovery males)                                  | 20 September 2018             | 32                  |

| Procedure   | Date                          | Study day           |
|---|-------------------------------|---------------------|
| <b>Necropsy date (principal males)</b>                      | 19 September 2018             | 31                  |
| <b>Week 9</b>   |                               |                     |
| . Hematology,blood biochemistry,<br>CRP and immunogenicity  | 15 October 2018               | 57                  |
| . Ophthalmology   | 15 October 2018               | 57                  |
| <b>Necropsy date (recovery males)</b>                       | 15 October 2018               | 57                  |
| <b>Females</b>  |                               |                     |
| . First day of acclimation period                           | 14 August 2018                | -14                 |
| . Randomization and weighing                                | 14 August 2018                | -14                 |
| . Hematology, blood biochemistry, CRP<br>and immunogenicity | 16 and 17 August 2018         | -12 and -11         |
| . Rectal temperature  | 16, 17, 21 and 24 August 2018 | -12, -11, -7 and -4 |
| . Ophthalmology   | 24 August 2018                | -4                  |
| <b>First injection (site 1)</b>                             | 28 August 2018                | 1                   |
| <b>Week 1</b>   |                               |                     |
| . Rectal temperature  | 28 and 29 August 2018         | 1 and 2             |
| . Hematology, blood biochemistry and CRP                    | 30 August 2018                | 3                   |
| . Ophthalmology   | 30 August 2018                | 3                   |
| <b>Second injection (site 2)</b>                            | 11 September 2018             | 15                  |
| <b>Week 3</b>   |                               |                     |
| . Rectal temperature  | 11 and 12 September 2018      | 15 and 16           |
| <b>Third injection (site 3)</b>                             | 25 September 2018             | 29                  |
| <b>Week 5</b>   |                               |                     |
| . Rectal temperature  | 25 and 26 September 2018      | 29 and 30           |
| . Hematology, blood biochemistry,<br>CRP and immunogenicity | 27 September 2018             | 31                  |
| . Ophthalmology   | 27 September 2018             | 31                  |
| <b>Necropsy date (principal females)</b>                    | 27 September 2018             | 31                  |

| Procedure   | Date            | Study day |
|---|-----------------|-----------|
| <b>Week 9</b>   |                 |           |
| . Hematology, blood biochemistry,<br>CRP and immunogenicity | 23 October 2018 | 57        |
| . Ophthalmology   | 23 October 2018 | 57        |
| <b>Necropsy date (recovery females)</b>                     | 23 October 2018 | 57        |
| <b>Experimental completion date</b>                         | 23 October 2018 |           |

## 2.15 STUDY PLAN ADHERENCE

The study was performed in accordance with study plan No. and subsequent amendments, with the following deviations from the agreed study plan:

*Environmental conditions:*

- . the temperature recorded in the animal rooms were outside the target range specified in the study plan several times at the beginning of the study (up to +2°C above the range for temperature),
- . the relative humidity was once (towards the end of the recovery period for one animal room out of two) outside the target range specified in the study plan (up to 91.3%).

*Administration:*

- . injections were performed using a limiting device on the 25G (16 mm) needle ensuring 12 mm depth of injection instead of the entire length of the needle.

*Clinical signs/Local reactions:*

- . on pre-test, detailed physical examination of females was not documented. Therefore there is no evidence that it was performed but it was considered with no impact on the study: no relevant clinical signs were observed on the next sessions,
- . on Day 5, clinical signs were not recorded for test item-treated recovery animals by omission,
- . there was no indication in the raw data of the localization of hematomas observed on the injection sites of control group 1 male N30646 (on Day 15) and of SENDVACC99 males N30661 (on Day 15), N30664 (on Days 1 to 3) and N30666 (on Days 16, 18 to 20). However, there was no reasonable doubt on the localization of hematomas which could only be linked to the last injection site used,
- . there was no indication in the raw data of the localization of induration observed on Day 2 in SENDVACC99 female N30740. However, there was no doubt on its localization since only the site 1 was injected before this observation on Day 2,
- . there was no indication in the raw data of the type and localization of the local finding observed on Day 51 in SENDVACC99 female N30738. However, this had no impact on the study since it was not considered as a test item-related local reaction (noted in one animal on one day during the recovery period only).

*Body weight:*

- . body weight was recorded outside the requested time (24 hours  $\pm$  1 hour after treatment) as follows:

| Group/Sex | Day | Animal number    | Deviation from the 24h |
|-----------|-----|------------------|------------------------|
| 3M        | 2   | N30670           | -2h05                  |
| 1M        |     | N30648 to N30650 | +1h31 to +1h32         |
| 2M        | 16  | N30656 to N30660 | +1h26 to +1h29         |

M: Male.

*Food consumption:*

- . for the interval Days -1/1, due to a planning error, no food consumption was measured for the first five males of all groups (principal males),
- . for the interval Days 2/3, due to a technical error, no food consumption was measured for any males.

*Rectal temperature:*

- . on Day 16 (at time-point 24 hours after dosing on Day 15), male N30655 rectal temperature was above 40°C but no recording was performed on the following day(s) as requested by the study plan. This animal clinical condition was ok on these days.

*Immunogenicity:*

- . the following samples were not centrifuged in 30 to 60 min after blood collection:

| Animal | Period   | Time between blood collection and centrifugation (min) |
|--------|----------|--|
| N30733 | Pre-test | 27   |
| N30734 | Pre-test | 28   |
| N30735 | Pre-test | 21   |
| N30712 | Day 31   | 27   |
| N30713 | Day 31   | 20   |
| N30714 | Day 31   | 19   |
| N30715 | Day 31   | 14   |

The centrifugation step for serum preparation is performed within 60 min  $\pm$  10 min after blood collection at Test Site for this ELISA analytical method. In consequence this deviation was considered not to have affected the validity and reliability of the data:

- . due to some prolonged door opening, the storage temperature for the reference item and QC sample in the Laboratory o was above the -70°C target range on several occasion and for up to a maximum of 4 hours 10 minutes on 27 July 2018 (max temperature: -53.7°C). Taking into account the short duration of this event and the slight drop in temperature, it was considered that there was not impact on the study objectives.

*C-Reactive Protein:*

- . on Day -12, for females N30733, N30734 and N30735 , the blood was allowed to clot for 27, 28 and 21 minutes, respectively, instead of 30 to 60 minutes. This was not considered to have had an impact on their results which were within the range of the other animals' tubes analyzed on Day -12,
- . on pre-test, the supernumerary animal samples were analyzed for CRP in excess (the data are not presented in the study report),
- . on pre-test, CRP analysis was performed by error on the tube dedicated for immunogenicity and sera were therefore stored at -80°C instead of -20°C. This was not considered to have an impact on the results since this storage temperature is also validated and covers this analysis, and since the immunogenicity tube was also a plain tube with a clot activator.

*Clinical pathology:*

- . on Day 31, recovery males were not fasted before blood sampling by omission. Blood was taken anyway (it was considered that fasting was not mandatory for hematology, CRP and coagulation), except for blood biochemistry which was postponed to Day 32 after an overnight fasting,
- . there was no analysis or calculation of total protein, globulin and albumin/globulin ratio for male N30650 (control group) at pre-test by omission,
- . the blood samples of control female N30716 for coagulation and blood biochemistry were centrifuged 92 min after blood sampling instead of within 90 min.

*Preservation of tissues:*

- . for all animals, the Harderian glands were preserved in 10% buffered formalin instead of in Modified Davidson's Fixative (writing error in the study plan).

These deviations were considered not to have compromised the validity or integrity of the study.

### 3. RESULTS

#### 3.1 IMMUNOGENICITY

Immunogenicity data are presented in [Appendix 12](#).

The immunogenicity evaluation confirmed the exposure of all rabbits to vaccines as sustained specific IgG ELISA humoral responses were induced by these vaccines.

Results are summarized in the text-table below:

IgG titers ( $\log_{10}$  EU  $\pm$  sd)<sup>(1)</sup>

| Group     | 1                          | 2                          | 3                          |
|-----------|----------------------------|----------------------------|----------------------------|
| Treatment | NaCl 0.9%                  | SENDVACC10                 | SENDVACC99                 |
| Pre-dose  | 1.181 $\pm$ 0.283          | 1.161 $\pm$ 0.376          | 1.124 $\pm$ 0.281          |
| Day 31    | 1.381 $\pm$ 0.400<br>+ 0.2 | 5.372 $\pm$ 0.086<br>+ 4.2 | 5.853 $\pm$ 0.119<br>+ 4.7 |
| Day 57    | 1.529 $\pm$ 0.485<br>+ 0.3 | 5.417 $\pm$ 0.150<br>+ 4.3 | 5.677 $\pm$ 0.139<br>+ 4.6 |

<sup>(1)</sup>: sd: standard deviation. *In italics*: Log<sub>10</sub> increase from pre-dose.

#### 3.2 CLINICAL EXAMINATIONS

##### 3.2.1 Mortality

Individual fates are presented in [Appendix 4](#).

No unscheduled deaths occurred during the study.

##### 3.2.2 Clinical signs

The clinical signs are presented in [Tables 1 to 4](#) and [Appendix 5](#).

No test item-related adverse clinical signs were recorded during the study.

The following observations were considered not related to the test items:

- . papules were observed in the back of several animals among all groups, including the control group. It was therefore considered not to be test item-related,
- . hematomas were observed in the interscapular region of some animals in the test item-treated groups (one male and one female given SENDVACC10 one female given SENDVACC99). Since they were observed with a low incidence, independently of administrations and apart from injection sites, they were considered as incidental findings, likely related to the housing conditions or handling procedures, abnormal reddish color and scabs on the right ear were observed in one female given SENDVACC99

These findings were due to the fact that a hemostatic clip had been placed on this animal's ear after the Day 31 blood collection and withdrawn only on Day 32 by omission.

### 3.2.3 Local reactions

The local reactions observed at the injection sites are presented in [Table 5](#) and [Appendix 6](#).

The local findings observed throughout the study were generally limited to minimal to slight hematoma and are summarized in the following table:

Summary of local reactions at the injection site

| Group<br>Treatment                      | 1<br>NaCl 0.9%          |           |   | 2<br>SENDVACC10 |   |           | 3<br>SENDVACC99 |           |           |
|---|-------------------------|-----------|---|-----------------|---|-----------|-----------------|-----------|-----------|
|   | 1<br>Injection site No. | 2         | 3 | 1               | 2 | 3         | 1               | 2         | 3         |
| <b>Incidence<br/>(grade)</b>            | 2<br>(G2)               | 1<br>(G1) | - | 1<br>(G2)       | - | 1<br>(G1) | 3<br>(G2)       | 2<br>(G2) | 3<br>(G2) |
| <b>Total number of affected animals</b> |                         | 3         |   |                 | 2 |           |                 | 8         |           |

G: up to grade; 1: area ≤ 1 cm<sup>2</sup>; 2: area > 1 cm<sup>2</sup> and ≤ 2 cm<sup>2</sup>; -: no hematoma.

Hematomas were observed in all groups with a slightly higher incidence and severity in animals given 99 as compared with controls. An effect of the adjuvanted test item could not be excluded, but considered as non-adverse considering the low incidence and severity.

One induration was observed in the 99 group and was considered as not test item-related in view of the isolated incidence. The local finding observed on Day 51 in one 99 female was not considered to be a test item-related local reaction since it was noted in one animal on 1 day towards the end of the recovery period only.

### 3.2.4 Body weight

The body weight data are presented in [Figures 1 to 4](#), [Tables 6 to 17](#) and [Appendices 7 and 8](#).

Mean body weight was not considered to be affected by the test items treatment (very low differences from Day 1 before treatment). The few statistically significantly differences from controls were considered to be mainly due to the slight differences already noted on the days of treatment before treatment.

Most relevant mean body weight changes are summarized in the following table:

Summary of mean body weight changes (g) and % from controls

| Sex<br>Group                              | Male              |      |       | Female         |      |       |
|---|-------------------|------|-------|----------------|------|-------|
|   | 1<br>NaCl<br>0.9% | 2    | 3     | 1<br>NaCl 0.9% | 2    | 3     |
| <b>1 - 2 (post 1<sup>st</sup> dose)</b>   | +5                | +4   | +0    | +16            | -7   | -18** |
| <b>15 - 16 (post 2<sup>nd</sup> dose)</b> | +13               | -24  | -60** | +22            | -1   | -2    |
| <b>29 - 30 (post 3<sup>rd</sup> dose)</b> | -4                | 6    | -4    | -7             | 6    | 14    |
| <b>1 - 30 (treatment)</b>                 | +555              | +490 | +493  | +697           | +724 | +630  |
|   | -                 | -12% | -11%  | -              | +4%  | -10%  |
| <b>30 - 56 (recovery)</b>                 | +371              | +349 | +418  | +456           | +431 | +461  |
|   | -                 | -6%  | +13%  | -              | -5%  | +1%   |

-: not applicable; Statistically significant from controls: \*\*: p<0.01; *In italics*: % of changes as compared to control group.

Minimal mean body weight loss was noted in both test item-treated groups after the first injection in females and after the second injection in both sexes, which reached statistical significance in 99 group. No relevant changes were noted for recovery animals between Day 31 and Day 56. An effect of the adjuvanted test item was considered likely, but non-adverse in view of the absence of changes after the third dose, the low magnitude, the transient effect and the absence of impact on the terminal mean body weight.

These changes were associated with a decrease in food consumption around dosing days (Days 1 and 15, see below).

Other changes in mean body weight and mean body weight change were considered as normal biological variations.

### 3.2.5 Food consumption

The food consumption data are presented in [Tables 18 to 21](#) and [Appendix 9](#).

Most relevant mean food consumption data are summarized in the following table:

Summary of mean food consumptions (g) and % from controls

| Sex Group            | Male      |            |             | Female    |             |             |
|----------------------|-----------|------------|-------------|-----------|-------------|-------------|
|                      | 1         | 2          | 3           | 1         | 2           | 3           |
| Treatment            | NaCl 0.9% | SENDVACC10 | SEND VACC99 | NaCl 0.9% | SEND VACC10 | SEND VACC99 |
| <b>Days -1 to 1</b>  | 208.0     | 191.0      | 187.0       | 227.0     | 207.5       | 209.5       |
|                      | -         | -8%        | -10%        | -         | -9%         | -8%         |
| <b>Days 1 to 2</b>   | 212.0     | 186.0      | 180.0*      | 234.5     | 229.0       | 207.0*      |
|                      | -         | -12%       | -15%        | -         | -2%         | -12%        |
| <b>Days 2 to 3</b>   | np        | np         | np          | 98        | 42          | 37*         |
|                      | -         | -          | -           | -         | -57%        | -62%        |
| <b>Days 5 to 6</b>   | 213.0     | 192.5*     | 192.0*      | 231.5     | 240.5       | 227.0       |
|                      | -         | -10%       | -10%        | -         | +4%         | -2%         |
| <b>Days 15 to 16</b> | 211.0     | 178.5*     | 163.5**     | 219.5     | 207.0       | 201.0       |
|                      | -         | -15%       | -23%        | -         | -6%         | -8%         |
| <b>Days 16 to 17</b> | 205.5     | 178.5*     | 179.0*      | 229.5     | 222.8       | 209.5*      |
|                      | -         | -13%       | -13%        | -         | -3%         | -9%         |
| <b>Days 17 to 18</b> | 204.5     | 172.5*     | 171.5*      | 220.5     | 238.0       | 217.5       |
|                      | -         | -16%       | -16%        | -         | +8%         | -1%         |

-: not applicable; np: not performed; Statistically significant from controls: \*: p<0.05; \*\*: p<0.01.

*In italics*: % of changes as compared to control group.

Mean food consumption was minimally reduced in males given VACC10 or VACC99 and in females given VACC99. Changes were observed on the days of treatment or within a few days after administration at Day 1 and Day 15, when compared with the control group and the previous food consumption. These changes in mean food consumption were considered to be related to the adjuvanted test items since they were observed just after administrations of the test items formulations, but as non-adverse in view of the minimal differences from controls and the transient effects.

Of note, the low food consumption in females on Days 2-3 was likely related to the food fasting for blood sampling on Day 3.

No relevant changes were noted for recovery animals between Day 31 and Day 56.

### 3.2.6 Rectal temperature

The rectal temperature data are presented in [Tables 22 to 35](#) and [Appendix 10](#).

There were no test item-related changes and the few statistical significances were considered to be incidental or of no biological significance in view of the magnitude of the changes. The mean temperatures in the test item groups remained within  $\pm 1\%$  of the control mean data (or up to 2% once, but difference from controls just before treatment was already at +1%).

### 3.2.7 Ophthalmology

Ophthalmology data are presented in [Appendix 11](#).

There were no abnormalities observed at ophthalmological examination throughout the study.

## 3.3 CLINICAL PATHOLOGY

### 3.3.1 Hematology

Hematology results are presented in [Tables 36 to 43](#) and [Appendix 13](#).

Main hematology changes are summarized in the following table:

Summary of hematology changes (mean values in G/L) and % from controls

| Study Day | Group                 | Sex                   |                   |                     | Male                |                   |                     | Female              |  |  |
|-----------|-----------------------|-----------------------|-------------------|---------------------|---------------------|-------------------|---------------------|---------------------|--|--|
|           |                       | Treatment             | 1<br>NaCl<br>0.9% | 2<br>SEND<br>VACC10 | 3<br>SEND<br>VACC99 | 1<br>NaCl<br>0.9% | 2<br>SEND<br>VACC10 | 3<br>SEND<br>VACC99 |  |  |
| Day 31    | White blood cells     | White blood cells     | 5.99              | 5.64                | 6.03                | 5.30              | 6.67*               | 5.76                |  |  |
|           |                       | -                     | -                 | -6%                 | +1%                 | -                 | +26%                | +9%                 |  |  |
|           |                       | Neutrophils           | 1.97              | 1.76                | 2.11                | 1.72              | 2.30*               | 1.81                |  |  |
|           |                       | -                     | -                 | -11%                | +7%                 | -                 | +34%                | +5%                 |  |  |
|           |                       | Monocytes             | 0.31              | 0.30                | 0.36                | 0.24              | 0.37                | 0.33                |  |  |
|           |                       | -                     | -                 | -3%                 | +16%                | -                 | +54%                | +38%                |  |  |
|           | Large unstained cells | Large unstained cells | 0.02              | 0.05**              | 0.04**              | 0.03              | 0.05*               | 0.05                |  |  |
|           |                       | -                     | -                 | +150%               | +100%               | -                 | +67%                | +67%                |  |  |

-: not applicable; Statistically significant from controls: \*: p<0.05; \*\*: p<0.01; *In italics*:% of changes as compared to control group.

On Day 31, an increase in large unstained cells was observed in both test item-treated groups in both sexes when compared to controls, without reaching statistical significance in females given

VA . The mean white blood cell count was minimally higher in females given SENDVACC10 when compared with controls, with related increase in mean neutrophil counts and similar trend in mean monocyte count. These changes were not seen in males and of low magnitude compared with controls and pre-dose; an effect of the test item treatment could not be excluded and might be related to the pharmacology activity of the adjuvanted vaccines and correlate with inflammation seen at the histopathological examination, but was considered to be of non-adverse.

On Day 57, after recovery, there were no changes observed at hematological examination anymore.

The decrease in the mean eosinophil counts which reached statistical significance in VA females on Day 1 and all test-item treated groups on Day 31 was considered of no toxicological significance. Other changes from controls (*i.e.* decrease in reticulocyte counts in SENDFlublock males on Day 3) were considered to be incidental due to the low magnitude of changes as compared to control and/or pretest values.

### 3.3.2 Biochemistry

Blood biochemistry results are presented in [Tables 44 to 51](#) and [Appendix 14](#).

Main biochemistry changes are summarized in the following table:

Summary of biochemistry changes and % from controls

| Study Day    | Sex Group              | Male        |               |               | Female      |               |               |
|--------------|------------------------|-------------|---------------|---------------|-------------|---------------|---------------|
|              |                        | 1 NaCl 0.9% | 2 SEND VACC10 | 3 SEND VACC99 | 1 NaCl 0.9% | 2 SEND VACC10 | 3 SEND VACC99 |
| Day 3        | Albumin (g/L)          | 44          | 43            | 42            | 44          | 43            | 43            |
|              | -                      | -           | -2%           | -5%           | -           | -2%           | -2%           |
|              | Globulin (g/L)         | 19          | 20            | 20            | 17          | 18            | 18            |
|              | -                      | -           | +5%           | +5%           | -           | +6%           | +6%           |
| Day 31 or 32 | Albumin/Globulin ratio | 2.29        | 2.21          | 2.11**        | 2.54        | 2.42          | 2.38*         |
|              | -                      | -           | -3%           | -8%           | -           | -5%           | -6%           |
|              | Cholesterol (mmol/L)   | 0.99        | 0.83          | 0.84          | 1.48        | 1.16*         | 1.26          |
|              | -                      | -           | -16%          | -15%          | -           | -22%          | -15%          |
| Day 57       | Albumin (g/L)          | 43          | 41*           | 41**          | 43          | 41*           | 41            |
|              | -                      | -           | -5%           | -5%           | -           | -5%           | -5%           |
|              | Globulin (g/L)         | 19          | 20            | 20*           | 19          | 19            | 19            |
|              | -                      | -           | +5%           | +5%           | -           | 0%            | 0%            |
|              | Albumin/Globulin ratio | 2.26        | 2.07**        | 2.02**        | 2.32        | 2.13*         | 2.12**        |
|              | -                      | -           | -8%           | -11%          | -           | -8%           | -9%           |
|              | Cholesterol (mmol/L)   | 0.93        | 0.78          | 0.88          | 1.58        | 1.05**        | 1.42          |
|              | -                      | -           | -16%          | -5%           | -           | -34%          | -10%          |

-: not applicable; Statistically significant from controls: \*: p<0.05; \*\*: p<0.01; *In italics*: % of changes as compared to control group.

On Day 3 and 31/32, mean albumin/globulin ratio (A/G) was decreased in test item-treated groups as compared with controls. This was due to changes in mean albumin and/or globulin concentrations. However, the differences from controls in mean albumin and globulin levels were minimal ( $\leq \pm 6\%$  and differences in these parameters between Days 3 and 31/32 or between pre-dose and Day 31/32 were also minimal or non-existent. These changes in mean albumin/globulin ratio (A/G) were not considered to be adverse and might be related to the pharmacology activity of the adjuvanted vaccines and correlate with inflammation seen at the histopathological examination. The effect was not seen at recovery.

Mean cholesterol level was slightly lower in test item-treated groups on Day 31/32 as compared to control mean values, especially in females given SENDVACC10. This effect related to the adjuvanted test items was still present at the end of the recovery period on Day 57, with statistical significance in females previously given with SENDVACC10. It was considered to be of no biological significance in view of the magnitude and direction of the changes and in absence of correlating findings.

Statistically significant decreases in mean enzyme activities were observed in test items-treated groups on several occasions. However they were considered to be not biologically relevant in view of the direction or minimal magnitude of the changes.

Other changes were considered as normal biological variations due to their low magnitude and/or the fact that values were similar to pre-test values, or in the absence of correlating findings in other electrolytes.

### 3.3.3 Coagulation

Coagulation results are presented in [Tables 36 to 43](#) and [Appendix 13](#).

Main coagulation changes are summarized in the following table:

Summary of coagulation changes and % from controls

| Study Day | Sex              |           | Male      |             |             | Female    |             |             |
|-----------|------------------|-----------|-----------|-------------|-------------|-----------|-------------|-------------|
|           | Group            | 1         | 2         | 3           | 1           | 2         | 3           |             |
|           |                  | Treatment | NaCl 0.9% | SEND VACC10 | SEND VACC99 | NaCl 0.9% | SEND VACC10 | SEND VACC99 |
| Day 3     | Fibrinogen (g/L) | 3.34      | 4.71**    | 5.12**      | 2.45        | 3.92**    | 4.25**      |             |
|           |                  | -         | +41%      | +53%        | -           | +60%      | +73%        |             |
| Day 31    | Fibrinogen (g/L) | 2.81      | 4.11**    | 4.28**      | 2.09        | 2.99**    | 3.26**      |             |
|           |                  | -         | +46%      | +52%        | -           | +43%      | +56%        |             |

-: not applicable; Statistically significant from controls: \*: p<0.05; \*\*: p<0.01; *In italics*: % of changes as compared to control group.

On Days 3 and 31, mean fibrinogen concentration was higher in both test item-treated groups and in both sexes when compared with controls and pre-test, and showed complete recovery by the end of the recovery period. These test item-related effects were considered to be non-adverse and related to the pharmacology activity of the activity of the adjuvanted vaccines. They correlated with inflammation seen at the histopathological examination.

Other changes, including those reaching statistical significance, were considered as normal biological variations due to their low amplitude and/or the fact that values remained within the range of pre-test values.

### 3.4 C-REACTIVE PROTEIN LEVELS

C-Reactive Protein (CRP) results are presented in [Appendix 15](#).

Main changes observed in CRP are summarized in the following table:

Summary of CRP changes and % from controls

| Study Day | Sex         |           | Male      |             |             | Female    |             |             |
|-----------|-------------|-----------|-----------|-------------|-------------|-----------|-------------|-------------|
|           | Group       | 1         | 2         | 3           | 1           | 2         | 3           |             |
|           |             | Treatment | NaCl 0.9% | SEND VACC10 | SEND VACC99 | NaCl 0.9% | SEND VACC10 | SEND VACC99 |
| Day 3     | CRP (µg/mL) | 9.36      | 45.14**   | 65.58**     | 14.33       | 62.80**   | 67.05**     |             |
|           |             | -         | +382%     | +611%       | -           | +338%     | +368%       |             |
| Day 31    | CRP (µg/mL) | 7.55      | 58.23**   | 62.61**     | 8.49        | 41.99**   | 40.04**     |             |
|           |             | -         | +671%     | +729%       | -           | +395%     | +372%       |             |

-: not applicable; Statistically significant from controls: \*\*: p<0.01; *In italics*: % of changes as compared to control group.

On Days 3 and 31, mean CRP levels were statistically significantly higher in both test item-treated groups and sexes. At the end of the recovery period, no statistical significant changes were observed and mean CRP levels were comparable to controls. These changes were considered to be test item-related and due to the pharmacological mechanism of the adjuvanted test items.

### 3.5 PATHOLOGY

#### 3.5.1 Organ weights

Organ weights results are presented in [Appendix 16](#).

##### 3.5.1.1 At the end of the treatment period

Relevant changes in mean final body weights and organ weights in test items-treated groups  
(% changes from controls)

| Sex                 | Male       |     | Female     |     |
|---------------------|------------|-----|------------|-----|
|                     | 2          | 3   | 2          | 3   |
| Group               | SENDVACC10 |     | SENDVACC10 |     |
| Treatment           |            |     |            |     |
| - Final body weight | -7*        | -5  | +5         | -4  |
| - Spleen            |            |     |            |     |
| . absolute          | +47*       | +26 | +63**      | +22 |
| . relative to body  | +57**      | +32 | +56**      | +27 |
| . relative to brain | +52*       | +27 | +57**      | +23 |

Statistically significant from controls: \*: p<0.05; \*\*: p<0.01.

The significance concerned the organ weights values and not the percentages.

#### SENDVACC10

There was a treatment-related statistically significant increase in absolute and relative (to body and brain weight of the spleen in males and females (correlating with lymphoid hyperplasia at histopathological examination).

There was an increase in absolute and relative (to body and brain weight of the spleen in males and females. This was not statistically significant; however it correlated with lymphoid hyperplasia at histopathological examination, and was therefore considered treatment-related.

##### 3.5.1.2 At the end of the recovery period

Relevant changes in mean final body weights and organ weights in test items-treated groups  
(% changes from controls:

| Sex                 | Male       |     | Female     |    |
|---------------------|------------|-----|------------|----|
|                     | 2          | 3   | 2          | 3  |
| Group               | SENDVACC10 |     | SENDVACC10 |    |
| Treatment           |            |     |            |    |
| - Final body weight | -3         | -2  | -2         | -3 |
| - Spleen            |            |     |            |    |
| . absolute          | +38        | +26 | -1         | -3 |
| . relative to body  | +42        | +29 | 0          | -1 |
| . relative to brain | +37        | +25 | 0          | -2 |

## **SENDVACC10**

There was a test item treatment-related increase in absolute and relative (to body and brain) weight of the spleen in males (correlating with lymphoid hyperplasia at histopathological examination). There was partial recovery in males, and complete recovery in females.

There was a test item treatment-related increase in absolute and relative (to body and brain) weight of the spleen in males (correlating with lymphoid hyperplasia at histopathological examination). There was partial recovery in males, and complete recovery in females.

### **Other findings**

All other variations in absolute/relative organ weights were considered to be incidental and unrelated to treatment with test items.

#### **3.5.2 Macroscopic post-mortem examination**

Macroscopic post-mortem examination results are presented in [Appendix 16](#).

##### **3.5.2.1 At the end of the treatment period**

Incidence and severity of macroscopic findings at the inguinal lymph node right, Adipose tissue at the end of the treatment period (n = 5)

| Sex<br>Group               | Male              |                     |                     | Female            |                     |                     |
|----------------------------|-------------------|---------------------|---------------------|-------------------|---------------------|---------------------|
|                            | 1<br>NaCl<br>0.9% | 2<br>SEND<br>VACC10 | 3<br>SEND<br>VACC99 | 1<br>NaCl<br>0.9% | 2<br>SEND<br>VACC10 | 3<br>SEND<br>VACC99 |
| Inguinal lymph node, right |                   |                     |                     |                   |                     |                     |
| Enlarged                   | -                 | -                   | 3                   | -                 | -                   | -                   |
| Adipose tissue             |                   |                     |                     |                   |                     |                     |
| Gelatinous                 | -                 | -                   | -                   | -                 | 4                   | 3                   |

-: finding not present.

## **SENDVACC10**

Gelatinous abdominal adipose tissue (correlating with edema at microscopic examination was present in females. There were no other test compound-related macroscopic findings.

Enlarged right inguinal lymph node (correlating with lymphoid hyperplasia at microscopic examination was present in males. Gelatinous abdominal adipose tissue (correlating with edema at microscopic examination was present in females. There were no other test compound-related macroscopic findings.

## **Other findings**

Red discoloration (correlating with hemorrhage at histopathological examination) at the injection sites of control and treated animals was considered to be due to the injection procedure, and unrelated to the test compounds.

The remaining macroscopic findings were considered to be incidental because they were consistent with spontaneously occurring findings described in the literature, the findings were distributed randomly among groups, or their appearance was similar to findings found in controls.

### **3.5.2.2 At the end of the recovery period**

#### **SENDVACC10**

There were no test item treatment-related macroscopic findings.

There were no test item treatment-related macroscopic findings.

### **3.5.3 Microscopic examination**

Microscopic examination results are presented in [Appendix 16](#).

#### **3.5.3.1 At the end of the treatment period**

#### **SENDVACC10**

Test item treatment-related microscopic observations consisted of lymphoid hyperplasia (which was mostly follicular) and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia (mostly follicular) in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue (on the right side only).

Test item treatment-related microscopic observations consisted of lymphoid hyperplasia (mostly follicular) and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia (mostly follicular) in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue (on the right side only).

## **Other findings**

Hemorrhage, minimal to slight focal muscle necrosis, needle tract lesions, and degeneration/regeneration of muscle at the injection sites were considered to be due to the injection procedure, and unrelated to the test compounds.

Incidence and severity of selected microscopic findings at the end of the treatment period (n = 5)

| Sex<br>Group<br>Treatment         | 1<br>NaCl<br>0.9% | Male<br>2<br>SEND<br>VACC10 | 3<br>SEND | 1<br>NaCl<br>0.9% | Female<br>2<br>SEND<br>VACC10 | 3<br>SEND |
|-----------------------------------|-------------------|-----------------------------|-----------|-------------------|-------------------------------|-----------|
| <b>Inguinal lymph node, right</b> |                   |                             |           |                   |                               |           |
| Hyperplasia lymphoid              |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | 3                           | 3         | 1                 | 3                             | 4         |
| Slight (grade 2)                  | -                 | -                           | 1         | -                 | 2                             | 1         |
| Infiltrate granulocyte            |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | 1                 | 2                           | 2         | 1                 | -                             | 3         |
| <b>Inguinal lymph node, left</b>  |                   |                             |           |                   |                               |           |
| Hyperplasia lymphoid              |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | 5                           | 5         | 2                 | 4                             | 4         |
| Slight (grade 2)                  | -                 | -                           | -         | -                 | 1                             | 1         |
| Infiltrate granulocyte            |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | 1                 | 3                           | 4         | 2                 | -                             | 1         |
| Slight (grade 2)                  | -                 | -                           | -         | -                 | -                             | 1         |
| <b>Iliac lymph node, right</b>    |                   |                             |           |                   |                               |           |
| Hyperplasia lymphoid              |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | 3                           | 2         | -                 | 2                             | 2         |
| Slight (grade 2)                  | -                 | 1                           | -         | -                 | -                             | 2         |
| Infiltrate granulocyte            |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | 1                           | 1         | -                 | -                             | 3         |
| <b>Iliac lymph node, left</b>     |                   |                             |           |                   |                               |           |
| Hyperplasia lymphoid              |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | 2                           | 4         | -                 | 2                             | 2         |
| Infiltrate granulocyte            |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | -                           | 1         | -                 | -                             | -         |
| <b>Sacral lymph node</b>          |                   |                             |           |                   |                               |           |
| Hyperplasia lymphoid              |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | -                           | 1         | -                 | 1                             | 3         |
| Infiltrate granulocyte            |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | -                           | -         | -                 | -                             | 1         |
| <b>Spleen</b>                     |                   |                             |           |                   |                               |           |
| Hyperplasia lymphoid              |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | 3                           | 3         | -                 | 4                             | 4         |
| Slight (grade 2)                  | -                 | -                           | -         | -                 | 1                             | -         |
| <b>Injection site 1</b>           |                   |                             |           |                   |                               |           |
| Inflammation                      |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | 2                           | 2         | 1                 | 2                             | 2         |
| Slight (grade 2)                  | -                 | 2                           | 2         | -                 | 2                             | 2         |
| Moderate (grade 3)                | -                 | 1                           | -         | -                 | -                             | -         |
| <b>Injection site 2</b>           |                   |                             |           |                   |                               |           |
| Inflammation                      |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | 3                           | 2         | 1                 | 2                             | 4         |
| Slight (grade 2)                  | -                 | 1                           | 1         | -                 | 1                             | -         |
| <b>Injection site 3</b>           |                   |                             |           |                   |                               |           |
| Inflammation                      |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | 1                 | -                           | -         | 2                 | -                             | -         |
| Slight (grade 2)                  | -                 | 3                           | 5         | -                 | 5                             | 5         |
| Moderate (grade 3)                | -                 | 1                           | -         | -                 | -                             | -         |
| <b>Adipose tissue</b>             |                   |                             |           |                   |                               |           |
| Edema                             |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | -                           | -         | -                 | 1                             | 1         |
| Slight (grade 2)                  | -                 | -                           | -         | -                 | 3                             | 2         |
| Hemorrhage                        |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | -                           | -         | -                 | 3                             | 2         |
| Slight (grade 2)                  | -                 | -                           | -         | -                 | 1                             | -         |
| <b>Inflammation</b>               |                   |                             |           |                   |                               |           |
| Minimal (grade 1)                 | -                 | -                           | -         | -                 | 1                             | 1         |
| Slight (grade 2)                  | -                 | -                           | -         | -                 | 3                             | 2         |

-: not observed.

The remaining microscopic findings were considered to be incidental because they were consistent with spontaneously occurring findings described in the literature, the findings were distributed randomly among groups, or their appearance was similar to findings found in controls.

3.5.3.2 At the end of the recovery period

**SENDVACC10**

The incidence and severity of lymphoid hyperplasia in the spleen and lymph nodes was similar to the treatment period, however the secondary follicles in the spleen of recovery animals were less cellular, consistent with involution. There was partial recovery at the injection sites, as the incidence and severity of subacute inflammation was decreased when compared to the treatment period. There was complete recovery in the abdominal adipose tissue.

The incidence and severity of lymphoid hyperplasia in the spleen and lymph nodes was similar to the treatment period, however the secondary follicles in the spleen of recovery animals were less cellular, consistent with involution. There was partial recovery at the injection sites as the incidence and severity of subacute inflammation was decreased when compared to the treatment period. There was complete recovery in the abdominal adipose tissue.

Incidence and severity of selected microscopic findings at the end of the observation period (n = 5)

| Sex<br>Group                      | Male           |                     |           | Female         |                     |           |
|-----------------------------------|----------------|---------------------|-----------|----------------|---------------------|-----------|
|                                   | 1<br>NaCl 0.9% | 2<br>SEND<br>VACC10 | 3<br>SEND | 1<br>NaCl 0.9% | 2<br>SEND<br>VACC10 | 3<br>SEND |
| Treatment                         |                |                     |           |                |                     |           |
| <b>Inguinal lymph node, right</b> |                |                     |           |                |                     |           |
| Hyperplasia lymphoid              |                |                     |           |                |                     |           |
| Minimal (grade 1)                 | -              | 3                   | 4         | 2              | 4                   | 4         |
| Slight (grade 2)                  | -              | 1                   | -         | -              | -                   | -         |
| Infiltrate granulocyte            |                |                     |           |                |                     |           |
| Minimal (grade 1)                 | 1              | -                   | 2         | -              | -                   | -         |
| <b>Inguinal lymph node, left</b>  |                |                     |           |                |                     |           |
| Hyperplasia lymphoid              |                |                     |           |                |                     |           |
| Minimal (grade 1)                 | 1              | 3                   | 3         | 3              | 3                   | 2         |
| Slight (grade 2)                  | -              | 1                   | 1         | -              | -                   | -         |
| Infiltrate granulocyte            |                |                     |           |                |                     |           |
| Minimal (grade 1)                 | -              | 1                   | 3         | -              | -                   | -         |
| <b>Iliac lymph node, right</b>    |                |                     |           |                |                     |           |
| Hyperplasia lymphoid              |                |                     |           |                |                     |           |
| Minimal (grade 1)                 | -              | 1                   | 2         | -              | 1                   | 4         |
| Slight (grade 2)                  | -              | 2                   | -         | -              | -                   | -         |
| <b>Iliac lymph node, left</b>     |                |                     |           |                |                     |           |
| Hyperplasia lymphoid              |                |                     |           |                |                     |           |
| Minimal (grade 1)                 | -              | 3                   | 3         | -              | 1                   | 2         |
| <b>Sacral lymph node</b>          |                |                     |           |                |                     |           |
| Hyperplasia lymphoid              |                |                     |           |                |                     |           |
| Minimal (grade 1)                 | -              | 1                   | 1         | -              | 1                   | 1         |
| Slight (grade 2)                  | -              | -                   | 1         | -              | -                   | -         |

-: not observed.

| Sex<br>Group            | Male           |                     |   | Female         |                     |   |  |  |  |  |  |  |
|-------------------------|----------------|---------------------|---|----------------|---------------------|---|--|--|--|--|--|--|
|                         | 1<br>NaCl 0.9% | 2<br>SEND<br>VACC10 | 3 | 1<br>NaCl 0.9% | 2<br>SEND<br>VACC10 | 3 |  |  |  |  |  |  |
| Treatment               |                |                     |   |                |                     |   |  |  |  |  |  |  |
| <b>Spleen</b>           |                |                     |   |                |                     |   |  |  |  |  |  |  |
| Hyperplasia lymphoid    |                |                     |   |                |                     |   |  |  |  |  |  |  |
| Minimal (grade 1)       | 1              | 4                   | 4 | 1              | 5                   | 4 |  |  |  |  |  |  |
| Slight (grade 2)        | -              | 1                   | - | -              | -                   | - |  |  |  |  |  |  |
| <b>Injection site 1</b> |                |                     |   |                |                     |   |  |  |  |  |  |  |
| Inflammation            |                |                     |   |                |                     |   |  |  |  |  |  |  |
| Minimal (grade 1)       | -              | -                   | 1 | -              | -                   | 2 |  |  |  |  |  |  |
| Slight (grade 2)        | -              | 1                   | - | -              | -                   | - |  |  |  |  |  |  |
| <b>Injection site 2</b> |                |                     |   |                |                     |   |  |  |  |  |  |  |
| Inflammation            |                |                     |   |                |                     |   |  |  |  |  |  |  |
| Minimal (grade 1)       | -              | 1                   | - | -              | -                   | 1 |  |  |  |  |  |  |
| <b>Injection site 3</b> |                |                     |   |                |                     |   |  |  |  |  |  |  |
| Inflammation            |                |                     |   |                |                     |   |  |  |  |  |  |  |
| Minimal (grade 1)       | -              | 3                   | 2 | 1              | 3                   | 3 |  |  |  |  |  |  |

-: not observed.

There were no other test item treatment-related microscopic findings.

### 3.5.4 Pathology discussion

Treatment-related findings with both SENDVACC10 and VA were present in the spleen (increased weight and lymphoid hyperplasia, the regional lymph nodes (lymphoid hyperplasia and granulocyte infiltration and injection sites (subacute inflammation). The severity was minimal to moderate, with most findings being minimal to slight. There was partial recovery.

The inflammation was characterized by the presence of mixed inflammatory cells, as well as clear spaces with faint eosinophilic or basophilic staining, considered to be exudate and serum proteins. These clear spaces were no longer present after the recovery period.

Injection site 1 was used on Day 1, injection site 2 on Day 15, and injection site 3 on Day 29 of the study. It would be expected that the findings would increase in incidence/severity from injection site 1 (first site, with most time for recovery to injection site 3 (most recent site, with least time for recovery, however findings at injection site 1 were slightly higher in incidence/severity than at injection site 2. Both sites 1 and 3 were on the same side of the animal, and approximately 4 cm apart. There appears to have been some cross-over between the two injection sites due to their proximity and to the liquid nature of the injection. This was not considered to have affected the interpretation of the study. Edema, hemorrhage and inflammation in abdominal adipose tissue was also present on the right side only (*i.e.* the same side as injection sites 1 and 3, and is likely to have been due to extension downwards (due to gravity of edema and hemorrhage at the injection sites, rather than a direct effect of the test compounds.

These findings were considered non-adverse and related to the pharmacological activity of the adjuvanted vaccines.

#### **4. CONCLUSION**

The three intramuscular administrations of SENDAdjuvanted VACC10 Quadrivalent and VA Quadrivalent, in the New Zealand White rabbit, two weeks apart, at the anticipated human dose, were both locally and systemically well tolerated. Both adjuvanted test items induced non-adverse transient minimal mean body weight loss associated with minimal reduction in mean food consumption shortly after the first two administrations. Other adjuvanted vaccines-related effects included reversible increase in mean fibrinogen and CRP concentrations, reversible decrease in mean albumin/globulin ratio, as well as potentially short minimal to slight hematomas at the injection sites and reversible increase in some white blood cell subpopulations. Adjuvanted test items induced lymphoid hyperplasia and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue. These histopathological findings showed partial recovery at the end of the 4-week observation period.

These changes were considered non-adverse and generally consistent with the pharmacology activity of adjuvanted vaccines.

The immunogenicity assay confirmed the exposure of all vaccinated rabbits to the adjuvanted vaccines.

#### **5. BIBLIOGRAPHICAL REFERENCES**

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## FIGURES

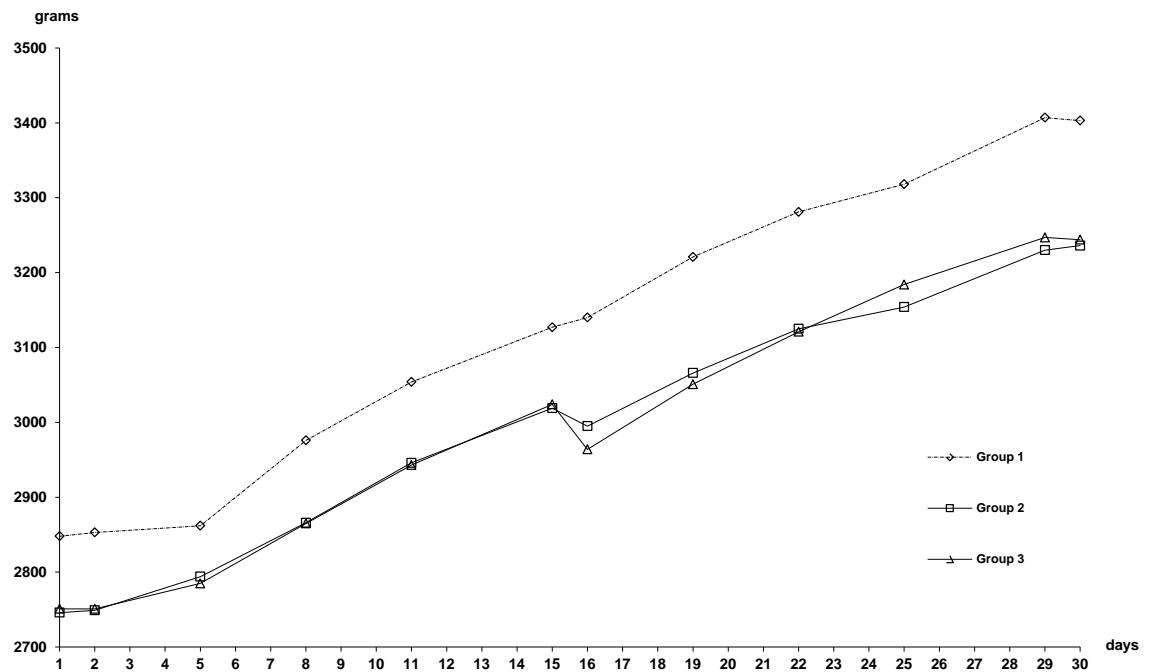


Figure 2. Mean body weight - females (principal and recovery animals) (treatment period)

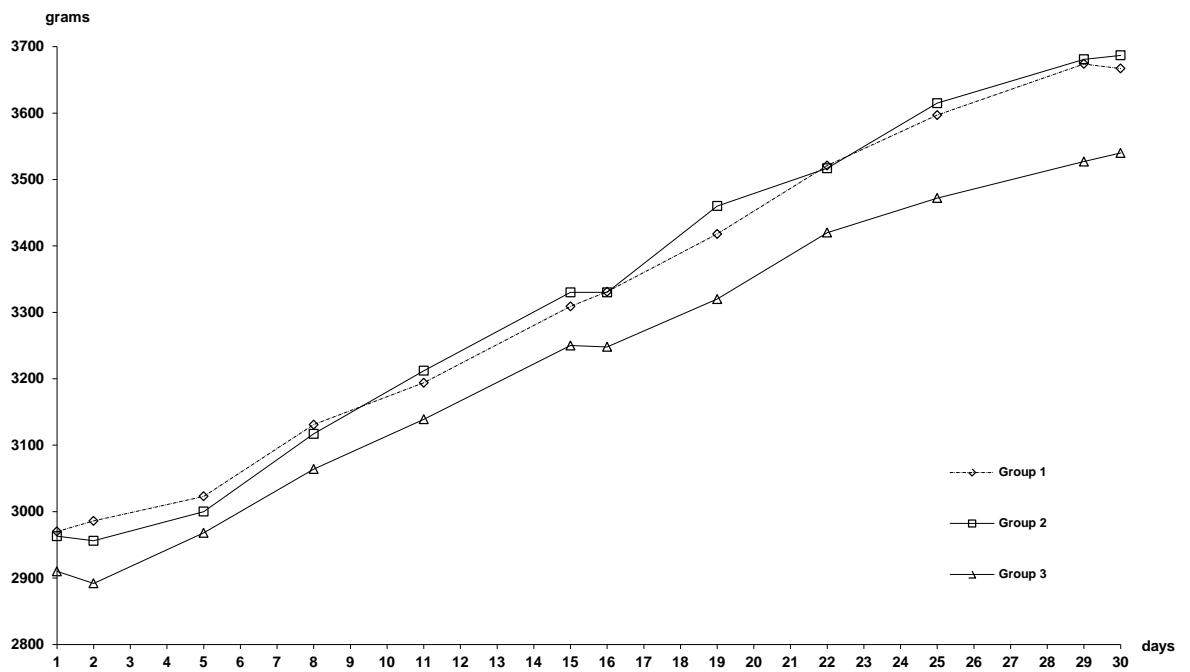


Figure 3. Mean body weight - males (recovery animals) (recovery period)

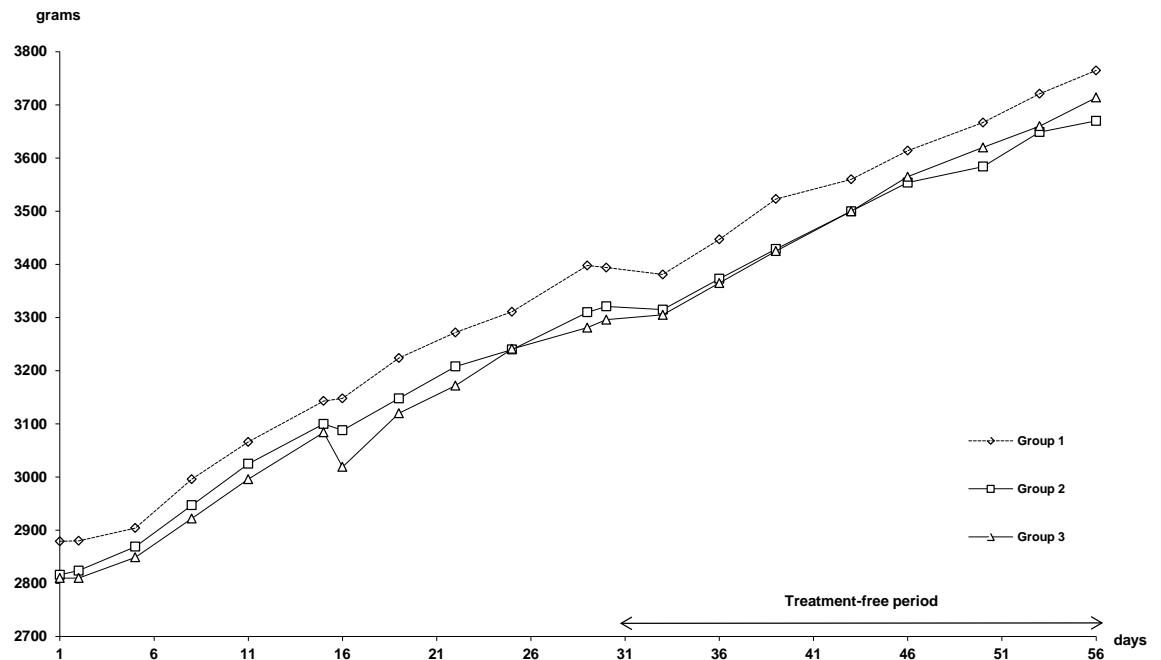
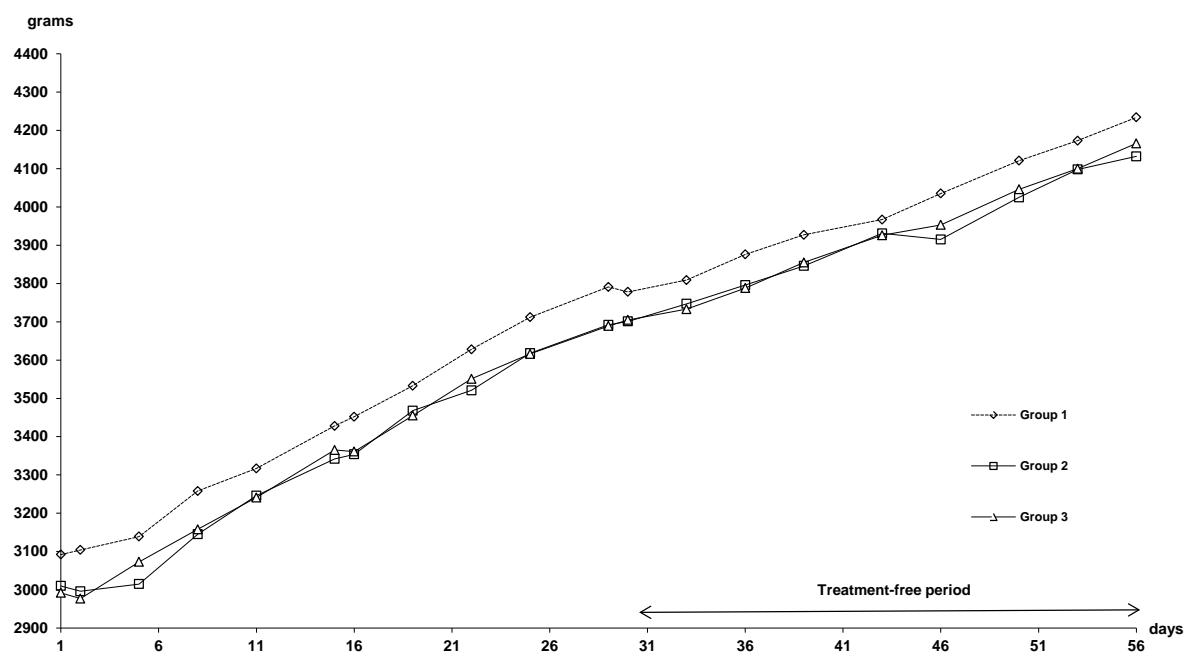


Figure 4. Mean body weight - females (recovery animals) (recovery period)



TABLES

Tables 1 to 4. Clinical signs (summary tables)

Table: 1

CLINICAL SIGNS (SUMMARY TABLES)

Study No.:

Sex: Male

Period: Days 1 to 31

Principal animals + Recovery animals

---

| Group                           | 1  | 2  | 3  |    |    |    |
|---------------------------------|----|----|----|----|----|----|
| Number of animals               | 10 | 10 | 10 |    |    |    |
| Observations                    | No | %  | No | %  | No | %  |
| Papule / Back                   | 3  | 30 |    |    | 3  | 30 |
| Hematoma / interscapular region |    |    | 1  | 10 |    |    |
| No clinical history             | 7  | 70 | 9  | 90 | 7  | 70 |

Table: 2

CLINICAL SIGNS (SUMMARY TABLES)

Study No.:

Sex: Female

Period: Days 1 to 31

Principal animals + Recovery animals

---

| Group                           | 1  | 2   | 3  |    |    |    |
|---------------------------------|----|-----|----|----|----|----|
| Number of animals               | 10 | 10  | 10 |    |    |    |
| Observations                    | No | %   | No | %  | No | %  |
| Papule / Back                   | 1  | 10  |    |    |    |    |
| Hematoma / interscapular region | 1  | 10  | 1  | 10 | 1  | 10 |
| No clinical history             | 10 | 100 | 8  | 80 | 9  | 90 |

Table: 3

CLINICAL SIGNS (SUMMARY TABLES)

Study No.:

Sex: Male

Period: Days 31 to 57

Recovery animals

--

| Group               | 1  | 2  | 3  |     |    |    |
|---------------------|----|----|----|-----|----|----|
| Number of animals   | 5  | 5  | 5  |     |    |    |
| Observations        | No | %  | No | %   | No | %  |
| Papule / Back       | 2  | 40 |    |     | 3  | 60 |
| No clinical history | 3  | 60 | 5  | 100 | 2  | 40 |

Table: 4

CLINICAL SIGNS (SUMMARY TABLES)

Study No.:

Sex: Female

Period: Days 31 to 57

Recovery animals

--

| Group                                | 1  | 2   | 3  |     |    |    |
|--------------------------------------|----|-----|----|-----|----|----|
| Number of animals                    | 5  | 5   | 5  |     |    |    |
| Observations                         | No | %   | No | %   | No | %  |
| Abnormal color / Reddish / right ear |    |     |    |     | 1  | 20 |
| Scabs / right ear                    |    |     |    |     | 1  | 20 |
| Papule / Back                        |    |     |    |     | 1  | 20 |
| No clinical history                  | 5  | 100 | 5  | 100 | 3  | 60 |

Table 5. Local reactions (summary table)

## LOCAL REACTIONS

(Summary table)

Study No. [REDACTED]

Sex: Male

Group: 1

Control item (NaCl)

| Animal No. | Local reaction                         | Site No. | Day                              |
|------------|--|----------|----------------------------------|
| N30646     | Hematoma (area $\leq 1 \text{ cm}^2$ ) | 2        | Day 15 (3 hours after treatment) |

Group: 3

| Animal No. | Local reaction  | Site No. | Day   |
|------------|---|----------|---|
| N30664     | Hematoma (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ ) | 1        | Day 1 (3 hours after treatment), Days 2 and 3 |
| N30661     | Hematoma (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ ) | 2        | Day 15 (3 hours after treatment)              |
| N30666     | Hematoma (area $\leq 1 \text{ cm}^2$ )                        | 2        | Days 16 and 19                                |
|            | Hematoma (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ ) |          | Day 18  |
| N30668     | Hematoma (area $\leq 1 \text{ cm}^2$ )                        | 3        | Day 29 (3 hours after treatment)              |
|            | Hematoma (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ ) |          | Day 32  |
| N30669     | Hematoma (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ ) | 3        | Days 30 and 31                                |

## LOCAL REACTIONS

(Summary table)

Study No. 46501 TCL

Sex: Female

Group: 1

Control item (NaCl)

| Animal No. | Local reaction  | Site No. | Day                             |
|------------|---|----------|---------------------------------|
| N30718     | Hematoma (area $\leq 1 \text{ cm}^2$ )                        | 1        | Day 1 (3 hours after treatment) |
| N30713     | Hematoma (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ ) | 1        | Day 2                           |

Group: 2

| Animal No. | Local reaction  | Site No. | Day   |
|------------|---|----------|---|
| N30725     | Hematoma (area $\leq 1 \text{ cm}^2$ )                        | 1        | Day 1 (3 hours after treatment)             |
|            | Hematoma (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ ) |          | Day 2                                       |
| N30724     | Hematoma (area $\leq 1 \text{ cm}^2$ )                        | 3        | Day 29 (3 hours after treatment) and Day 30 |

Group: 3

| Animal No. | Local reaction  | Site No. | Day  |
|------------|---|----------|--|
| N30736     | Hematoma (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ )   | 1        | Day 1 (3 hours after treatment), Days 2, 3 and 4     |
| N30740     | Induration (area $> 1 \text{ cm}^2$ and $\leq 2 \text{ cm}^2$ ) | 1        | Day 2  |
| N30739     | Hematoma (area $\leq 1 \text{ cm}^2$ )                          | 3        | Day 29 (3 hours after treatment), Days 30, 31 and 32 |
| N30738     | Other   | P        | Day 51   |

P: Presence (site and reaction not documented)

Tables 6 to 9. Body weight (mean values)

BODY WEIGHT  
(mean values - g)

Table: 6

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group |             | 1     | 2     | 3      |
|-------|-------------|-------|-------|--------|
| Day   |             |       |       |        |
| -14   | M (1)       | 2463  | 2439  | 2441   |
|       | SD          | 54.8  | 128.0 | 129.1  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -1    | -1    |        |
| ..... | .....       | ..... | ..... | .....  |
| -7    | M (1)       | 2666  | 2598  | 2612   |
|       | SD          | 71.8  | 78.6  | 124.7  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -3    | -2    |        |
| ..... | .....       | ..... | ..... | .....  |
| 1     | M (1)       | 2848  | 2746  | 2751   |
|       | SD          | 94.7  | 102.3 | 139.7  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -4    | -3    |        |
| ..... | .....       | ..... | ..... | .....  |
| 2     | M (1)       | 2853  | 2749  | 2751   |
|       | SD          | 92.6  | 107.6 | 137.2  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -4    | -4    |        |
| ..... | .....       | ..... | ..... | .....  |
| 5     | M (1)       | 2862  | 2794  | 2785   |
|       | SD          | 110.8 | 111.7 | 141.1  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -2    | -3    |        |
| ..... | .....       | ..... | ..... | .....  |
| 8     | M (1)       | 2976  | 2866  | 2865   |
|       | SD          | 104.3 | 128.2 | 149.9  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -4    | -4    |        |
| ..... | .....       | ..... | ..... | .....  |
| 11    | M (1)       | 3054  | 2946  | 2943   |
|       | SD          | 114.2 | 131.6 | 156.4  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -4    | -4    |        |
| ..... | .....       | ..... | ..... | .....  |
| 15    | M (1)       | 3127  | 3019  | 3024   |
|       | SD          | 132.7 | 137.0 | 164.0  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -3    | -3    |        |
| ..... | .....       | ..... | ..... | .....  |
| 16    | M (1)       | 3140  | 2995  | 2964 * |
|       | SD          | 127.2 | 148.0 | 148.7  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -5    | -6    |        |
| ..... | .....       | ..... | ..... | .....  |
| 19    | M (1)       | 3221  | 3066  | 3051 * |
|       | SD          | 133.6 | 144.4 | 190.9  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -5    | -5    |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

BODY WEIGHT  
(mean values - g)

Table: (continued)

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group |             | 1     | 2     | 3      |
|-------|-------------|-------|-------|--------|
| Day   |             |       |       |        |
| 22    | M (1)       | 3281  | 3125  | 3121   |
|       | SD          | 143.6 | 148.1 | 172.9  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group |       | -5    | -5     |
| 25    | M (1)       | 3318  | 3154  | 3184   |
|       | SD          | 152.8 | 150.6 | 193.4  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group |       | -5    | -4     |
| 29    | M (1)       | 3407  | 3230  | * 3247 |
|       | SD          | 153.4 | 147.9 | 197.6  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group |       | -5    | -5     |
| 30    | M (1)       | 3403  | 3236  | 3244   |
|       | SD          | 158.5 | 164.5 | 188.3  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group |       | -5    | -5     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BODY WEIGHT  
(mean values - g)

Table: 7

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| -14   | M (1)       | 2562  | 2534  | 2520  |
|       | SD          | 144.5 | 135.0 | 139.4 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -1    | -2    |       |
| ..... | .....       | ..... | ..... | ..... |
| -7    | M (1)       | 2740  | 2741  | 2711  |
|       | SD          | 137.9 | 155.9 | 124.2 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -1    |       |
| ..... | .....       | ..... | ..... | ..... |
| 1     | M (1)       | 2970  | 2963  | 2910  |
|       | SD          | 151.8 | 167.6 | 127.2 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -2    |       |
| ..... | .....       | ..... | ..... | ..... |
| 2     | M (1)       | 2986  | 2956  | 2892  |
|       | SD          | 147.4 | 177.3 | 135.5 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -1    | -3    |       |
| ..... | .....       | ..... | ..... | ..... |
| 5     | M (1)       | 3023  | 3000  | 2968  |
|       | SD          | 153.0 | 190.5 | 143.0 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -1    | -2    |       |
| ..... | .....       | ..... | ..... | ..... |
| 8     | M (1)       | 3131  | 3117  | 3064  |
|       | SD          | 155.4 | 191.2 | 143.0 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -2    |       |
| ..... | .....       | ..... | ..... | ..... |
| 11    | M (1)       | 3194  | 3212  | 3139  |
|       | SD          | 156.4 | 193.0 | 150.4 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 1     | -2    |       |
| ..... | .....       | ..... | ..... | ..... |
| 15    | M (1)       | 3309  | 3330  | 3250  |
|       | SD          | 159.2 | 198.1 | 185.4 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 1     | -2    |       |
| ..... | .....       | ..... | ..... | ..... |
| 16    | M (1)       | 3331  | 3330  | 3248  |
|       | SD          | 166.2 | 227.2 | 168.1 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -2    |       |
| ..... | .....       | ..... | ..... | ..... |
| 19    | M (1)       | 3418  | 3460  | 3320  |
|       | SD          | 154.7 | 246.0 | 190.2 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 1     | -3    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

BODY WEIGHT  
(mean values - g)

Table: (continued)

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 22    | M (1)       | 3521  | 3517  | 3420  |
|       | SD          | 159.1 | 249.9 | 204.8 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -3    |       |
| 25    | M (1)       | 3597  | 3615  | 3472  |
|       | SD          | 169.3 | 262.6 | 214.0 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 1     | -3    |       |
| 29    | M (1)       | 3674  | 3681  | 3527  |
|       | SD          | 182.6 | 262.8 | 239.6 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -4    |       |
| 30    | M (1)       | 3667  | 3687  | 3540  |
|       | SD          | 169.5 | 269.9 | 241.0 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 1     | -3    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BODY WEIGHT  
(mean values - g)

Table: 8

Study No.:  
Sex: Male  
Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| -14   | M (1)       | 2493  | 2472  | 2529  |
|       | SD          | 53.1  | 169.2 | 89.8  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -1    | 1     |
| ..... | .....       | ..... | ..... | ..... |
| -7    | M (1)       | 2692  | 2654  | 2666  |
|       | SD          | 85.9  | 67.0  | 118.0 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -1    | -1    |
| ..... | .....       | ..... | ..... | ..... |
| 1     | M (1)       | 2879  | 2816  | 2810  |
|       | SD          | 107.4 | 80.4  | 125.6 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 2     | M (1)       | 2880  | 2824  | 2810  |
|       | SD          | 110.4 | 94.6  | 106.5 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 5     | M (1)       | 2904  | 2869  | 2849  |
|       | SD          | 127.0 | 78.6  | 122.6 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -1    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 8     | M (1)       | 2996  | 2947  | 2922  |
|       | SD          | 126.7 | 110.6 | 117.3 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 11    | M (1)       | 3066  | 3025  | 2996  |
|       | SD          | 137.1 | 109.4 | 144.1 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -1    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 15    | M (1)       | 3143  | 3100  | 3084  |
|       | SD          | 155.5 | 117.4 | 149.8 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -1    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 16    | M (1)       | 3148  | 3088  | 3019  |
|       | SD          | 145.3 | 131.4 | 120.3 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -4    |
| ..... | .....       | ..... | ..... | ..... |
| 19    | M (1)       | 3224  | 3148  | 3120  |
|       | SD          | 162.5 | 118.8 | 166.1 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -3    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

Study No. RABBITV1 SENDAdjuvanted VACC10  
 Quadrivalent and VA      Quadrivalent

BODY WEIGHT  
 (mean values - g)

Table: (continued)

Study No.:  
 Sex: Male  
 Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 22    | M (1)       | 3272  | 3208  | 3172  |
|       | SD          | 168.8 | 122.5 | 168.5 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -3    |
| 25    | M (1)       | 3311  | 3240  | 3241  |
|       | SD          | 180.7 | 118.3 | 185.2 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 29    | M (1)       | 3398  | 3310  | 3281  |
|       | SD          | 186.6 | 105.5 | 211.5 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -3    |
| 30    | M (1)       | 3394  | 3321  | 3296  |
|       | SD          | 189.1 | 118.3 | 187.1 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -3    |
| 33    | M (1)       | 3381  | 3315  | 3305  |
|       | SD          | 183.5 | 132.1 | 190.8 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 36    | M (1)       | 3447  | 3373  | 3365  |
|       | SD          | 204.9 | 136.7 | 201.6 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 39    | M (1)       | 3523  | 3429  | 3425  |
|       | SD          | 204.1 | 148.4 | 192.5 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -3    |
| 43    | M (1)       | 3560  | 3500  | 3500  |
|       | SD          | 213.1 | 152.8 | 205.6 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 46    | M (1)       | 3614  | 3554  | 3565  |
|       | SD          | 223.6 | 158.7 | 230.4 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -1    |
| 50    | M (1)       | 3667  | 3584  | 3620  |
|       | SD          | 218.3 | 99.2  | 244.9 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -1    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
 TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
 \*\* P<0.01  
 (1) : DUNNETT TEST  
 (2) : MANN-WHITNEY TEST  
 (3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
 (F) FISHER TEST P<0.01  
 (K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
 (L) LOGARITHMIC TRANSFORMATION  
 - STATISTICS EXCLUDED GROUP

BODY WEIGHT  
(mean values - g)

Table: (continued)

Study No.:

Sex: Male

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 53    | M (1)       | 3721  | 3649  | 3660  |
|       | SD          | 225.0 | 161.7 | 219.2 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 56    | M (1)       | 3765  | 3670  | 3714  |
|       | SD          | 235.3 | 179.7 | 240.6 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -1    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BODY WEIGHT  
(mean values - g)

Table: 9

Study No.:  
Sex: Female  
Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| -14   | M (1)       | 2687  | 2608  | 2617  |
|       | SD          | 32.1  | 77.7  | 98.3  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -3    |
| ..... | .....       | ..... | ..... | ..... |
| -7    | M (1)       | 2845  | 2826  | 2796  |
|       | SD          | 55.0  | 136.9 | 84.7  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -1    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 1     | M (1)       | 3092  | 3010  | 2992  |
|       | SD          | 78.9  | 154.8 | 74.5  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -3    |
| ..... | .....       | ..... | ..... | ..... |
| 2     | M (1)       | 3104  | 2996  | 2977  |
|       | SD          | 66.9  | 163.6 | 98.4  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -4    |
| ..... | .....       | ..... | ..... | ..... |
| 5     | M (1)       | 3139  | 3015  | 3073  |
|       | SD          | 106.3 | 197.9 | 85.4  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -4    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 8     | M (1)       | 3258  | 3145  | 3158  |
|       | SD          | 98.4  | 183.1 | 103.4 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -3    |
| ..... | .....       | ..... | ..... | ..... |
| 11    | M (1)       | 3317  | 3246  | 3241  |
|       | SD          | 110.0 | 201.1 | 112.5 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 15    | M (1)       | 3428  | 3342  | 3365  |
|       | SD          | 126.5 | 210.1 | 142.0 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -2    |
| ..... | .....       | ..... | ..... | ..... |
| 16    | M (1)       | 3452  | 3354  | 3361  |
|       | SD          | 137.7 | 221.4 | 124.2 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -3    |
| ..... | .....       | ..... | ..... | ..... |
| 19    | M (1)       | 3533  | 3468  | 3455  |
|       | SD          | 127.0 | 233.2 | 142.7 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BODY WEIGHT  
(mean values - g)

Table: (continued)

Study No.:  
Sex: Female  
Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 22    | M (1)       | 3628  | 3521  | 3551  |
|       | SD          | 135.1 | 242.8 | 168.3 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -2    |
| 25    | M (1)       | 3712  | 3618  | 3616  |
|       | SD          | 145.5 | 266.0 | 187.5 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -3    |
| 29    | M (1)       | 3791  | 3692  | 3689  |
|       | SD          | 178.7 | 252.2 | 182.4 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -3    |
| 30    | M (1)       | 3778  | 3701  | 3705  |
|       | SD          | 149.2 | 261.8 | 190.0 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 33    | M (1)       | 3809  | 3747  | 3733  |
|       | SD          | 159.4 | 282.3 | 166.9 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 36    | M (1)       | 3876  | 3796  | 3788  |
|       | SD          | 157.1 | 278.1 | 159.6 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 39    | M (1)       | 3927  | 3846  | 3855  |
|       | SD          | 166.5 | 265.1 | 165.5 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 43    | M (1)       | 3967  | 3931  | 3926  |
|       | SD          | 208.4 | 270.6 | 184.4 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -1    | -1    |
| 46    | M (1)       | 4035  | 3915  | 3953  |
|       | SD          | 182.5 | 338.1 | 213.2 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -2    |
| 50    | M (1)       | 4121  | 4025  | 4046  |
|       | SD          | 181.4 | 326.8 | 171.6 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BODY WEIGHT  
(mean values - g)

Table: (continued)

Study No.:  
Sex: Female  
Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 53    | M (1)       | 4173  | 4098  | 4100  |
|       | SD          | 204.4 | 324.0 | 164.4 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 56    | M (1)       | 4234  | 4132  | 4166  |
|       | SD          | 193.1 | 326.3 | 157.7 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

Tables 10 to 17. Body weight change (mean values)

BODY WEIGHT CHANGE  
(mean values - g)

Table: 10

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group |             | 1    | 2    | 3      |
|-------|-------------|------|------|--------|
| Day   |             |      |      |        |
| 1/2   | M (1)       | 5    | 4    | 0      |
|       | SD          | 18.9 | 25.8 | 29.3   |
|       | n           | 10   | 10   | 10     |
|       | %/1st group | -20  | -100 |        |
| 2/5   | M (3)       | 9    | 45   | 35     |
|       | SD (K)      | 58.4 | 35.8 | 24.4   |
|       | n           | 10   | 10   | 10     |
|       | %/1st group | 400  | 289  |        |
| 5/8   | M (1)       | 115  | 72 * | 80     |
|       | SD (L)      | 51.4 | 27.8 | 25.3   |
|       | n           | 10   | 10   | 10     |
|       | %/1st group | -37  | -30  |        |
| 8/11  | M (3)       | 78   | 80   | 78     |
|       | SD (K)      | 22.3 | 17.6 | 24.4   |
|       | n           | 10   | 10   | 10     |
|       | %/1st group | 3    | 0    |        |
| 11/15 | M (3)       | 73   | 73   | 82     |
|       | SD          | 45.9 | 18.1 | 20.4   |
|       | n (B)       | 10   | 10   | 10     |
|       | %/1st group | 0    | 12   |        |
| 15/16 | M (3)       | 13   | -24  | -60 ** |
|       | SD (K)      | 47.0 | 27.5 | 28.8   |
|       | n           | 10   | 10   | 10     |
|       | %/1st group | -285 | -562 |        |
| 16/19 | M (3)       | 81   | 71   | 87     |
|       | SD          | 16.2 | 32.5 | 58.1   |
|       | n (B)       | 10   | 10   | 10     |
|       | %/1st group | -12  | 7    |        |
| 19/22 | M (3)       | 61   | 59   | 70     |
|       | SD (K)      | 28.9 | 28.8 | 38.5   |
|       | n           | 10   | 10   | 10     |
|       | %/1st group | -3   | 15   |        |
| 22/25 | M (1)       | 37   | 29   | 63 *   |
|       | SD          | 14.9 | 22.9 | 31.9   |
|       | n           | 10   | 10   | 10     |
|       | %/1st group | -22  | 70   |        |
| 25/29 | M (1)       | 89   | 77   | 64     |
|       | SD          | 16.5 | 19.6 | 35.7   |
|       | n           | 10   | 10   | 10     |
|       | %/1st group | -13  | -28  |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: (continued)

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group |             | 1    | 2    | 3    |
|-------|-------------|------|------|------|
| Day   |             |      |      |      |
| 29/30 | M (1)       | -4   | 6    | -4   |
|       | SD          | 15.2 | 24.5 | 42.1 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group | 250  |      | 0    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: 11

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group |             | 1    | 2    | 3    |
|-------|-------------|------|------|------|
| Day   |             |      |      |      |
| 1/30  | M (1)       | 555  | 490  | 493  |
|       | SD          | 91.1 | 89.3 | 95.7 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group |      | -12  | -11  |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: 12

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group<br>Day |             | 1    | 2    | 3    |     |
|--------------|-------------|------|------|------|-----|
| 1/2          | M (1)       | 16   | -7   | -18  | **  |
|              | SD          | 26.9 | 21.9 | 20.4 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | -144 | -213 |     |
| 2/5          | M (3)       | 38   | 44   | 76   |     |
|              | SD (K)      | 42.3 | 60.2 | 31.8 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | 16   | 100  |     |
| 5/8          | M (1)       | 108  | 118  | 96   |     |
|              | SD          | 33.8 | 40.2 | 30.2 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | 9    | -11  |     |
| 8/11         | M (1)       | 63   | 95   | **   | 75  |
|              | SD          | 26.8 | 23.1 | 20.1 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | 51   | 19   |     |
| 11/15        | M (1)       | 116  | 118  | 111  |     |
|              | SD          | 22.2 | 47.8 | 45.6 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | 2    | -4   |     |
| 15/16        | M (1)       | 22   | -1   | -2   |     |
|              | SD          | 17.0 | 45.2 | 29.6 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | -105 | -109 |     |
| 16/19        | M (1)       | 87   | 130  | *    | 72  |
|              | SD (L)      | 29.5 | 33.2 | 38.7 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | 49   | -17  |     |
| 19/22        | M (1)       | 103  | 57   | **   | 100 |
|              | SD          | 32.4 | 24.1 | 33.4 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | -45  | -3   |     |
| 22/25        | M (1)       | 76   | 98   | 52   |     |
|              | SD          | 17.8 | 40.2 | 40.3 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | 29   | -32  |     |
| 25/29        | M (1)       | 77   | 67   | 55   |     |
|              | SD          | 28.9 | 26.7 | 50.7 |     |
|              | n           | 10   | 10   | 10   |     |
|              | %/1st group |      | -13  | -29  |     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: (continued)

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group |             | 1    | 2    | 3    |
|-------|-------------|------|------|------|
| Day   |             |      |      |      |
| 29/30 | M (1)       | -7   | 6    | 14   |
|       | SD          | 27.0 | 15.2 | 15.5 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group | 186  | 300  |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: 13

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group |             | 1    | 2     | 3     |
|-------|-------------|------|-------|-------|
| Day   |             |      |       |       |
| 1/30  | M (1)       | 697  | 724   | 630   |
|       | SD          | 70.3 | 141.6 | 152.0 |
|       | n           | 10   | 10    | 10    |
|       | %/1st group | 4    |       | -10   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: 14

Study No.:  
Sex: Male  
Recovery animals

| Group<br>Day |             | 1    | 2     | 3      |
|--------------|-------------|------|-------|--------|
| 1/2          | M (1)       | 1    | 8     | 0      |
|              | SD          | 18.5 | 29.7  | 39.2   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | 700  | -100  |        |
| 2/5          | M (1)       | 24   | 45    | 39     |
|              | SD          | 17.8 | 31.0  | 34.2   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | 88   | 63    |        |
| 5/8          | M (1)       | 92   | 78    | 73     |
|              | SD          | 13.0 | 37.5  | 14.8   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | -15  | -21   |        |
| 8/11         | M (1)       | 70   | 78    | 74     |
|              | SD          | 18.4 | 12.5  | 32.7   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | 11   | 6     |        |
| 11/15        | M (1)       | 77   | 75    | 88     |
|              | SD          | 26.1 | 12.2  | 17.9   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | -3   | 14    |        |
| 15/16        | M (1)       | 5    | -12   | -65 ** |
|              | SD          | 12.7 | 34.4  | 32.2   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | -340 | -1400 |        |
| 16/19        | M (1)       | 76   | 60    | 101    |
|              | SD          | 19.8 | 30.2  | 59.8   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | -21  | 33    |        |
| 19/22        | M (1)       | 48   | 60    | 52     |
|              | SD          | 25.9 | 35.2  | 10.4   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | 25   | 8     |        |
| 22/25        | M (1)       | 39   | 32    | 69     |
|              | SD          | 13.9 | 29.7  | 29.7   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | -18  | 77    |        |
| 25/29        | M (1)       | 87   | 70    | 40 *   |
|              | SD          | 11.0 | 20.6  | 37.6   |
|              | n           | 5    | 5     | 5      |
|              | %/1st group | -20  | -54   |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: (continued)

Study No.:

Sex: Male

Recovery animals

| Group |             | 1    | 2    | 3    |
|-------|-------------|------|------|------|
| Day   |             |      |      |      |
| 29/30 | M (1)       | -4   | 11   | 15   |
|       | SD          | 13.9 | 22.7 | 52.4 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | 375  | 475  |      |
| 30/33 | M (1)       | -13  | -6   | 9    |
|       | SD          | 16.8 | 29.0 | 53.8 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | 54   | 169  |      |
| 33/36 | M (1)       | 66   | 58   | 60   |
|       | SD          | 28.8 | 21.4 | 27.8 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | -12  | -9   |      |
| 36/39 | M (1)       | 76   | 56   | 60   |
|       | SD          | 16.4 | 21.3 | 13.2 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | -26  | -21  |      |
| 39/43 | M (1)       | 37   | 71   | 75 * |
|       | SD          | 27.5 | 22.2 | 18.4 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | 92   | 103  |      |
| 43/46 | M (1)       | 54   | 54   | 65   |
|       | SD          | 24.6 | 20.1 | 34.1 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | 0    | 20   |      |
| 46/50 | M (1)       | 53   | 30   | 55   |
|       | SD          | 45.2 | 75.7 | 46.4 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | -43  | 4    |      |
| 50/53 | M (1)       | 54   | 65   | 40   |
|       | SD          | 14.3 | 72.3 | 54.4 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | 20   | -26  |      |
| 53/56 | M (3)       | 44   | 21   | 54   |
|       | SD (K)      | 25.3 | 19.2 | 38.8 |
|       | n           | 5    | 5    | 5    |
|       | %/1st group | -52  | 23   |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: 15

Study No.:

Sex: Male

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 1/30  | M (1)       | 515   | 505   | 486   |
|       | SD          | 88.5  | 70.4  | 115.1 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -6    |
| 30/56 | M (1)       | 371   | 349   | 418   |
|       | SD          | 66.6  | 83.6  | 82.9  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -6    | 13    |
| 1/56  | M (1)       | 886   | 854   | 904   |
|       | SD          | 140.1 | 146.0 | 179.6 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -4    | 2     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: 16

Study No.:  
Sex: Female  
Recovery animals

| Group<br>Day |             | 1    | 2    | 3    |
|--------------|-------------|------|------|------|
| 1/2          | M (1)       | 12   | -14  | -15  |
|              | SD          | 37.2 | 25.3 | 26.2 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | -217 | -225 |
| 2/5          | M (1)       | 35   | 19   | 96   |
|              | SD          | 56.2 | 79.3 | 27.7 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | -46  | 174  |
| 5/8          | M (1)       | 119  | 130  | 85   |
|              | SD          | 31.7 | 50.4 | 33.4 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | 9    | -29  |
| 8/11         | M (1)       | 59   | 101  | *    |
|              | SD          | 29.9 | 24.8 | 15.2 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | 71   | 41   |
| 11/15        | M (1)       | 111  | 96   | 124  |
|              | SD          | 22.2 | 39.0 | 38.1 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | -14  | 12   |
| 15/16        | M (1)       | 24   | 12   | -4   |
|              | SD          | 12.9 | 43.1 | 33.8 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | -50  | -117 |
| 16/19        | M (1)       | 81   | 114  | 94   |
|              | SD (L)      | 24.3 | 21.6 | 42.6 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | 41   | 16   |
| 19/22        | M (1)       | 95   | 53   | 96   |
|              | SD          | 25.2 | 26.6 | 31.1 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | -44  | 1    |
| 22/25        | M (1)       | 84   | 97   | 65   |
|              | SD          | 23.3 | 52.3 | 31.8 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | 15   | -23  |
| 25/29        | M (1)       | 79   | 74   | 73   |
|              | SD          | 38.3 | 25.1 | 32.5 |
|              | n           | 5    | 5    | 5    |
|              | %/1st group |      | -6   | -8   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: (continued)

Study No.:

Sex: Female

Recovery animals

| Group |             | 1    | 2     | 3     |
|-------|-------------|------|-------|-------|
| Day   |             |      |       |       |
| 29/30 | M (1)       | -13  | 9     | 16    |
|       | SD          | 34.4 | 19.8  | 8.2   |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | 169  | 223   |       |
| 30/33 | M (1)       | 31   | 46    | 28    |
|       | SD          | 29.5 | 44.9  | 28.6  |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | 48   | -10   |       |
| 33/36 | M (1)       | 67   | 49    | 55    |
|       | SD          | 35.6 | 9.6   | 21.8  |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | -27  | -18   |       |
| 36/39 | M (1)       | 51   | 50    | 67    |
|       | SD          | 31.1 | 39.2  | 18.2  |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | -2   | 31    |       |
| 39/43 | M (1)       | 40   | 85    | 71    |
|       | SD          | 67.6 | 18.4  | 28.6  |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | 113  | 78    |       |
| 43/46 | M (1)       | 68   | -16   | 27    |
|       | SD (L)      | 28.0 | 146.0 | 100.7 |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | -124 | -60   |       |
| 46/50 | M (1)       | 86   | 110   | 93    |
|       | SD (L)      | 11.4 | 80.2  | 51.3  |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | 28   | 8     |       |
| 50/53 | M (1)       | 52   | 73    | 54    |
|       | SD          | 32.5 | 20.2  | 18.8  |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | 40   | 4     |       |
| 53/56 | M (1)       | 61   | 34    | 66    |
|       | SD          | 12.9 | 42.5  | 10.8  |
|       | n           | 5    | 5     | 5     |
|       | %/1st group | -44  | 8     |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

BODY WEIGHT CHANGE  
(mean values - g)

Table: 17

Study No.:  
Sex: Female  
Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 1/30  | M (1)       | 686   | 691   | 713   |
|       | SD          | 75.4  | 136.1 | 137.0 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 1     | 4     |
| 30/56 | M (1)       | 456   | 431   | 461   |
|       | SD          | 82.9  | 108.7 | 133.2 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -5    | 1     |
| 1/56  | M (1)       | 1142  | 1122  | 1174  |
|       | SD          | 117.3 | 218.3 | 161.8 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | 3     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

Tables 18 to 21. Food consumption (mean values)

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: 18

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group |             | 1     | 2       | 3       |
|-------|-------------|-------|---------|---------|
| Day   |             |       |         |         |
| -5/-4 | M (1)       | 233.8 | 214.6   | 209.9   |
|       | SD          | 28.18 | 13.55   | 24.42   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -8    | -10     |         |
| -4/-3 | M (1)       | 231.2 | 216.5   | 210.9   |
|       | SD          | 40.28 | 22.80   | 23.32   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -6    | -9      |         |
| -3/-2 | M (3)       | 207.7 | 216.4   | 181.5   |
|       | SD (K)      | 33.09 | 107.36  | 20.59   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | 4     | -13     |         |
| -2/-1 | M (3)       | 214.5 | 213.5   | 193.0   |
|       | SD (K)      | 30.77 | 46.37   | 21.11   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | 0     | -10     |         |
| -1/1  | M (3)       | 208.0 | 191.0   | 187.0   |
|       | SD (K)      | 16.81 | 28.59   | 11.51   |
|       | n           | 5     | 5       | 5       |
|       | %/1st group | -8    | -10     |         |
| 1/2   | M (1)       | 212.0 | 186.0   | 180.0 * |
|       | SD          | 35.13 | 13.08   | 26.03   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -12   | -15     |         |
| 3/4   | M (1)       | 218.5 | 192.0   | 197.0   |
|       | SD          | 26.46 | 13.37   | 33.85   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -12   | -10     |         |
| 4/5   | M (1)       | 201.5 | 196.5   | 199.5   |
|       | SD          | 15.10 | 12.03   | 20.20   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -2    | -1      |         |
| 5/6   | M (1)       | 213.0 | 192.5 * | 192.0 * |
|       | SD          | 17.98 | 13.59   | 19.75   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -10   | -10     |         |
| 6/7   | M (1)       | 224.5 | 213.5   | 209.0   |
|       | SD          | 18.77 | 13.34   | 22.71   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -5    | -7      |         |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group<br>Day |             | 1     | 2       | 3        |
|--------------|-------------|-------|---------|----------|
| 7/8          | M (3)       | 225.5 | 215.5   | 218.5    |
|              | SD (K)      | 19.92 | 12.79   | 25.50    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -4    | -3      |          |
| 8/9          | M (1)       | 217.5 | 200.5   | 195.5 *  |
|              | SD          | 27.71 | 11.17   | 18.77    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -8    | -10     |          |
| 9/10         | M (1)       | 227.5 | 217.5   | 221.0    |
|              | SD          | 20.03 | 13.99   | 24.81    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -4    | -3      |          |
| 10/11        | M (1)       | 204.5 | 191.0   | 194.5    |
|              | SD          | 21.01 | 12.20   | 16.91    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -7    | -5      |          |
| 11/12        | M (1)       | 230.5 | 218.0   | 224.5    |
|              | SD (L)      | 24.20 | 15.13   | 23.27    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -5    | -3      |          |
| 12/13        | M (1)       | 203.0 | 182.5 * | 188.5    |
|              | SD          | 20.71 | 13.99   | 18.27    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -10   | -7      |          |
| 13/14        | M (1)       | 237.0 | 216.0   | 211.0 *  |
|              | SD          | 33.43 | 18.07   | 19.26    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -9    | -11     |          |
| 14/15        | M (1)       | 216.0 | 199.5   | 209.5    |
|              | SD          | 21.58 | 21.40   | 25.22    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -8    | -3      |          |
| 15/16        | M (1)       | 211.0 | 178.5 * | 163.5 ** |
|              | SD          | 29.14 | 23.81   | 24.50    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -15   | -23     |          |
| 16/17        | M (1)       | 205.5 | 178.5 * | 179.0 *  |
|              | SD          | 24.99 | 16.84   | 26.44    |
|              | n           | 10    | 10      | 10       |
|              | %/1st group | -13   | -13     |          |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFOR'S TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group<br>Day |             | 1     | 2       | 3       |
|--------------|-------------|-------|---------|---------|
| 17/18        | M (1)       | 204.5 | 172.5 * | 171.5 * |
|              | SD          | 22.29 | 27.71   | 31.01   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -16     | -16     |
| 18/19        | M (1)       | 213.0 | 190.0   | 195.0   |
|              | SD          | 26.89 | 13.54   | 33.83   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -11     | -8      |
| 19/20        | M (1)       | 215.0 | 196.0   | 199.5   |
|              | SD          | 24.61 | 19.12   | 21.53   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -9      | -7      |
| 20/21        | M (1)       | 220.0 | 200.0   | 203.0   |
|              | SD          | 24.49 | 12.91   | 27.10   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -9      | -8      |
| 21/22        | M (1)       | 215.5 | 198.5   | 207.0   |
|              | SD          | 24.66 | 16.67   | 33.60   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -8      | -4      |
| 22/23        | M (3)       | 200.0 | 181.0 * | 202.5   |
|              | SD          | 31.45 | 10.22   | 21.11   |
|              | n (B)       | 10    | 10      | 10      |
|              | %/1st group |       | -10     | 1       |
| 23/24        | M (1)       | 197.5 | 182.5   | 193.5   |
|              | SD (L)      | 15.86 | 8.58    | 26.25   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -8      | -2      |
| 24/25        | M (1)       | 201.0 | 184.5   | 195.0   |
|              | SD          | 21.45 | 18.63   | 23.69   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -8      | -3      |
| 25/26        | M (1)       | 210.5 | 191.0   | 198.5   |
|              | SD          | 23.39 | 16.12   | 20.55   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -9      | -6      |
| 26/27        | M (1)       | 217.0 | 200.5   | 199.5   |
|              | SD          | 25.63 | 17.55   | 32.36   |
|              | n           | 10    | 10      | 10      |
|              | %/1st group |       | -8      | -8      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Male

Principal animals + Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 27/28 | M (1)       | 208.5 | 188.0 | 202.5 |
|       | SD          | 32.06 | 15.31 | 22.02 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -10   | -3    |
| 28/29 | M (3)       | 207.5 | 196.0 | 202.0 |
|       | SD          | 36.31 | 11.01 | 28.11 |
|       | n (B)       | 10    | 10    | 10    |
|       | %/1st group |       | -6    | -3    |
| 29/30 | M (1)       | 191.5 | 168.0 | 169.5 |
|       | SD          | 26.78 | 24.06 | 19.21 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -12   | -11   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: 19

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group |             | 1     | 2     | 3       |
|-------|-------------|-------|-------|---------|
| Day   |             |       |       |         |
| -5/-4 | M (1)       | 208.0 | 215.5 | 209.0   |
|       | SD          | 17.83 | 22.04 | 15.24   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | 4     | 0     |         |
| -4/-3 | M (1)       | 225.0 | 219.0 | 204.5   |
|       | SD          | 35.90 | 36.88 | 19.50   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | -3    | -9    |         |
| -3/-2 | M (1)       | 226.0 | 240.5 | 215.0   |
|       | SD          | 19.12 | 40.72 | 20.00   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | 6     | -5    |         |
| -2/-1 | M (1)       | 245.0 | 244.0 | 234.0   |
|       | SD (L)      | 13.54 | 34.79 | 15.42   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | 0     | -4    |         |
| -1/1  | M (3)       | 227.0 | 207.5 | 209.5   |
|       | SD (K)      | 20.84 | 71.42 | 12.79   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | -9    | -8    |         |
| 1/2   | M (1)       | 234.5 | 229.0 | 207.0 * |
|       | SD          | 11.17 | 32.81 | 23.59   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | -2    | -12   |         |
| 2/3   | M (3)       | 98.0  | 42.0  | 37.0 *  |
|       | SD (K)      | 77.79 | 10.06 | 16.02   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | -57   | -62   |         |
| 3/4   | M (1)       | 229.5 | 221.0 | 232.5   |
|       | SD          | 24.09 | 48.69 | 26.69   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | -4    | 1     |         |
| 4/5   | M (1)       | 218.0 | 210.5 | 202.0   |
|       | SD          | 20.30 | 30.23 | 13.37   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | -3    | -7    |         |
| 5/6   | M (1)       | 231.5 | 240.5 | 227.0   |
|       | SD          | 17.33 | 23.86 | 18.59   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group | 4     | -2    |         |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 6/7   | M (1)       | 237.0 | 238.0 | 228.5 |
|       | SD          | 15.49 | 33.10 | 13.34 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -4    |       |
| 7/8   | M (1)       | 247.0 | 253.0 | 239.0 |
|       | SD          | 13.58 | 29.83 | 18.07 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 2     | -3    |       |
| 8/9   | M (1)       | 211.5 | 216.0 | 212.5 |
|       | SD          | 15.64 | 20.66 | 17.83 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 2     | 0     |       |
| 9/10  | M (1)       | 216.0 | 229.5 | 216.5 |
|       | SD          | 12.43 | 25.76 | 24.16 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 6     | 0     |       |
| 10/11 | M (1)       | 231.5 | 236.0 | 228.5 |
|       | SD          | 16.17 | 23.66 | 13.55 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 2     | -1    |       |
| 11/12 | M (3)       | 239.0 | 236.5 | 229.5 |
|       | SD (K)      | 16.30 | 22.61 | 20.61 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -1    | -4    |       |
| 12/13 | M (1)       | 242.0 | 244.5 | 235.0 |
|       | SD          | 14.94 | 27.23 | 21.47 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 1     | -3    |       |
| 13/14 | M (1)       | 238.0 | 242.5 | 233.5 |
|       | SD          | 13.58 | 19.76 | 13.95 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 2     | -2    |       |
| 14/15 | M (1)       | 221.5 | 236.0 | 221.5 |
|       | SD          | 16.17 | 29.51 | 20.69 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 7     | 0     |       |
| 15/16 | M (3)       | 219.5 | 207.0 | 201.0 |
|       | SD          | 20.88 | 43.41 | 14.10 |
|       | n (B)       | 10    | 10    | 10    |
|       | %/1st group | -6    | -8    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group<br>Day |             | 1     | 2     | 3       |
|--------------|-------------|-------|-------|---------|
| 16/17        | M (3)       | 229.5 | 222.8 | 209.5 * |
|              | SD (K)      | 11.89 | 20.33 | 24.55   |
|              | n           | 10    | 9     | 10      |
|              | %/1st group |       | -3    | -9      |
| 17/18        | M (1)       | 220.5 | 238.0 | 217.5   |
|              | SD          | 21.27 | 26.89 | 30.12   |
|              | n           | 10    | 10    | 10      |
|              | %/1st group |       | 8     | -1      |
| 18/19        | M (3)       | 240.0 | 250.5 | 222.5   |
|              | SD          | 17.48 | 40.51 | 12.53   |
|              | n (B)       | 10    | 10    | 10      |
|              | %/1st group |       | 4     | -7      |
| 19/20        | M (1)       | 230.5 | 231.0 | 219.0   |
|              | SD          | 16.24 | 29.04 | 17.76   |
|              | n           | 10    | 10    | 10      |
|              | %/1st group |       | 0     | -5      |
| 20/21        | M (1)       | 235.0 | 234.5 | 217.0   |
|              | SD          | 20.00 | 31.49 | 30.02   |
|              | n           | 10    | 10    | 10      |
|              | %/1st group |       | 0     | -8      |
| 21/22        | M (1)       | 213.5 | 214.5 | 206.0   |
|              | SD          | 16.17 | 27.33 | 23.55   |
|              | n           | 10    | 10    | 10      |
|              | %/1st group |       | 0     | -4      |
| 22/23        | M (1)       | 248.0 | 252.5 | 226.5   |
|              | SD          | 16.02 | 31.73 | 24.73   |
|              | n           | 10    | 10    | 10      |
|              | %/1st group |       | 2     | -9      |
| 23/24        | M (1)       | 213.0 | 211.5 | 196.0   |
|              | SD          | 15.85 | 21.86 | 27.67   |
|              | n           | 10    | 10    | 10      |
|              | %/1st group |       | -1    | -8      |
| 24/25        | M (1)       | 228.5 | 233.0 | 205.5   |
|              | SD          | 14.92 | 31.64 | 30.77   |
|              | n           | 10    | 10    | 10      |
|              | %/1st group |       | 2     | -10     |
| 25/26        | M (1)       | 206.0 | 209.0 | 192.0   |
|              | SD          | 18.83 | 22.34 | 19.32   |
|              | n           | 10    | 10    | 10      |
|              | %/1st group |       | 1     | -7      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Female

Principal animals + Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 26/27 | M (3)       | 218.0 | 221.0 | 200.0 |
|       | SD (K)      | 15.67 | 30.26 | 14.53 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 1     | -8    |
| 27/28 | M (1)       | 238.0 | 239.5 | 225.0 |
|       | SD          | 17.19 | 34.52 | 32.06 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 1     | -5    |
| 28/29 | M (3)       | 218.5 | 225.5 | 205.5 |
|       | SD (K)      | 16.51 | 25.98 | 27.53 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 3     | -6    |
| 29/30 | M (1)       | 217.2 | 213.5 | 204.0 |
|       | SD          | 15.63 | 26.67 | 22.46 |
|       | n           | 9     | 10    | 10    |
|       | %/1st group |       | -2    | -6    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: 20

Study No.:

Sex: Male

Recovery animals

| Group |             | 1     | 2      | 3       |
|-------|-------------|-------|--------|---------|
| Day   |             |       |        |         |
| -5/-4 | M (1)       | 221.6 | 217.1  | 205.9   |
|       | SD          | 16.13 | 3.75   | 6.75    |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | -2     | -7      |
| -4/-3 | M (1)       | 216.3 | 230.0  | 219.9   |
|       | SD          | 30.93 | 18.93  | 14.72   |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | 6      | 2       |
| -3/-2 | M (3)       | 198.4 | 258.8  | 185.1   |
|       | SD          | 12.37 | 145.33 | 14.65   |
|       | n (B)       | 5     | 5      | 5       |
|       | %/1st group |       | 30     | -7      |
| -2/-1 | M (1)       | 207.0 | 234.0  | 192.0   |
|       | SD          | 17.54 | 59.83  | 17.54   |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | 13     | -7      |
| -1/1  | M (3)       | 208.0 | 191.0  | 187.0   |
|       | SD (K)      | 16.81 | 28.59  | 11.51   |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | -8     | -10     |
| 1/2   | M (1)       | 208.0 | 188.0  | 181.0 * |
|       | SD          | 14.83 | 8.37   | 18.51   |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | -10    | -13     |
| 3/4   | M (1)       | 208.0 | 198.0  | 195.0   |
|       | SD          | 11.51 | 14.83  | 15.41   |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | -5     | -6      |
| 4/5   | M (1)       | 202.0 | 196.0  | 203.0   |
|       | SD          | 9.08  | 12.94  | 12.55   |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | -3     | 0       |
| 5/6   | M (1)       | 206.0 | 192.0  | 192.0   |
|       | SD          | 15.57 | 14.40  | 9.08    |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | -7     | -7      |
| 6/7   | M (1)       | 220.0 | 213.0  | 208.0   |
|       | SD          | 15.81 | 12.55  | 10.95   |
|       | n           | 5     | 5      | 5       |
|       | %/1st group |       | -3     | -5      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Male

Recovery animals

| Group |             | 1     | 2     | 3        |
|-------|-------------|-------|-------|----------|
| Day   |             |       |       |          |
| 7/8   | M (3)       | 218.0 | 223.0 | 215.0    |
|       | SD (K)      | 6.71  | 4.47  | 14.14    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | 2     | -1       |
| 8/9   | M (1)       | 213.0 | 204.0 | 197.0    |
|       | SD          | 16.43 | 6.52  | 13.51    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | -4    | -8       |
| 9/10  | M (1)       | 224.0 | 222.0 | 214.0    |
|       | SD          | 19.49 | 14.40 | 14.32    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | -1    | -4       |
| 10/11 | M (1)       | 195.0 | 191.0 | 192.0    |
|       | SD          | 14.14 | 9.62  | 16.05    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | -2    | -2       |
| 11/12 | M (1)       | 218.0 | 222.0 | 218.0    |
|       | SD          | 11.51 | 13.51 | 15.25    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | 2     | 0        |
| 12/13 | M (1)       | 195.0 | 182.0 | 182.0    |
|       | SD          | 11.73 | 16.05 | 9.75     |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | -7    | -7       |
| 13/14 | M (1)       | 242.0 | 224.0 | 213.0    |
|       | SD          | 42.37 | 21.04 | 12.55    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | -7    | -12      |
| 14/15 | M (1)       | 210.0 | 200.0 | 205.0    |
|       | SD          | 18.37 | 30.21 | 22.64    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | -5    | -2       |
| 15/16 | M (1)       | 198.0 | 190.0 | 156.0 ** |
|       | SD          | 14.40 | 20.92 | 16.73    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | -4    | -21      |
| 16/17 | M (1)       | 191.0 | 185.0 | 173.0    |
|       | SD          | 8.94  | 12.75 | 30.54    |
|       | n           | 5     | 5     | 5        |
|       | %/1st group |       | -3    | -9       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Male

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 17/18 | M (1)       | 207.0 | 190.0 | 187.0 |
|       | SD          | 18.91 | 22.36 | 21.97 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -8    | -10   |       |
| 18/19 | M (1)       | 197.0 | 186.0 | 188.0 |
|       | SD          | 18.23 | 14.32 | 24.39 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -6    | -5    |       |
| 19/20 | M (1)       | 211.0 | 206.0 | 193.0 |
|       | SD          | 21.62 | 18.51 | 24.90 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    | -9    |       |
| 20/21 | M (1)       | 211.0 | 199.0 | 199.0 |
|       | SD          | 19.81 | 14.75 | 24.85 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -6    | -6    |       |
| 21/22 | M (1)       | 199.0 | 196.0 | 193.0 |
|       | SD          | 17.82 | 21.04 | 25.88 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    | -3    |       |
| 22/23 | M (1)       | 210.0 | 188.0 | 203.0 |
|       | SD          | 15.81 | 6.71  | 18.23 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -10   | -3    |       |
| 23/24 | M (1)       | 190.0 | 181.0 | 186.0 |
|       | SD          | 12.75 | 6.52  | 25.10 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -5    | -2    |       |
| 24/25 | M (1)       | 190.0 | 197.0 | 195.0 |
|       | SD          | 18.03 | 16.05 | 19.04 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 4     | 3     |       |
| 25/26 | M (1)       | 201.0 | 191.0 | 196.0 |
|       | SD          | 20.43 | 9.62  | 18.17 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -5    | -2    |       |
| 26/27 | M (1)       | 205.0 | 203.0 | 198.0 |
|       | SD          | 22.36 | 24.39 | 19.24 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    | -3    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Male

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 27/28 | M (1)       | 213.0 | 192.0 | 196.0 |
|       | SD          | 34.75 | 13.51 | 18.17 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -10   | -8    |
| 28/29 | M (1)       | 193.0 | 198.0 | 189.0 |
|       | SD          | 38.50 | 13.51 | 29.03 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 3     | -2    |
| 29/30 | M (1)       | 181.0 | 175.0 | 168.0 |
|       | SD          | 12.45 | 17.32 | 23.35 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -7    |
| 30/31 | M (1)       | 193.0 | 183.0 | 188.0 |
|       | SD          | 14.83 | 15.65 | 21.39 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -5    | -3    |
| 31/32 | M (1)       | 25.0  | 25.0  | 17.0  |
|       | SD          | 3.54  | 3.54  | 9.08  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 0     | -32   |
| 32/33 | M (1)       | 191.0 | 188.0 | 198.0 |
|       | SD          | 10.25 | 15.25 | 18.23 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | 4     |
| 33/34 | M (1)       | 190.0 | 186.0 | 188.0 |
|       | SD          | 16.20 | 19.81 | 22.25 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -1    |
| 34/35 | M (1)       | 189.0 | 191.0 | 187.0 |
|       | SD          | 16.36 | 19.17 | 18.91 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 1     | -1    |
| 35/36 | M (1)       | 214.0 | 208.0 | 212.0 |
|       | SD          | 17.82 | 22.80 | 16.43 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -1    |
| 36/37 | M (1)       | 205.0 | 197.0 | 201.0 |
|       | SD          | 14.58 | 16.43 | 17.82 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -4    | -2    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Male

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 37/38 | M (1)       | 191.0 | 189.0 | 199.0 |
|       | SD          | 14.32 | 10.84 | 12.94 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    |       | 4     |
| 38/39 | M (1)       | 221.0 | 207.0 | 206.0 |
|       | SD          | 13.87 | 21.97 | 19.17 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -6    |       | -7    |
| 39/40 | M (1)       | 193.0 | 188.0 | 189.0 |
|       | SD          | 14.40 | 7.58  | 18.51 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -3    |       | -2    |
| 40/41 | M (1)       | 211.0 | 207.0 | 204.0 |
|       | SD          | 25.84 | 21.68 | 10.25 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    |       | -3    |
| 41/42 | M (1)       | 196.0 | 193.0 | 208.0 |
|       | SD          | 18.51 | 18.23 | 15.65 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    |       | 6     |
| 42/43 | M (1)       | 198.0 | 198.0 | 198.0 |
|       | SD          | 22.25 | 19.56 | 16.05 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 0     |       | 0     |
| 43/44 | M (1)       | 202.0 | 200.0 | 203.0 |
|       | SD          | 22.53 | 17.68 | 26.36 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    |       | 0     |
| 44/45 | M (1)       | 199.0 | 203.0 | 192.0 |
|       | SD          | 25.35 | 16.05 | 18.91 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 2     |       | -4    |
| 45/46 | M (1)       | 197.0 | 192.0 | 200.0 |
|       | SD          | 24.14 | 23.08 | 18.37 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -3    |       | 2     |
| 46/47 | M (1)       | 197.0 | 194.0 | 205.0 |
|       | SD          | 17.18 | 18.84 | 16.96 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    |       | 4     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFOR'S TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Male

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 47/48 | M (1)       | 192.0 | 184.0 | 187.0 |
|       | SD          | 17.54 | 21.62 | 19.87 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -4    | -3    |       |
| 48/49 | M (1)       | 192.0 | 182.0 | 195.0 |
|       | SD          | 16.05 | 30.12 | 29.79 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -5    | 2     |       |
| 49/50 | M (1)       | 207.0 | 196.0 | 195.0 |
|       | SD          | 10.95 | 20.74 | 39.21 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -5    | -6    |       |
| 50/51 | M (1)       | 210.0 | 204.0 | 205.0 |
|       | SD          | 17.68 | 24.34 | 21.51 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -3    | -2    |       |
| 51/52 | M (1)       | 196.0 | 185.0 | 198.0 |
|       | SD          | 17.10 | 17.68 | 12.55 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -6    | 1     |       |
| 52/53 | M (1)       | 191.0 | 191.0 | 188.0 |
|       | SD          | 15.17 | 11.40 | 15.65 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 0     | -2    |       |
| 53/54 | M (1)       | 208.0 | 187.0 | 207.0 |
|       | SD          | 10.95 | 23.35 | 18.91 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -10   | 0     |       |
| 54/55 | M (1)       | 174.0 | 171.0 | 177.0 |
|       | SD          | 27.25 | 20.12 | 26.60 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    | 2     |       |
| 55/56 | M (1)       | 197.0 | 198.0 | 207.0 |
|       | SD          | 21.68 | 20.19 | 21.39 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 1     | 5     |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: 21

Study No.:  
Sex: Female  
Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| -5/-4 | M (1)       | 203.0 | 213.0 | 216.0 |
|       | SD          | 18.91 | 24.65 | 13.87 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 5     | 6     |
| -4/-3 | M (1)       | 234.0 | 206.0 | 208.0 |
|       | SD          | 48.53 | 21.04 | 15.25 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -12   | -11   |
| -3/-2 | M (1)       | 227.0 | 228.0 | 228.0 |
|       | SD          | 16.81 | 34.93 | 6.71  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 0     | 0     |
| -2/-1 | M (1)       | 244.0 | 238.0 | 242.0 |
|       | SD          | 16.73 | 27.97 | 13.04 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -1    |
| -1/1  | M (1)       | 239.0 | 224.0 | 215.0 |
|       | SD          | 13.42 | 23.29 | 12.75 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -6    | -10   |
| 1/2   | M (1)       | 236.0 | 228.0 | 220.0 |
|       | SD          | 11.40 | 35.46 | 16.58 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -7    |
| 2/3   | M (1)       | 39.0  | 49.0  | 48.0  |
|       | SD          | 5.48  | 9.62  | 16.05 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 26    | 23    |
| 3/4   | M (1)       | 228.0 | 234.0 | 246.0 |
|       | SD          | 32.90 | 51.28 | 10.84 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 3     | 8     |
| 4/5   | M (1)       | 213.0 | 195.0 | 212.0 |
|       | SD          | 21.97 | 30.62 | 8.37  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -8    | 0     |
| 5/6   | M (1)       | 236.0 | 246.0 | 239.0 |
|       | SD          | 11.94 | 27.02 | 12.94 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 4     | 1     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFOR TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Female

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 6/7   | M (1)       | 241.0 | 229.0 | 236.0 |
|       | SD          | 17.82 | 34.71 | 11.40 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -5    | -2    |       |
| 7/8   | M (1)       | 241.0 | 241.0 | 250.0 |
|       | SD          | 12.94 | 29.03 | 14.14 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 0     | 4     |       |
| 8/9   | M (1)       | 204.0 | 209.0 | 220.0 |
|       | SD          | 17.82 | 12.94 | 16.96 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 2     | 8     |       |
| 9/10  | M (1)       | 219.0 | 233.0 | 236.0 |
|       | SD          | 8.94  | 23.35 | 16.73 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 6     | 8     |       |
| 10/11 | M (1)       | 222.0 | 231.0 | 232.0 |
|       | SD          | 15.65 | 23.82 | 9.75  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 4     | 5     |       |
| 11/12 | M (1)       | 238.0 | 239.0 | 243.0 |
|       | SD          | 20.19 | 16.36 | 7.58  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 0     | 2     |       |
| 12/13 | M (1)       | 234.0 | 234.0 | 246.0 |
|       | SD          | 17.82 | 25.59 | 8.22  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 0     | 5     |       |
| 13/14 | M (1)       | 231.0 | 239.0 | 232.0 |
|       | SD          | 11.94 | 19.49 | 12.55 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 3     | 0     |       |
| 14/15 | M (1)       | 227.0 | 223.0 | 235.0 |
|       | SD          | 18.91 | 24.39 | 16.96 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    | 4     |       |
| 15/16 | M (1)       | 211.0 | 196.0 | 207.0 |
|       | SD          | 20.43 | 55.16 | 10.37 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -7    | -2    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Female

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 16/17 | M (1)       | 228.0 | 224.0 | 225.0 |
|       | SD          | 4.47  | 17.82 | 17.68 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -1    |
| 17/18 | M (1)       | 211.0 | 230.0 | 235.0 |
|       | SD          | 21.91 | 26.22 | 10.00 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 9     | 11    |
| 18/19 | M (1)       | 229.0 | 237.0 | 230.0 |
|       | SD          | 13.87 | 31.74 | 7.91  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 3     | 0     |
| 19/20 | M (1)       | 229.0 | 220.0 | 230.0 |
|       | SD          | 20.43 | 24.24 | 13.69 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -4    | 0     |
| 20/21 | M (1)       | 225.0 | 221.0 | 220.0 |
|       | SD          | 11.73 | 27.93 | 40.77 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -2    |
| 21/22 | M (1)       | 207.0 | 201.0 | 221.0 |
|       | SD          | 13.96 | 26.32 | 15.57 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | 7     |
| 22/23 | M (1)       | 240.0 | 242.0 | 233.0 |
|       | SD          | 13.69 | 33.28 | 16.05 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 1     | -3    |
| 23/24 | M (1)       | 215.0 | 215.0 | 215.0 |
|       | SD          | 19.36 | 28.50 | 24.24 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 0     | 0     |
| 24/25 | M (1)       | 220.0 | 216.0 | 219.0 |
|       | SD          | 14.58 | 19.49 | 22.75 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | 0     |
| 25/26 | M (1)       | 198.0 | 202.0 | 200.0 |
|       | SD          | 20.80 | 16.05 | 16.96 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 2     | 1     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Female

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 26/27 | M (1)       | 214.0 | 211.0 | 207.0 |
|       | SD          | 15.17 | 25.84 | 9.08  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    | -3    |       |
| 27/28 | M (1)       | 243.0 | 241.0 | 246.0 |
|       | SD          | 23.08 | 28.37 | 17.10 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    | 1     |       |
| 28/29 | M (1)       | 220.0 | 218.0 | 218.0 |
|       | SD          | 21.51 | 24.90 | 18.91 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    | -1    |       |
| 29/30 | M (3)       | 211.3 | 201.0 | 216.0 |
|       | SD          | 16.52 | 24.85 | 14.32 |
|       | n           | 4     | 5     | 5     |
|       | %/1st group | -5    | 2     |       |
| 30/31 | M (1)       | 46.0  | 43.0  | 36.0  |
|       | SD          | 4.18  | 11.51 | 9.62  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -7    | -22   |       |
| 31/32 | M (1)       | 221.0 | 230.0 | 223.0 |
|       | SD          | 20.12 | 22.64 | 16.43 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 4     | 1     |       |
| 32/33 | M (1)       | 249.0 | 248.0 | 246.0 |
|       | SD          | 21.62 | 29.71 | 9.62  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 0     | -1    |       |
| 33/34 | M (3)       | 214.0 | 231.0 | 273.0 |
|       | SD (K)      | 20.74 | 27.02 | 85.19 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 8     | 28    |       |
| 34/35 | M (3)       | 250.0 | 228.0 | 222.5 |
|       | SD          | 56.42 | 17.18 | 8.66  |
|       | n           | 4     | 5     | 4     |
|       | %/1st group | -9    | -11   |       |
| 35/36 | M (1)       | 203.0 | 224.0 | 232.0 |
|       | SD          | 51.06 | 21.62 | 10.95 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 10    | 14    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFOR'S TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Female

Recovery animals

| Group |             | 1     | 2      | 3     |
|-------|-------------|-------|--------|-------|
| Day   |             |       |        |       |
| 36/37 | M (1)       | 227.0 | 227.0  | 259.0 |
|       | SD          | 27.97 | 15.25  | 71.19 |
|       | n           | 5     | 5      | 5     |
|       | %/1st group | 0     | 14     |       |
| 37/38 | M (1)       | 222.0 | 222.0  | 232.0 |
|       | SD          | 16.43 | 18.23  | 17.89 |
|       | n           | 5     | 5      | 5     |
|       | %/1st group | 0     | 5      |       |
| 38/39 | M (3)       | 221.0 | 192.5  | 231.0 |
|       | SD          | 17.82 | 51.07  | 11.40 |
|       | n           | 5     | 4      | 5     |
|       | %/1st group | -13   | 5      |       |
| 39/40 | M (1)       | 205.0 | 216.0  | 218.0 |
|       | SD          | 11.73 | 21.04  | 14.83 |
|       | n           | 5     | 5      | 5     |
|       | %/1st group | 5     | 6      |       |
| 40/41 | M (3)       | 214.0 | 215.0  | 226.3 |
|       | SD          | 12.94 | 14.58  | 20.16 |
|       | n           | 5     | 5      | 4     |
|       | %/1st group | 0     | 6      |       |
| 41/42 | M (3)       | 217.0 | 222.0  | 230.0 |
|       | SD          | 22.53 | 30.54  | 16.83 |
|       | n           | 5     | 5      | 4     |
|       | %/1st group | 2     | 6      |       |
| 42/43 | M (3)       | 210.0 | 235.0  | 256.0 |
|       | SD          | 36.57 | 24.83  | 56.94 |
|       | n           | 5     | 4      | 5     |
|       | %/1st group | 12    | 22     |       |
| 43/44 | M (3)       | 200.0 | 227.5  | 225.0 |
|       | SD          | 35.18 | 24.66  | 12.25 |
|       | n           | 5     | 4      | 4     |
|       | %/1st group | 14    | 13     |       |
| 44/45 | M (3)       | 196.0 | 306.0  | 181.0 |
|       | SD (K)      | 27.02 | 206.80 | 79.95 |
|       | n           | 5     | 5      | 5     |
|       | %/1st group | 56    | -8     |       |
| 45/46 | M (1)       | 226.0 | 199.0  | 214.0 |
|       | SD          | 26.32 | 90.99  | 53.55 |
|       | n           | 5     | 5      | 5     |
|       | %/1st group | -12   | -5     |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

FOOD CONSUMPTION  
(mean values - g/animal/day)

Table: (continued)

Study No.:

Sex: Female

Recovery animals

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| Day   |             |       |       |       |
| 46/47 | M (1)       | 188.0 | 178.0 | 191.0 |
|       | SD          | 20.19 | 60.58 | 28.15 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -5    | 2     |
| 47/48 | M (1)       | 211.0 | 221.0 | 224.0 |
|       | SD          | 20.12 | 36.98 | 26.32 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 5     | 6     |
| 48/49 | M (1)       | 213.0 | 220.0 | 223.0 |
|       | SD          | 17.89 | 20.92 | 14.83 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 3     | 5     |
| 49/50 | M (1)       | 222.0 | 235.0 | 248.0 |
|       | SD          | 12.04 | 28.06 | 13.04 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 6     | 12    |
| 50/51 | M (1)       | 213.0 | 215.0 | 216.0 |
|       | SD          | 15.25 | 15.81 | 14.75 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 1     | 1     |
| 51/52 | M (1)       | 202.0 | 221.0 | 212.0 |
|       | SD          | 16.05 | 17.10 | 22.25 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 9     | 5     |
| 52/53 | M (1)       | 222.0 | 226.0 | 233.0 |
|       | SD          | 18.91 | 25.35 | 18.23 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 2     | 5     |
| 53/54 | M (1)       | 212.0 | 213.0 | 220.0 |
|       | SD          | 15.65 | 16.43 | 19.69 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 0     | 4     |
| 54/55 | M (3)       | 218.0 | 258.0 | 225.0 |
|       | SD          | 10.37 | 86.07 | 20.62 |
|       | n (B)       | 5     | 5     | 5     |
|       | %/1st group |       | 18    | 3     |
| 55/56 | M (3)       | 213.0 | 226.3 | 233.0 |
|       | SD          | 19.24 | 28.39 | 35.11 |
|       | n           | 5     | 4     | 5     |
|       | %/1st group |       | 6     | 9     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

Tables 22 to 35. Rectal temperature (mean values)

RECTAL TEMPERATURE - AM  
(mean values)

Table: 22

Study No.:

Sex: Male

Predose 1

Principal animals + Recovery animals

| Group | 1           | 2    | 3    |      |
|-------|-------------|------|------|------|
| AM    | M (1)       | 39.0 | 39.0 | 39.0 |
| °C    | SD          | 0.38 | 0.45 | 0.23 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group | 0    | 0    |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE - AM  
(mean values)

Table: 23

Study No.:

Sex: Male

Predose 2

Principal animals + Recovery animals

| Group | 1           | 2    | 3    |      |
|-------|-------------|------|------|------|
| AM    | M (1)       | 39.1 | 39.0 | 39.2 |
| °C    | SD          | 0.40 | 0.58 | 0.57 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group | 0    | 0    | 0    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE - AM  
(mean values)

Table: 24

Study No.:

Sex: Male

Predose 3

Principal animals + Recovery animals

| Group | 1           | 2    | 3      |      |
|-------|-------------|------|--------|------|
| AM    | M (1)       | 38.6 | 38.9 * | 38.7 |
| °C    | SD          | 0.27 | 0.21   | 0.23 |
|       | n           | 10   | 10     | 10   |
|       | %/1st group | 1    | 0      |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE - AM  
(mean values)

Table: 25

Study No.:

Sex: Male

Predose 4

Principal animals + Recovery animals

| Group | 1           | 2    | 3    |      |
|-------|-------------|------|------|------|
| AM    | M (1)       | 39.2 | 39.1 | 39.3 |
| °C    | SD          | 0.37 | 0.48 | 0.26 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group | 0    | 0    |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE  
(mean values)

Table: 26

Study No.:

Sex: Male

Time: Week 1

Principal animals + Recovery animals

| Group  |             | 1    | 2    | 3    |    |
|--------|-------------|------|------|------|----|
| BD     | M (3)       | 38.6 | 38.7 | 39.0 | *  |
| °C     | SD (K)      | 0.23 | 0.39 | 0.27 |    |
|        | n           | 10   | 10   | 10   |    |
|        | %/1st group | 0    | 1    |      |    |
| T+3 h  | M (1)       | 38.2 | 38.4 | 38.8 | ** |
| °C     | SD          | 0.40 | 0.44 | 0.22 |    |
|        | n           | 10   | 10   | 10   |    |
|        | %/1st group | 1    | 2    |      |    |
| T+6 h  | M (1)       | 38.9 | 39.1 | 39.1 |    |
| °C     | SD          | 0.36 | 0.23 | 0.23 |    |
|        | n           | 10   | 10   | 10   |    |
|        | %/1st group | 1    | 1    |      |    |
| T+24 h | M (1)       | 38.4 | 38.5 | 38.7 |    |
| °C     | SD          | 0.30 | 0.23 | 0.30 |    |
|        | n           | 10   | 10   | 10   |    |
|        | %/1st group | 0    | 1    |      |    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE  
(mean values)

Table: 27

Study No.:

Sex: Male

Time: Week 3

Principal animals + Recovery animals

| Group  |             | 1    | 2      | 3    |
|--------|-------------|------|--------|------|
| BD     | M (1)       | 38.5 | 38.8   | 38.7 |
| °C     | SD          | 0.30 | 0.39   | 0.29 |
|        | n           | 10   | 10     | 10   |
|        | %/1st group | 1    | 1      |      |
| T+3 h  | M (1)       | 38.7 | 38.8   | 38.5 |
| °C     | SD          | 0.29 | 0.31   | 0.31 |
|        | n           | 10   | 10     | 10   |
|        | %/1st group | 0    | -1     |      |
| T+6 h  | M (1)       | 38.8 | 38.7   | 38.7 |
| °C     | SD          | 0.36 | 0.33   | 0.34 |
|        | n           | 10   | 10     | 10   |
|        | %/1st group | 0    | 0      |      |
| T+24 h | M (3)       | 38.8 | 39.2 * | 38.6 |
| °C     | SD          | 0.18 | 0.57   | 0.35 |
|        | n (B)       | 10   | 10     | 10   |
|        | %/1st group | 1    | -1     |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE  
(mean values)

Table: 28

Study No.:

Sex: Male

Time: Week 5

Principal animals + Recovery animals

| Group  |             | 1    | 2    | 3    |
|--------|-------------|------|------|------|
| BD     | M (1)       | 39.0 | 39.2 | 39.1 |
| °C     | SD          | 0.33 | 0.31 | 0.22 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 1    | 0    |      |
| T+3 h  | M (1)       | 38.9 | 39.0 | 39.2 |
| °C     | SD          | 0.18 | 0.21 | 0.29 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 1    |      |
| T+6 h  | M (1)       | 39.1 | 39.4 | 39.1 |
| °C     | SD          | 0.42 | 0.28 | 0.21 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 1    | 0    |      |
| T+24 h | M (1)       | 38.1 | 38.3 | 38.3 |
| °C     | SD          | 0.43 | 0.27 | 0.31 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 1    | 1    |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE - AM  
(mean values)

Table: 29

Study No.:

Sex: Female

Predose 1

Principal animals + Recovery animals

| Group |             | 1    | 2    | 3    |
|-------|-------------|------|------|------|
| AM    | M (1)       | 39.0 | 38.9 | 38.9 |
| °C    | SD          | 0.22 | 0.28 | 0.14 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group | 0    | 0    | 0    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE - AM  
(mean values)

Table: 30

Study No.:

Sex: Female

Predose 2

Principal animals + Recovery animals

| Group | 1           | 2    | 3    |      |
|-------|-------------|------|------|------|
| AM    | M (1)       | 38.7 | 38.9 | 38.8 |
| °C    | SD          | 0.44 | 0.46 | 0.27 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group | 1    | 0    |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE - AM  
(mean values)

Table: 31

Study No.:

Sex: Female

Predose 3

Principal animals + Recovery animals

| Group | 1           | 2    | 3      |      |
|-------|-------------|------|--------|------|
| AM    | M (1)       | 38.7 | 39.0 * | 38.9 |
| °C    | SD          | 0.26 | 0.33   | 0.40 |
|       | n           | 10   | 10     | 10   |
|       | %/1st group | 1    | 1      | 1    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE - AM  
(mean values)

Table: 32

Study No.:

Sex: Female

Predose 4

Principal animals + Recovery animals

| Group | 1           | 2    | 3    |      |
|-------|-------------|------|------|------|
| AM    | M (1)       | 39.0 | 38.8 | 38.9 |
| °C    | SD          | 0.25 | 0.19 | 0.37 |
|       | n           | 10   | 10   | 10   |
|       | %/1st group | -1   | 0    |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE  
(mean values)

Table: 33

Study No.:

Sex: Female

Time: Week 1

Principal animals + Recovery animals

| Group  |             | 1    | 2    | 3    |
|--------|-------------|------|------|------|
| BD     | M (1)       | 38.7 | 38.7 | 38.8 |
| °C     | SD          | 0.38 | 0.52 | 0.34 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 0    | 0    |
| T+3 h  | M (3)       | 38.9 | 38.9 | 38.9 |
| °C     | SD (K)      | 0.29 | 0.24 | 0.24 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 0    | 0    |
| T+6 h  | M (1)       | 39.2 | 39.2 | 39.1 |
| °C     | SD          | 0.19 | 0.21 | 0.16 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 0    | 0    |
| T+24 h | M (1)       | 38.5 | 38.7 | 38.6 |
| °C     | SD          | 0.26 | 0.29 | 0.34 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 1    | 0    | 0    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE  
(mean values)

Table: 34

Study No.:

Sex: Female

Time: Week 3

Principal animals + Recovery animals

| Group  |             | 1    | 2    | 3    |
|--------|-------------|------|------|------|
| BD     | M (1)       | 38.9 | 39.1 | 39.0 |
| °C     | SD          | 0.39 | 0.43 | 0.42 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 1    | 0    |      |
| T+3 h  | M (1)       | 39.0 | 39.0 | 39.0 |
| °C     | SD          | 0.21 | 0.25 | 0.26 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 0    |      |
| T+6 h  | M (1)       | 39.3 | 39.3 | 39.3 |
| °C     | SD          | 0.16 | 0.17 | 0.24 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 0    |      |
| T+24 h | M (1)       | 38.2 | 38.6 | 38.6 |
| °C     | SD          | 0.56 | 0.43 | 0.45 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 1    | 1    |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

RECTAL TEMPERATURE  
(mean values)

Table: 35

Study No.:

Sex: Female

Time: Week 5

Principal animals + Recovery animals

| Group  |             | 1    | 2    | 3    |
|--------|-------------|------|------|------|
| BD     | M (1)       | 39.2 | 39.4 | 39.2 |
| °C     | SD          | 0.20 | 0.16 | 0.24 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 1    | 0    |      |
| T+3 h  | M (1)       | 39.0 | 39.0 | 39.0 |
| °C     | SD          | 0.18 | 0.16 | 0.15 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 0    |      |
| T+6 h  | M (3)       | 39.1 | 39.1 | 39.1 |
| °C     | SD (K)      | 0.24 | 0.17 | 0.25 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 0    |      |
| T+24 h | M (1)       | 38.8 | 38.9 | 39.0 |
| °C     | SD          | 0.44 | 0.33 | 0.55 |
|        | n           | 10   | 10   | 10   |
|        | %/1st group | 0    | 1    |      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

Tables 36 to 43. Hematology (mean values)

HEMATOLOGY  
(mean values)

Table: 36

Study No.:

Sex: Male

Time: Predose

| Group |             | 1     | 2       | 3      |
|-------|-------------|-------|---------|--------|
| WBC   | M (1)       | 7.60  | 6.46    | 7.53   |
| G/L   | SD (L)      | 3.063 | 0.972   | 2.553  |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | -15     | -1     |
| RBC   | M (1)       | 6.64  | 6.67    | 6.89   |
| T/L   | SD          | 0.375 | 0.230   | 0.230  |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | 0       | 4      |
| HB    | M (1)       | 13.8  | 14.0    | 14.3   |
| g/dL  | SD          | 0.66  | 0.48    | 0.43   |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | 1       | 4      |
| PCV   | M (1)       | 0.42  | 0.43    | 0.43 * |
| L/L   | SD          | 0.020 | 0.015   | 0.013  |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | 2       | 2      |
| MCV   | M (1)       | 62.5  | 64.2 *  | 62.9   |
| fL    | SD          | 1.84  | 0.94    | 1.30   |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | 3       | 1      |
| MCH   | M (1)       | 20.8  | 20.9    | 20.8   |
| pg    | SD          | 0.69  | 0.34    | 0.40   |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | 0       | 0      |
| MCHC  | M (1)       | 33.2  | 32.6 ** | 33.0   |
| g/dL  | SD          | 0.35  | 0.44    | 0.41   |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | -2      | -1     |
| PLT   | M (1)       | 392   | 400     | 427    |
| G/L   | SD          | 46.9  | 79.1    | 78.5   |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | 2       | 9      |
| RTC   | M (1)       | 3.09  | 3.03    | 2.78   |
| %     | SD          | 0.429 | 0.851   | 0.498  |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | -2      | -10    |
| RTC   | M (1)       | 0.21  | 0.20    | 0.19   |
| T/L   | SD          | 0.028 | 0.056   | 0.037  |
|       | n           | 10    | 10      | 10     |
|       | %/1st group |       | -5      | -10    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Predose

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| N     | M (3)       | 3.18  | 2.90  | 3.76  |
| G/L   | SD (L)      | 1.594 | 0.489 | 2.214 |
|       | n (B)       | 10    | 10    | 10    |
|       | %/1st group | -9    | 18    |       |
| E     | M (1)       | 0.09  | 0.07  | 0.08  |
| G/L   | SD          | 0.049 | 0.018 | 0.025 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -22   | -11   |       |
| B     | M (1)       | 0.26  | 0.23  | 0.29  |
| G/L   | SD          | 0.081 | 0.046 | 0.120 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -12   | 12    |       |
| L     | M (1)       | 3.71  | 3.00  | 2.94  |
| G/L   | SD          | 1.246 | 0.636 | 0.483 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -19   | -21   |       |
| LUC   | M (3)       | 0.02  | 0.02  | 0.02  |
| G/L   | SD (K)      | 0.010 | 0.018 | 0.012 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | 0     |       |
| M     | M (1)       | 0.34  | 0.25  | 0.44  |
| G/L   | SD          | 0.201 | 0.101 | 0.156 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -26   | 29    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Predose

| Group |             | 1     | 2     | 3      |
|-------|-------------|-------|-------|--------|
| PT    | M (1)       | 7.4   | 7.1   | 7.3    |
| s     | SD          | 0.53  | 0.36  | 0.49   |
| n     |             | 10    | 10    | 10     |
|       | %/1st group | -4    | -1    |        |
| FIB   | M (1)       | 3.47  | 3.52  | 3.88   |
| g/L   | SD          | 0.404 | 0.646 | 0.394  |
| n     |             | 10    | 10    | 10     |
|       | %/1st group | 1     | 12    |        |
| APTT  | M (3)       | 13.5  | 13.7  | 14.1 * |
| s     | SD          | 0.43  | 1.21  | 0.43   |
| n (B) |             | 10    | 10    | 10     |
|       | %/1st group | 1     | 4     |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: 37

Study No.:

Sex: Female

Time: Predose

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| WBC   | M (1)       | 6.24  | 6.88  | 6.68  |
| G/L   | SD          | 1.288 | 1.258 | 1.438 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 10    | 7     |
| RBC   | M (1)       | 6.35  | 6.37  | 6.41  |
| T/L   | SD          | 0.329 | 0.411 | 0.297 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | 1     |
| HB    | M (1)       | 13.4  | 13.4  | 13.3  |
| g/dL  | SD          | 0.67  | 0.47  | 0.55  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | -1    |
| PCV   | M (3)       | 0.41  | 0.42  | 0.41  |
| L/L   | SD (K)      | 0.022 | 0.017 | 0.018 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 2     | 0     |
| MCV   | M (1)       | 64.8  | 65.1  | 64.5  |
| fL    | SD          | 1.99  | 1.97  | 1.12  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | 0     |
| MCH   | M (1)       | 21.1  | 21.1  | 20.8  |
| pg    | SD          | 0.62  | 0.65  | 0.50  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | -1    |
| MCHC  | M (1)       | 32.5  | 32.5  | 32.3  |
| g/dL  | SD          | 0.60  | 0.38  | 0.38  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | -1    |
| PLT   | M (1)       | 434   | 421   | 458   |
| G/L   | SD          | 72.4  | 69.4  | 86.0  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -3    | 6     |
| RTC   | M (1)       | 3.39  | 3.47  | 2.91  |
| %     | SD          | 0.451 | 1.121 | 0.566 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 2     | -14   |
| RTC   | M (1)       | 0.22  | 0.22  | 0.19  |
| T/L   | SD          | 0.026 | 0.069 | 0.037 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | -14   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

(-) STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Predose

| Group       |       | 1     | 2     | 3     |
|-------------|-------|-------|-------|-------|
| N           | M (1) | 2.40  | 2.82  | 2.49  |
| G/L         | SD    | 0.744 | 1.267 | 0.774 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 18    | 4     |       |
| E           | M (1) | 0.07  | 0.07  | 0.08  |
| G/L         | SD    | 0.020 | 0.022 | 0.027 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 0     | 14    |       |
| B           | M (1) | 0.32  | 0.25  | 0.33  |
| G/L         | SD    | 0.084 | 0.059 | 0.123 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | -22   | 3     |       |
| L           | M (1) | 3.09  | 3.40  | 3.45  |
| G/L         | SD    | 0.587 | 0.486 | 0.818 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 10    | 12    |       |
| LUC         | M (1) | 0.03  | 0.02  | 0.02  |
| G/L         | SD    | 0.019 | 0.008 | 0.009 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | -33   | -33   |       |
| M           | M (1) | 0.33  | 0.33  | 0.31  |
| G/L         | SD    | 0.131 | 0.154 | 0.109 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 0     | -6    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Predose

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| PT    | M (1)       | 7.0   | 6.9   | 6.9   |
| s     | SD          | 0.32  | 0.39  | 0.61  |
| n     |             | 10    | 10    | 10    |
|       | %/1st group |       | -1    | -1    |
| FIB   | M (1)       | 2.61  | 2.70  | 2.68  |
| g/L   | SD          | 0.458 | 0.505 | 0.327 |
| n     |             | 10    | 10    | 10    |
|       | %/1st group |       | 3     | 3     |
| APTT  | M (1)       | 13.9  | 14.1  | 14.0  |
| s     | SD          | 0.90  | 1.05  | 0.72  |
| n     |             | 10    | 10    | 10    |
|       | %/1st group |       | 1     | 1     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: 38

Study No.:

Sex: Male

Time: Week 1

| Group |             | 1     | 2     | 3       |
|-------|-------------|-------|-------|---------|
| WBC   | M (1)       | 7.57  | 6.17  | 6.66    |
| G/L   | SD          | 2.498 | 1.487 | 1.494   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | -18   | -12     |
| RBC   | M (1)       | 6.98  | 6.82  | 7.07    |
| T/L   | SD          | 0.435 | 0.184 | 0.300   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | -2    | 1       |
| HB    | M (1)       | 14.6  | 14.3  | 14.6    |
| g/dL  | SD          | 0.78  | 0.39  | 0.52    |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | -2    | 0       |
| PCV   | M (1)       | 0.45  | 0.44  | 0.45    |
| L/L   | SD          | 0.021 | 0.010 | 0.018   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | -2    | 0       |
| MCV   | M (1)       | 63.8  | 65.0  | 63.1    |
| fL    | SD          | 1.76  | 0.86  | 1.56    |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | 2     | -1      |
| MCH   | M (1)       | 20.9  | 20.9  | 20.7    |
| pg    | SD          | 0.70  | 0.30  | 0.45    |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | 0     | -1      |
| MCHC  | M (3)       | 32.8  | 32.2  | 32.8    |
| g/dL  | SD (K)      | 0.67  | 0.46  | 0.66    |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | -2    | 0       |
| PLT   | M (1)       | 439   | 381   | 395     |
| G/L   | SD          | 69.9  | 110.8 | 96.7    |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | -13   | -10     |
| RTC   | M (1)       | 4.33  | 3.99  | 3.70 ** |
| %     | SD          | 0.528 | 0.367 | 0.464   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | -8    | -15     |
| RTC   | M (1)       | 0.30  | 0.27  | 0.26 *  |
| T/L   | SD          | 0.037 | 0.023 | 0.032   |
|       | n           | 10    | 10    | 10      |
|       | %/1st group |       | -10   | -13     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

(-) STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 1

| Group       |        | 1     | 2     | 3     |
|-------------|--------|-------|-------|-------|
| N           | M (1)  | 3.60  | 2.38  | 2.90  |
| G/L         | SD     | 1.554 | 1.014 | 1.006 |
| n           |        | 10    | 10    | 10    |
| %/1st group |        | -34   | -19   |       |
| E           | M (1)  | 0.07  | 0.05  | 0.06  |
| G/L         | SD     | 0.033 | 0.020 | 0.027 |
| n           |        | 10    | 10    | 10    |
| %/1st group |        | -29   | -14   |       |
| B           | M (1)  | 0.28  | 0.24  | 0.27  |
| G/L         | SD (L) | 0.091 | 0.063 | 0.120 |
| n           |        | 10    | 10    | 10    |
| %/1st group |        | -14   | -4    |       |
| L           | M (1)  | 3.25  | 3.13  | 3.11  |
| G/L         | SD     | 1.054 | 0.663 | 0.672 |
| n           |        | 10    | 10    | 10    |
| %/1st group |        | -4    | -4    |       |
| LUC         | M (3)  | 0.02  | 0.02  | 0.02  |
| G/L         | SD (K) | 0.010 | 0.007 | 0.013 |
| n           |        | 10    | 10    | 10    |
| %/1st group |        | 0     | 0     |       |
| M           | M (1)  | 0.35  | 0.36  | 0.31  |
| G/L         | SD     | 0.225 | 0.195 | 0.146 |
| n           |        | 10    | 10    | 10    |
| %/1st group |        | 3     | -11   |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 1

| Group |             | 1     | 2       | 3       |
|-------|-------------|-------|---------|---------|
| PT    | M (1)       | 6.8   | 6.6     | 6.5     |
| s     | SD          | 0.46  | 0.53    | 0.52    |
| n     |             | 10    | 10      | 10      |
|       | %/1st group |       | -3      | -4      |
| FIB   | M (1)       | 3.34  | 4.71 ** | 5.12 ** |
| g/L   | SD          | 0.451 | 0.642   | 0.836   |
| n     |             | 10    | 10      | 10      |
|       | %/1st group |       | 41      | 53      |
| APTT  | M (1)       | 13.1  | 12.7    | 13.2    |
| s     | SD          | 0.52  | 0.69    | 0.65    |
| n     |             | 10    | 10      | 10      |
|       | %/1st group |       | -3      | 1       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: 39

Study No.:  
Sex: Female  
Time: Week 1

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| WBC   | M (1)       | 5.87  | 5.90  | 5.64  |
| G/L   | SD          | 0.857 | 0.969 | 0.938 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 1     | -4    |
| RBC   | M (1)       | 6.38  | 6.33  | 6.36  |
| T/L   | SD          | 0.248 | 0.318 | 0.380 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -1    | 0     |
| HB    | M (1)       | 13.7  | 13.6  | 13.4  |
| g/dL  | SD          | 0.47  | 0.55  | 0.60  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -1    | -2    |
| PCV   | M (1)       | 0.42  | 0.42  | 0.42  |
| L/L   | SD          | 0.013 | 0.023 | 0.021 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | 0     |
| MCV   | M (1)       | 66.2  | 66.5  | 65.6  |
| fL    | SD          | 1.73  | 1.64  | 1.32  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | -1    |
| MCH   | M (1)       | 21.5  | 21.6  | 21.1  |
| pg    | SD          | 0.58  | 0.57  | 0.60  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | -2    |
| MCHC  | M (1)       | 32.5  | 32.5  | 32.1  |
| g/dL  | SD          | 0.42  | 0.55  | 0.50  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | -1    |
| PLT   | M (1)       | 414   | 410   | 434   |
| G/L   | SD          | 61.9  | 72.0  | 91.6  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -1    | 5     |
| RTC   | M (1)       | 4.78  | 4.51  | 4.38  |
| %     | SD          | 0.409 | 0.528 | 0.769 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -6    | -8    |
| RTC   | M (1)       | 0.30  | 0.29  | 0.28  |
| T/L   | SD          | 0.026 | 0.041 | 0.048 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -3    | -7    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 1

| Group       |        | 1     | 2     | 3       |
|-------------|--------|-------|-------|---------|
| N           | M (1)  | 2.28  | 2.10  | 1.82    |
| G/L         | SD     | 0.368 | 0.733 | 0.463   |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | -8    | -20   |         |
| E           | M (1)  | 0.08  | 0.06  | 0.05 ** |
| G/L         | SD     | 0.023 | 0.023 | 0.011   |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | -25   | -38   |         |
| B           | M (1)  | 0.29  | 0.24  | 0.30    |
| G/L         | SD     | 0.068 | 0.054 | 0.104   |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | -17   | 3     |         |
| L           | M (1)  | 2.90  | 3.09  | 3.13    |
| G/L         | SD     | 0.473 | 0.579 | 0.807   |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | 7     | 8     |         |
| LUC         | M (3)  | 0.02  | 0.02  | 0.03    |
| G/L         | SD (K) | 0.011 | 0.009 | 0.014   |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | 0     | 50    |         |
| M           | M (1)  | 0.31  | 0.40  | 0.31    |
| G/L         | SD     | 0.123 | 0.166 | 0.090   |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | 29    | 0     |         |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 1

| Group |             | 1     | 2       | 3       |
|-------|-------------|-------|---------|---------|
| PT    | M (1)       | 7.2   | 6.8     | 6.6 **  |
| s     | SD          | 0.31  | 0.62    | 0.41    |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -6    | -8      |         |
| FIB   | M (1)       | 2.45  | 3.92 ** | 4.25 ** |
| g/L   | SD          | 0.341 | 0.695   | 0.495   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | 60    | 73      |         |
| APTT  | M (1)       | 13.3  | 13.9    | 13.5    |
| s     | SD          | 1.09  | 0.64    | 1.27    |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | 5     | 2       |         |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: 40

Study No.:

Sex: Male

Time: Week 5

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| WBC   | M (1)       | 5.99  | 5.64  | 6.03  |
| G/L   | SD          | 1.722 | 0.731 | 2.059 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -6    | 1     |       |
| RBC   | M (1)       | 7.14  | 7.08  | 7.10  |
| T/L   | SD          | 0.410 | 0.360 | 0.449 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -1    | -1    |       |
| HB    | M (1)       | 15.1  | 14.9  | 14.9  |
| g/dL  | SD          | 0.78  | 0.69  | 0.79  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -1    | -1    |       |
| PCV   | M (3)       | 0.45  | 0.45  | 0.45  |
| L/L   | SD (K)      | 0.025 | 0.022 | 0.025 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | 0     |       |
| MCV   | M (1)       | 63.8  | 64.1  | 63.1  |
| fL    | SD          | 2.10  | 1.19  | 2.02  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -1    |       |
| MCH   | M (1)       | 21.2  | 21.1  | 20.9  |
| pg    | SD          | 0.84  | 0.46  | 0.51  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -1    |       |
| MCHC  | M (1)       | 33.2  | 32.9  | 33.2  |
| g/dL  | SD          | 0.75  | 0.35  | 0.46  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -1    | 0     |       |
| PLT   | M (1)       | 349   | 315   | 356   |
| G/L   | SD          | 40.8  | 69.3  | 70.1  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -10   | 2     |       |
| RTC   | M (1)       | 2.64  | 2.37  | 2.46  |
| %     | SD          | 0.461 | 0.297 | 0.508 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -10   | -7    |       |
| RTC   | M (3)       | 0.19  | 0.17  | 0.17  |
| T/L   | SD (K)      | 0.036 | 0.019 | 0.034 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -11   | -11   |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 5

| Group       |        | 1     | 2       | 3      |
|-------------|--------|-------|---------|--------|
| N           | M (1)  | 1.97  | 1.76    | 2.11   |
| G/L         | SD     | 0.563 | 0.370   | 1.017  |
| n           |        | 10    | 10      | 10     |
| %/1st group |        | -11   | 7       |        |
| E           | M (3)  | 0.08  | 0.03 ** | 0.04 * |
| G/L         | SD (K) | 0.027 | 0.007   | 0.009  |
| n           |        | 10    | 10      | 10     |
| %/1st group |        | -63   | -50     |        |
| B           | M (1)  | 0.26  | 0.28    | 0.27   |
| G/L         | SD     | 0.075 | 0.072   | 0.090  |
| n           |        | 10    | 10      | 10     |
| %/1st group |        | 8     | 4       |        |
| L           | M (1)  | 3.35  | 3.23    | 3.20   |
| G/L         | SD     | 1.191 | 0.638   | 1.378  |
| n           |        | 10    | 10      | 10     |
| %/1st group |        | -4    | -4      |        |
| LUC         | M (1)  | 0.02  | 0.05 ** | 0.04 * |
| G/L         | SD (L) | 0.012 | 0.033   | 0.022  |
| n           |        | 10    | 10      | 10     |
| %/1st group |        | 150   | 100     |        |
| M           | M (3)  | 0.31  | 0.30    | 0.36   |
| G/L         | SD     | 0.172 | 0.043   | 0.157  |
| n (B)       |        | 10    | 10      | 10     |
| %/1st group |        | -3    | 16      |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 5

| Group |             | 1     | 2       | 3       |
|-------|-------------|-------|---------|---------|
| PT    | M (1)       | 6.9   | 6.8     | 6.9     |
| s     | SD          | 0.38  | 0.33    | 0.30    |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | -1    | 0       |         |
| FIB   | M (1)       | 2.81  | 4.11 ** | 4.28 ** |
| g/L   | SD          | 0.399 | 0.506   | 0.531   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group | 46    | 52      |         |
| APTT  | M (1)       | 13.7  | 13.8    | 14.3    |
| s     | SD          | 0.67  | 0.69    | 0.96    |
|       | n           | 10    | 9       | 10      |
|       | %/1st group | 1     | 4       |         |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: 41

Study No.:  
Sex: Female  
Time: Week 5

| Group |             | 1     | 2      | 3      |
|-------|-------------|-------|--------|--------|
| WBC   | M (1)       | 5.30  | 6.67 * | 5.76   |
| G/L   | SD          | 0.992 | 0.910  | 1.242  |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | 26     | 9      |
| RBC   | M (1)       | 6.55  | 6.57   | 6.65   |
| T/L   | SD          | 0.376 | 0.301  | 0.408  |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | 0      | 2      |
| HB    | M (1)       | 14.2  | 14.0   | 13.9   |
| g/dL  | SD          | 0.80  | 0.51   | 0.63   |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | -1     | -2     |
| PCV   | M (3)       | 0.43  | 0.43   | 0.43   |
| L/L   | SD (K)      | 0.024 | 0.018  | 0.021  |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | 0      | 0      |
| MCV   | M (1)       | 65.9  | 65.4   | 64.6   |
| fL    | SD          | 2.01  | 1.06   | 1.48   |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | -1     | -2     |
| MCH   | M (1)       | 21.7  | 21.4   | 21.0 * |
| pg    | SD          | 0.74  | 0.41   | 0.49   |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | -1     | -3     |
| MCHC  | M (1)       | 32.9  | 32.7   | 32.5   |
| g/dL  | SD          | 0.37  | 0.61   | 0.47   |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | -1     | -1     |
| PLT   | M (1)       | 342   | 349    | 380    |
| G/L   | SD          | 76.5  | 50.8   | 83.3   |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | 2      | 11     |
| RTC   | M (1)       | 3.34  | 3.24   | 2.88   |
| %     | SD          | 0.613 | 0.780  | 0.471  |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | -3     | -14    |
| RTC   | M (1)       | 0.22  | 0.21   | 0.19   |
| T/L   | SD          | 0.031 | 0.050  | 0.034  |
|       | n           | 10    | 10     | 10     |
|       | %/1st group |       | -5     | -14    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORS TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 5

| Group       |        | 1     | 2       | 3       |
|-------------|--------|-------|---------|---------|
| N           | M (1)  | 1.72  | 2.30 *  | 1.81    |
| G/L         | SD     | 0.531 | 0.639   | 0.495   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | 34    | 5       |         |
| E           | M (1)  | 0.07  | 0.04 ** | 0.04 ** |
| G/L         | SD     | 0.020 | 0.015   | 0.014   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | -43   | -43     |         |
| B           | M (1)  | 0.28  | 0.30    | 0.34    |
| G/L         | SD     | 0.090 | 0.086   | 0.103   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | 7     | 21      |         |
| L           | M (1)  | 2.95  | 3.60    | 3.19    |
| G/L         | SD     | 0.471 | 0.585   | 0.767   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | 22    | 8       |         |
| LUC         | M (1)  | 0.03  | 0.05 *  | 0.05    |
| G/L         | SD (L) | 0.020 | 0.017   | 0.024   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | 67    | 67      |         |
| M           | M (1)  | 0.24  | 0.37    | 0.33    |
| G/L         | SD     | 0.124 | 0.136   | 0.168   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | 54    | 38      |         |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 5

| Group |             | 1     | 2       | 3       |
|-------|-------------|-------|---------|---------|
| PT    | M (1)       | 6.7   | 6.9     | 6.6     |
| s     | SD          | 0.31  | 0.49    | 0.29    |
|       | n           | 10    | 10      | 10      |
|       | %/1st group |       | 3       | -1      |
| FIB   | M (1)       | 2.09  | 2.99 ** | 3.26 ** |
| g/L   | SD          | 0.331 | 0.549   | 0.491   |
|       | n           | 10    | 10      | 10      |
|       | %/1st group |       | 43      | 56      |
| APTT  | M (1)       | 14.5  | 14.3    | 14.1    |
| s     | SD          | 1.09  | 0.76    | 0.90    |
|       | n           | 10    | 10      | 10      |
|       | %/1st group |       | -1      | -3      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: 42

Study No.:

Sex: Male

Time: Week 9

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| WBC   | M (1)       | 6.77  | 4.95  | 6.18  |
| G/L   | SD          | 1.848 | 0.739 | 1.287 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -27   | -9    |       |
| RBC   | M (1)       | 6.99  | 7.10  | 7.01  |
| T/L   | SD          | 0.423 | 0.132 | 0.274 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 2     | 0     |       |
| HB    | M (1)       | 15.0  | 14.9  | 15.0  |
| g/dL  | SD          | 0.69  | 0.38  | 0.54  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    | 0     |       |
| PCV   | M (1)       | 0.45  | 0.46  | 0.45  |
| L/L   | SD          | 0.024 | 0.005 | 0.023 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 2     | 0     |       |
| MCV   | M (1)       | 64.9  | 64.3  | 64.7  |
| fL    | SD          | 2.60  | 1.16  | 2.04  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    | 0     |       |
| MCH   | M (1)       | 21.5  | 21.1  | 21.4  |
| pg    | SD          | 0.57  | 0.40  | 0.30  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    | 0     |       |
| MCHC  | M (3)       | 33.1  | 32.8  | 33.0  |
| g/dL  | SD (K)      | 0.58  | 0.64  | 0.75  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -1    | 0     |       |
| PLT   | M (1)       | 342   | 344   | 369   |
| G/L   | SD          | 53.7  | 61.4  | 68.4  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 1     | 8     |       |
| RTC   | M (1)       | 2.56  | 2.29  | 2.44  |
| %     | SD          | 0.364 | 0.395 | 0.376 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -11   | -5    |       |
| RTC   | M (1)       | 0.18  | 0.16  | 0.17  |
| T/L   | SD          | 0.033 | 0.029 | 0.023 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -11   | -6    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 9

| Group       |        | 1     | 2      | 3     |
|-------------|--------|-------|--------|-------|
| N           | M (1)  | 2.05  | 1.49   | 1.93  |
| G/L         | SD     | 0.754 | 0.297  | 0.265 |
| n           |        | 5     | 5      | 5     |
| %/1st group |        | -27   | -6     |       |
| E           | M (1)  | 0.10  | 0.09   | 0.11  |
| G/L         | SD     | 0.031 | 0.018  | 0.030 |
| n           |        | 5     | 5      | 5     |
| %/1st group |        | -10   | 10     |       |
| B           | M (1)  | 0.29  | 0.25   | 0.23  |
| G/L         | SD     | 0.075 | 0.038  | 0.087 |
| n           |        | 5     | 5      | 5     |
| %/1st group |        | -14   | -21    |       |
| L           | M (1)  | 4.01  | 2.90   | 3.69  |
| G/L         | SD     | 0.916 | 0.704  | 1.095 |
| n           |        | 5     | 5      | 5     |
| %/1st group |        | -28   | -8     |       |
| LUC         | M (3)  | 0.03  | 0.01 * | 0.02  |
| G/L         | SD (K) | 0.016 | 0.004  | 0.008 |
| n           |        | 5     | 5      | 5     |
| %/1st group |        | -67   | -33    |       |
| M           | M (1)  | 0.28  | 0.22   | 0.21  |
| G/L         | SD     | 0.152 | 0.084  | 0.096 |
| n           |        | 5     | 5      | 5     |
| %/1st group |        | -21   | -25    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 9

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| PT    | M (1)       | 7.0   | 6.8   | 7.1   |
| s     | SD          | 0.38  | 0.15  | 0.45  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -3    | 1     |       |
| FIB   | M (1)       | 2.85  | 2.46  | 2.69  |
| g/L   | SD          | 0.311 | 0.359 | 0.404 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -14   | -6    |       |
| APTT  | M (1)       | 13.2  | 13.0  | 14.1  |
| s     | SD          | 0.36  | 0.82  | 0.65  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -2    | 7     |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: 43

Study No.:  
Sex: Female  
Time: Week 9

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| WBC   | M (1)       | 5.45  | 5.69  | 4.33  |
| G/L   | SD          | 1.098 | 1.124 | 0.519 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 4     | -21   |
| RBC   | M (1)       | 6.50  | 6.32  | 6.41  |
| T/L   | SD          | 0.452 | 0.111 | 0.442 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -3    | -1    |
| HB    | M (1)       | 14.2  | 13.9  | 13.7  |
| g/dL  | SD          | 0.65  | 0.24  | 0.64  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -2    | -4    |
| PCV   | M (3)       | 0.44  | 0.42  | 0.42  |
| L/L   | SD (K)      | 0.023 | 0.009 | 0.026 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -5    | -5    |
| MCV   | M (1)       | 67.3  | 66.8  | 66.2  |
| fL    | SD          | 2.22  | 0.38  | 1.25  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -1    | -2    |
| MCH   | M (1)       | 22.0  | 22.0  | 21.4  |
| pg    | SD          | 1.00  | 0.31  | 0.54  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 0     | -3    |
| MCHC  | M (1)       | 32.6  | 32.9  | 32.3  |
| g/dL  | SD          | 0.66  | 0.47  | 0.57  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 1     | -1    |
| PLT   | M (1)       | 325   | 336   | 378   |
| G/L   | SD          | 76.7  | 33.8  | 91.6  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 3     | 16    |
| RTC   | M (1)       | 3.07  | 2.87  | 2.77  |
| %     | SD          | 0.331 | 0.869 | 0.658 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -7    | -10   |
| RTC   | M (1)       | 0.20  | 0.18  | 0.18  |
| T/L   | SD          | 0.011 | 0.054 | 0.046 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -10   | -10   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

- \* P<0.05
- \*\* P<0.01
- (1) : DUNNETT TEST
- (2) : MANN-WHITNEY TEST
- (3) : DUNN TEST

- (B) BARTLETT TEST P<0.01
- (F) FISHER TEST P<0.01
- (K) KOLMOGOROV-LILLIEFORS TEST P<0.01
- (L) LOGARITHMIC TRANSFORMATION
- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 9

| Group       |        | 1     | 2     | 3     |
|-------------|--------|-------|-------|-------|
| N           | M (3)  | 1.64  | 1.78  | 1.42  |
| G/L         | SD (K) | 0.467 | 0.458 | 0.413 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | 9     | -13   |       |
| E           | M (1)  | 0.13  | 0.14  | 0.12  |
| G/L         | SD     | 0.019 | 0.015 | 0.029 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | 8     | -8    |       |
| B           | M (1)  | 0.32  | 0.27  | 0.25  |
| G/L         | SD     | 0.090 | 0.125 | 0.083 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | -16   | -22   |       |
| L           | M (1)  | 3.13  | 3.23  | 2.35  |
| G/L         | SD     | 0.737 | 0.819 | 0.368 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | 3     | -25   |       |
| LUC         | M (3)  | 0.05  | 0.04  | 0.03  |
| G/L         | SD (K) | 0.042 | 0.015 | 0.013 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | -20   | -40   |       |
| M           | M (1)  | 0.20  | 0.24  | 0.15  |
| G/L         | SD     | 0.069 | 0.107 | 0.035 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | 20    | -25   |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

HEMATOLOGY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 9

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| PT    | M (1)       | 7.2   | 7.2   | 7.1   |
| s     | SD          | 0.36  | 0.28  | 0.74  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 0     | -1    |       |
| FIB   | M (1)       | 2.02  | 1.92  | 2.04  |
| g/L   | SD          | 0.327 | 0.171 | 0.147 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -5    | 1     |       |
| APTT  | M (1)       | 13.7  | 14.1  | 14.8  |
| s     | SD          | 1.08  | 0.52  | 1.32  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 3     | 8     |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

Tables 44 to 51. Blood biochemistry (mean values)

BLOOD BIOCHEMISTRY  
(mean values)

Table: 44

Study No.:

Sex: Male

Time: Predose

| Group       |        | 1     | 2      | 3     |
|-------------|--------|-------|--------|-------|
| Na+         | M (1)  | 141.6 | 142.1  | 140.7 |
| mmol/L      | SD     | 1.14  | 0.94   | 1.77  |
| n           |        | 10    | 10     | 10    |
| %/1st group |        | 0     | -1     |       |
| K+          | M (3)  | 4.07  | 4.21   | 3.95  |
| mmol/L      | SD (K) | 0.340 | 0.537  | 0.205 |
| n           |        | 10    | 10     | 10    |
| %/1st group |        | 3     | -3     |       |
| Cl-         | M (1)  | 102.3 | 103.2  | 102.4 |
| mmol/L      | SD     | 3.06  | 2.32   | 3.06  |
| n           |        | 10    | 10     | 10    |
| %/1st group |        | 1     | 0      |       |
| Ca++        | M (1)  | 3.54  | 3.57   | 3.55  |
| mmol/L      | SD     | 0.087 | 0.132  | 0.071 |
| n           |        | 10    | 10     | 10    |
| %/1st group |        | 1     | 0      |       |
| PHOS        | M (1)  | 2.20  | 2.36   | 2.31  |
| mmol/L      | SD     | 0.169 | 0.264  | 0.182 |
| n           |        | 10    | 10     | 10    |
| %/1st group |        | 7     | 5      |       |
| GLUC        | M (3)  | 7.00  | 7.00   | 7.15  |
| mmol/L      | SD (K) | 0.564 | 0.733  | 0.512 |
| n           |        | 10    | 10     | 10    |
| %/1st group |        | 0     | 2      |       |
| UREA        | M (1)  | 7.0   | 7.8    | 8.0   |
| mmol/L      | SD     | 0.60  | 1.62   | 1.61  |
| n           |        | 10    | 10     | 10    |
| %/1st group |        | 11    | 14     |       |
| CREAT       | M (1)  | 94.02 | 94.73  | 94.38 |
| µmol/L      | SD     | 7.327 | 12.852 | 8.657 |
| n           |        | 10    | 10     | 10    |
| %/1st group |        | 1     | 0      |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFOR TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Predose

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| ALP   | M (1)       | 494   | 512   | 568   |
| U/L   | SD          | 102.4 | 145.6 | 131.2 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 4     | 15    |
| ..... | .....       | ..... | ..... | ..... |
| ALAT  | M (1)       | 49    | 46    | 50    |
| U/L   | SD          | 12.3  | 10.3  | 12.4  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -6    | 2     |
| ..... | .....       | ..... | ..... | ..... |
| ASAT  | M (1)       | 23    | 21    | 18 *  |
| U/L   | SD          | 4.3   | 4.5   | 3.2   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -9    | -22   |
| ..... | .....       | ..... | ..... | ..... |
| CK    | M (1)       | 758   | 686   | 649   |
| U/L   | SD (L)      | 212.8 | 367.3 | 200.7 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -9    | -14   |
| ..... | .....       | ..... | ..... | ..... |
| LDH   | M (1)       | 280   | 220   | 192   |
| U/L   | SD          | 100.0 | 85.7  | 86.8  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -21   | -31   |
| ..... | .....       | ..... | ..... | ..... |
| GGT   | M (1)       | 6     | 7     | 6     |
| U/L   | SD          | 1.9   | 1.9   | 1.1   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 17    | 0     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Predose

| Group         | 1     | 2     | 3     |
|---------------|-------|-------|-------|
| TOT.BIL M     | 0.0   | 0.0   | 0.0   |
| µmol/L SD (K) | 0.00  | 0.00  | 0.00  |
| n             | 10    | 10    | 10    |
| %/1st group   | -     | -     | -     |
| CHOL M (1)    | 1.53  | 1.44  | 1.52  |
| mmol/L SD     | 0.273 | 0.330 | 0.229 |
| n             | 10    | 10    | 10    |
| %/1st group   | -6    | -1    | -     |
| TRIG M (1)    | 0.79  | 0.76  | 0.92  |
| mmol/L SD     | 0.233 | 0.328 | 0.311 |
| n             | 10    | 10    | 10    |
| %/1st group   | -4    | 16    | -     |
| PROT M (1)    | 62.8  | 61.8  | 62.5  |
| g/L SD        | 2.42  | 3.11  | 2.62  |
| n             | 9     | 10    | 10    |
| %/1st group   | -2    | 0     | -     |
| ALB M (1)     | 40    | 40    | 40    |
| g/L SD        | 1.5   | 2.3   | 1.7   |
| n             | 10    | 10    | 10    |
| %/1st group   | 0     | 0     | -     |
| A/G M (1)     | 1.81  | 1.80  | 1.72  |
| - SD          | 0.061 | 0.058 | 0.116 |
| n             | 9     | 10    | 10    |
| %/1st group   | -1    | -5    | -     |
| GLOB M (3)    | 23    | 22    | 23    |
| g/L SD (K)    | 1.1   | 0.9   | 1.3   |
| n             | 9     | 10    | 10    |
| %/1st group   | -4    | 0     | -     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: 45

Study No.:

Sex: Female

Time: Predose

| Group       |       | 1     | 2      | 3      |
|-------------|-------|-------|--------|--------|
| Na+         | M (1) | 140.4 | 140.8  | 141.1  |
| mmol/L      | SD    | 1.34  | 1.04   | 0.87   |
| n           |       | 10    | 10     | 10     |
| %/1st group |       | 0     | 0      |        |
| K+          | M (1) | 3.87  | 3.93   | 3.78   |
| mmol/L      | SD    | 0.222 | 0.299  | 0.160  |
| n           |       | 10    | 10     | 10     |
| %/1st group |       | 2     | -2     |        |
| Cl-         | M (1) | 103.4 | 103.0  | 102.8  |
| mmol/L      | SD    | 2.24  | 1.22   | 1.43   |
| n           |       | 10    | 10     | 10     |
| %/1st group |       | 0     | -1     |        |
| Ca++        | M (1) | 3.49  | 3.44   | 3.42   |
| mmol/L      | SD    | 0.093 | 0.097  | 0.074  |
| n           |       | 10    | 10     | 10     |
| %/1st group |       | -1    | -2     |        |
| PHOS        | M (1) | 2.21  | 2.26   | 2.25   |
| mmol/L      | SD    | 0.125 | 0.131  | 0.089  |
| n           |       | 10    | 10     | 10     |
| %/1st group |       | 2     | 2      |        |
| GLUC        | M (1) | 6.57  | 6.76   | 6.63   |
| mmol/L      | SD    | 0.465 | 0.395  | 0.419  |
| n           |       | 10    | 10     | 10     |
| %/1st group |       | 3     | 1      |        |
| UREA        | M (1) | 9.2   | 8.7    | 9.6    |
| mmol/L      | SD    | 0.98  | 0.84   | 1.07   |
| n           |       | 10    | 10     | 10     |
| %/1st group |       | -5    | 4      |        |
| CREAT       | M (1) | 92.98 | 87.42  | 93.43  |
| µmol/L      | SD    | 5.941 | 10.469 | 10.265 |
| n           |       | 10    | 10     | 10     |
| %/1st group |       | -6    | 0      |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Predose

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| ALP   | M (1)       | 499   | 510   | 519   |
| U/L   | SD          | 69.5  | 65.1  | 102.0 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 2     | 4     |
| ..... | .....       | ..... | ..... | ..... |
| ALAT  | M (1)       | 45    | 50    | 48    |
| U/L   | SD          | 13.7  | 8.6   | 11.3  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 11    | 7     |
| ..... | .....       | ..... | ..... | ..... |
| ASAT  | M (1)       | 16    | 17    | 16    |
| U/L   | SD (L)      | 3.3   | 4.3   | 2.8   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 6     | 0     |
| ..... | .....       | ..... | ..... | ..... |
| CK    | M (3)       | 487   | 567   | 517   |
| U/L   | SD (K)      | 148.5 | 291.6 | 142.7 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 16    | 6     |
| ..... | .....       | ..... | ..... | ..... |
| LDH   | M (1)       | 145   | 149   | 190 * |
| U/L   | SD          | 49.2  | 32.0  | 34.3  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 3     | 31    |
| ..... | .....       | ..... | ..... | ..... |
| GGT   | M (1)       | 7     | 5     | *     |
| U/L   | SD (L)      | 1.8   | 1.2   | 1.5   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -29   | -29   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Predose

| Group                | 1                                  | 2                          | 3                         |
|----------------------|------------------------------------|----------------------------|---------------------------|
| TOT.BIL M<br>µmol/L  | 0.0<br>SD (K)<br>n<br>%/1st group  | 0.0<br>0.00<br>10<br>-     | 0.0<br>0.00<br>10<br>-    |
| CHOL M (3)<br>mmol/L | 1.68<br>SD<br>n (B)<br>%/1st group | 1.51<br>0.322<br>10<br>-10 | 1.71<br>0.378<br>10<br>2  |
| TRIG M (1)<br>mmol/L | 0.77<br>SD<br>n<br>%/1st group     | 0.72<br>0.241<br>10<br>-6  | 0.86<br>0.192<br>10<br>12 |
| PROT M (1)<br>g/L    | 60.4<br>SD<br>n<br>%/1st group     | 61.0<br>1.62<br>10<br>1    | 60.2<br>2.18<br>10<br>0   |
| ALB M (1)<br>g/L     | 41<br>SD<br>n<br>%/1st group       | 41<br>1.6<br>10<br>0       | 41<br>1.8<br>10<br>0      |
| A/G -                | M (1)<br>SD<br>n<br>%/1st group    | 2.10<br>0.122<br>10<br>-2  | 2.05<br>0.112<br>10<br>0  |
| GLOB M (3)<br>g/L    | 20<br>SD (K)<br>n<br>%/1st group   | 20<br>1.5<br>10<br>0       | 20<br>0.8<br>10<br>0      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: 46

Study No.:

Sex: Male

Time: Week 1

| Group       |       | 1     | 2     | 3     |
|-------------|-------|-------|-------|-------|
| Na+         | M (1) | 141.4 | 140.7 | 140.9 |
| mmol/L      | SD    | 0.79  | 1.09  | 0.73  |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 0     | 0     |       |
| K+          | M (1) | 3.59  | 3.53  | 3.55  |
| mmol/L      | SD    | 0.229 | 0.258 | 0.292 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | -2    | -1    |       |
| Cl-         | M (1) | 105.1 | 105.6 | 105.4 |
| mmol/L      | SD    | 1.38  | 1.74  | 1.16  |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 0     | 0     |       |
| Ca++        | M (1) | 3.58  | 3.54  | 3.54  |
| mmol/L      | SD    | 0.083 | 0.066 | 0.076 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | -1    | -1    |       |
| PHOS        | M (1) | 1.82  | 1.93  | 1.94  |
| mmol/L      | SD    | 0.109 | 0.130 | 0.151 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 6     | 7     |       |
| GLUC        | M (1) | 6.71  | 6.80  | 6.73  |
| mmol/L      | SD    | 0.422 | 0.452 | 0.397 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 1     | 0     |       |
| UREA        | M (1) | 6.7   | 6.9   | 7.3   |
| mmol/L      | SD    | 0.70  | 0.42  | 1.21  |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 3     | 9     |       |
| CREAT       | M (1) | 78.64 | 81.57 | 83.87 |
| µmol/L      | SD    | 7.144 | 5.170 | 9.794 |
| n           |       | 10    | 10    | 10    |
| %/1st group |       | 4     | 7     |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 1

| Group |             | 1     | 2     | 3      |
|-------|-------------|-------|-------|--------|
| ALP   | M (1)       | 532   | 490   | 504    |
| U/L   | SD          | 98.6  | 69.9  | 104.1  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -8    | -5    |        |
| ..... | .....       | ..... | ..... | .....  |
| ALAT  | M (1)       | 58    | 48    | 52     |
| U/L   | SD          | 19.5  | 10.6  | 8.5    |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -17   | -10   |        |
| ..... | .....       | ..... | ..... | .....  |
| ASAT  | M (1)       | 28    | 19    | 16 **  |
| U/L   | SD (L)      | 15.5  | 4.3   | 4.5    |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -32   | -43   |        |
| ..... | .....       | ..... | ..... | .....  |
| CK    | M (1)       | 713   | 778   | 619    |
| U/L   | SD          | 169.8 | 368.2 | 204.3  |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | 9     | -13   |        |
| ..... | .....       | ..... | ..... | .....  |
| LDH   | M (1)       | 215   | 163 * | 118 ** |
| U/L   | SD          | 65.3  | 40.8  | 27.6   |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -24   | -45   |        |
| ..... | .....       | ..... | ..... | .....  |
| GGT   | M (1)       | 7     | 6     | 7      |
| U/L   | SD          | 1.4   | 1.8   | 1.4    |
|       | n           | 10    | 10    | 10     |
|       | %/1st group | -14   | 0     |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 1

| Group       |        | 1     | 2     | 3       |
|-------------|--------|-------|-------|---------|
| TOT.BIL     | M      | 0.0   | 0.0   | 0.0     |
| µmol/L      | SD (K) | 0.00  | 0.00  | 0.00    |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | -     | -     | -       |
| CHOL        | M (1)  | 1.11  | 1.05  | 1.04    |
| mmol/L      | SD     | 0.170 | 0.234 | 0.201   |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | -5    | -6    | -       |
| TRIG        | M (1)  | 0.55  | 0.48  | 0.56    |
| mmol/L      | SD     | 0.135 | 0.125 | 0.181   |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | -13   | 2     | -       |
| PROT        | M (1)  | 62.9  | 63.0  | 62.4    |
| g/L         | SD     | 1.67  | 1.58  | 2.87    |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | 0     | -1    | -       |
| ALB         | M (1)  | 44    | 43    | 42      |
| g/L         | SD     | 1.0   | 1.2   | 2.0     |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | -2    | -5    | -       |
| A/G         | M (3)  | 2.29  | 2.21  | 2.11 ** |
| -           | SD     | 0.063 | 0.083 | 0.171   |
| n (B)       |        | 10    | 10    | 10      |
| %/1st group |        | -3    | -8    | -       |
| GLOB        | M (1)  | 19    | 20    | 20      |
| g/L         | SD     | 0.7   | 0.9   | 1.7     |
| n           |        | 10    | 10    | 10      |
| %/1st group |        | 5     | 5     | -       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: 47

Study No.:

Sex: Female

Time: Week 1

| Group       |        | 1     | 2      | 3      |
|-------------|--------|-------|--------|--------|
| Na+         | M (3)  | 140.9 | 140.8  | 141.6  |
| mmol/L      | SD (K) | 0.77  | 0.98   | 1.36   |
| n           |        | 10    | 10     | 10     |
| %/1st group |        | 0     | 0      |        |
| K+          | M (1)  | 3.85  | 3.62 * | 3.64 * |
| mmol/L      | SD     | 0.146 | 0.211  | 0.219  |
| n           |        | 10    | 10     | 10     |
| %/1st group |        | -6    | -5     |        |
| Cl-         | M (1)  | 106.0 | 105.6  | 105.9  |
| mmol/L      | SD     | 1.53  | 2.27   | 1.98   |
| n           |        | 10    | 10     | 10     |
| %/1st group |        | 0     | 0      |        |
| Ca++        | M (1)  | 3.57  | 3.55   | 3.54   |
| mmol/L      | SD     | 0.081 | 0.064  | 0.047  |
| n           |        | 10    | 10     | 10     |
| %/1st group |        | -1    | -1     |        |
| PHOS        | M (1)  | 2.01  | 1.93   | 2.00   |
| mmol/L      | SD     | 0.100 | 0.116  | 0.143  |
| n           |        | 10    | 10     | 10     |
| %/1st group |        | -4    | 0      |        |
| GLUC        | M (1)  | 6.89  | 6.78   | 6.84   |
| mmol/L      | SD     | 0.298 | 0.456  | 0.409  |
| n           |        | 10    | 10     | 10     |
| %/1st group |        | -2    | -1     |        |
| UREA        | M (1)  | 8.8   | 8.4    | 8.8    |
| mmol/L      | SD     | 0.86  | 0.95   | 0.51   |
| n           |        | 10    | 10     | 10     |
| %/1st group |        | -5    | 0      |        |
| CREAT       | M (1)  | 88.95 | 82.25  | 85.35  |
| µmol/L      | SD     | 9.444 | 6.735  | 7.532  |
| n           |        | 10    | 10     | 10     |
| %/1st group |        | -8    | -4     |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 1

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| ALP   | M (1)       | 519   | 520   | 476   |
| U/L   | SD          | 116.5 | 75.8  | 94.1  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 0     | -8    |       |
| ..... | .....       | ..... | ..... | ..... |
| ALAT  | M (1)       | 50    | 58    | 52    |
| U/L   | SD          | 15.2  | 12.0  | 12.9  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 16    | 4     |       |
| ..... | .....       | ..... | ..... | ..... |
| ASAT  | M (1)       | 21    | 25    | 17    |
| U/L   | SD (L)      | 3.9   | 16.1  | 5.3   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 19    | -19   |       |
| ..... | .....       | ..... | ..... | ..... |
| CK    | M (1)       | 592   | 695   | 743   |
| U/L   | SD (L)      | 192.4 | 236.7 | 698.3 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 17    | 26    |       |
| ..... | .....       | ..... | ..... | ..... |
| LDH   | M (1)       | 184   | 208   | 139 * |
| U/L   | SD          | 53.0  | 25.9  | 33.8  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | 13    | -24   |       |
| ..... | .....       | ..... | ..... | ..... |
| GGT   | M (3)       | 9     | 7 *   | 8     |
| U/L   | SD (K)      | 1.4   | 1.6   | 1.3   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group | -22   | -11   |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 1

| Group                | 1                                 | 2                           | 3                         |
|----------------------|-----------------------------------|-----------------------------|---------------------------|
| TOT.BIL M<br>µmol/L  | 0.0<br>SD (K)<br>n<br>%/1st group | 0.00<br>0.00<br>10<br>-     | 0.00<br>0.00<br>10<br>-   |
| CHOL M (1)<br>mmol/L | 1.42<br>SD<br>n<br>%/1st group    | 0.179<br>0.219<br>10<br>-17 | 1.37<br>0.277<br>10<br>-4 |
| TRIG M (1)<br>mmol/L | 0.44<br>SD<br>n<br>%/1st group    | 0.083<br>0.081<br>10<br>-5  | 0.47<br>0.089<br>10<br>7  |
| PROT M (1)<br>g/L    | 60.8<br>SD<br>n<br>%/1st group    | 3.24<br>1.90<br>10<br>1     | 61.1<br>2.53<br>10<br>0   |
| ALB M (1)<br>g/L     | 44<br>SD<br>n<br>%/1st group      | 2.3<br>1.6<br>10<br>-2      | 43<br>2.0<br>10<br>-2     |
| A/G -                | M (1)<br>SD<br>n<br>%/1st group   | 2.54<br>0.144<br>10<br>-5   | 2.42<br>0.168<br>10<br>-6 |
| GLOB M (1)<br>g/L    | 17<br>SD<br>n<br>%/1st group      | 1.3<br>1.2<br>10<br>6       | 18<br>1.0<br>10<br>6      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: 48

Study No.:

Sex: Male

Time: Week 5

| Group       |       | 1     | 2       | 3      |
|-------------|-------|-------|---------|--------|
| Na+         | M (1) | 142.8 | 141.8 * | 142.0  |
| mmol/L      | SD    | 0.61  | 1.18    | 0.81   |
| n           |       | 10    | 10      | 10     |
| %/1st group |       | -1    | -1      |        |
| K+          | M (1) | 3.89  | 3.89    | 3.69   |
| mmol/L      | SD    | 0.171 | 0.264   | 0.364  |
| n           |       | 10    | 10      | 10     |
| %/1st group |       | 0     | -5      |        |
| Cl-         | M (1) | 106.5 | 106.5   | 107.4  |
| mmol/L      | SD    | 1.33  | 1.44    | 1.89   |
| n           |       | 10    | 10      | 10     |
| %/1st group |       | 0     | 1       |        |
| Ca++        | M (1) | 3.52  | 3.47    | 3.41   |
| mmol/L      | SD    | 0.106 | 0.112   | 0.102  |
| n           |       | 10    | 10      | 10     |
| %/1st group |       | -1    | -3      |        |
| PHOS        | M (1) | 1.48  | 1.59 *  | 1.59   |
| mmol/L      | SD    | 0.062 | 0.116   | 0.124  |
| n           |       | 10    | 10      | 10     |
| %/1st group |       | 7     | 7       |        |
| GLUC        | M (1) | 7.17  | 7.28    | 6.78   |
| mmol/L      | SD    | 0.513 | 0.379   | 0.518  |
| n           |       | 10    | 10      | 10     |
| %/1st group |       | 2     | -5      |        |
| UREA        | M (1) | 7.2   | 7.2     | 7.8    |
| mmol/L      | SD    | 1.04  | 1.07    | 1.56   |
| n           |       | 10    | 10      | 10     |
| %/1st group |       | 0     | 8       |        |
| CREAT       | M (1) | 85.35 | 91.53   | 89.89  |
| µmol/L      | SD    | 8.140 | 8.758   | 12.120 |
| n           |       | 10    | 10      | 10     |
| %/1st group |       | 7     | 5       |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 5

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| ALP   | M (1)       | 513   | 385   | *     |
| U/L   | SD          | 123.2 | 69.2  | 109.6 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -25   | -16   |
| ..... | .....       | ..... | ..... | ..... |
| ALAT  | M (1)       | 48    | 41    | 46    |
| U/L   | SD          | 13.9  | 8.6   | 10.0  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -15   | -4    |
| ..... | .....       | ..... | ..... | ..... |
| ASAT  | M (1)       | 25    | 22    | 19 *  |
| U/L   | SD          | 5.0   | 5.1   | 2.1   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -12   | -24   |
| ..... | .....       | ..... | ..... | ..... |
| CK    | M (1)       | 826   | 663   | 1232  |
| U/L   | SD (L)      | 349.2 | 177.8 | 734.5 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -20   | 49    |
| ..... | .....       | ..... | ..... | ..... |
| LDH   | M (1)       | 210   | 186   | 200   |
| U/L   | SD          | 53.7  | 46.9  | 59.0  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -11   | -5    |
| ..... | .....       | ..... | ..... | ..... |
| GGT   | M (3)       | 5     | 5     | 4     |
| U/L   | SD (K)      | 1.6   | 1.3   | 1.0   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 0     | -20   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 5

| Group       |        | 1     | 2       | 3       |
|-------------|--------|-------|---------|---------|
| TOT.BIL     | M      | 0.0   | 0.0     | 0.0     |
| µmol/L      | SD (K) | 0.00  | 0.00    | 0.00    |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | -     | -       | -       |
| CHOL        | M (1)  | 0.99  | 0.83    | 0.84    |
| mmol/L      | SD     | 0.203 | 0.175   | 0.163   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | -16   | -15     | -       |
| TRIG        | M (1)  | 0.57  | 0.54    | 0.58    |
| mmol/L      | SD     | 0.120 | 0.165   | 0.179   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | -5    | 2       | -       |
| PROT        | M (1)  | 61.5  | 60.4    | 60.7    |
| g/L         | SD     | 1.52  | 2.25    | 2.26    |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | -2    | -1      | -       |
| ALB         | M (3)  | 43    | 41      | *       |
| g/L         | SD (K) | 1.0   | 1.7     | 1.6     |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | -5    | -5      | -       |
| A/G         | M (1)  | 2.26  | 2.07 ** | 2.02 ** |
| -           | SD     | 0.120 | 0.115   | 0.120   |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | -8    | -11     | -       |
| GLOB        | M (3)  | 19    | 20      | 20 *    |
| g/L         | SD (K) | 0.8   | 1.2     | 1.3     |
| n           |        | 10    | 10      | 10      |
| %/1st group |        | 5     | 5       | -       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: 49

Study No.:

Sex: Female

Time: Week 5

| Group       |        | 1      | 2      | 3      |
|-------------|--------|--------|--------|--------|
| Na+         | M (1)  | 140.7  | 140.0  | 140.6  |
| mmol/L      | SD     | 1.11   | 0.59   | 0.51   |
| n           |        | 10     | 10     | 10     |
| %/1st group |        | 0      | 0      |        |
| K+          | M (1)  | 3.72   | 3.61   | 3.77   |
| mmol/L      | SD     | 0.121  | 0.189  | 0.148  |
| n           |        | 10     | 10     | 10     |
| %/1st group |        | -3     | 1      |        |
| Cl-         | M (1)  | 106.3  | 105.4  | 107.0  |
| mmol/L      | SD     | 1.25   | 2.30   | 1.88   |
| n           |        | 10     | 10     | 10     |
| %/1st group |        | -1     | 1      |        |
| Ca++        | M (1)  | 3.61   | 3.55   | 3.55   |
| mmol/L      | SD     | 0.096  | 0.097  | 0.050  |
| n           |        | 10     | 10     | 10     |
| %/1st group |        | -2     | -2     |        |
| PHOS        | M (3)  | 1.53   | 1.51   | 1.57   |
| mmol/L      | SD (K) | 0.098  | 0.102  | 0.150  |
| n           |        | 10     | 10     | 10     |
| %/1st group |        | -1     | 3      |        |
| GLUC        | M (1)  | 6.86   | 6.65   | 6.65   |
| mmol/L      | SD     | 0.376  | 0.504  | 0.323  |
| n           |        | 10     | 10     | 10     |
| %/1st group |        | -3     | -3     |        |
| UREA        | M (1)  | 9.6    | 9.5    | 10.6   |
| mmol/L      | SD     | 1.21   | 1.11   | 1.42   |
| n           |        | 10     | 10     | 10     |
| %/1st group |        | -1     | 10     |        |
| CREAT       | M (1)  | 104.61 | 101.35 | 105.17 |
| µmol/L      | SD     | 11.006 | 9.658  | 15.808 |
| n           |        | 10     | 10     | 10     |
| %/1st group |        | -3     | 1      |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 5

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| ALP   | M (3)       | 446   | 397   | 358 * |
| U/L   | SD (K)      | 104.7 | 64.0  | 90.4  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -11   | -20   |
| ..... | .....       | ..... | ..... | ..... |
| ALAT  | M (1)       | 45    | 52    | 49    |
| U/L   | SD          | 14.2  | 13.2  | 11.9  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 16    | 9     |
| ..... | .....       | ..... | ..... | ..... |
| ASAT  | M (1)       | 23    | 29    | 21    |
| U/L   | SD (L)      | 4.8   | 14.2  | 5.1   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 26    | -9    |
| ..... | .....       | ..... | ..... | ..... |
| CK    | M (1)       | 664   | 619   | 636   |
| U/L   | SD (L)      | 274.6 | 154.6 | 351.7 |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -7    | -4    |
| ..... | .....       | ..... | ..... | ..... |
| LDH   | M (1)       | 154   | 195   | 194   |
| U/L   | SD          | 45.3  | 66.8  | 52.1  |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | 27    | 26    |
| ..... | .....       | ..... | ..... | ..... |
| GGT   | M (3)       | 8     | 7     | 7     |
| U/L   | SD (K)      | 0.7   | 0.9   | 0.7   |
|       | n           | 10    | 10    | 10    |
|       | %/1st group |       | -13   | -13   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 5

| Group       |        | 1     | 2      | 3       |
|-------------|--------|-------|--------|---------|
| TOT.BIL     | M      | 0.0   | 0.0    | 0.0     |
| μmol/L      | SD (K) | 0.00  | 0.00   | 0.00    |
| n           |        | 10    | 10     | 10      |
| %/1st group |        | -     | -      | -       |
| CHOL        | M (1)  | 1.48  | 1.16 * | 1.26    |
| mmol/L      | SD     | 0.261 | 0.250  | 0.311   |
| n           |        | 10    | 10     | 10      |
| %/1st group |        | -22   | -15    | -       |
| TRIG        | M (1)  | 0.44  | 0.42   | 0.43    |
| mmol/L      | SD     | 0.107 | 0.076  | 0.080   |
| n           |        | 10    | 10     | 10      |
| %/1st group |        | -5    | -2     | -       |
| PROT        | M (1)  | 61.6  | 60.2   | 60.3    |
| g/L         | SD     | 2.81  | 1.59   | 2.14    |
| n           |        | 10    | 10     | 10      |
| %/1st group |        | -2    | -2     | -       |
| ALB         | M (3)  | 43    | 41 *   | 41      |
| g/L         | SD (K) | 1.8   | 1.3    | 1.7     |
| n           |        | 10    | 10     | 10      |
| %/1st group |        | -5    | -5     | -       |
| A/G         | M (1)  | 2.32  | 2.13 * | 2.12 ** |
| -           | SD     | 0.154 | 0.153  | 0.098   |
| n           |        | 10    | 10     | 10      |
| %/1st group |        | -8    | -9     | -       |
| GLOB        | M (1)  | 19    | 19     | 19      |
| g/L         | SD     | 1.4   | 1.3    | 1.0     |
| n           |        | 10    | 10     | 10      |
| %/1st group |        | 0     | 0      | -       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: 50

Study No.:

Sex: Male

Time: Week 9

| Group       |       | 1      | 2      | 3      |
|-------------|-------|--------|--------|--------|
| Na+         | M (1) | 142.9  | 143.0  | 142.8  |
| mmol/L      | SD    | 1.61   | 0.53   | 1.13   |
| n           |       | 5      | 5      | 5      |
| %/1st group |       | 0      | 0      |        |
| K+          | M (1) | 3.59   | 3.57   | 3.58   |
| mmol/L      | SD    | 0.276  | 0.171  | 0.273  |
| n           |       | 5      | 5      | 5      |
| %/1st group |       | -1     | 0      |        |
| Cl-         | M (1) | 107.2  | 108.0  | 108.2  |
| mmol/L      | SD    | 2.05   | 0.77   | 2.03   |
| n           |       | 5      | 5      | 5      |
| %/1st group |       | 1      | 1      |        |
| Ca++        | M (1) | 3.45   | 3.44   | 3.42   |
| mmol/L      | SD    | 0.093  | 0.033  | 0.087  |
| n           |       | 5      | 5      | 5      |
| %/1st group |       | 0      | -1     |        |
| PHOS        | M (1) | 1.44   | 1.55   | 1.53   |
| mmol/L      | SD    | 0.033  | 0.076  | 0.179  |
| n           |       | 5      | 5      | 5      |
| %/1st group |       | 8      | 6      |        |
| GLUC        | M (1) | 6.51   | 6.47   | 6.43   |
| mmol/L      | SD    | 0.296  | 0.920  | 0.192  |
| n           |       | 5      | 5      | 5      |
| %/1st group |       | -1     | -1     |        |
| UREA        | M (1) | 8.7    | 8.0    | 8.7    |
| mmol/L      | SD    | 1.80   | 0.40   | 1.28   |
| n           |       | 5      | 5      | 5      |
| %/1st group |       | -8     | 0      |        |
| CREAT       | M (1) | 97.97  | 101.81 | 100.48 |
| µmol/L      | SD    | 14.125 | 5.108  | 9.772  |
| n           |       | 5      | 5      | 5      |
| %/1st group |       | 4      | 3      |        |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 9

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| ALP   | M (1)       | 337   | 298   | 335   |
| U/L   | SD          | 81.0  | 93.9  | 94.2  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -12   | -1    |
| ..... | .....       | ..... | ..... | ..... |
| ALAT  | M (1)       | 45    | 41    | 53    |
| U/L   | SD          | 17.8  | 11.6  | 15.0  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -9    | 18    |
| ..... | .....       | ..... | ..... | ..... |
| ASAT  | M (1)       | 24    | 20    | 21    |
| U/L   | SD          | 7.1   | 2.5   | 5.4   |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -17   | -13   |
| ..... | .....       | ..... | ..... | ..... |
| CK-L  | M (1)       | 669   | 670   | 879   |
| U/L   | SD          | 102.5 | 186.0 | 368.7 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 0     | 31    |
| ..... | .....       | ..... | ..... | ..... |
| LDH   | M (1)       | 266   | 206   | 172   |
| U/L   | SD          | 56.3  | 31.3  | 82.8  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | -23   | -35   |
| ..... | .....       | ..... | ..... | ..... |
| GGT   | M (1)       | 6     | 6     | 6     |
| U/L   | SD          | 2.1   | 0.7   | 1.2   |
|       | n           | 5     | 5     | 5     |
|       | %/1st group |       | 0     | 0     |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Male

Time: Week 9

| Group       |        | 1     | 2     | 3     |
|-------------|--------|-------|-------|-------|
| TOT.BIL     | M      | 0.0   | 0.0   | 0.0   |
| μmol/L      | SD (K) | 0.00  | 0.00  | 0.00  |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | -     | -     |       |
| CHOL        | M (1)  | 0.93  | 0.78  | 0.88  |
| mmol/L      | SD     | 0.189 | 0.103 | 0.084 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | -16   | -5    |       |
| TRIG        | M (1)  | 0.49  | 0.57  | 0.57  |
| mmol/L      | SD     | 0.065 | 0.199 | 0.108 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | 16    | 16    |       |
| PROT        | M (1)  | 61.3  | 59.3  | 58.9  |
| g/L         | SD     | 1.82  | 1.66  | 2.02  |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | -3    | -4    |       |
| ALB         | M (1)  | 43    | 42    | 41    |
| g/L         | SD     | 1.5   | 1.0   | 2.2   |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | -2    | -5    |       |
| A/G         | M (1)  | 2.40  | 2.44  | 2.37  |
| -           | SD     | 0.195 | 0.157 | 0.203 |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | 2     | -1    |       |
| GLOB        | M (1)  | 18    | 17    | 17    |
| g/L         | SD     | 1.1   | 1.1   | 1.1   |
| n           |        | 5     | 5     | 5     |
| %/1st group |        | -6    | -6    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFOR TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: 51

Study No.:

Sex: Female

Time: Week 9

| Group       |       | 1      | 2      | 3        |
|-------------|-------|--------|--------|----------|
| Na+         | M (1) | 142.9  | 140.9  | ** 142.0 |
| mmol/L      | SD    | 0.92   | 1.04   | 0.55     |
| n           |       | 5      | 5      | 5        |
| %/1st group |       | -1     | -1     |          |
| K+          | M (1) | 3.76   | 3.60   | 3.56     |
| mmol/L      | SD    | 0.101  | 0.065  | 0.193    |
| n           |       | 5      | 5      | 5        |
| %/1st group |       | -4     | -5     |          |
| Cl-         | M (1) | 107.2  | 106.9  | 108.8    |
| mmol/L      | SD    | 1.94   | 1.27   | 1.28     |
| n           |       | 5      | 5      | 5        |
| %/1st group |       | 0      | 1      |          |
| Ca++        | M (1) | 3.60   | 3.55   | 3.55     |
| mmol/L      | SD    | 0.198  | 0.096  | 0.099    |
| n           |       | 5      | 5      | 5        |
| %/1st group |       | -1     | -1     |          |
| PHOS        | M (1) | 1.44   | 1.37   | 1.42     |
| mmol/L      | SD    | 0.136  | 0.090  | 0.116    |
| n           |       | 5      | 5      | 5        |
| %/1st group |       | -5     | -1     |          |
| GLUC        | M (1) | 6.62   | 6.82   | 6.94     |
| mmol/L      | SD    | 0.463  | 0.458  | 0.207    |
| n           |       | 5      | 5      | 5        |
| %/1st group |       | 3      | 5      |          |
| UREA        | M (1) | 10.8   | 10.1   | 11.0     |
| mmol/L      | SD    | 1.53   | 1.06   | 1.23     |
| n           |       | 5      | 5      | 5        |
| %/1st group |       | -6     | 2      |          |
| CREAT       | M (1) | 129.20 | 114.95 | 115.54   |
| µmol/L      | SD    | 11.533 | 12.093 | 8.044    |
| n           |       | 5      | 5      | 5        |
| %/1st group |       | -11    | -11    |          |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 9

| Group |             | 1     | 2     | 3     |
|-------|-------------|-------|-------|-------|
| ALP   | M (1)       | 227   | 292   | 250   |
| U/L   | SD          | 51.2  | 50.5  | 78.0  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 29    | 10    |       |
| ..... | .....       | ..... | ..... | ..... |
| ALAT  | M (1)       | 46    | 68    | 60    |
| U/L   | SD          | 17.1  | 16.9  | 15.2  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 48    | 30    |       |
| ..... | .....       | ..... | ..... | ..... |
| ASAT  | M (1)       | 25    | 32    | 24    |
| U/L   | SD          | 7.9   | 17.9  | 3.1   |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 28    | -4    |       |
| ..... | .....       | ..... | ..... | ..... |
| CK-L  | M (1)       | 597   | 615   | 541   |
| U/L   | SD          | 201.4 | 149.0 | 277.2 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 3     | -9    |       |
| ..... | .....       | ..... | ..... | ..... |
| LDH   | M (3)       | 247   | 200   | 83    |
| U/L   | SD (K)      | 242.3 | 41.7  | 33.5  |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | -19   | -66   |       |
| ..... | .....       | ..... | ..... | ..... |
| GGT   | M (1)       | 4     | 5     | 4     |
| U/L   | SD          | 1.5   | 1.9   | 1.3   |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 25    | 0     |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

BLOOD BIOCHEMISTRY  
(mean values)

Table: (continued)

Study No.:

Sex: Female

Time: Week 9

| Group                | 1                               | 2                        | 3                       |                         |
|----------------------|---------------------------------|--------------------------|-------------------------|-------------------------|
| TOT.BIL M<br>µmol/L  | 0.0<br>0.00                     | 0.0<br>0.00              | 0.0<br>0.00             |                         |
| n                    | 5                               | 5                        | 5                       |                         |
| %/1st group          | -                               | -                        | -                       |                         |
| CHOL M (1)<br>mmol/L | 1.58<br>0.219                   | 1.05 **<br>0.215         | 1.42<br>0.191           |                         |
| n                    | 5                               | 5                        | 5                       |                         |
| %/1st group          | -34                             | -10                      | -                       |                         |
| TRIG M (1)<br>mmol/L | 0.45<br>0.077                   | 0.42<br>0.067            | 0.45<br>0.041           |                         |
| n                    | 5                               | 5                        | 5                       |                         |
| %/1st group          | -7                              | 0                        | -                       |                         |
| PROT M (1)<br>g/L    | 59.8<br>3.48                    | 59.6<br>1.33             | 59.6<br>1.64            |                         |
| n                    | 5                               | 5                        | 5                       |                         |
| %/1st group          | 0                               | 0                        | -                       |                         |
| ALB M (1)<br>g/L     | 42<br>2.8                       | 42<br>1.1                | 42<br>1.6               |                         |
| n                    | 5                               | 5                        | 5                       |                         |
| %/1st group          | 0                               | 0                        | -                       |                         |
| A/G -                | M (1)<br>SD<br>n<br>%/1st group | 2.41<br>0.268<br>5<br>-4 | 2.32<br>0.113<br>5<br>0 | 2.42<br>0.099<br>5<br>0 |
| GLOB M (1)<br>g/L    | 18<br>1.7                       | 18<br>0.7                | 18<br>0.5               |                         |
| n                    | 5                               | 5                        | 5                       |                         |
| %/1st group          | 0                               | 0                        | -                       |                         |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

## APPENDICES

4. Individual fate

## INDIVIDUAL FATE

Study No.: RABBITV1  
Group 1  
Control item (NaCl)  
Sex: Male  
Period : Days 1 to 57  
Principal animals + Recovery animals

---

| Animal No. | Week of death | Day of death | Date       | Reason for sacrifice or death |
|------------|---------------|--------------|------------|-------------------------------|
| N30641     | 5             | 31           | 19/09/2018 | Final sacrifice               |
| N30642     | 5             | 31           | 19/09/2018 | Final sacrifice               |
| N30643     | 5             | 31           | 19/09/2018 | Final sacrifice               |
| N30644     | 5             | 31           | 19/09/2018 | Final sacrifice               |
| N30645     | 5             | 31           | 19/09/2018 | Final sacrifice               |
| N30646     | 9             | 57           | 15/10/2018 | Sacrifice after reversibility |
| N30647     | 9             | 57           | 15/10/2018 | Sacrifice after reversibility |
| N30648     | 9             | 57           | 15/10/2018 | Sacrifice after reversibility |
| N30649     | 9             | 57           | 15/10/2018 | Sacrifice after reversibility |
| N30650     | 9             | 57           | 15/10/2018 | Sacrifice after reversibility |

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## INDIVIDUAL FATE

Study No.: RABBITV1

Group 2

SENDVACC10

Sex: Male

Period : Days 1 to 57

Principal animals + Recovery animals

---

| Animal<br>No. | Week of<br>death | Day of<br>death | Date | Reason for sacrifice or death |
|---------------|------------------|-----------------|------|-------------------------------|
|---------------|------------------|-----------------|------|-------------------------------|

|        |   |    |            |                               |
|--------|---|----|------------|-------------------------------|
| N30651 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30652 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30653 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30654 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30655 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30656 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |
| N30657 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |
| N30658 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |
| N30659 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |
| N30660 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |

## INDIVIDUAL FATE

Study No.:  
Group 3

Sex: Male  
Period : Days 1 to 57  
Principal animals + Recovery animals

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| Animal<br>No. | Week of<br>death | Day of<br>death | Date | Reason for sacrifice or death |
|---------------|------------------|-----------------|------|-------------------------------|
|---------------|------------------|-----------------|------|-------------------------------|

|        |   |    |            |                               |
|--------|---|----|------------|-------------------------------|
| N30661 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30662 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30663 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30664 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30665 | 5 | 31 | 19/09/2018 | Final sacrifice               |
| N30666 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |
| N30667 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |
| N30668 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |
| N30669 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |
| N30670 | 9 | 57 | 15/10/2018 | Sacrifice after reversibility |

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## INDIVIDUAL FATE

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Period : Days 1 to 57

Principal animals + Recovery animals

-

| Animal<br>No. | Week of<br>death | Day of<br>death | Date | Reason for sacrifice or death |
|---------------|------------------|-----------------|------|-------------------------------|
|---------------|------------------|-----------------|------|-------------------------------|

|        |   |    |            |                               |
|--------|---|----|------------|-------------------------------|
| N30711 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30712 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30713 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30714 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30715 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30716 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30717 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30718 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30719 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30720 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |

## INDIVIDUAL FATE

Study No.:  
Group 2

Sex: Female  
Period : Days 1 to 57  
Principal animals + Recovery animals

-----  
---

| Animal<br>No. | Week of<br>death | Day of<br>death | Date | Reason for sacrifice or death |
|---------------|------------------|-----------------|------|-------------------------------|
|---------------|------------------|-----------------|------|-------------------------------|

|        |   |    |            |                               |
|--------|---|----|------------|-------------------------------|
| N30721 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30722 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30723 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30724 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30725 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30726 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30727 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30728 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30729 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30730 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |

## INDIVIDUAL FATE

Study No.:  
Group 3

Sex: Female  
Period : Days 1 to 57  
Principal animals + Recovery animals

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| Animal<br>No. | Week of<br>death | Day of<br>death | Date | Reason for sacrifice or death |
|---------------|------------------|-----------------|------|-------------------------------|
|---------------|------------------|-----------------|------|-------------------------------|

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|        |   |    |            |                               |
|--------|---|----|------------|-------------------------------|
| N30731 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30732 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30733 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30734 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30735 | 5 | 31 | 27/09/2018 | Final sacrifice               |
| N30736 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30737 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30738 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30739 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |
| N30740 | 9 | 57 | 23/10/2018 | Sacrifice after reversibility |

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5. Clinical signs: individual findings

Bet.treat: before treatment  
Aft.Treat: after treatment

CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

-- Animal Clinical history

Latency

No.

|        |                   |                  |            |
|--------|-------------------|------------------|------------|
| N30641 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30           | 24h        |
|        | No clinical signs | Day 31           |            |
|        | Final sacrifice   | Day 31           |            |
| <hr/>  |                   |                  |            |
| N30642 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30           | 24h        |
|        | No clinical signs | Day 31           |            |
|        | Final sacrifice   | Day 31           |            |
| <hr/>  |                   |                  |            |
| N30643 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 24 |            |
|        | Papule / Back     | From day 25      |            |
|        | Final sacrifice   | Day 31           |            |
| <hr/>  |                   |                  |            |

CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

---

| -- Animal | Clinical history | Latency |
|-----------|------------------|---------|
| No.       |                  |         |

---

|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30644 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30           | 24h        |
|        | No clinical signs             | Day 31           |            |
|        | Final sacrifice               | Day 31           |            |
| .....  |                               |                  |            |
| N30645 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 24 |            |
|        | Papule / Back                 | From day 25      |            |
|        | Final sacrifice               | Day 31           |            |
| .....  |                               |                  |            |
| N30646 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 27 |            |
|        | Papule / Back                 | Day 28 to day 38 |            |
|        | No clinical signs             | Day 39 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |
| .....  |                               |                  |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal | Clinical history | Latency |
|-----------|------------------|---------|
| No.       |                  |         |

--

|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30647 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |
| .....  | .....                         | .....            | .....      |
| N30648 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |
| .....  | .....                         | .....            | .....      |
| N30649 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 50 |            |
|        | Papule / Back                 | From day 51      |            |
|        | Sacrifice after reversibility | Day 57           |            |
| .....  | .....                         | .....            | .....      |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

| Animal<br>No. | Clinical history              | Latency          |            |
|---------------|-------------------------------|------------------|------------|
| -             |                               |                  |            |
| N30650        | No clinical signs             | Day 1            | Bef.treat. |
|               | No clinical signs             | Day 1            | Aft.Treat. |
|               | No clinical signs             | Day 2 to day 14  |            |
|               | No clinical signs             | Day 15           | Bef.treat. |
|               | No clinical signs             | Day 15           | Aft.Treat. |
|               | No clinical signs             | Day 16 to day 28 |            |
|               | No clinical signs             | Day 29           | Bef.treat. |
|               | No clinical signs             | Day 29           | Aft.Treat. |
|               | No clinical signs             | Day 30 to day 57 |            |
|               | Sacrifice after reversibility | Day 57           |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No. :  
Group 2

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

|        |                                 |                  |            |
|--------|---------------------------------|------------------|------------|
| N30651 | No clinical signs               | Day 1            | Bef.treat. |
|        | No clinical signs               | Day 1            | Aft.Treat. |
|        | No clinical signs               | Day 2 to day 14  |            |
|        | No clinical signs               | Day 15           | Bef.treat. |
|        | No clinical signs               | Day 15           | Aft.Treat. |
|        | No clinical signs               | Day 16 to day 28 |            |
|        | No clinical signs               | Day 29           | Bef.treat. |
|        | No clinical signs               | Day 29           | Aft.Treat. |
|        | No clinical signs               | Day 30           | 24h        |
|        | No clinical signs               | Day 31           |            |
|        | Final sacrifice                 | Day 31           |            |
| .....  |                                 |                  |            |
| N30652 | No clinical signs               | Day 1            | Bef.treat. |
|        | No clinical signs               | Day 1            | Aft.Treat. |
|        | No clinical signs               | Day 2 to day 14  |            |
|        | No clinical signs               | Day 15           | Bef.treat. |
|        | No clinical signs               | Day 15           | Aft.Treat. |
|        | No clinical signs               | Day 16 to day 21 |            |
|        | Hematoma / interscapular region | Day 22           |            |
|        | No clinical signs               | Day 23 to day 28 |            |
|        | No clinical signs               | Day 29           | Bef.treat. |
|        | No clinical signs               | Day 29           | Aft.Treat. |
|        | No clinical signs               | Day 30           | 24h        |
|        | No clinical signs               | Day 31           |            |
|        | Final sacrifice                 | Day 31           |            |
| .....  |                                 |                  |            |
| N30653 | No clinical signs               | Day 1            | Bef.treat. |
|        | No clinical signs               | Day 1            | Aft.Treat. |
|        | No clinical signs               | Day 2 to day 14  |            |
|        | No clinical signs               | Day 15           | Bef.treat. |
|        | No clinical signs               | Day 15           | Aft.Treat. |
|        | No clinical signs               | Day 16 to day 28 |            |
|        | No clinical signs               | Day 29           | Bef.treat. |
|        | No clinical signs               | Day 29           | Aft.Treat. |
|        | No clinical signs               | Day 30           | 24h        |
|        | No clinical signs               | Day 31           |            |
|        | Final sacrifice                 | Day 31           |            |
| .....  |                                 |                  |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No. :  
Group 2

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

|           |                               |                  |            |
|-----------|-------------------------------|------------------|------------|
| N30654    | No clinical signs             | Day 1            | Bef.treat. |
|           | No clinical signs             | Day 1            | Aft.Treat. |
|           | No clinical signs             | Day 2 to day 14  |            |
|           | No clinical signs             | Day 15           | Bef.treat. |
|           | No clinical signs             | Day 15           | Aft.Treat. |
|           | No clinical signs             | Day 16 to day 28 |            |
|           | No clinical signs             | Day 29           | Bef.treat. |
|           | No clinical signs             | Day 29           | Aft.Treat. |
|           | No clinical signs             | Day 30           | 24h        |
|           | No clinical signs             | Day 31           |            |
|           | Final sacrifice               | Day 31           |            |
| <br>..... |                               |                  |            |
| N30655    | No clinical signs             | Day 1            | Bef.treat. |
|           | No clinical signs             | Day 1            | Aft.Treat. |
|           | No clinical signs             | Day 2 to day 14  |            |
|           | No clinical signs             | Day 15           | Bef.treat. |
|           | No clinical signs             | Day 15           | Aft.Treat. |
|           | No clinical signs             | Day 16 to day 28 |            |
|           | No clinical signs             | Day 29           | Bef.treat. |
|           | No clinical signs             | Day 29           | Aft.Treat. |
|           | No clinical signs             | Day 30 to day 31 |            |
|           | Final sacrifice               | Day 31           |            |
| <br>..... |                               |                  |            |
| N30656    | No clinical signs             | Day 1            | Bef.treat. |
|           | No clinical signs             | Day 1            | Aft.Treat. |
|           | No clinical signs             | Day 2 to day 4   |            |
|           | No clinical signs             | Day 6 to day 14  |            |
|           | No clinical signs             | Day 15           |            |
|           | No clinical signs             | Day 15           | Bef.treat. |
|           | No clinical signs             | Day 15           | Aft.Treat. |
|           | No clinical signs             | Day 16 to day 28 |            |
|           | No clinical signs             | Day 29           | Bef.treat. |
|           | No clinical signs             | Day 29           | Aft.Treat. |
|           | No clinical signs             | Day 30 to day 57 |            |
|           | Sacrifice after reversibility | Day 57           |            |
| <br>..... |                               |                  |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 2

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

--

|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30657 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 4   |            |
|        | No clinical signs             | Day 6 to day 14  |            |
|        | No clinical signs             | Day 15           |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16           |            |
|        | No clinical signs             | Day 18 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |
| N30658 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 4   |            |
|        | No clinical signs             | Day 6 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |
| N30659 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 4   |            |
|        | No clinical signs             | Day 6 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 2

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

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-- Animal Clinical history  
No.

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Latency

N30660 No clinical signs Day 1 Bef.treat.  
No clinical signs Day 1 Aft.Treat.  
No clinical signs Day 2 to day 4  
No clinical signs Day 6 to day 14  
No clinical signs Day 15 Bef.treat.  
No clinical signs Day 15 Aft.Treat.  
No clinical signs Day 16 to day 28  
No clinical signs Day 29 Bef.treat.  
No clinical signs Day 29 Aft.Treat.  
No clinical signs Day 30 to day 57  
Sacrifice after reversibility Day 57

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## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 3

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

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|        |                   |                  |            |
|--------|-------------------|------------------|------------|
| N30661 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |
| <hr/>  |                   |                  |            |
| N30662 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |
| <hr/>  |                   |                  |            |
| N30663 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 3

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30664 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 30 to day 31 | Aft.Treat. |
|        | Final sacrifice               | Day 31           |            |
| <hr/>  |                               |                  |            |
| N30665 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | Papule / Back                 | From day 30      | Aft.Treat. |
|        | Final sacrifice               | Day 31           |            |
| <hr/>  |                               |                  |            |
| N30666 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 4   |            |
|        | No clinical signs             | Day 6 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 30 to day 57 | Aft.Treat. |
|        | Sacrifice after reversibility | Day 57           |            |

#### CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No. :  
Group 3

Sex: Male  
Period: Days -14 to 57  
Principal animals + Recovery animals

-- Animal Clinical history Latency  
No.

|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30667 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 4   |            |
|        | No clinical signs             | Day 6 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 24 |            |
|        | Papule / Back                 | From day 25      |            |
|        | Sacrifice after reversibility | Day 57           |            |

|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30668 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 4   |            |
|        | No clinical signs             | Day 6 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | Papule / Back                 | Day 30 to day 43 |            |
|        | No clinical signs             | Day 44 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |

|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30669 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 4   |            |
|        | No clinical signs             | Day 6 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 3

Sex: Male

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

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|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30670 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 4   |            |
|        | No clinical signs             | Day 6 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 33 |            |
|        | Papule / Back                 | Day 34 to day 42 |            |
|        | No clinical signs             | Day 44 to day 50 |            |
|        | Papule / Back                 | Day 51 to day 52 |            |
|        | No clinical signs             | Day 53 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

|        |                   |                  |            |
|--------|-------------------|------------------|------------|
| N30711 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |
| .....  |                   |                  |            |
| N30712 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |
| .....  |                   |                  |            |
| N30713 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |
| .....  |                   |                  |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| - Animal No. | Clinical history | Latency |
|--------------|------------------|---------|
|--------------|------------------|---------|

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|        |  |   |  |
|--------|--|---|--|
| N30714 | No clinical signs<br>No clinical signs<br>Final sacrifice               | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 31<br>Day 31 | Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat. |
| N30715 | No clinical signs<br>No clinical signs<br>Final sacrifice               | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 31<br>Day 31 | Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat. |
| N30716 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57 | Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat. |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

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|        |  |   |  |
|--------|--|---|--|
| N30717 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57 | Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat. |
| N30718 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57 | Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat. |
| N30719 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57 | Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat.<br>Bef.treat.<br>Aft.Treat. |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

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-- Animal Clinical history Latency  
No.

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|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30720 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |

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## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No. :  
Group 2

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

|        |                   |                  |            |
|--------|-------------------|------------------|------------|
| N30721 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |
| .....  |                   |                  |            |
| N30722 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |
| .....  |                   |                  |            |
| N30723 | No clinical signs | Day 1            | Bef.treat. |
|        | No clinical signs | Day 1            | Aft.Treat. |
|        | No clinical signs | Day 2 to day 14  |            |
|        | No clinical signs | Day 15           | Bef.treat. |
|        | No clinical signs | Day 15           | Aft.Treat. |
|        | No clinical signs | Day 16 to day 28 |            |
|        | No clinical signs | Day 29           | Bef.treat. |
|        | No clinical signs | Day 29           | Aft.Treat. |
|        | No clinical signs | Day 30 to day 31 |            |
|        | Final sacrifice   | Day 31           |            |
| .....  |                   |                  |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No. :  
Group 2

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

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|        |                                 |                  |            |
|--------|---------------------------------|------------------|------------|
| N30724 | No clinical signs               | Day 1            | Bef.treat. |
|        | No clinical signs               | Day 1            | Aft.Treat. |
|        | No clinical signs               | Day 2 to day 14  |            |
|        | No clinical signs               | Day 15           | Bef.treat. |
|        | No clinical signs               | Day 15           | Aft.Treat. |
|        | No clinical signs               | Day 16 to day 26 |            |
|        | Papule / Back                   | From day 27      |            |
|        | Papule / Back                   | Day 29 to day 30 |            |
|        | Final sacrifice                 | Day 31           |            |
| .....  | .....                           | .....            | .....      |
| N30725 | No clinical signs               | Day 1            | Bef.treat. |
|        | No clinical signs               | Day 1            | Aft.Treat. |
|        | No clinical signs               | Day 2 to day 14  |            |
|        | No clinical signs               | Day 15           | Bef.treat. |
|        | No clinical signs               | Day 15           | Aft.Treat. |
|        | No clinical signs               | Day 16           |            |
|        | Hematoma / interscapular region | Day 17 to day 18 |            |
|        | No clinical signs               | Day 19 to day 28 |            |
|        | No clinical signs               | Day 29           | Bef.treat. |
|        | No clinical signs               | Day 29           | Aft.Treat. |
|        | No clinical signs               | Day 30 to day 31 |            |
|        | Final sacrifice                 | Day 31           |            |
| .....  | .....                           | .....            | .....      |
| N30726 | No clinical signs               | Day 1            | Bef.treat. |
|        | No clinical signs               | Day 1            | Aft.Treat. |
|        | No clinical signs               | Day 2 to day 14  |            |
|        | No clinical signs               | Day 15           | Bef.treat. |
|        | No clinical signs               | Day 15           | Aft.Treat. |
|        | No clinical signs               | Day 16 to day 28 |            |
|        | No clinical signs               | Day 29           | Bef.treat. |
|        | No clinical signs               | Day 29           | Aft.Treat. |
|        | No clinical signs               | Day 30 to day 57 |            |
|        | Sacrifice after reversibility   | Day 57           |            |
| .....  | .....                           | .....            | .....      |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 2

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| - Animal No. | Clinical history | Latency |
|--------------|------------------|---------|
|--------------|------------------|---------|

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|        |  |   |  |
|--------|--|---|--|
| N30727 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57 | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat. |
| N30728 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57 | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat. |
| N30729 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57 | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.                                 |

CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 2

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

-- Animal Clinical history  
No.

Latency

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|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30730 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 3

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

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|        |  |   |  |
|--------|--|---|--|
| N30731 | No clinical signs<br>No clinical signs<br>Final sacrifice   | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 31<br>Day 31                               | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat. |
| N30732 | No clinical signs<br>No clinical signs<br>No clinical signs<br>Hematoma / interscapular region<br>No clinical signs<br>No clinical signs<br>No clinical signs<br>No clinical signs<br>No clinical signs<br>No clinical signs<br>No clinical signs<br>Final sacrifice | Day 1<br>Day 1<br>Day 2 to day 10<br>Day 11 to day 13<br>Day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 31<br>Day 31 | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat. |
| N30733 | No clinical signs<br>No clinical signs<br>Final sacrifice   | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 31<br>Day 31                               | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.                                 |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 3

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| - Animal No. | Clinical history | Latency |
|--------------|------------------|---------|
|--------------|------------------|---------|

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|        |  |   |  |
|--------|--|---|--|
| N30734 | No clinical signs<br>No clinical signs<br>Final sacrifice               | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 31<br>Day 31 | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat. |
| N30735 | No clinical signs<br>No clinical signs<br>Final sacrifice               | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 31<br>Day 31 | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat. |
| N30736 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57 | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.                                 |

## CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No. :  
Group 3

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

| -- Animal No. | Clinical history | Latency |
|---------------|------------------|---------|
|---------------|------------------|---------|

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|        |   |  |  |
|--------|---|--|--|
| N30737 | No clinical signs<br>No clinical signs<br>Abnormal color / Reddish / right ear<br>Scabs / right ear<br>Sacrifice after reversibility | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 31<br>Day 32 to day 39<br>From day 35<br>Day 57 | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat. |
| N30738 | No clinical signs<br>No clinical signs<br>Papule / Back<br>Sacrifice after reversibility   | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 42<br>From day 43<br>Day 57                     | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.                                 |
| N30739 | No clinical signs<br>No clinical signs<br>Sacrifice after reversibility  | Day 1<br>Day 1<br>Day 2 to day 14<br>Day 15<br>Day 15<br>Day 16 to day 28<br>Day 29<br>Day 29<br>Day 30 to day 57<br>Day 57                                    | Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.<br><br>Bef.treat.<br>Aft.Treat.   |

CLINICAL HISTORY - INDIVIDUAL FINDINGS

Study No.:  
Group 3

Sex: Female

Period: Days -14 to 57

Principal animals + Recovery animals

- Animal Clinical history Latency  
No.

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|        |                               |                  |            |
|--------|-------------------------------|------------------|------------|
| N30740 | No clinical signs             | Day 1            | Bef.treat. |
|        | No clinical signs             | Day 1            | Aft.Treat. |
|        | No clinical signs             | Day 2 to day 14  |            |
|        | No clinical signs             | Day 15           | Bef.treat. |
|        | No clinical signs             | Day 15           | Aft.Treat. |
|        | No clinical signs             | Day 16 to day 28 |            |
|        | No clinical signs             | Day 29           | Bef.treat. |
|        | No clinical signs             | Day 29           | Aft.Treat. |
|        | No clinical signs             | Day 30 to day 57 |            |
|        | Sacrifice after reversibility | Day 57           |            |

6. Local reactions: individual findings

**Erythema and edema:**

- . 0: no observation

**Hematoma and induration:**

- . 0: no hematoma/induration,
- . 1: area  $\leq 1 \text{ cm}^2$ ,
- . 2: area  $> 1 \text{ cm}^2$  and  $\leq 2 \text{ cm}^2$

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Male

| Group  | Animal No. | Local reactions | Day            |               |                 |                 |                 |                 |                 |                 |                 |                 |                  |                  |                  |                  |
|--------|------------|-----------------|----------------|---------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|------------------|
|        |            |                 | Bef.<br>Site 1 | 3 h<br>Site 1 | Day 2<br>Site 1 | Day 3<br>Site 1 | Day 4<br>Site 1 | Day 5<br>Site 1 | Day 6<br>Site 1 | Day 7<br>Site 1 | Day 8<br>Site 1 | Day 9<br>Site 1 | Day 10<br>Site 1 | Day 11<br>Site 1 | Day 12<br>Site 1 | Day 13<br>Site 1 |
| N30641 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30642 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30643 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30644 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30645 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1      | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30646 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30647 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30648 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30649 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30650 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |

/ : No other local reactions  
 Bef.: Before administration  
 3 h: 3 hours after administration

### LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day            |               |                 |                 |                 |                 |                 |                 |                 |                 |                  |                  |                  |                  |
|--------|------------|-----------------|----------------|---------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|------------------|
|        |            |                 | Bef.<br>Site 1 | 3 h<br>Site 1 | Day 2<br>Site 1 | Day 3<br>Site 1 | Day 4<br>Site 1 | Day 5<br>Site 1 | Day 6<br>Site 1 | Day 7<br>Site 1 | Day 8<br>Site 1 | Day 9<br>Site 1 | Day 10<br>Site 1 | Day 11<br>Site 1 | Day 12<br>Site 1 | Day 13<br>Site 1 |
| N30651 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30652 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30653 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30654 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30655 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30656 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30657 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30658 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30659 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30660 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No.

Sex: Male

*f*: No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]  
 \* Control item (NaCl)  
 Sex: Male

| Group | Animal No. | Local reactions | Day 15 |        |        | Day 16 |        |        | Day 17 |        |        | Day 18 |        |        | Day 19 |        |        | Day 20 |        |        | Day 21 |        |  |
|-------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--|
|       |            |                 | Bef.   | Site 1 | Site 2 | 3 h    | Site 1 | Site 2 |  |
| 1     | N30641     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30642     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30643     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30644     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30645     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30646     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 1      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30647     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30648     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30649     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |
| 1     | N30650     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |  |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |  |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 15 |                  | Day 16 |                  | Day 17           |                  | Day 18           |                  | Day 19           |                  | Day 20           |                  | Day 21           |                  |
|--------|------------|-----------------|--------|------------------|--------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
|        |            |                 | Bef.   | Site 1<br>Site 2 | 3 h    | Site 1<br>Site 2 |
| N30651 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30652 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30653 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30654 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30655 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30656 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30657 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30658 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30659 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |
| N30660 | Erythema   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0      | 0                | 0      | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                | 0                |
|        | Other      | /               | /      | /                | /      | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                | /                |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 15 |                |               | Day 16 |        |        | Day 17 |        |        | Day 18 |        |        | Day 19 |        |        | Day 20 |        |   |
|--------|------------|-----------------|--------|----------------|---------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|---|
|        |            |                 | Site 1 | Bef.<br>Site 2 | 3 h<br>Site 2 | Site 1 | Site 2 |   |
| N30661 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 2              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30662 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | U               | U      | U              | U             | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30663 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30664 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30665 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30666 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 0              | 0             | 0      | 0      | 1      | 0      | 0      | 0      | 0      | 2      | 0      | 1      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30667 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30668 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30669 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |
| N30670 | Erythema   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Edema      | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Hematoma   | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Induration | 0               | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0 |
|        | Other      | /               | /      | /              | /             | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | / |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Male

| Group  | Animal No. | Local reactions | Day 22 |        | Day 23 |        | Day 24 |        | Day 25 |        | Day 26 |        | Day 27 |        | Day 28 |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 |
| N30641 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30642 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30643 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30644 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30645 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30646 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30647 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30648 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30649 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30650 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/: No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 22 |        | Day 23 |        | Day 24 |        | Day 25 |        | Day 26 |        | Day 27 |        | Day 28 |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 |
| N30651 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30652 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30653 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30654 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30655 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30656 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30657 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30658 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30659 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30660 | Erythema   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 3      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 22 |        | Day 23 |        | Day 24 |        | Day 25 |        | Day 26 |        | Day 27 |        | Day 28 |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 |
| N30661 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30662 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30663 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30664 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30665 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30666 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30667 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30668 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30669 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30670 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Control item (NaCl)

Sex: Male

| Group  | Animal No. | Local reactions | Day 29 |        |      |     | Day 30 |        |        | Day 31 |        |        |
|--------|------------|-----------------|--------|--------|------|-----|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Bef. | 3 h | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30641 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30642 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30643 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30644 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30645 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30646 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30647 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30648 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30649 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30650 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 29 |        |      |     | Day 30 |        |        | Day 31 |        |        |
|--------|------------|-----------------|--------|--------|------|-----|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Bef. | 3 h | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30651 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30652 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30653 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30654 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30655 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30656 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30657 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30658 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30659 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30660 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

~~05/05/2000~~

Sex: Male

| Group  | Animal No. | Local reactions | Day 29 |        |      |     | Day 30 |        |        | Day 31 |        |        |
|--------|------------|-----------------|--------|--------|------|-----|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Bef. | 3 h | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30661 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30662 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30663 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30664 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30665 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30666 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30667 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30668 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 1    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30669 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 2      | 0      | 0      | 2      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30670 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Male

| Group | Animal No. | Local reactions | Day 32 |        |        | Day 33 |        |        | Day 34 |        |        | Day 35 |        |        | Day 36 |        |        |
|-------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|       |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| 1     | N30646     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30647     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30648     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30649     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30650     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 32 |        |        | Day 33 |        |        | Day 34 |        |        | Day 35 |        |        | Day 36 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30656 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30657 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30658 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30659 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30660 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 32 |        |        | Day 33 |        |        | Day 34 |        |        | Day 35 |        |        | Day 36 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30666 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30667 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | U               | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | N30668     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 2      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30669 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30670 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Male

| Group | Animal No. | Local reactions | Day 37 |        |        | Day 38 |        |        | Day 39 |        |        | Day 40 |        |        | Day 41 |        |        |
|-------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|       |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| 1     | N30646     | Erythema        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30647     | Erythema        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | U      | C      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      |
|       |            | Induration      | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30648     | Erythema        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30649     | Erythema        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30650     | Erythema        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 37 |        |        | Day 38 |        |        | Day 39 |        |        | Day 40 |        |        | Day 41 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30656 | [REDACTED] | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30657 | [REDACTED] | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 2      | N30658     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30659 | [REDACTED] | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30660 | [REDACTED] | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 37 |        |        | Day 38 |        |        | Day 39 |        |        | Day 40 |        |        | Day 41 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30666 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30667 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | U               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | N30668     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30669 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30670 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Control item (NaCl)\*

Sex: Male

| Group  | Animal No. | Local reactions | Day 42 |        |        | Day 43 |        |        | Day 44 |        |        | Day 45 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30646 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30647 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30648 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30649 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30650 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/: No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group    | Animal No. | Local reactions | Day 42 |        |        | Day 43 |        |        | Day 44 |        |        | Day 45 |        |        |
|----------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|          |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30656   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30657   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 2 N30658 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30659   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30660   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

<sup>1</sup> Study No<sup>2</sup> [REDACTED]

Sex: Male

| Group  | Animal No. | Local reactions | Day 42 |        |        | Day 43 |        |        | Day 44 |        |        | Day 45 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30666 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30667 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | N30668     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30669 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30670 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Male

| Group | Animal No. | Local reactions | Day 46 |        |        | Day 47 |        |        | Day 48 |        |        | Day 49 |        |        | Day 50 |        |        | Day 51 |        |        |
|-------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|       |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| I     | N30646     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| I     | N30647     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| I     | N30648     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| I     | N30649     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| I     | N30650     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]  
Sex: Male

| Group    | Animal No. | Local reactions | Day 46 |        |        | Day 47 |        |        | Day 48 |        |        | Day 49 |        |        | Day 50 |        |        | Day 51 |        |        |
|----------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|          |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30651   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30652   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 2 N30653 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30654   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30655   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]

Sex: Male

| Group    | Animal No. | Local reactions | Day 46 |        |        | Day 47 |        |        | Day 48 |        |        | Day 49 |        |        | Day 50 |        |        | Day 51 |        |        |
|----------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|          |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30666   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30667   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3 N30668 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30669   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30670   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. **[REDACTED]**  
 Control item (NaCl)  
 Sex: Male

| Group    | Animal No. | Local reactions | Day 52 |        |        | Day 53 |        |        | Day 54 |        |        | Day 55 |        |        | Day 56 |        |        | Day 57 |        |        |
|----------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|          |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30646   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30647   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1 N30648 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30649   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30650   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]  
 Sex: Male

| Group    | Animal No. | Local reactions | Day 52 |        |        | Day 53 |        |        | Day 54 |        |        | Day 55 |        |        | Day 56 |        |        | Day 57 |        |        |
|----------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|          |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30651   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |
| N30652   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |
| 2 N30653 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |
| N30654   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |
| N30655   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |

/ : No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]  
Sex: Male

| Group  | Animal No  | Local reactions | Day 52 |        |        | Day 53 |        |        | Day 54 |        |        | Day 55 |        |        | Day 56 |        |        | Day 57 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30666 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30667 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30668 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30669 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30670 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ - No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Female

| Group | Animal No. | Local reactions | Day            |               |                 |                 |                 |                 |                 |                 |                 |                 |                  |                  |                  |                  |
|-------|------------|-----------------|----------------|---------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|------------------|
|       |            |                 | Bef.<br>Site 1 | 3 h<br>Site 1 | Day 2<br>Site 1 | Day 3<br>Site 1 | Day 4<br>Site 1 | Day 5<br>Site 1 | Day 6<br>Site 1 | Day 7<br>Site 1 | Day 8<br>Site 1 | Day 9<br>Site 1 | Day 10<br>Site 1 | Day 11<br>Site 1 | Day 12<br>Site 1 | Day 13<br>Site 1 |
| 1     | N30711     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30712     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30713     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 2               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30714     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30715     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30716     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30717     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30718     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 1             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30719     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| 1     | N30720     | Erythema        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Edema           | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Hematoma        | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Induration      | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|       |            | Other           | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

**Study No.**

**Sex: Females**

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

### LOCAL REACTIONS

Study No.

Sex: Female

| Group  | Animal No. | Local reactions | Day            |               |                 |                 |                 |                 |                 |                 |                 |                 |                 |                  |                  |                  |                  |
|--------|------------|-----------------|----------------|---------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|------------------|------------------|
|        |            |                 | Bef.<br>Site 1 | 3 h<br>Site 1 | Day 1<br>Site 1 | Day 2<br>Site 1 | Day 3<br>Site 1 | Day 4<br>Site 1 | Day 5<br>Site 1 | Day 6<br>Site 1 | Day 7<br>Site 1 | Day 8<br>Site 1 | Day 9<br>Site 1 | Day 10<br>Site 1 | Day 11<br>Site 1 | Day 12<br>Site 1 | Day 13<br>Site 1 |
| N30731 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
| N30732 | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
|        | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
| N30733 | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30734 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
| N30735 | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
|        | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
| N30736 | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30737 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
| N30738 | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
|        | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
| N30739 | Induration | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |
| N30740 | Erythema   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Edema      | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Hematoma   | 0               | 0              | 0             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Induration | 0               | 0              | 2             | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0               | 0                | 0                | 0                | 0                |
|        | Other      | /               | /              | /             | /               | /               | /               | /               | /               | /               | /               | /               | /               | /                | /                | /                | /                |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]  
 [REDACTED] (CL)  
 Sex: Female

| Group | Animal No. | Local reactions | Day 15 |     |        | Day 16 |        | Day 17 |        | Day 18 |        | Day 19 |        | Day 20 |        | Day 21 |        |
|-------|------------|-----------------|--------|-----|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|       |            |                 | Bef.   | 3 h | Site 1 | Site 2 | Site 2 | Site 1 | Site 2 |
| 1     | N30711     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30712     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      | U      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30713     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30714     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30715     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30716     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30717     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30718     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30719     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30720     | Erythema        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 15 |      |     | Day 16 |        | Day 17 |        | Day 18 |        | Day 19 |        | Day 20 |        | Day 21 |        |
|--------|------------|-----------------|--------|------|-----|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Bef. | 3 h | Site 1 | Site 2 |
| N30721 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30722 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30723 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30724 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30725 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30726 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30727 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30728 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30729 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30730 | Erythema   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group | Animal No. | Local reactions | Day 15 |      |     | Day 16 |        |        | Day 17 |        |        | Day 18 |        |        | Day 19 |        |        | Day 20 |        |        |        |
|-------|------------|-----------------|--------|------|-----|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|       |            |                 | Site 1 | Bef. | 3 h | Site 1 | Site 2 |
| 3     | N30731     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30732     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30733     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30734     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30735     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30736     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30737     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30738     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30739     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3     | N30740     | Erythema        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /    | /   | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/: No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Control item (NaCl)

Sex: Female

| Group | Animal No. | Local reactions | Day 22 |        | Day 23 |        | Day 24 |        | Day 25 |        | Day 26 |        | Day 27 |        | Day 28 |        |
|-------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|       |            |                 | Site 1 | Site 2 |
| 1     | N30711     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30712     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30713     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30714     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30715     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30716     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30717     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30718     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30719     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30720     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No.

Sex: Female

| Group  | Animal No. | Local reactions | Day 22 |        | Day 23 |        | Day 24 |        | Day 25 |        | Day 26 |        | Day 27 |        | Day 28 |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 |
| N30721 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30722 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30723 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30724 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30725 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30726 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30727 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30728 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30729 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30730 | Erythema   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | C      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 22 |        | Day 23 |        | Day 24 |        | Day 25 |        | Day 26 |        | Day 27 |        | Day 28 |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 |
| N30731 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| N30732 | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|        | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| N30733 | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30734 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| N30735 | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| N30736 | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30737 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| N30738 | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30739 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| N30740 | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Female

| Group  | Animal No. | Local reactions | Day 29 |        |      |     | Day 30 |        |        | Day 31 |        |        |
|--------|------------|-----------------|--------|--------|------|-----|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Bef. | 3 h | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30711 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30712 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30713 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30714 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30715 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30716 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30717 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30718 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30719 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30720 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 29 |        |      |     | Day 30 |        |        | Day 31 |        |        |
|--------|------------|-----------------|--------|--------|------|-----|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Bef. | 3 h | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30721 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30722 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30723 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30724 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 1    | 0   | 0      | 0      | 1      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30725 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30726 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30727 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30728 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30729 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |
| N30730 | Erythema   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0    | 0   | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /    | /   | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 29 |        |                |               | Day 30 |        |        | Day 31 |        |        |
|--------|------------|-----------------|--------|--------|----------------|---------------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Bef.<br>Site 3 | 3 h<br>Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30731 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30732 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30733 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30734 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30735 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| 3      | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30736 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30737 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30738 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30739 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 1              | 0             | 0      | 0      | 1      | 0      | 0      | 1      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |
| N30740 | Erythema   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0              | 0             | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /              | /             | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

Bef.: Before administration

3 h: 3 hours after administration

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Female

| Group | Animal No. | Local reactions | Day 32 |        |        | Day 33 |        |        | Day 34 |        |        | Day 35 |        |        | Day 36 |        |        |
|-------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|       |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| I     | N30716     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|       | N30717     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|       | N30718     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|       | N30719     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|       | N30720     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 32 |        |        | Day 33 |        |        | Day 34 |        |        | Day 35 |        |        | Day 36 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30726 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30727 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 2      | N30728     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30729 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30730 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 32 |        |        | Day 33 |        |        | Day 34 |        |        | Day 35 |        |        | Day 36 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30736 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30737 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | N30738     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30739 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 1      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30740 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Female

| Group  | Animal No. | Local reactions | Day 37 |        |        | Day 38 |        |        | Day 39 |        |        | Day 40 |        |        | Day 41 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30716 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30717 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1      | N30718     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30719 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30720 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]  
Sex: Female

| Group  | Animal No. | Local reactions | Day 37 |        |        | Day 38 |        |        | Day 39 |        |        | Day 40 |        |        | Day 41 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30726 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30727 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 2      | N30728     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30729 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30730 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 37 |        |        | Day 38 |        |        | Day 39 |        |        | Day 40 |        |        | Day 41 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30736 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30737 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | N30738     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30739 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30740 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Control item (NaCl)

Sex: Female

| Group  | Animal No. | Local reactions | Day 42 |        |        | Day 43 |        |        | Day 44 |        |        | Day 45 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30716 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30717 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1      | N30718     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30719 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30720 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 42 |        |        | Day 43 |        |        | Day 44 |        |        | Day 45 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30726 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30727 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30728 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30729 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30730 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 42 |        |        | Day 43 |        |        | Day 44 |        |        | Day 45 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30736 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30737 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | N30738     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30739 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30740 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Female

| Group | Animal No. | Local reactions | Day 46 |        |        | Day 47 |        |        | Day 48 |        |        | Day 49 |        |        | Day 50 |        |        | Day 51 |        |        |
|-------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|       |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| 1     | N30716     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|       |            | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| 1     | N30717     | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|       |            | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| 1     | N30718     | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|       |            | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| 1     | N30719     | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
|       |            | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1     | N30720     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Edema           | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Hematoma        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Induration      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|       |            | Other           | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

Study No. 46501 TCL

Sex: Female

| Group    | Animal No. | Local reactions | Day 46 |        |        | Day 47 |        |        | Day 48 |        |        | Day 49 |        |        | Day 50 |        |        | Day 51 |        |        |
|----------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|          |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30726   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30727   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 2 N30728 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30729   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30730   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

\* Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 46 |        |        | Day 47 |        |        | Day 48 |        |        | Day 49 |        |        | Day 50 |        |        | Day 51 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30736 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30737 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 3      | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | P      |
| N30738 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30739 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30740 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

P: Presence (site not documented)

## LOCAL REACTIONS

Study No. [REDACTED]  
 Control item (NaCl)  
 Sex: Female

| Group  | Animal No. | Local reactions | Day 52 |        |        | Day 53 |        |        | Day 54 |        |        | Day 55 |        |        | Day 56 |        |        | Day 57 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30716 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30717 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 1      | N30718     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30719 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30720 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/: No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group    | Animal No. | Local reactions | Day 52 |        |        | Day 53 |        |        | Day 54 |        |        | Day 55 |        |        | Day 56 |        |        | Day 57 |        |        |
|----------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|          |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30726   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30727   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| 2 N30728 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30729   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |
| N30730   | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|          | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |

/ : No other local reactions

### LOCAL REACTIONS

Study No. [REDACTED]

Sex: Female

| Group  | Animal No. | Local reactions | Day 52 |        |        | Day 53 |        |        | Day 54 |        |        | Day 55 |        |        | Day 56 |        |        | Day 57 |        |        |
|--------|------------|-----------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|        |            |                 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 | Site 1 | Site 2 | Site 3 |
| N30736 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |
| N30737 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |
| 3      | N30738     | Erythema        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |
| N30739 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |
| N30740 | Erythema   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Edema      | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Hematoma   | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Induration | 0               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|        | Other      | /               | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      | /      |        |

/ : No other local reactions

7. Body weight: individual values

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

| Day        | -14  | -7   | 1    | 2    | 5     | 8     | 11    | 15    | 16    | 19    |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30641     | 2375 | 2705 | 2930 | 2915 | 2955  | 3085  | 3180  | 3325  | 3300  | 3365  |
| N30642     | 2440 | 2600 | 2770 | 2760 | 2795  | 2895  | 2995  | 3070  | 3060  | 3155  |
| N30643     | 2460 | 2665 | 2870 | 2890 | 2740  | 2995  | 3110  | 3080  | 3220  | 3315  |
| N30644     | 2410 | 2650 | 2755 | 2790 | 2835  | 2935  | 2995  | 3060  | 3075  | 3160  |
| N30645     | 2475 | 2580 | 2760 | 2770 | 2770  | 2870  | 2930  | 3020  | 3005  | 3090  |
| N30646     | 2470 | 2575 | 2725 | 2715 | 2720  | 2800  | 2850  | 2900  | 2925  | 2970  |
| N30647     | 2470 | 2640 | 2825 | 2830 | 2835  | 2945  | 3025  | 3110  | 3105  | 3175  |
| N30648     | 2560 | 2705 | 2890 | 2910 | 2940  | 3040  | 3095  | 3150  | 3160  | 3255  |
| N30649     | 2535 | 2750 | 2975 | 2950 | 2990  | 3080  | 3175  | 3290  | 3290  | 3380  |
| N30650     | 2430 | 2790 | 2980 | 2995 | 3035  | 3115  | 3185  | 3265  | 3260  | 3340  |
| Mean       | 2463 | 2666 | 2848 | 2853 | 2862  | 2976  | 3054  | 3127  | 3140  | 3221  |
| SD         | 54.8 | 71.8 | 94.7 | 92.6 | 110.8 | 104.3 | 114.2 | 132.7 | 127.2 | 133.6 |

Group 2

Sex: Male

Principal animals + Recovery animals

| -- Day        | -14   | -7   | 1     | 2     | 5     | 8     | 11    | 15    | 16    |       |
|---------------|-------|------|-------|-------|-------|-------|-------|-------|-------|-------|
| 19 Animal No. |       |      |       |       |       |       |       |       |       |       |
| <hr/>         |       |      |       |       |       |       |       |       |       |       |
| N30651        | 2275  | 2515 | 2655  | 2660  | 2690  | 2760  | 2850  | 2945  | 2910  | 3040  |
| N30652        | 2450  | 2520 | 2635  | 2640  | 2685  | 2730  | 2820  | 2865  | 2840  | 2885  |
| N30653        | 2440  | 2545 | 2700  | 2665  | 2755  | 2810  | 2905  | 2950  | 2930  | 3005  |
| N30654        | 2415  | 2605 | 2780  | 2770  | 2850  | 2930  | 3020  | 3105  | 3050  | 3150  |
| N30655        | 2445  | 2520 | 2605  | 2635  | 2615  | 2695  | 2735  | 2820  | 2780  | 2835  |
| N30656        | 2510  | 2585 | 2695  | 2705  | 2770  | 2830  | 2920  | 3000  | 2965  | 3040  |
| N30657        | 2175  | 2615 | 2820  | 2780  | 2870  | 2945  | 3005  | 3065  | 3005  | 3105  |
| N30658        | 2525  | 2620 | 2790  | 2795  | 2815  | 2855  | 2930  | 2995  | 3015  | 3060  |
| N30659        | 2555  | 2710 | 2900  | 2935  | 2960  | 3100  | 3175  | 3265  | 3265  | 3325  |
| N30660        | 2595  | 2740 | 2875  | 2905  | 2930  | 3005  | 3095  | 3175  | 3190  | 3210  |
| Mean          | 2439  | 2598 | 2746  | 2749  | 2794  | 2866  | 2946  | 3019  | 2995  | 3066  |
| SD            | 128.0 | 78.6 | 102.3 | 107.6 | 111.7 | 128.2 | 131.6 | 137.0 | 148.0 | 144.4 |

BODY WEIGHT  
(g)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

|               | -14   | -7    | 1     | 2     | 5     | 8     | 11    | 15    | 16    |
|---------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Day           |       |       |       |       |       |       |       |       |       |
| 19 Animal No. |       |       |       |       |       |       |       |       |       |
| --            |       |       |       |       |       |       |       |       |       |
| N30661        | 2330  | 2445  | 2540  | 2545  | 2575  | 2610  | 2715  | 2775  | 2760  |
| N30662        | 2255  | 2450  | 2615  | 2580  | 2625  | 2715  | 2790  | 2875  | 2790  |
| N30663        | 2395  | 2540  | 2630  | 2635  | 2670  | 2745  | 2815  | 2880  | 2815  |
| N30664        | 2280  | 2640  | 2795  | 2810  | 2835  | 2955  | 3025  | 3135  | 3095  |
| N30665        | 2505  | 2710  | 2875  | 2885  | 2900  | 3010  | 3100  | 3155  | 3085  |
| N30666        | 2385  | 2490  | 2600  | 2645  | 2650  | 2740  | 2775  | 2870  | 2845  |
| N30667        | 2565  | 2680  | 2815  | 2840  | 2845  | 2920  | 2980  | 3055  | 3015  |
| N30668        | 2535  | 2650  | 2830  | 2800  | 2865  | 2915  | 3015  | 3100  | 3025  |
| N30669        | 2530  | 2690  | 2875  | 2825  | 2905  | 2975  | 3035  | 3105  | 3025  |
| N30670        | 2630  | 2820  | 2930  | 2940  | 2980  | 3060  | 3175  | 3290  | 3185  |
| Mean          | 2441  | 2612  | 2751  | 2751  | 2785  | 2865  | 2943  | 3024  | 2964  |
| SD            | 129.1 | 124.7 | 139.7 | 137.2 | 141.1 | 149.9 | 156.4 | 164.0 | 148.7 |
|               |       |       |       |       |       |       |       |       | 190.9 |

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

| Day        | 22    | 25    | 29    | 30    |
|------------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |
| N30641     | 3440  | 3495  | 3585  | 3590  |
| N30642     | 3260  | 3280  | 3380  | 3350  |
| N30643     | 3410  | 3435  | 3495  | 3500  |
| N30644     | 3215  | 3265  | 3385  | 3400  |
| N30645     | 3125  | 3145  | 3230  | 3215  |
| N30646     | 3020  | 3045  | 3115  | 3095  |
| N30647     | 3230  | 3270  | 3360  | 3370  |
| N30648     | 3260  | 3285  | 3385  | 3395  |
| N30649     | 3455  | 3510  | 3595  | 3580  |
| N30650     | 3395  | 3445  | 3535  | 3530  |
| Mean       | 3281  | 3318  | 3407  | 3403  |
| SD         | 143.6 | 152.8 | 153.4 | 158.5 |

Group 2

Sex: Male

Principal animals + Recovery animals

| Day        | 22    | 25    | 29    | 30    |
|------------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |
| --         |       |       |       |       |
| N30651     | 3075  | 3115  | 3220  | 3220  |
| N30652     | 2950  | 2980  | 3065  | 3040  |
| N30653     | 3035  | 3075  | 3145  | 3125  |
| N30654     | 3240  | 3260  | 3355  | 3400  |
| N30655     | 2905  | 2905  | 2965  | 2965  |
| N30656     | 3115  | 3145  | 3250  | 3240  |
| N30657     | 3180  | 3185  | 3250  | 3265  |
| N30658     | 3120  | 3155  | 3225  | 3215  |
| N30659     | 3415  | 3425  | 3480  | 3495  |
| N30660     | 3210  | 3290  | 3345  | 3390  |
| Mean       | 3125  | 3154  | 3230  | 3236  |
| SD         | 148.1 | 150.6 | 147.9 | 164.5 |

BODY WEIGHT  
(g)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

-----  
-- Day            22        25        29        30  
Animal No.

---  
N30661      2895      2950      3035      3030  
N30662      2960      3020      3120      3110  
N30663      2965      2965      3050      3015  
N30664      3285      3355      3430      3420  
N30665      3240      3340      3430      3380  
N30666      2955      3025      3010      3110  
N30667      3085      3105      3155      3160  
N30668      3200      3270      3345      3305  
N30669      3210      3305      3325      3315  
N30670      3410      3500      3570      3590

-----  
Mean      3121      3184      3247      3244  
SD        172.9     193.4     197.6     188.3

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

| Day        | -14   | -7    | 1     | 2     | 5     | 8     | 11    | 15    | 16    | 19    |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| N30711     | 2315  | 2455  | 2700  | 2705  | 2780  | 2915  | 2985  | 3120  | 3120  | 3230  |
| N30712     | 2455  | 2695  | 2865  | 2905  | 2955  | 3000  | 3080  | 3170  | 3185  | 3320  |
| N30713     | 2405  | 2605  | 2830  | 2855  | 2850  | 2970  | 3030  | 3130  | 3155  | 3235  |
| N30714     | 2475  | 2695  | 2915  | 2935  | 2970  | 3075  | 3170  | 3300  | 3305  | 3345  |
| N30715     | 2530  | 2720  | 2930  | 2935  | 2980  | 3060  | 3085  | 3230  | 3285  | 3385  |
| N30716     | 2695  | 2870  | 3170  | 3135  | 3245  | 3360  | 3445  | 3565  | 3595  | 3685  |
| N30717     | 2710  | 2805  | 3020  | 3055  | 3030  | 3190  | 3200  | 3305  | 3315  | 3430  |
| N30718     | 2715  | 2820  | 3050  | 3110  | 3095  | 3235  | 3300  | 3425  | 3460  | 3515  |
| N30719     | 2635  | 2800  | 3035  | 3025  | 3065  | 3145  | 3225  | 3300  | 3310  | 3395  |
| N30720     | 2680  | 2930  | 3185  | 3195  | 3260  | 3360  | 3415  | 3545  | 3580  | 3640  |
| Mean       | 2562  | 2740  | 2970  | 2986  | 3023  | 3131  | 3194  | 3309  | 3331  | 3418  |
| SD         | 144.5 | 137.9 | 151.8 | 147.4 | 153.0 | 155.4 | 156.4 | 159.2 | 166.2 | 154.7 |

Group 2

Sex: Female

Principal animals + Recovery animals

| -- Day        | -14   | -7    | 1     | 2     | 5     | 8     | 11    | 15    | 16    |       |
|---------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 19 Animal No. |       |       |       |       |       |       |       |       |       |       |
| N30721        | 2325  | 2505  | 2730  | 2710  | 2790  | 2875  | 2980  | 3160  | 3115  | 3250  |
| N30722        | 2310  | 2560  | 2790  | 2785  | 2835  | 2970  | 3045  | 3210  | 3175  | 3275  |
| N30723        | 2445  | 2625  | 2835  | 2825  | 2885  | 2955  | 3075  | 3130  | 3070  | 3205  |
| N30724        | 2605  | 2805  | 3130  | 3140  | 3195  | 3315  | 3385  | 3535  | 3590  | 3750  |
| N30725        | 2610  | 2780  | 3095  | 3120  | 3215  | 3330  | 3405  | 3555  | 3575  | 3775  |
| N30726        | 2505  | 2700  | 2800  | 2775  | 2835  | 2920  | 2985  | 3055  | 3090  | 3175  |
| N30727        | 2550  | 2785  | 3010  | 2995  | 2920  | 3100  | 3215  | 3375  | 3330  | 3455  |
| N30728        | 2660  | 3040  | 3225  | 3235  | 3350  | 3430  | 3550  | 3645  | 3705  | 3825  |
| N30729        | 2690  | 2875  | 3060  | 3010  | 2960  | 3145  | 3230  | 3325  | 3305  | 3405  |
| N30730        | 2635  | 2730  | 2955  | 2965  | 3010  | 3130  | 3250  | 3310  | 3340  | 3480  |
| Mean          | 2534  | 2741  | 2963  | 2956  | 3000  | 3117  | 3212  | 3330  | 3330  | 3460  |
| SD            | 135.0 | 155.9 | 167.6 | 177.3 | 190.5 | 191.2 | 193.0 | 198.1 | 227.2 | 246.0 |

BODY WEIGHT  
(g)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

| Day        | -14   | -7    | 1     | 2     | 5     | 8     | 11    | 15    | 16    | 19    |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| <hr/>      |       |       |       |       |       |       |       |       |       |       |
| N30731     | 2295  | 2515  | 2725  | 2690  | 2750  | 2870  | 2930  | 3035  | 3060  | 3135  |
| N30732     | 2335  | 2530  | 2685  | 2675  | 2760  | 2855  | 2955  | 3005  | 3020  | 3080  |
| N30733     | 2485  | 2720  | 2860  | 2850  | 2875  | 2945  | 2995  | 3035  | 3055  | 3080  |
| N30734     | 2465  | 2660  | 2910  | 2900  | 2955  | 3070  | 3115  | 3245  | 3225  | 3270  |
| N30735     | 2535  | 2705  | 2960  | 2920  | 2970  | 3105  | 3185  | 3350  | 3310  | 3355  |
| N30736     | 2455  | 2650  | 2870  | 2815  | 2930  | 2990  | 3055  | 3135  | 3145  | 3220  |
| N30737     | 2620  | 2795  | 2980  | 2970  | 3060  | 3135  | 3225  | 3320  | 3365  | 3445  |
| N30738     | 2655  | 2855  | 3020  | 3025  | 3140  | 3190  | 3270  | 3445  | 3435  | 3510  |
| N30739     | 2635  | 2835  | 3025  | 3000  | 3110  | 3225  | 3330  | 3475  | 3430  | 3600  |
| N30740     | 2720  | 2845  | 3065  | 3075  | 3125  | 3250  | 3325  | 3450  | 3430  | 3500  |
| Mean       | 2520  | 2711  | 2910  | 2892  | 2968  | 3064  | 3139  | 3250  | 3248  | 3320  |
| SD         | 139.4 | 124.2 | 127.2 | 135.5 | 143.0 | 143.0 | 150.4 | 185.4 | 168.1 | 190.2 |

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BODY WEIGHT  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

| Day        | 22    | 25    | 29    | 30    |
|------------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |
| N30711     | 3325  | 3390  | 3490  | 3475  |
| N30712     | 3435  | 3500  | 3580  | 3570  |
| N30713     | 3295  | 3365  | 3435  | 3420  |
| N30714     | 3515  | 3585  | 3665  | 3670  |
| N30715     | 3495  | 3565  | 3610  | 3640  |
| N30716     | 3765  | 3855  | 3975  | 3945  |
| N30717     | 3505  | 3585  | 3630  | 3665  |
| N30718     | 3595  | 3710  | 3755  | 3735  |
| N30719     | 3500  | 3550  | 3615  | 3620  |
| N30720     | 3775  | 3860  | 3980  | 3925  |
| Mean       | 3521  | 3597  | 3674  | 3667  |
| SD         | 159.1 | 169.3 | 182.6 | 169.5 |

Group 2

Sex: Female

Principal animals + Recovery animals

| -- Day     | 22    | 25    | 29    | 30    |
|------------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |
| --         |       |       |       |       |
| N30721     | 3320  | 3430  | 3455  | 3465  |
| N30722     | 3365  | 3440  | 3535  | 3525  |
| N30723     | 3235  | 3340  | 3375  | 3370  |
| N30724     | 3795  | 3860  | 3935  | 3950  |
| N30725     | 3845  | 3985  | 4050  | 4055  |
| N30726     | 3220  | 3300  | 3385  | 3390  |
| N30727     | 3540  | 3575  | 3670  | 3700  |
| N30728     | 3895  | 4030  | 4085  | 4110  |
| N30729     | 3455  | 3525  | 3620  | 3600  |
| N30730     | 3495  | 3660  | 3700  | 3705  |
| Mean       | 3517  | 3615  | 3681  | 3687  |
| SD         | 249.9 | 262.6 | 262.8 | 269.9 |

BODY WEIGHT  
(g)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

-----  
-- Day            22        25        29        30  
Animal No.

-----  
-  
N30731      3280      3315      3400      3400  
N30732      3145      3210      3195      3215  
N30733      3145      3200      3180      3200  
N30734      3375      3455      3470      3505  
N30735      3495      3455      3575      3555  
N30736      3280      3320      3420      3425  
N30737      3520      3605      3660      3670  
N30738      3645      3700      3725      3745  
N30739      3720      3830      3930      3955  
N30740      3590      3625      3710      3730

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Mean      3420      3472      3527      3540  
SD        204.8     214.0     239.6     241.0

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

| Day        | -14  | -7   | 1     | 2     | 5     | 8     | 11    | 15    | 16    | 19    |
|------------|------|------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |       |       |       |       |       |       |       |       |
| N30646     | 2470 | 2575 | 2725  | 2715  | 2720  | 2800  | 2850  | 2900  | 2925  | 2970  |
| N30647     | 2470 | 2640 | 2825  | 2830  | 2835  | 2945  | 3025  | 3110  | 3105  | 3175  |
| N30648     | 2560 | 2705 | 2890  | 2910  | 2940  | 3040  | 3095  | 3150  | 3160  | 3255  |
| N30649     | 2535 | 2750 | 2975  | 2950  | 2990  | 3080  | 3175  | 3290  | 3290  | 3380  |
| N30650     | 2430 | 2790 | 2980  | 2995  | 3035  | 3115  | 3185  | 3265  | 3260  | 3340  |
| Mean       | 2493 | 2692 | 2879  | 2880  | 2904  | 2996  | 3066  | 3143  | 3148  | 3224  |
| SD         | 53.1 | 85.9 | 107.4 | 110.4 | 127.0 | 126.7 | 137.1 | 155.5 | 145.3 | 162.5 |

Group 2

Sex: Male

Recovery animals

| -- Day        | -14   | -7   | 1    | 2    | 5    | 8     | 11    | 15    | 16    |       |
|---------------|-------|------|------|------|------|-------|-------|-------|-------|-------|
| 19 Animal No. |       |      |      |      |      |       |       |       |       |       |
| N30656        | 2510  | 2585 | 2695 | 2705 | 2770 | 2830  | 2920  | 3000  | 2965  | 3040  |
| N30657        | 2175  | 2615 | 2820 | 2780 | 2870 | 2945  | 3005  | 3065  | 3005  | 3105  |
| N30658        | 2525  | 2620 | 2790 | 2795 | 2815 | 2855  | 2930  | 2995  | 3015  | 3060  |
| N30659        | 2555  | 2710 | 2900 | 2935 | 2960 | 3100  | 3175  | 3265  | 3265  | 3325  |
| N30660        | 2595  | 2740 | 2875 | 2905 | 2930 | 3005  | 3095  | 3175  | 3190  | 3210  |
| Mean          | 2472  | 2654 | 2816 | 2824 | 2869 | 2947  | 3025  | 3100  | 3088  | 3148  |
| SD            | 169.2 | 67.0 | 80.4 | 94.6 | 78.6 | 110.6 | 109.4 | 117.4 | 131.4 | 118.8 |

Group 3

Sex: Male

Recovery animals

| -- Day        | -14  | -7    | 1     | 2     | 5     | 8     | 11    | 15    | 16    |       |
|---------------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 19 Animal No. |      |       |       |       |       |       |       |       |       |       |
| N30666        | 2385 | 2490  | 2600  | 2645  | 2650  | 2740  | 2775  | 2870  | 2845  | 2915  |
| N30667        | 2565 | 2680  | 2815  | 2840  | 2845  | 2920  | 2980  | 3055  | 3015  | 3035  |
| N30668        | 2535 | 2650  | 2830  | 2800  | 2865  | 2915  | 3015  | 3100  | 3025  | 3140  |
| N30669        | 2530 | 2690  | 2875  | 2825  | 2905  | 2975  | 3035  | 3105  | 3025  | 3145  |
| N30670        | 2630 | 2820  | 2930  | 2940  | 2980  | 3060  | 3175  | 3290  | 3185  | 3365  |
| Mean          | 2529 | 2666  | 2810  | 2810  | 2849  | 2922  | 2996  | 3084  | 3019  | 3120  |
| SD            | 89.8 | 118.0 | 125.6 | 106.5 | 122.6 | 117.3 | 144.1 | 149.8 | 120.3 | 166.1 |

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

| Day        | 22    | 25    | 29    | 30    | 33    | 36    | 39    | 43    | 46    | 50    |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| N30646     | 3020  | 3045  | 3115  | 3095  | 3100  | 3125  | 3215  | 3250  | 3300  | 3350  |
| N30647     | 3230  | 3270  | 3360  | 3370  | 3340  | 3425  | 3475  | 3530  | 3605  | 3615  |
| N30648     | 3260  | 3285  | 3385  | 3395  | 3375  | 3440  | 3515  | 3505  | 3520  | 3645  |
| N30649     | 3455  | 3510  | 3595  | 3580  | 3555  | 3655  | 3745  | 3800  | 3875  | 3935  |
| N30650     | 3395  | 3445  | 3535  | 3530  | 3535  | 3590  | 3665  | 3715  | 3770  | 3790  |
| Mean       | 3272  | 3311  | 3398  | 3394  | 3381  | 3447  | 3523  | 3560  | 3614  | 3667  |
| SD         | 168.8 | 180.7 | 186.6 | 189.1 | 183.5 | 204.9 | 204.1 | 213.1 | 223.6 | 218.3 |

Group 2

Sex: Male

Recovery animals

| -- Day        | 22    | 25    | 29    | 30    | 33    | 36    | 39    | 43    | 46    |      |
|---------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|
| 50 Animal No. |       |       |       |       |       |       |       |       |       |      |
| --            |       |       |       |       |       |       |       |       |       |      |
| N30656        | 3115  | 3145  | 3250  | 3240  | 3235  | 3305  | 3350  | 3455  | 3500  | 3595 |
| N30657        | 3180  | 3185  | 3250  | 3265  | 3225  | 3300  | 3325  | 3380  | 3410  | 3480 |
| N30658        | 3120  | 3155  | 3225  | 3215  | 3200  | 3230  | 3295  | 3345  | 3420  | 3485 |
| N30659        | 3415  | 3425  | 3480  | 3495  | 3485  | 3560  | 3625  | 3690  | 3765  | 3670 |
| N30660        | 3210  | 3290  | 3345  | 3390  | 3430  | 3470  | 3550  | 3630  | 3675  | 3690 |
| Mean          | 3208  | 3240  | 3310  | 3321  | 3315  | 3373  | 3429  | 3500  | 3554  | 3584 |
| SD            | 122.5 | 118.3 | 105.5 | 118.3 | 132.1 | 136.7 | 148.4 | 152.8 | 158.7 | 99.2 |

Group 3

Sex: Male

Recovery animals

| -- Day        | 22    | 25    | 29    | 30    | 33    | 36    | 39    | 43    | 46    |       |
|---------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 50 Animal No. |       |       |       |       |       |       |       |       |       |       |
| --            |       |       |       |       |       |       |       |       |       |       |
| N30666        | 2955  | 3025  | 3010  | 3110  | 3085  | 3150  | 3225  | 3285  | 3330  | 3430  |
| N30667        | 3085  | 3105  | 3155  | 3160  | 3155  | 3195  | 3250  | 3325  | 3345  | 3325  |
| N30668        | 3200  | 3270  | 3345  | 3305  | 3315  | 3390  | 3455  | 3510  | 3585  | 3665  |
| N30669        | 3210  | 3305  | 3325  | 3315  | 3415  | 3440  | 3505  | 3590  | 3700  | 3745  |
| N30670        | 3410  | 3500  | 3570  | 3590  | 3555  | 3650  | 3690  | 3790  | 3865  | 3935  |
| Mean          | 3172  | 3241  | 3281  | 3296  | 3305  | 3365  | 3425  | 3500  | 3565  | 3620  |
| SD            | 168.5 | 185.2 | 211.5 | 187.1 | 190.8 | 201.6 | 192.5 | 205.6 | 230.4 | 244.9 |

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

-----  
Day            53        56  
Animal No.

-----  
N30646      3395      3435  
N30647      3685      3735  
N30648      3680      3685  
N30649      4000      4050  
N30650      3845      3920

-----  
Mean          3721      3765  
SD            225.0     235.3

Group 2

Sex: Male

Recovery animals

-----  
-- Day            53        56  
Animal No.

-----  
--  
N30656      3620      3640  
N30657      3510      3510  
N30658      3485      3490  
N30659      3850      3885  
N30660      3780      3825

-----  
Mean          3649      3670  
SD            161.7     179.7

Group 3

Sex: Male

Recovery animals

-----  
-- Day            53        56  
Animal No.

-----  
--  
N30666      3465      3535  
N30667      3450      3435  
N30668      3675      3750  
N30669      3725      3800  
N30670      3985      4050

-----  
Mean          3660      3714  
SD            219.2     240.6

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

| Day        | -14  | -7   | 1    | 2    | 5     | 8    | 11    | 15    | 16    | 19    |
|------------|------|------|------|------|-------|------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |      |       |       |       |       |
| N30716     | 2695 | 2870 | 3170 | 3135 | 3245  | 3360 | 3445  | 3565  | 3595  | 3685  |
| N30717     | 2710 | 2805 | 3020 | 3055 | 3030  | 3190 | 3200  | 3305  | 3315  | 3430  |
| N30718     | 2715 | 2820 | 3050 | 3110 | 3095  | 3235 | 3300  | 3425  | 3460  | 3515  |
| N30719     | 2635 | 2800 | 3035 | 3025 | 3065  | 3145 | 3225  | 3300  | 3310  | 3395  |
| N30720     | 2680 | 2930 | 3185 | 3195 | 3260  | 3360 | 3415  | 3545  | 3580  | 3640  |
| Mean       | 2687 | 2845 | 3092 | 3104 | 3139  | 3258 | 3317  | 3428  | 3452  | 3533  |
| SD         | 32.1 | 55.0 | 78.9 | 66.9 | 106.3 | 98.4 | 110.0 | 126.5 | 137.7 | 127.0 |

Group 2

Sex: Female

Recovery animals

| Day        | -14  | -7    | 1     | 2     | 5     | 8     | 11    | 15    | 16    | 19    |
|------------|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |       |       |       |       |       |       |       |       |       |
| -          |      |       |       |       |       |       |       |       |       |       |
| N30726     | 2505 | 2700  | 2800  | 2775  | 2835  | 2920  | 2985  | 3055  | 3090  | 3175  |
| N30727     | 2550 | 2785  | 3010  | 2995  | 2920  | 3100  | 3215  | 3375  | 3330  | 3455  |
| N30728     | 2660 | 3040  | 3225  | 3235  | 3350  | 3430  | 3550  | 3645  | 3705  | 3825  |
| N30729     | 2690 | 2875  | 3060  | 3010  | 2960  | 3145  | 3230  | 3325  | 3305  | 3405  |
| N30730     | 2635 | 2730  | 2955  | 2965  | 3010  | 3130  | 3250  | 3310  | 3340  | 3480  |
| Mean       | 2608 | 2826  | 3010  | 2996  | 3015  | 3145  | 3246  | 3342  | 3354  | 3468  |
| SD         | 77.7 | 136.9 | 154.8 | 163.6 | 197.9 | 183.1 | 201.1 | 210.1 | 221.4 | 233.2 |

Group 3

Sex: Female

Recovery animals

| -- Day        | -14  | -7   | 1    | 2    | 5    | 8     | 11    | 15    | 16    |       |
|---------------|------|------|------|------|------|-------|-------|-------|-------|-------|
| 19 Animal No. |      |      |      |      |      |       |       |       |       |       |
| --            |      |      |      |      |      |       |       |       |       |       |
| N30736        | 2455 | 2650 | 2870 | 2815 | 2930 | 2990  | 3055  | 3135  | 3145  | 3220  |
| N30737        | 2620 | 2795 | 2980 | 2970 | 3060 | 3135  | 3225  | 3320  | 3365  | 3445  |
| N30738        | 2655 | 2855 | 3020 | 3025 | 3140 | 3190  | 3270  | 3445  | 3435  | 3510  |
| N30739        | 2635 | 2835 | 3025 | 3000 | 3110 | 3225  | 3330  | 3475  | 3430  | 3600  |
| N30740        | 2720 | 2845 | 3065 | 3075 | 3125 | 3250  | 3325  | 3450  | 3430  | 3500  |
| Mean          | 2617 | 2796 | 2992 | 2977 | 3073 | 3158  | 3241  | 3365  | 3361  | 3455  |
| SD            | 98.3 | 84.7 | 74.5 | 98.4 | 85.4 | 103.4 | 112.5 | 142.0 | 124.2 | 142.7 |

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

| Day        | 22    | 25    | 29    | 30    | 33    | 36    | 39    | 43    | 46    | 50    |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| N30716     | 3765  | 3855  | 3975  | 3945  | 3985  | 4030  | 4060  | 4175  | 4205  | 4285  |
| N30717     | 3505  | 3585  | 3630  | 3665  | 3660  | 3710  | 3760  | 3695  | 3800  | 3890  |
| N30718     | 3595  | 3710  | 3755  | 3735  | 3810  | 3840  | 3855  | 3890  | 3970  | 4040  |
| N30719     | 3500  | 3550  | 3615  | 3620  | 3640  | 3750  | 3815  | 3895  | 3965  | 4065  |
| N30720     | 3775  | 3860  | 3980  | 3925  | 3950  | 4050  | 4145  | 4180  | 4235  | 4325  |
| Mean       | 3628  | 3712  | 3791  | 3778  | 3809  | 3876  | 3927  | 3967  | 4035  | 4121  |
| SD         | 135.1 | 145.5 | 178.7 | 149.2 | 159.4 | 157.1 | 166.5 | 208.4 | 182.5 | 181.4 |

Group 2

Sex: Female

Recovery animals

| Day        | 22    | 25    | 29    | 30    | 33    | 36    | 39    | 43    | 46    | 50    |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| -          |       |       |       |       |       |       |       |       |       |       |
| N30726     | 3220  | 3300  | 3385  | 3390  | 3410  | 3465  | 3510  | 3605  | 3640  | 3680  |
| N30727     | 3540  | 3575  | 3670  | 3700  | 3680  | 3730  | 3790  | 3845  | 3870  | 3930  |
| N30728     | 3895  | 4030  | 4085  | 4110  | 4190  | 4235  | 4240  | 4340  | 4405  | 4510  |
| N30729     | 3455  | 3525  | 3620  | 3600  | 3685  | 3745  | 3775  | 3855  | 3580  | 3825  |
| N30730     | 3495  | 3660  | 3700  | 3705  | 3770  | 3805  | 3915  | 4010  | 4080  | 4180  |
| Mean       | 3521  | 3618  | 3692  | 3701  | 3747  | 3796  | 3846  | 3931  | 3915  | 4025  |
| SD         | 242.8 | 266.0 | 252.2 | 261.8 | 282.3 | 278.1 | 265.1 | 270.6 | 338.1 | 326.8 |

Group 3

Sex: Female

Recovery animals

| -- Day        | 22    | 25    | 29    | 30    | 33    | 36    | 39    | 43    | 46    |       |
|---------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 50 Animal No. |       |       |       |       |       |       |       |       |       |       |
| -             |       |       |       |       |       |       |       |       |       |       |
| N30736        | 3280  | 3320  | 3420  | 3425  | 3500  | 3580  | 3660  | 3725  | 3800  | 3950  |
| N30737        | 3520  | 3605  | 3660  | 3670  | 3675  | 3735  | 3780  | 3860  | 3950  | 4025  |
| N30738        | 3645  | 3700  | 3725  | 3745  | 3775  | 3830  | 3905  | 3960  | 4040  | 4080  |
| N30739        | 3720  | 3830  | 3930  | 3955  | 3960  | 4020  | 4105  | 4220  | 4260  | 4315  |
| N30740        | 3590  | 3625  | 3710  | 3730  | 3755  | 3775  | 3825  | 3865  | 3715  | 3860  |
| Mean          | 3551  | 3616  | 3689  | 3705  | 3733  | 3788  | 3855  | 3926  | 3953  | 4046  |
| SD            | 168.3 | 187.5 | 182.4 | 190.0 | 166.9 | 159.6 | 165.5 | 184.4 | 213.2 | 171.6 |

BODY WEIGHT  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

-- Day 53 56

Animal No.

N30716 4345 4390  
N30717 3935 4005  
N30718 4085 4160  
N30719 4075 4140  
N30720 4425 4475

Mean 4173 4234  
SD 204.4 193.1

Group 2

Sex: Female

Recovery animals

-- Day 53 56

Animal No.

--  
N30726 3745 3740  
N30727 4030 4035  
N30728 4585 4595  
N30729 3905 3990  
N30730 4225 4300

Mean 4098 4132  
SD 324.0 326.3

Group 3

Sex: Female

Recovery animals

-- Day 53 56

Animal No.

--  
N30736 4000 4075  
N30737 4070 4145  
N30738 4115 4185  
N30739 4370 4420  
N30740 3945 4005

Mean 4100 4166  
SD 164.4 157.7

8. Body weight change: individual values

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

| Day        | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30641     | -15  | 40   | 130  | 95   | 145   | -25   | 65    | 75    | 55    | 90    |
| N30642     | -10  | 35   | 100  | 100  | 75    | -10   | 95    | 105   | 20    | 100   |
| N30643     | 20   | -150 | 255  | 115  | -30   | 140   | 95    | 95    | 25    | 60    |
| N30644     | 35   | 45   | 100  | 60   | 65    | 15    | 85    | 55    | 50    | 120   |
| N30645     | 10   | 0    | 100  | 60   | 90    | -15   | 85    | 35    | 20    | 85    |
| N30646     | -10  | 5    | 80   | 50   | 50    | 25    | 45    | 50    | 25    | 70    |
| N30647     | 5    | 5    | 110  | 80   | 85    | -5    | 70    | 55    | 40    | 90    |
| N30648     | 20   | 30   | 100  | 55   | 55    | 10    | 95    | 5     | 25    | 100   |
| N30649     | -25  | 40   | 90   | 95   | 115   | 0     | 90    | 75    | 55    | 85    |
| N30650     | 15   | 40   | 80   | 70   | 80    | -5    | 80    | 55    | 50    | 90    |
| Mean       | 5    | 9    | 115  | 78   | 73    | 13    | 81    | 61    | 37    | 89    |
| SD         | 18.9 | 58.4 | 51.4 | 22.3 | 45.9  | 47.0  | 16.2  | 28.9  | 14.9  | 16.5  |

Group 2

Sex: Male

Principal animals + Recovery animals

| Day        | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30651     | 5    | 30   | 70   | 90   | 95    | -35   | 130   | 35    | 40    | 105   |
| N30652     | 5    | 45   | 45   | 90   | 45    | -25   | 45    | 65    | 30    | 85    |
| N30653     | -35  | 90   | 55   | 95   | 45    | -20   | 75    | 30    | 40    | 70    |
| N30654     | -10  | 80   | 80   | 90   | 85    | -55   | 100   | 90    | 20    | 95    |
| N30655     | 30   | -20  | 80   | 40   | 85    | -40   | 55    | 70    | 0     | 60    |
| N30656     | 10   | 65   | 60   | 90   | 80    | -35   | 75    | 75    | 30    | 105   |
| N30657     | -40  | 90   | 75   | 60   | 60    | -60   | 100   | 75    | 5     | 65    |
| N30658     | 5    | 20   | 40   | 75   | 65    | 20    | 45    | 60    | 35    | 70    |
| N30659     | 35   | 25   | 140  | 75   | 90    | 0     | 60    | 90    | 10    | 55    |
| N30660     | 30   | 25   | 75   | 90   | 80    | 15    | 20    | 0     | 80    | 55    |
| Mean       | 4    | 45   | 72   | 80   | 73    | -23   | 71    | 59    | 29    | 77    |
| SD         | 25.8 | 35.8 | 27.8 | 17.6 | 18.1  | 27.5  | 32.5  | 28.8  | 22.9  | 19.6  |

BODY WEIGHT CHANGE  
(g)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

| Day<br>Animal No. | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|-------------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| N30661            | 5    | 30   | 35   | 105  | 60    | -15   | 60    | 75    | 55    | 85    |
| N30662            | -35  | 45   | 90   | 75   | 85    | -85   | 100   | 70    | 60    | 100   |
| N30663            | 5    | 35   | 75   | 70   | 65    | -65   | -25   | 175   | 0     | 85    |
| N30664            | 15   | 25   | 120  | 70   | 110   | -40   | 125   | 65    | 70    | 75    |
| N30665            | 10   | 15   | 110  | 90   | 55    | -70   | 100   | 55    | 100   | 90    |
| N30666            | 45   | 5    | 90   | 35   | 95    | -25   | 70    | 40    | 70    | -15   |
| N30667            | 25   | 5    | 75   | 60   | 75    | -40   | 20    | 50    | 20    | 50    |
| N30668            | -30  | 65   | 50   | 100  | 85    | -75   | 115   | 60    | 70    | 75    |
| N30669            | -50  | 80   | 70   | 60   | 70    | -80   | 120   | 65    | 95    | 20    |
| N30670            | 10   | 40   | 80   | 115  | 115   | -105  | 180   | 45    | 90    | 70    |
| Mean              | 0    | 35   | 80   | 78   | 82    | -60   | 87    | 70    | 63    | 64    |
| SD                | 29.3 | 24.4 | 25.3 | 24.4 | 20.4  | 28.8  | 58.1  | 38.5  | 31.9  | 35.7  |

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

-----  
Day 29/30

Animal No.

-----  
N30641 5  
N30642 -30  
N30643 5  
N30644 15  
N30645 -15  
N30646 -20  
N30647 10  
N30648 10  
N30649 -15  
N30650 -5

-----  
Mean -4  
SD 15.2

Group 2

Sex: Male

Principal animals + Recovery animals

-----  
- Day 29/30

Animal No.

-----  
-- N30651 0  
  
N30652 -25  
N30653 -20  
N30654 45  
N30655 0  
N30656 -10  
N30657 15  
N30658 -10  
N30659 15  
N30660 45

-----  
Mean 6  
SD 24.5

BODY WEIGHT CHANGE  
(g)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

-----  
Day 29/30  
Animal No.

---  
N30661 -5  
N30662 -10  
N30663 -35  
N30664 -10  
N30665 -50  
N30666 100  
N30667 5  
N30668 -40  
N30669 -10  
N30670 20

-----  
Mean -3  
SD 42.1

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

-----  
Day            1/30  
Animal No.

-----  
N30641        660  
N30642        580  
N30643        630  
N30644        645  
N30645        455  
N30646        370  
N30647        545  
N30648        505  
N30649        605  
N30650        550

-----  
Mean          555  
SD            91.1

Group 2

Sex: Male

Principal animals + Recovery animals

-----  
-- Day        1/30  
Animal No.

-----  
--  
N30651        565  
N30652        405  
N30653        425  
N30654        620  
N30655        360  
N30656        545  
N30657        445  
N30658        425  
N30659        595  
N30660        515

-----  
Mean          490  
SD            89.3

BODY WEIGHT CHANGE  
(g)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

-----  
-- Day 1/30  
Animal No.

-----  
-  
N30661 490  
N30662 495  
N30663 385  
N30664 625  
N30665 505  
N30666 510  
N30667 345  
N30668 475  
N30669 440  
N30670 660

-----  
Mean 493  
SD 95.7

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

| Day<br>Animal No. | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|-------------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| N30711            | 5    | 75   | 135  | 70   | 135   | 0     | 110   | 95    | 65    | 100   |
| N30712            | 40   | 50   | 45   | 80   | 90    | 15    | 135   | 115   | 65    | 80    |
| N30713            | 25   | -5   | 120  | 60   | 100   | 25    | 80    | 60    | 70    | 70    |
| N30714            | 20   | 35   | 105  | 95   | 130   | 5     | 40    | 170   | 70    | 80    |
| N30715            | 5    | 45   | 80   | 25   | 145   | 55    | 100   | 110   | 70    | 45    |
| N30716            | -35  | 110  | 115  | 85   | 120   | 30    | 90    | 80    | 90    | 120   |
| N30717            | 35   | -25  | 160  | 10   | 105   | 10    | 115   | 75    | 80    | 45    |
| N30718            | 60   | -15  | 140  | 65   | 125   | 35    | 55    | 80    | 115   | 45    |
| N30719            | -10  | 40   | 80   | 80   | 75    | 10    | 85    | 105   | 50    | 65    |
| N30720            | 10   | 65   | 100  | 55   | 130   | 35    | 60    | 135   | 85    | 120   |
| Mean              | 16   | 38   | 108  | 63   | 116   | 22    | 87    | 103   | 76    | 77    |
| SD                | 26.9 | 42.3 | 33.8 | 26.8 | 22.2  | 17.0  | 29.5  | 32.4  | 17.8  | 28.9  |

Group 2

Sex: Female

Principal animals + Recovery animals

| Day<br>Animal No. | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|-------------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| N30721            | -20  | 80   | 85   | 105  | 180   | -45   | 135   | 70    | 110   | 25    |
| N30722            | -5   | 50   | 135  | 75   | 165   | -35   | 100   | 90    | 75    | 95    |
| N30723            | -10  | 60   | 70   | 120  | 55    | -60   | 135   | 30    | 105   | 35    |
| N30724            | 10   | 55   | 120  | 70   | 150   | 55    | 160   | 45    | 65    | 75    |
| N30725            | 25   | 95   | 115  | 75   | 150   | 20    | 200   | 70    | 140   | 65    |
| N30726            | -25  | 60   | 85   | 65   | 70    | 35    | 85    | 45    | 80    | 85    |
| N30727            | -15  | -75  | 180  | 115  | 160   | -45   | 125   | 85    | 35    | 95    |
| N30728            | 10   | 115  | 80   | 120  | 95    | 60    | 120   | 70    | 135   | 55    |
| N30729            | -50  | -50  | 185  | 85   | 95    | -20   | 100   | 50    | 70    | 95    |
| N30730            | 10   | 45   | 120  | 120  | 60    | 30    | 140   | 15    | 165   | 40    |
| Mean              | -7   | 44   | 118  | 95   | 118   | 0     | 130   | 57    | 98    | 67    |
| SD                | 21.9 | 60.2 | 40.2 | 23.1 | 47.8  | 45.2  | 33.2  | 24.1  | 40.2  | 26.7  |

BODY WEIGHT CHANGE  
(g)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

| Day<br>Animal No. | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|-------------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| N30731            | -35  | 60   | 120  | 60   | 105   | 25    | 75    | 145   | 35    | 85    |
| N30732            | -10  | 85   | 95   | 100  | 50    | 15    | 60    | 65    | 65    | -15   |
| N30733            | -10  | 25   | 70   | 50   | 40    | 20    | 25    | 65    | 55    | -20   |
| N30734            | -10  | 55   | 115  | 45   | 130   | -20   | 45    | 105   | 80    | 15    |
| N30735            | -40  | 50   | 135  | 80   | 165   | -40   | 45    | 140   | -40   | 120   |
| N30736            | -55  | 115  | 60   | 65   | 80    | 10    | 75    | 60    | 40    | 100   |
| N30737            | -10  | 90   | 75   | 90   | 95    | 45    | 80    | 75    | 85    | 55    |
| N30738            | 5    | 115  | 50   | 80   | 175   | -10   | 75    | 135   | 55    | 25    |
| N30739            | -25  | 110  | 115  | 105  | 145   | -45   | 170   | 120   | 110   | 100   |
| N30740            | 10   | 50   | 125  | 75   | 125   | -20   | 70    | 90    | 35    | 85    |
| Mean              | -18  | 76   | 96   | 75   | 111   | -2    | 72    | 100   | 52    | 55    |
| SD                | 20.4 | 31.8 | 30.2 | 20.1 | 45.6  | 29.6  | 38.7  | 33.4  | 40.3  | 50.7  |

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

-----  
Day 29/30

Animal No.

-----  
N30711 -15  
N30712 -10  
N30713 -15  
N30714 5  
N30715 30  
N30716 -30  
N30717 35  
N30718 -20  
N30719 5  
N30720 -55

-----  
Mean -7  
SD 27.0

Group 2

Sex: Female

Principal animals + Recovery animals

-----  
- Day 29/30

Animal No.

-----  
-- N30721 10  
  
N30722 -10  
N30723 -5  
N30724 15  
N30725 5  
N30726 5  
N30727 30  
N30728 25  
N30729 -20  
N30730 5

-----  
Mean 6  
SD 15.2

BODY WEIGHT CHANGE  
(g)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

-----  
Day 29/30  
Animal No.

---  
N30731 0  
N30732 20  
N30733 20  
N30734 35  
N30735 -20  
N30736 5  
N30737 10  
N30738 20  
N30739 25  
N30740 20

-----  
Mean 14  
SD 15.5

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

-----  
Day 1/30

Animal No.

-----  
N30711 775  
N30712 705  
N30713 590  
N30714 755  
N30715 710  
N30716 775  
N30717 645  
N30718 685  
N30719 585  
N30720 740

-----  
Mean 697  
SD 70.3

Group 2

Sex: Female

Principal animals + Recovery animals

-----  
-- Day 1/30  
Animal No.

-----  
N30721 735  
N30722 735  
N30723 535  
N30724 820  
N30725 960  
N30726 590  
N30727 690  
N30728 885  
N30729 540  
N30730 750

-----  
Mean 724  
SD 141.6

BODY WEIGHT CHANGE  
(g)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

-----  
-- Day 1/30  
Animal No.

-----  
-  
N30731 675  
N30732 530  
N30733 340  
N30734 595  
N30735 595  
N30736 555  
N30737 690  
N30738 725  
N30739 930  
N30740 665

-----  
Mean 630  
SD 152.0

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

| Day        | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30646     | -10  | 5    | 80   | 50   | 50    | 25    | 45    | 50    | 25    | 70    |
| N30647     | 5    | 5    | 110  | 80   | 85    | -5    | 70    | 55    | 40    | 90    |
| N30648     | 20   | 30   | 100  | 55   | 55    | 10    | 95    | 5     | 25    | 100   |
| N30649     | -25  | 40   | 90   | 95   | 115   | 0     | 90    | 75    | 55    | 85    |
| N30650     | 15   | 40   | 80   | 70   | 80    | -5    | 80    | 55    | 50    | 90    |
| Mean       | 1    | 24   | 92   | 70   | 77    | 5     | 76    | 48    | 39    | 87    |
| SD         | 18.5 | 17.8 | 13.0 | 18.4 | 26.1  | 12.7  | 19.8  | 25.9  | 13.9  | 11.0  |

Group 2

Sex: Male

Recovery animals

| Day        | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30656     | 10   | 65   | 60   | 90   | 80    | -35   | 75    | 75    | 30    | 105   |
| N30657     | -40  | 90   | 75   | 60   | 60    | -60   | 100   | 75    | 5     | 65    |
| N30658     | 5    | 20   | 40   | 75   | 65    | 20    | 45    | 60    | 35    | 70    |
| N30659     | 35   | 25   | 140  | 75   | 90    | 0     | 60    | 90    | 10    | 55    |
| N30660     | 30   | 25   | 75   | 90   | 80    | 15    | 20    | 0     | 80    | 55    |
| Mean       | 8    | 45   | 78   | 78   | 75    | -12   | 60    | 60    | 32    | 70    |
| SD         | 29.7 | 31.0 | 37.5 | 12.5 | 12.2  | 34.4  | 30.2  | 35.2  | 29.7  | 20.6  |

Group 3

Sex: Male

Recovery animals

| Day        | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30666     | 45   | 5    | 90   | 35   | 95    | -25   | 70    | 40    | 70    | -15   |
| N30667     | 25   | 5    | 75   | 60   | 75    | -40   | 20    | 50    | 20    | 50    |
| N30668     | -30  | 65   | 50   | 100  | 85    | -75   | 115   | 60    | 70    | 75    |
| N30669     | -50  | 80   | 70   | 60   | 70    | -80   | 120   | 65    | 95    | 20    |
| N30670     | 10   | 40   | 80   | 115  | 115   | -105  | 180   | 45    | 90    | 70    |
| Mean       | 0    | 39   | 73   | 74   | 88    | -65   | 101   | 52    | 69    | 40    |
| SD         | 39.2 | 34.2 | 14.8 | 32.7 | 17.9  | 32.2  | 59.8  | 10.4  | 29.7  | 37.6  |

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

| Day        | 29/30 | 30/33 | 33/36 | 36/39 | 39/43 | 43/46 | 46/50 | 50/53 | 53/56 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |
| N30646     | -20   | 5     | 25    | 90    | 35    | 50    | 50    | 45    | 40    |
| N30647     | 10    | -30   | 85    | 50    | 55    | 75    | 10    | 70    | 50    |
| N30648     | 10    | -20   | 65    | 75    | -10   | 15    | 125   | 35    | 5     |
| N30649     | -15   | -25   | 100   | 90    | 55    | 75    | 60    | 65    | 50    |
| N30650     | -5    | 5     | 55    | 75    | 50    | 55    | 20    | 55    | 75    |
| Mean       | -4    | -13   | 66    | 76    | 37    | 54    | 53    | 54    | 44    |
| SD         | 13.9  | 16.8  | 28.8  | 16.4  | 27.5  | 24.6  | 45.2  | 14.3  | 25.3  |

Group 2

Sex: Male

Recovery animals

| Day        | 29/30 | 30/33 | 33/36 | 36/39 | 39/43 | 43/46 | 46/50 | 50/53 | 53/56 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |
| N30656     | -10   | -5    | 70    | 45    | 105   | 45    | 95    | 25    | 20    |
| N30657     | 15    | -40   | 75    | 25    | 55    | 30    | 70    | 30    | 0     |
| N30658     | -10   | -15   | 30    | 65    | 50    | 75    | 65    | 0     | 5     |
| N30659     | 15    | -10   | 75    | 65    | 65    | 75    | -95   | 180   | 35    |
| N30660     | 45    | 40    | 40    | 80    | 80    | 45    | 15    | 90    | 45    |
| Mean       | 11    | -6    | 58    | 56    | 71    | 54    | 30    | 65    | 21    |
| SD         | 22.7  | 29.0  | 21.4  | 21.3  | 22.2  | 20.1  | 75.7  | 72.3  | 19.2  |

Group 3

Sex: Male

Recovery animals

| Day        | 29/30 | 30/33 | 33/36 | 36/39 | 39/43 | 43/46 | 46/50 | 50/53 | 53/56 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |
| N30666     | 100   | -25   | 65    | 75    | 60    | 45    | 100   | 35    | 70    |
| N30667     | 5     | -5    | 40    | 55    | 75    | 20    | -20   | 125   | -15   |
| N30668     | -40   | 10    | 75    | 65    | 55    | 75    | 80    | 10    | 75    |
| N30669     | -10   | 100   | 25    | 65    | 85    | 110   | 45    | -20   | 75    |
| N30670     | 20    | -35   | 95    | 40    | 100   | 75    | 70    | 50    | 65    |
| Mean       | 15    | 9     | 60    | 60    | 75    | 65    | 55    | 40    | 54    |
| SD         | 52.4  | 53.8  | 27.8  | 13.2  | 18.4  | 34.1  | 46.4  | 54.4  | 38.8  |

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

| Day    | 1/30 | 30/56 | 1/56  |
|--------|------|-------|-------|
| <hr/>  |      |       |       |
| N30646 | 370  | 340   | 710   |
| N30647 | 545  | 365   | 910   |
| N30648 | 505  | 290   | 795   |
| N30649 | 605  | 470   | 1075  |
| N30650 | 550  | 390   | 940   |
| Mean   | 515  | 371   | 886   |
| SD     | 88.5 | 66.6  | 140.1 |

---

Group 2

Sex: Male

Recovery animals

| Day    | 1/30 | 30/56 | 1/56  |
|--------|------|-------|-------|
| <hr/>  |      |       |       |
| N30656 | 545  | 400   | 945   |
| N30657 | 445  | 245   | 690   |
| N30658 | 425  | 275   | 700   |
| N30659 | 595  | 390   | 985   |
| N30660 | 515  | 435   | 950   |
| Mean   | 505  | 349   | 854   |
| SD     | 70.4 | 83.6  | 146.0 |

---

Group 3

Sex: Male

Recovery animals

| Day    | 1/30  | 30/56 | 1/56  |
|--------|-------|-------|-------|
| <hr/>  |       |       |       |
| N30666 | 510   | 425   | 935   |
| N30667 | 345   | 275   | 620   |
| N30668 | 475   | 445   | 920   |
| N30669 | 440   | 485   | 925   |
| N30670 | 660   | 460   | 1120  |
| Mean   | 486   | 418   | 904   |
| SD     | 115.1 | 82.9  | 179.6 |

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BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

| Day        | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30716     | -35  | 110  | 115  | 85   | 120   | 30    | 90    | 80    | 90    | 120   |
| N30717     | 35   | -25  | 160  | 10   | 105   | 10    | 115   | 75    | 80    | 45    |
| N30718     | 60   | -15  | 140  | 65   | 125   | 35    | 55    | 80    | 115   | 45    |
| N30719     | -10  | 40   | 80   | 80   | 75    | 10    | 85    | 105   | 50    | 65    |
| N30720     | 10   | 65   | 100  | 55   | 130   | 35    | 60    | 135   | 85    | 120   |
| Mean       | 12   | 35   | 119  | 59   | 111   | 24    | 81    | 95    | 84    | 79    |
| SD         | 37.2 | 56.2 | 31.7 | 29.9 | 22.2  | 12.9  | 24.3  | 25.2  | 23.3  | 38.3  |

Group 2

Sex: Female

Recovery animals

| Day        | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30726     | -25  | 60   | 85   | 65   | 70    | 35    | 85    | 45    | 80    | 85    |
| N30727     | -15  | -75  | 180  | 115  | 160   | -45   | 125   | 85    | 35    | 95    |
| N30728     | 10   | 115  | 80   | 120  | 95    | 60    | 120   | 70    | 135   | 55    |
| N30729     | -50  | -50  | 185  | 85   | 95    | -20   | 100   | 50    | 70    | 95    |
| N30730     | 10   | 45   | 120  | 120  | 60    | 30    | 140   | 15    | 165   | 40    |
| Mean       | -14  | 19   | 130  | 101  | 96    | 12    | 114   | 53    | 97    | 74    |
| SD         | 25.3 | 79.3 | 50.4 | 24.8 | 39.0  | 43.1  | 21.6  | 26.6  | 52.3  | 25.1  |

Group 3

Sex: Female

Recovery animals

| Day        | 1/2  | 2/5  | 5/8  | 8/11 | 11/15 | 15/16 | 16/19 | 19/22 | 22/25 | 25/29 |
|------------|------|------|------|------|-------|-------|-------|-------|-------|-------|
| Animal No. |      |      |      |      |       |       |       |       |       |       |
| N30736     | -55  | 115  | 60   | 65   | 80    | 10    | 75    | 60    | 40    | 100   |
| N30737     | -10  | 90   | 75   | 90   | 95    | 45    | 80    | 75    | 85    | 55    |
| N30738     | 5    | 115  | 50   | 80   | 175   | -10   | 75    | 135   | 55    | 25    |
| N30739     | -25  | 110  | 115  | 105  | 145   | -45   | 170   | 120   | 110   | 100   |
| N30740     | 10   | 50   | 125  | 75   | 125   | -20   | 70    | 90    | 35    | 85    |
| Mean       | -15  | 96   | 85   | 83   | 124   | -4    | 94    | 96    | 65    | 73    |
| SD         | 26.2 | 27.7 | 33.4 | 15.2 | 38.1  | 33.8  | 42.6  | 31.1  | 31.8  | 32.5  |

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

| Day        | 29/30 | 30/33 | 33/36 | 36/39 | 39/43 | 43/46 | 46/50 | 50/53 | 53/56 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |
| N30716     | -30   | 40    | 45    | 30    | 115   | 30    | 80    | 60    | 45    |
| N30717     | 35    | -5    | 50    | 50    | -65   | 105   | 90    | 45    | 70    |
| N30718     | -20   | 75    | 30    | 15    | 35    | 80    | 70    | 45    | 75    |
| N30719     | 5     | 20    | 110   | 65    | 80    | 70    | 100   | 10    | 65    |
| N30720     | -55   | 25    | 100   | 95    | 35    | 55    | 90    | 100   | 50    |
| Mean       | -13   | 31    | 67    | 51    | 40    | 68    | 86    | 52    | 61    |
| SD         | 34.4  | 29.5  | 35.6  | 31.1  | 67.6  | 28.0  | 11.4  | 32.5  | 12.9  |

Group 2

Sex: Female

Recovery animals

| Day        | 29/30 | 30/33 | 33/36 | 36/39 | 39/43 | 43/46 | 46/50 | 50/53 | 53/56 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |
| N30726     | 5     | 20    | 55    | 45    | 95    | 35    | 40    | 65    | -5    |
| N30727     | 30    | -20   | 50    | 60    | 55    | 25    | 60    | 100   | 5     |
| N30728     | 25    | 80    | 45    | 5     | 100   | 65    | 105   | 75    | 10    |
| N30729     | -20   | 85    | 60    | 30    | 80    | -275  | 245   | 80    | 85    |
| N30730     | 5     | 65    | 35    | 110   | 95    | 70    | 100   | 45    | 75    |
| Mean       | 9     | 46    | 49    | 50    | 85    | -16   | 110   | 73    | 34    |
| SD         | 19.8  | 44.9  | 9.6   | 39.2  | 18.4  | 146.0 | 80.2  | 20.2  | 42.5  |

Group 3

Sex: Female

Recovery animals

| Day        | 29/30 | 30/33 | 33/36 | 36/39 | 39/43 | 43/46 | 46/50 | 50/53 | 53/56 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |
| N30736     | 5     | 75    | 80    | 80    | 65    | 75    | 150   | 50    | 75    |
| N30737     | 10    | 5     | 60    | 45    | 80    | 90    | 75    | 45    | 75    |
| N30738     | 20    | 30    | 55    | 75    | 55    | 80    | 40    | 35    | 70    |
| N30739     | 25    | 5     | 60    | 85    | 115   | 40    | 55    | 55    | 50    |
| N30740     | 20    | 25    | 20    | 50    | 40    | -150  | 145   | 85    | 60    |
| Mean       | 16    | 28    | 55    | 67    | 71    | 27    | 93    | 54    | 66    |
| SD         | 8.2   | 28.6  | 21.8  | 18.2  | 28.6  | 100.7 | 51.3  | 18.8  | 10.8  |

BODY WEIGHT CHANGE  
(g)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

| Day    | 1/30 | 30/56 | 1/56  |
|--------|------|-------|-------|
| <hr/>  |      |       |       |
| N30716 | 775  | 445   | 1220  |
| N30717 | 645  | 340   | 985   |
| N30718 | 685  | 425   | 1110  |
| N30719 | 585  | 520   | 1105  |
| N30720 | 740  | 550   | 1290  |
| Mean   | 686  | 456   | 1142  |
| SD     | 75.4 | 82.9  | 117.3 |

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Group 2

Sex: Female

Recovery animals

| Day    | 1/30  | 30/56 | 1/56  |
|--------|-------|-------|-------|
| <hr/>  |       |       |       |
| N30726 | 590   | 350   | 940   |
| N30727 | 690   | 335   | 1025  |
| N30728 | 885   | 485   | 1370  |
| N30729 | 540   | 390   | 930   |
| N30730 | 750   | 595   | 1345  |
| Mean   | 691   | 431   | 1122  |
| SD     | 136.1 | 108.7 | 218.3 |

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Group 3

Sex: Female

Recovery animals

| Day    | 1/30  | 30/56 | 1/56  |
|--------|-------|-------|-------|
| <hr/>  |       |       |       |
| N30736 | 555   | 650   | 1205  |
| N30737 | 690   | 475   | 1165  |
| N30738 | 725   | 440   | 1165  |
| N30739 | 930   | 465   | 1395  |
| N30740 | 665   | 275   | 940   |
| Mean   | 713   | 461   | 1174  |
| SD     | 137.0 | 133.2 | 161.8 |

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9. Food consumption: individual values

/: missing value or spillage

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

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| Day<br>Animal No. | -5/-4 | -4/-3 | -3/-2 | -2/-1 | -1/1  | 1/2   | 3/4   | 4/5   | 5/6   | 6/7   |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30641            | 265.0 | 260.0 | 230.0 | 225.0 | /     | 215.0 | 250.0 | 235.0 | 240.0 | 250.0 |
| N30642            | 210.0 | 205.0 | 180.0 | 190.0 | /     | 180.0 | 190.0 | 185.0 | 205.0 | 205.0 |
| N30643            | 295.0 | 320.0 | 290.0 | 290.0 | /     | 300.0 | 275.0 | 185.0 | 240.0 | 255.0 |
| N30644            | 225.0 | 215.0 | 180.0 | 190.0 | /     | 175.0 | 205.0 | 195.0 | 215.0 | 215.0 |
| N30645            | 235.0 | 230.0 | 205.0 | 215.0 | /     | 210.0 | 225.0 | 205.0 | 200.0 | 220.0 |
| N30646            | 224.2 | 221.8 | 191.6 | 195.0 | 200.0 | 200.0 | 195.0 | 190.0 | 180.0 | 200.0 |
| N30647            | 214.8 | 239.1 | 206.6 | 215.0 | 210.0 | 210.0 | 225.0 | 205.0 | 210.0 | 240.0 |
| N30648            | 200.7 | 214.0 | 179.9 | 210.0 | 185.0 | 190.0 | 200.0 | 200.0 | 205.0 | 210.0 |
| N30649            | 223.3 | 241.6 | 209.0 | 230.0 | 215.0 | 210.0 | 210.0 | 200.0 | 215.0 | 230.0 |
| N30650            | 245.0 | 165.0 | 205.0 | 185.0 | 230.0 | 230.0 | 210.0 | 215.0 | 220.0 | 220.0 |
| Mean              | 233.8 | 231.2 | 207.7 | 214.5 | 208.0 | 212.0 | 218.5 | 201.5 | 213.0 | 224.5 |
| SD                | 28.18 | 40.28 | 33.09 | 30.77 | 16.81 | 35.13 | 26.46 | 15.10 | 17.98 | 18.77 |

Group 2

Sex: Male

Principal animals + Recovery animals

--

| Day<br>Animal No. | -5/-4 | -4/-3 | -3/-2  | -2/-1 | -1/1  | 1/2   | 3/4   | 4/5   | 5/6   | 6/7   |
|-------------------|-------|-------|--------|-------|-------|-------|-------|-------|-------|-------|
| N30651            | 225.0 | 235.0 | 190.0  | 210.0 | /     | 200.0 | 190.0 | 195.0 | 205.0 | 230.0 |
| N30652            | 195.0 | 200.0 | 155.0  | 185.0 | /     | 175.0 | 185.0 | 200.0 | 190.0 | 220.0 |
| N30653            | 200.0 | 200.0 | 180.0  | 190.0 | /     | 165.0 | 190.0 | 195.0 | 185.0 | 195.0 |
| N30654            | 240.0 | 195.0 | 190.0  | 205.0 | /     | 205.0 | 195.0 | 215.0 | 210.0 | 225.0 |
| N30655            | 200.0 | 185.0 | 155.0  | 175.0 | /     | 175.0 | 170.0 | 180.0 | 175.0 | 200.0 |
| N30656            | 216.9 | 201.3 | 515.2  | 340.0 | 140.0 | 195.0 | 180.0 | 175.0 | 185.0 | 215.0 |
| N30657            | 214.2 | 228.2 | 233.8  | 200.0 | 205.0 | 185.0 | 200.0 | 210.0 | 200.0 | 215.0 |
| N30658            | 223.5 | 234.8 | 177.4  | 200.0 | 205.0 | 175.0 | 190.0 | 195.0 | 170.0 | 195.0 |
| N30659            | 216.4 | 254.1 | 172.7  | 220.0 | 205.0 | 195.0 | 220.0 | 200.0 | 205.0 | 230.0 |
| N30660            | 214.6 | 231.4 | 194.9  | 210.0 | 200.0 | 190.0 | 200.0 | 200.0 | 200.0 | 210.0 |
| Mean              | 214.6 | 216.5 | 216.4  | 213.5 | 191.0 | 186.0 | 192.0 | 196.5 | 192.5 | 213.5 |
| SD                | 13.55 | 22.80 | 107.36 | 46.37 | 28.59 | 13.08 | 13.37 | 12.03 | 13.59 | 13.34 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

---

--

| Day        | -5/-4 | -4/-3 | -3/-2 | -2/-1 | -1/1  | 1/2   | 3/4   | 4/5   | 5/6   | 6/7   |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| N30661     | 170.0 | 170.0 | 150.0 | 160.0 | /     | 140.0 | 185.0 | 170.0 | 155.0 | 165.0 |
| N30662     | 195.0 | 185.0 | 170.0 | 190.0 | /     | 160.0 | 190.0 | 180.0 | 180.0 | 200.0 |
| N30663     | 205.0 | 200.0 | 165.0 | 180.0 | /     | 165.0 | 130.0 | 180.0 | 185.0 | 205.0 |
| N30664     | 245.0 | 210.0 | 185.0 | 215.0 | /     | 210.0 | 240.0 | 220.0 | 225.0 | 230.0 |
| N30665     | 255.0 | 245.0 | 220.0 | 225.0 | /     | 220.0 | 250.0 | 230.0 | 215.0 | 250.0 |
| N30666     | 200.5 | 210.7 | 190.6 | 180.0 | 190.0 | 205.0 | 180.0 | 195.0 | 195.0 | 205.0 |
| N30667     | 217.2 | 234.8 | 176.4 | 190.0 | 185.0 | 170.0 | 180.0 | 200.0 | 185.0 | 195.0 |
| N30668     | 201.3 | 205.0 | 165.7 | 175.0 | 175.0 | 160.0 | 215.0 | 200.0 | 200.0 | 210.0 |
| N30669     | 203.9 | 212.2 | 188.5 | 195.0 | 180.0 | 175.0 | 195.0 | 195.0 | 180.0 | 205.0 |
| N30670     | 206.5 | 236.6 | 204.2 | 220.0 | 205.0 | 195.0 | 205.0 | 225.0 | 200.0 | 225.0 |
| Mean       | 209.9 | 210.9 | 181.5 | 193.0 | 187.0 | 180.0 | 197.0 | 199.5 | 192.0 | 209.0 |
| SD         | 24.42 | 23.32 | 20.59 | 21.11 | 11.51 | 26.03 | 33.85 | 20.20 | 19.75 | 22.71 |

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FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

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| Day<br>Animal No. | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 | 16/17 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30641            | 270.0 | 240.0 | 265.0 | 240.0 | 270.0 | 235.0 | 250.0 | 260.0 | 245.0 | 225.0 |
| N30642            | 205.0 | 195.0 | 210.0 | 195.0 | 210.0 | 180.0 | 200.0 | 200.0 | 185.0 | 190.0 |
| N30643            | 250.0 | 280.0 | 240.0 | 240.0 | 275.0 | 240.0 | 265.0 | 200.0 | 275.0 | 265.0 |
| N30644            | 215.0 | 195.0 | 215.0 | 195.0 | 230.0 | 205.0 | 225.0 | 220.0 | 210.0 | 215.0 |
| N30645            | 225.0 | 200.0 | 225.0 | 200.0 | 230.0 | 195.0 | 220.0 | 230.0 | 205.0 | 205.0 |
| N30646            | 215.0 | 200.0 | 195.0 | 180.0 | 200.0 | 180.0 | 315.0 | 190.0 | 180.0 | 185.0 |
| N30647            | 215.0 | 230.0 | 245.0 | 210.0 | 220.0 | 200.0 | 225.0 | 220.0 | 195.0 | 195.0 |
| N30648            | 215.0 | 195.0 | 215.0 | 180.0 | 215.0 | 185.0 | 205.0 | 195.0 | 190.0 | 185.0 |
| N30649            | 230.0 | 230.0 | 230.0 | 205.0 | 230.0 | 205.0 | 235.0 | 235.0 | 215.0 | 205.0 |
| N30650            | 215.0 | 210.0 | 235.0 | 200.0 | 225.0 | 205.0 | 230.0 | 210.0 | 210.0 | 185.0 |
| Mean              | 225.5 | 217.5 | 227.5 | 204.5 | 230.5 | 203.0 | 237.0 | 216.0 | 211.0 | 205.5 |
| SD                | 19.92 | 27.71 | 20.03 | 21.01 | 24.20 | 20.71 | 33.43 | 21.58 | 29.14 | 24.99 |

Group 2

Sex: Male

Principal animals + Recovery animals

| Day<br>Animal No. | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 | 16/17 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30651            | 225.0 | 210.0 | 230.0 | 205.0 | 240.0 | 200.0 | 225.0 | 215.0 | 205.0 | 195.0 |
| N30652            | 205.0 | 195.0 | 205.0 | 190.0 | 210.0 | 175.0 | 200.0 | 185.0 | 145.0 | 165.0 |
| N30653            | 200.0 | 195.0 | 215.0 | 200.0 | 205.0 | 195.0 | 210.0 | 200.0 | 165.0 | 185.0 |
| N30654            | 220.0 | 210.0 | 220.0 | 195.0 | 220.0 | 175.0 | 210.0 | 200.0 | 160.0 | 170.0 |
| N30655            | 190.0 | 175.0 | 195.0 | 165.0 | 195.0 | 170.0 | 195.0 | 195.0 | 160.0 | 145.0 |
| N30656            | 220.0 | 200.0 | 210.0 | 175.0 | 225.0 | 160.0 | 230.0 | 225.0 | 180.0 | 175.0 |
| N30657            | 220.0 | 200.0 | 210.0 | 195.0 | 200.0 | 175.0 | 200.0 | 195.0 | 160.0 | 170.0 |
| N30658            | 225.0 | 200.0 | 235.0 | 190.0 | 230.0 | 180.0 | 210.0 | 210.0 | 195.0 | 185.0 |
| N30659            | 230.0 | 205.0 | 240.0 | 200.0 | 235.0 | 200.0 | 255.0 | 150.0 | 215.0 | 200.0 |
| N30660            | 220.0 | 215.0 | 215.0 | 195.0 | 220.0 | 195.0 | 225.0 | 220.0 | 200.0 | 195.0 |
| Mean              | 215.5 | 200.5 | 217.5 | 191.0 | 218.0 | 182.5 | 216.0 | 199.5 | 178.5 | 178.5 |
| SD                | 12.79 | 11.17 | 13.99 | 12.20 | 15.13 | 13.99 | 18.07 | 21.40 | 23.81 | 16.84 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

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| Day        | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 | 16/17 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| N30661     | 180.0 | 165.0 | 200.0 | 185.0 | 200.0 | 175.0 | 195.0 | 190.0 | 165.0 | 175.0 |
| N30662     | 200.0 | 175.0 | 200.0 | 175.0 | 210.0 | 175.0 | 180.0 | 185.0 | 135.0 | 160.0 |
| N30663     | 215.0 | 195.0 | 215.0 | 195.0 | 220.0 | 185.0 | 200.0 | 205.0 | 155.0 | 170.0 |
| N30664     | 250.0 | 210.0 | 255.0 | 205.0 | 265.0 | 215.0 | 225.0 | 240.0 | 215.0 | 210.0 |
| N30665     | 265.0 | 225.0 | 270.0 | 225.0 | 260.0 | 225.0 | 245.0 | 250.0 | 185.0 | 210.0 |
| N30666     | 215.0 | 205.0 | 215.0 | 185.0 | 225.0 | 185.0 | 205.0 | 210.0 | 165.0 | 165.0 |
| N30667     | 195.0 | 185.0 | 195.0 | 185.0 | 200.0 | 175.0 | 205.0 | 185.0 | 155.0 | 160.0 |
| N30668     | 215.0 | 205.0 | 210.0 | 190.0 | 210.0 | 185.0 | 210.0 | 205.0 | 155.0 | 170.0 |
| N30669     | 215.0 | 180.0 | 215.0 | 180.0 | 215.0 | 170.0 | 210.0 | 185.0 | 130.0 | 145.0 |
| N30670     | 235.0 | 210.0 | 235.0 | 220.0 | 240.0 | 195.0 | 235.0 | 240.0 | 175.0 | 225.0 |
| Mean       | 218.5 | 195.5 | 221.0 | 194.5 | 224.5 | 188.5 | 211.0 | 209.5 | 163.5 | 179.0 |
| SD         | 25.50 | 18.77 | 24.81 | 16.91 | 23.27 | 18.27 | 19.26 | 25.22 | 24.50 | 26.44 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

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| Day<br>Animal No. | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 | 26/27 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30641            | 195.0 | 240.0 | 240.0 | 240.0 | 240.0 | 215.0 | 220.0 | 220.0 | 240.0 | 225.0 |
| N30642            | 175.0 | 190.0 | 180.0 | 200.0 | 210.0 | 185.0 | 185.0 | 190.0 | 190.0 | 200.0 |
| N30643            | 245.0 | 260.0 | 255.0 | 270.0 | 260.0 | 235.0 | 190.0 | 240.0 | 245.0 | 265.0 |
| N30644            | 210.0 | 225.0 | 210.0 | 225.0 | 230.0 | 190.0 | 215.0 | 215.0 | 225.0 | 240.0 |
| N30645            | 185.0 | 230.0 | 210.0 | 210.0 | 220.0 | 125.0 | 215.0 | 195.0 | 200.0 | 215.0 |
| N30646            | 185.0 | 175.0 | 185.0 | 195.0 | 185.0 | 190.0 | 180.0 | 185.0 | 185.0 | 175.0 |
| N30647            | 210.0 | 210.0 | 220.0 | 215.0 | 190.0 | 220.0 | 190.0 | 185.0 | 205.0 | 210.0 |
| N30648            | 195.0 | 185.0 | 195.0 | 190.0 | 185.0 | 200.0 | 175.0 | 165.0 | 175.0 | 190.0 |
| N30649            | 235.0 | 220.0 | 240.0 | 240.0 | 225.0 | 230.0 | 200.0 | 210.0 | 220.0 | 220.0 |
| N30650            | 210.0 | 195.0 | 215.0 | 215.0 | 210.0 | 210.0 | 205.0 | 205.0 | 220.0 | 230.0 |
| Mean              | 204.5 | 213.0 | 215.0 | 220.0 | 215.5 | 200.0 | 197.5 | 201.0 | 210.5 | 217.0 |
| SD                | 22.29 | 26.89 | 24.61 | 24.49 | 24.66 | 31.45 | 15.86 | 21.45 | 23.39 | 25.63 |

Group 2

Sex: Male

Principal animals + Recovery animals

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| Day<br>Animal No. | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 | 26/27 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30651            | 185.0 | 205.0 | 195.0 | 220.0 | 220.0 | 180.0 | 200.0 | 180.0 | 220.0 | 210.0 |
| N30652            | 155.0 | 190.0 | 195.0 | 205.0 | 200.0 | 175.0 | 185.0 | 185.0 | 190.0 | 205.0 |
| N30653            | 165.0 | 185.0 | 185.0 | 190.0 | 185.0 | 175.0 | 170.0 | 170.0 | 175.0 | 195.0 |
| N30654            | 140.0 | 210.0 | 195.0 | 200.0 | 205.0 | 180.0 | 185.0 | 170.0 | 205.0 | 190.0 |
| N30655            | 130.0 | 180.0 | 160.0 | 190.0 | 195.0 | 160.0 | 180.0 | 155.0 | 165.0 | 190.0 |
| N30656            | 165.0 | 195.0 | 215.0 | 195.0 | 200.0 | 180.0 | 175.0 | 210.0 | 195.0 | 210.0 |
| N30657            | 180.0 | 170.0 | 185.0 | 195.0 | 190.0 | 185.0 | 180.0 | 175.0 | 190.0 | 175.0 |
| N30658            | 185.0 | 185.0 | 210.0 | 205.0 | 185.0 | 195.0 | 185.0 | 190.0 | 175.0 | 190.0 |
| N30659            | 225.0 | 205.0 | 230.0 | 220.0 | 230.0 | 195.0 | 190.0 | 215.0 | 195.0 | 240.0 |
| N30660            | 195.0 | 175.0 | 190.0 | 180.0 | 175.0 | 185.0 | 175.0 | 195.0 | 200.0 | 200.0 |
| Mean              | 172.5 | 190.0 | 196.0 | 200.0 | 198.5 | 181.0 | 182.5 | 184.5 | 191.0 | 200.5 |
| SD                | 27.71 | 13.54 | 19.12 | 12.91 | 16.67 | 10.22 | 8.58  | 18.63 | 16.12 | 17.55 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

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| Day        | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 | 26/27 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| N30661     | 155.0 | 180.0 | 190.0 | 190.0 | 180.0 | 180.0 | 180.0 | 170.0 | 180.0 | 190.0 |
| N30662     | 150.0 | 175.0 | 190.0 | 175.0 | 195.0 | 190.0 | 190.0 | 180.0 | 190.0 | 210.0 |
| N30663     | 105.0 | 160.0 | 200.0 | 190.0 | 210.0 | 180.0 | 175.0 | 170.0 | 180.0 | 130.0 |
| N30664     | 185.0 | 260.0 | 225.0 | 250.0 | 260.0 | 230.0 | 220.0 | 225.0 | 225.0 | 235.0 |
| N30665     | 185.0 | 235.0 | 225.0 | 230.0 | 260.0 | 230.0 | 240.0 | 230.0 | 230.0 | 240.0 |
| N30666     | 185.0 | 185.0 | 190.0 | 195.0 | 185.0 | 200.0 | 185.0 | 190.0 | 200.0 | 215.0 |
| N30667     | 175.0 | 160.0 | 160.0 | 170.0 | 165.0 | 175.0 | 155.0 | 175.0 | 170.0 | 175.0 |
| N30668     | 180.0 | 195.0 | 195.0 | 210.0 | 195.0 | 205.0 | 185.0 | 185.0 | 200.0 | 195.0 |
| N30669     | 170.0 | 175.0 | 190.0 | 185.0 | 185.0 | 210.0 | 180.0 | 200.0 | 190.0 | 185.0 |
| N30670     | 225.0 | 225.0 | 230.0 | 235.0 | 235.0 | 225.0 | 225.0 | 225.0 | 220.0 | 220.0 |
| Mean       | 171.5 | 195.0 | 199.5 | 203.0 | 207.0 | 202.5 | 193.5 | 195.0 | 198.5 | 199.5 |
| SD         | 31.01 | 33.83 | 21.53 | 27.10 | 33.60 | 21.11 | 26.25 | 23.69 | 20.55 | 32.36 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Principal animals + Recovery animals

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| Day | 27/28 | 28/29 | 29/30 |
|-----|-------|-------|-------|
|-----|-------|-------|-------|

Animal No.

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|        |       |       |       |
|--------|-------|-------|-------|
| N30641 | 240.0 | 225.0 | 205.0 |
| N30642 | 205.0 | 190.0 | 160.0 |
| N30643 | 155.0 | 270.0 | 250.0 |
| N30644 | 225.0 | 225.0 | 215.0 |
| N30645 | 195.0 | 200.0 | 180.0 |
| N30646 | 255.0 | 130.0 | 180.0 |
| N30647 | 170.0 | 205.0 | 185.0 |
| N30648 | 185.0 | 185.0 | 160.0 |
| N30649 | 230.0 | 225.0 | 190.0 |
| N30650 | 225.0 | 220.0 | 190.0 |

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|      |       |       |       |
|------|-------|-------|-------|
| Mean | 208.5 | 207.5 | 191.5 |
| SD   | 32.06 | 36.31 | 26.78 |

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Group 2

Sex: Male

Principal animals + Recovery animals

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| Day | 27/28 | 28/29 | 29/30 |
|-----|-------|-------|-------|
|-----|-------|-------|-------|

Animal No.

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|        |       |       |       |
|--------|-------|-------|-------|
| N30651 | 195.0 | 195.0 | 165.0 |
| N30652 | 195.0 | 200.0 | 165.0 |
| N30653 | 195.0 | 185.0 | 145.0 |
| N30654 | 180.0 | 205.0 | 205.0 |
| N30655 | 155.0 | 185.0 | 125.0 |
| N30656 | 200.0 | 205.0 | 190.0 |
| N30657 | 175.0 | 180.0 | 150.0 |
| N30658 | 180.0 | 190.0 | 165.0 |
| N30659 | 205.0 | 215.0 | 180.0 |
| N30660 | 200.0 | 200.0 | 190.0 |

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|      |       |       |       |
|------|-------|-------|-------|
| Mean | 188.0 | 196.0 | 168.0 |
| SD   | 15.31 | 11.01 | 24.06 |

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FOOD CONSUMPTION  
(g/animal/day)

Study No.:  
Group 3

Sex: Male  
Principal animals + Recovery animals

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Day            27/28    28/29    29/30  
Animal No.

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|        |       |       |       |
|--------|-------|-------|-------|
| N30661 | 180.0 | 200.0 | 155.0 |
| N30662 | 205.0 | 205.0 | 175.0 |
| N30663 | 190.0 | 195.0 | 155.0 |
| N30664 | 230.0 | 225.0 | 195.0 |
| N30665 | 240.0 | 250.0 | 175.0 |
| N30666 | 200.0 | 160.0 | 185.0 |
| N30667 | 170.0 | 165.0 | 135.0 |
| N30668 | 200.0 | 205.0 | 160.0 |
| N30669 | 190.0 | 185.0 | 165.0 |
| N30670 | 220.0 | 230.0 | 195.0 |

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|      |       |       |       |
|------|-------|-------|-------|
| Mean | 202.5 | 202.0 | 169.5 |
| SD   | 22.02 | 28.11 | 19.21 |

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FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

| -- Day | -5/-4 | -4/-3 | -3/-2 | -2/-1 | -1/1 | 1/2 | 2/3 | 3/4 | 4/5 |
|--------|-------|-------|-------|-------|------|-----|-----|-----|-----|
|--------|-------|-------|-------|-------|------|-----|-----|-----|-----|

5/6 Animal No.

|        |       |       |       |       |       |       |       |       |       |       |
|--------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30711 | 190.0 | 190.0 | 185.0 | 235.0 | 180.0 | 220.0 | 205.0 | 225.0 | 200.0 | 195.0 |
| N30712 | 220.0 | 230.0 | 245.0 | 255.0 | 220.0 | 240.0 | 200.0 | 235.0 | 230.0 | 230.0 |
| N30713 | 200.0 | 205.0 | 230.0 | 235.0 | 215.0 | 220.0 | 175.0 | 220.0 | 205.0 | 220.0 |
| N30714 | 225.0 | 235.0 | 235.0 | 260.0 | 235.0 | 240.0 | 170.0 | 255.0 | 245.0 | 255.0 |
| N30715 | 230.0 | 220.0 | 230.0 | 245.0 | 225.0 | 245.0 | 35.0  | 220.0 | 235.0 | 235.0 |
| N30716 | 225.0 | 235.0 | 250.0 | 265.0 | 260.0 | 250.0 | 40.0  | 265.0 | 245.0 | 250.0 |
| N30717 | 200.0 | 315.0 | 235.0 | 255.0 | 230.0 | 235.0 | 40.0  | 180.0 | 205.0 | 230.0 |
| N30718 | 175.0 | 190.0 | 205.0 | 225.0 | 225.0 | 225.0 | 40.0  | 230.0 | 190.0 | 235.0 |
| N30719 | 200.0 | 205.0 | 220.0 | 230.0 | 240.0 | 225.0 | 30.0  | 215.0 | 200.0 | 220.0 |
| N30720 | 215.0 | 225.0 | 225.0 | 245.0 | 240.0 | 245.0 | 45.0  | 250.0 | 225.0 | 245.0 |
| Mean   | 208.0 | 225.0 | 226.0 | 245.0 | 227.0 | 234.5 | 98.0  | 229.5 | 218.0 | 231.5 |
| SD     | 17.83 | 35.90 | 19.12 | 13.54 | 20.84 | 11.17 | 77.79 | 24.09 | 20.30 | 17.33 |

Group 2

Sex: Female

Principal animals + Recovery animals

| -- Day | -5/-4 | -4/-3 | -3/-2 | -2/-1 | -1/1 | 1/2 | 2/3 | 3/4 | 4/5 |
|--------|-------|-------|-------|-------|------|-----|-----|-----|-----|
|--------|-------|-------|-------|-------|------|-----|-----|-----|-----|

5/6 Animal No.

|        |       |       |       |       |       |       |       |       |       |       |
|--------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30721 | 185.0 | 185.0 | 200.0 | 200.0 | 195.0 | 195.0 | 30.0  | 205.0 | 195.0 | 210.0 |
| N30722 | 215.0 | 225.0 | 220.0 | 235.0 | 20.0  | 225.0 | 35.0  | 240.0 | 220.0 | 230.0 |
| N30723 | 215.0 | 195.0 | 315.0 | 225.0 | 210.0 | 200.0 | 35.0  | 155.0 | 220.0 | 220.0 |
| N30724 | 240.0 | 300.0 | 280.0 | 295.0 | 280.0 | 270.0 | 40.0  | 270.0 | 240.0 | 260.0 |
| N30725 | 235.0 | 255.0 | 250.0 | 295.0 | 250.0 | 260.0 | 35.0  | 170.0 | 255.0 | 255.0 |
| N30726 | 200.0 | 195.0 | 195.0 | 220.0 | 210.0 | 215.0 | 40.0  | 240.0 | 205.0 | 230.0 |
| N30727 | 215.0 | 210.0 | 235.0 | 230.0 | 220.0 | 220.0 | 45.0  | 255.0 | 175.0 | 250.0 |
| N30728 | 255.0 | 240.0 | 285.0 | 285.0 | 265.0 | 290.0 | 45.0  | 295.0 | 240.0 | 290.0 |
| N30729 | 200.0 | 200.0 | 215.0 | 240.0 | 215.0 | 215.0 | 65.0  | 155.0 | 160.0 | 240.0 |
| N30730 | 195.0 | 185.0 | 210.0 | 215.0 | 210.0 | 200.0 | 50.0  | 225.0 | 195.0 | 220.0 |
| Mean   | 215.5 | 219.0 | 240.5 | 244.0 | 207.5 | 229.0 | 42.0  | 221.0 | 210.5 | 240.5 |
| SD     | 22.04 | 36.88 | 40.72 | 34.79 | 71.42 | 32.81 | 10.06 | 48.69 | 30.23 | 23.86 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

|                | -5/-4 | -4/-3 | -3/-2 | -2/-1 | -1/1  | 1/2   | 2/3   | 3/4   | 4/5   |       |
|----------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| 5/6 Animal No. |       |       |       |       |       |       |       |       |       |       |
| <hr/>          |       |       |       |       |       |       |       |       |       |       |
| N30731         | 200.0 | 175.0 | 180.0 | 225.0 | 200.0 | 175.0 | 25.0  | 215.0 | 190.0 | 205.0 |
| N30732         | 180.0 | 175.0 | 180.0 | 210.0 | 190.0 | 175.0 | 20.0  | 255.0 | 205.0 | 215.0 |
| N30733         | 220.0 | 210.0 | 210.0 | 215.0 | 200.0 | 185.0 | 30.0  | 175.0 | 190.0 | 195.0 |
| N30734         | 205.0 | 225.0 | 215.0 | 245.0 | 220.0 | 230.0 | 30.0  | 205.0 | 195.0 | 225.0 |
| N30735         | 205.0 | 220.0 | 225.0 | 235.0 | 210.0 | 205.0 | 25.0  | 245.0 | 180.0 | 235.0 |
| N30736         | 195.0 | 190.0 | 225.0 | 225.0 | 220.0 | 200.0 | 35.0  | 250.0 | 225.0 | 220.0 |
| N30737         | 210.0 | 200.0 | 225.0 | 235.0 | 195.0 | 225.0 | 30.0  | 245.0 | 215.0 | 245.0 |
| N30738         | 220.0 | 205.0 | 235.0 | 245.0 | 215.0 | 235.0 | 70.0  | 230.0 | 210.0 | 235.0 |
| N30739         | 225.0 | 215.0 | 235.0 | 245.0 | 230.0 | 205.0 | 55.0  | 245.0 | 205.0 | 240.0 |
| N30740         | 230.0 | 230.0 | 220.0 | 260.0 | 215.0 | 235.0 | 50.0  | 260.0 | 205.0 | 255.0 |
| Mean           | 209.0 | 204.5 | 215.0 | 234.0 | 209.5 | 207.0 | 37.0  | 232.5 | 202.0 | 227.0 |
| SD             | 15.24 | 19.50 | 20.00 | 15.42 | 12.79 | 23.59 | 16.02 | 26.69 | 13.37 | 18.59 |

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FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

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| Day<br>Animal No. | 6/7   | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30711            | 235.0 | 255.0 | 220.0 | 200.0 | 235.0 | 230.0 | 250.0 | 240.0 | 215.0 | 210.0 |
| N30712            | 225.0 | 250.0 | 225.0 | 205.0 | 240.0 | 245.0 | 245.0 | 240.0 | 215.0 | 225.0 |
| N30713            | 220.0 | 235.0 | 205.0 | 210.0 | 235.0 | 225.0 | 245.0 | 230.0 | 215.0 | 210.0 |
| N30714            | 255.0 | 255.0 | 230.0 | 240.0 | 260.0 | 260.0 | 255.0 | 260.0 | 200.0 | 240.0 |
| N30715            | 230.0 | 270.0 | 215.0 | 210.0 | 235.0 | 240.0 | 255.0 | 255.0 | 235.0 | 255.0 |
| N30716            | 270.0 | 260.0 | 230.0 | 230.0 | 245.0 | 270.0 | 265.0 | 240.0 | 260.0 | 235.0 |
| N30717            | 245.0 | 245.0 | 210.0 | 210.0 | 215.0 | 225.0 | 225.0 | 225.0 | 220.0 | 215.0 |
| N30718            | 225.0 | 240.0 | 185.0 | 225.0 | 215.0 | 230.0 | 220.0 | 230.0 | 225.0 | 205.0 |
| N30719            | 230.0 | 225.0 | 190.0 | 220.0 | 230.0 | 245.0 | 230.0 | 215.0 | 215.0 | 180.0 |
| N30720            | 235.0 | 235.0 | 205.0 | 210.0 | 205.0 | 220.0 | 230.0 | 245.0 | 215.0 | 220.0 |
| Mean              | 237.0 | 247.0 | 211.5 | 216.0 | 231.5 | 239.0 | 242.0 | 238.0 | 221.5 | 219.5 |
| SD                | 15.49 | 13.58 | 15.64 | 12.43 | 16.17 | 16.30 | 14.94 | 13.58 | 16.17 | 20.88 |

Group 2

Sex: Female

Principal animals + Recovery animals

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| Day<br>Animal No. | 6/7   | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30721            | 205.0 | 230.0 | 180.0 | 195.0 | 220.0 | 210.0 | 220.0 | 235.0 | 230.0 | 190.0 |
| N30722            | 245.0 | 240.0 | 220.0 | 200.0 | 210.0 | 225.0 | 245.0 | 230.0 | 225.0 | 205.0 |
| N30723            | 230.0 | 280.0 | 230.0 | 220.0 | 250.0 | 230.0 | 245.0 | 230.0 | 225.0 | 195.0 |
| N30724            | 265.0 | 280.0 | 240.0 | 260.0 | 255.0 | 285.0 | 280.0 | 280.0 | 285.0 | 255.0 |
| N30725            | 290.0 | 295.0 | 245.0 | 255.0 | 270.0 | 220.0 | 285.0 | 255.0 | 280.0 | 245.0 |
| N30726            | 240.0 | 225.0 | 195.0 | 210.0 | 210.0 | 230.0 | 210.0 | 225.0 | 210.0 | 210.0 |
| N30727            | 185.0 | 245.0 | 225.0 | 220.0 | 225.0 | 245.0 | 235.0 | 240.0 | 235.0 | 210.0 |
| N30728            | 280.0 | 290.0 | 220.0 | 270.0 | 270.0 | 265.0 | 275.0 | 270.0 | 260.0 | 255.0 |
| N30729            | 220.0 | 220.0 | 200.0 | 225.0 | 215.0 | 230.0 | 215.0 | 220.0 | 210.0 | 105.0 |
| N30730            | 220.0 | 225.0 | 205.0 | 240.0 | 235.0 | 225.0 | 235.0 | 240.0 | 200.0 | 200.0 |
| Mean              | 238.0 | 253.0 | 216.0 | 229.5 | 236.0 | 236.5 | 244.5 | 242.5 | 236.0 | 207.0 |
| SD                | 33.10 | 29.83 | 20.66 | 25.76 | 23.66 | 22.61 | 27.23 | 19.76 | 29.51 | 43.41 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

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| Day        | 6/7   | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 |
|------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |       |       |       |       |       |       |
| N30731     | 210.0 | 225.0 | 215.0 | 205.0 | 230.0 | 220.0 | 210.0 | 230.0 | 205.0 | 210.0 |
| N30732     | 220.0 | 220.0 | 195.0 | 200.0 | 235.0 | 220.0 | 215.0 | 230.0 | 210.0 | 200.0 |
| N30733     | 210.0 | 210.0 | 180.0 | 185.0 | 195.0 | 180.0 | 195.0 | 215.0 | 185.0 | 170.0 |
| N30734     | 230.0 | 250.0 | 215.0 | 205.0 | 230.0 | 225.0 | 240.0 | 240.0 | 225.0 | 190.0 |
| N30735     | 235.0 | 235.0 | 220.0 | 190.0 | 235.0 | 235.0 | 260.0 | 260.0 | 215.0 | 205.0 |
| N30736     | 225.0 | 240.0 | 205.0 | 225.0 | 220.0 | 235.0 | 240.0 | 220.0 | 220.0 | 195.0 |
| N30737     | 245.0 | 240.0 | 230.0 | 235.0 | 225.0 | 240.0 | 245.0 | 220.0 | 215.0 | 205.0 |
| N30738     | 225.0 | 240.0 | 200.0 | 215.0 | 235.0 | 240.0 | 245.0 | 235.0 | 255.0 | 220.0 |
| N30739     | 235.0 | 270.0 | 225.0 | 255.0 | 245.0 | 255.0 | 260.0 | 250.0 | 240.0 | 200.0 |
| N30740     | 250.0 | 260.0 | 240.0 | 250.0 | 235.0 | 245.0 | 240.0 | 235.0 | 245.0 | 215.0 |
| Mean       | 228.5 | 239.0 | 212.5 | 216.5 | 228.5 | 229.5 | 235.0 | 233.5 | 221.5 | 201.0 |
| SD         | 13.34 | 18.07 | 17.83 | 24.16 | 13.55 | 20.61 | 21.47 | 13.95 | 20.69 | 14.10 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

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| Day<br>Animal No. | 16/17 | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30711            | 210.0 | 205.0 | 245.0 | 225.0 | 225.0 | 210.0 | 260.0 | 205.0 | 235.0 | 205.0 |
| N30712            | 245.0 | 240.0 | 260.0 | 230.0 | 255.0 | 235.0 | 260.0 | 220.0 | 230.0 | 230.0 |
| N30713            | 215.0 | 220.0 | 230.0 | 215.0 | 220.0 | 195.0 | 230.0 | 190.0 | 225.0 | 195.0 |
| N30714            | 240.0 | 235.0 | 265.0 | 245.0 | 250.0 | 230.0 | 260.0 | 220.0 | 250.0 | 225.0 |
| N30715            | 245.0 | 250.0 | 255.0 | 245.0 | 275.0 | 230.0 | 270.0 | 220.0 | 245.0 | 215.0 |
| N30716            | 235.0 | 225.0 | 250.0 | 250.0 | 240.0 | 220.0 | 250.0 | 230.0 | 230.0 | 210.0 |
| N30717            | 225.0 | 225.0 | 235.0 | 225.0 | 215.0 | 190.0 | 225.0 | 210.0 | 215.0 | 200.0 |
| N30718            | 230.0 | 225.0 | 225.0 | 215.0 | 215.0 | 195.0 | 250.0 | 200.0 | 210.0 | 175.0 |
| N30719            | 225.0 | 205.0 | 220.0 | 205.0 | 220.0 | 210.0 | 225.0 | 195.0 | 205.0 | 180.0 |
| N30720            | 225.0 | 175.0 | 215.0 | 250.0 | 235.0 | 220.0 | 250.0 | 240.0 | 240.0 | 225.0 |
| Mean              | 229.5 | 220.5 | 240.0 | 230.5 | 235.0 | 213.5 | 248.0 | 213.0 | 228.5 | 206.0 |
| SD                | 11.89 | 21.27 | 17.48 | 16.24 | 20.00 | 16.17 | 16.02 | 15.85 | 14.92 | 18.83 |

Group 2

Sex: Female

Principal animals + Recovery animals

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| Day<br>Animal No. | 16/17 | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30721            | 210.0 | 225.0 | 225.0 | 210.0 | 235.0 | 210.0 | 250.0 | 205.0 | 230.0 | 190.0 |
| N30722            | 210.0 | 240.0 | 235.0 | 220.0 | 220.0 | 215.0 | 235.0 | 200.0 | 240.0 | 205.0 |
| N30723            | 205.0 | 215.0 | 230.0 | 230.0 | 225.0 | 210.0 | 240.0 | 190.0 | 210.0 | 195.0 |
| N30724            | 260.0 | 275.0 | 305.0 | 265.0 | 265.0 | 245.0 | 295.0 | 215.0 | 280.0 | 240.0 |
| N30725            | /     | 275.0 | 325.0 | 285.0 | 295.0 | 260.0 | 295.0 | 230.0 | 290.0 | 250.0 |
| N30726            | 220.0 | 210.0 | 215.0 | 210.0 | 195.0 | 180.0 | 220.0 | 200.0 | 195.0 | 190.0 |
| N30727            | 215.0 | 240.0 | 250.0 | 235.0 | 240.0 | 205.0 | 240.0 | 205.0 | 210.0 | 200.0 |
| N30728            | 255.0 | 270.0 | 285.0 | 255.0 | 260.0 | 245.0 | 300.0 | 265.0 | 245.0 | 225.0 |
| N30729            | 210.0 | 205.0 | 205.0 | 200.0 | 200.0 | 185.0 | 225.0 | 195.0 | 205.0 | 185.0 |
| N30730            | 220.0 | 225.0 | 230.0 | 200.0 | 210.0 | 190.0 | 225.0 | 210.0 | 225.0 | 210.0 |
| Mean              | 222.8 | 238.0 | 250.5 | 231.0 | 234.5 | 214.5 | 252.5 | 211.5 | 233.0 | 209.0 |
| SD                | 20.33 | 26.89 | 40.51 | 29.04 | 31.49 | 27.33 | 31.73 | 21.86 | 31.64 | 22.34 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

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| Day<br>Animal No. | 16/17 | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30731            | 215.0 | 225.0 | 215.0 | 210.0 | 220.0 | 195.0 | 215.0 | 180.0 | 205.0 | 180.0 |
| N30732            | 205.0 | 215.0 | 215.0 | 200.0 | 205.0 | 200.0 | 220.0 | 170.0 | 210.0 | 180.0 |
| N30733            | 160.0 | 140.0 | 195.0 | 190.0 | 190.0 | 155.0 | 170.0 | 155.0 | 170.0 | 155.0 |
| N30734            | 190.0 | 205.0 | 225.0 | 210.0 | 215.0 | 195.0 | 245.0 | 195.0 | 230.0 | 200.0 |
| N30735            | 200.0 | 215.0 | 225.0 | 230.0 | 240.0 | 210.0 | 250.0 | 185.0 | 145.0 | 205.0 |
| N30736            | 200.0 | 230.0 | 220.0 | 215.0 | 150.0 | 205.0 | 220.0 | 180.0 | 200.0 | 175.0 |
| N30737            | 215.0 | 225.0 | 235.0 | 220.0 | 245.0 | 205.0 | 225.0 | 220.0 | 215.0 | 195.0 |
| N30738            | 235.0 | 240.0 | 225.0 | 235.0 | 220.0 | 230.0 | 235.0 | 225.0 | 225.0 | 210.0 |
| N30739            | 245.0 | 230.0 | 240.0 | 250.0 | 250.0 | 240.0 | 260.0 | 245.0 | 255.0 | 220.0 |
| N30740            | 230.0 | 250.0 | 230.0 | 230.0 | 235.0 | 225.0 | 225.0 | 205.0 | 200.0 | 200.0 |
| Mean              | 209.5 | 217.5 | 222.5 | 219.0 | 217.0 | 206.0 | 226.5 | 196.0 | 205.5 | 192.0 |
| SD                | 24.55 | 30.12 | 12.53 | 17.76 | 30.02 | 23.55 | 24.73 | 27.67 | 30.77 | 19.32 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Principal animals + Recovery animals

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| Day | 26/27 | 27/28 | 28/29 | 29/30 |
|-----|-------|-------|-------|-------|
|-----|-------|-------|-------|-------|

Animal No.

|        |       |       |       |       |
|--------|-------|-------|-------|-------|
| N30711 | 200.0 | 225.0 | 225.0 | 215.0 |
| N30712 | 230.0 | 235.0 | 220.0 | 225.0 |
| N30713 | 215.0 | 225.0 | 200.0 | 200.0 |
| N30714 | 245.0 | 245.0 | 230.0 | 235.0 |
| N30715 | 220.0 | 235.0 | 210.0 | 235.0 |
| N30716 | 225.0 | 275.0 | 250.0 | 235.0 |
| N30717 | 205.0 | 225.0 | 200.0 | 200.0 |
| N30718 | 200.0 | 225.0 | 210.0 | 200.0 |
| N30719 | 205.0 | 230.0 | 205.0 | /     |
| N30720 | 235.0 | 260.0 | 235.0 | 210.0 |

|      |       |       |       |       |
|------|-------|-------|-------|-------|
| Mean | 218.0 | 238.0 | 218.5 | 217.2 |
| SD   | 15.67 | 17.19 | 16.51 | 15.63 |

Group 2

Sex: Female

Principal animals + Recovery animals

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| Day | 26/27 | 27/28 | 28/29 | 29/30 |
|-----|-------|-------|-------|-------|
|-----|-------|-------|-------|-------|

Animal No.

|        |       |       |       |       |
|--------|-------|-------|-------|-------|
| N30721 | 205.0 | 230.0 | 215.0 | 210.0 |
| N30722 | 205.0 | 180.0 | 215.0 | 210.0 |
| N30723 | 210.0 | 220.0 | 210.0 | 205.0 |
| N30724 | 260.0 | 270.0 | 255.0 | 250.0 |
| N30725 | 275.0 | 290.0 | 270.0 | 255.0 |
| N30726 | 195.0 | 210.0 | 195.0 | 180.0 |
| N30727 | 205.0 | 230.0 | 215.0 | 200.0 |
| N30728 | 255.0 | 280.0 | 260.0 | 235.0 |
| N30729 | 190.0 | 225.0 | 205.0 | 175.0 |
| N30730 | 210.0 | 260.0 | 215.0 | 215.0 |

|      |       |       |       |       |
|------|-------|-------|-------|-------|
| Mean | 221.0 | 239.5 | 225.5 | 213.5 |
| SD   | 30.26 | 34.52 | 25.98 | 26.67 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:  
Group 3

Sex: Female  
Principal animals + Recovery animals

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| Day        | 26/27 | 27/28 | 28/29 | 29/30 |
|------------|-------|-------|-------|-------|
| Animal No. |       |       |       |       |

|        |       |       |       |       |
|--------|-------|-------|-------|-------|
| N30731 | 190.0 | 200.0 | 190.0 | 195.0 |
| N30732 | 190.0 | 190.0 | 175.0 | 185.0 |
| N30733 | 170.0 | 165.0 | 155.0 | 155.0 |
| N30734 | 200.0 | 220.0 | 210.0 | 215.0 |
| N30735 | 215.0 | 245.0 | 235.0 | 210.0 |
| N30736 | 205.0 | 220.0 | 210.0 | 205.0 |
| N30737 | 205.0 | 255.0 | 220.0 | 205.0 |
| N30738 | 210.0 | 240.0 | 205.0 | 215.0 |
| N30739 | 220.0 | 265.0 | 250.0 | 240.0 |
| N30740 | 195.0 | 250.0 | 205.0 | 215.0 |
| Mean   | 200.0 | 225.0 | 205.5 | 204.0 |
| SD     | 14.53 | 32.06 | 27.53 | 22.46 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

|        | -5/-4 | -4/-3      | -3/-2 | -2/-1 | -1/1  | 1/2   | 3/4   | 4/5   | 5/6   |
|--------|-------|------------|-------|-------|-------|-------|-------|-------|-------|
| -- Day | 6/7   | Animal No. |       |       |       |       |       |       |       |
| <hr/>  |       |            |       |       |       |       |       |       |       |
| N30646 | 224.2 | 221.8      | 191.6 | 195.0 | 200.0 | 200.0 | 195.0 | 190.0 | 180.0 |
| N30647 | 214.8 | 239.1      | 206.6 | 215.0 | 210.0 | 210.0 | 225.0 | 205.0 | 210.0 |
| N30648 | 200.7 | 214.0      | 179.9 | 210.0 | 185.0 | 190.0 | 200.0 | 200.0 | 205.0 |
| N30649 | 223.3 | 241.6      | 209.0 | 230.0 | 215.0 | 210.0 | 210.0 | 200.0 | 215.0 |
| N30650 | 245.0 | 165.0      | 205.0 | 185.0 | 230.0 | 230.0 | 210.0 | 215.0 | 220.0 |
| Mean   | 221.6 | 216.3      | 198.4 | 207.0 | 208.0 | 208.0 | 208.0 | 202.0 | 206.0 |
| SD     | 16.13 | 30.93      | 12.37 | 17.54 | 16.81 | 14.83 | 11.51 | 9.08  | 15.57 |
|        |       |            |       |       |       |       |       |       |       |

Group 2

Sex: Male

Recovery animals

|        | -5/-4 | -4/-3      | -3/-2  | -2/-1 | -1/1  | 1/2   | 3/4   | 4/5   | 5/6   |
|--------|-------|------------|--------|-------|-------|-------|-------|-------|-------|
| -- Day | 6/7   | Animal No. |        |       |       |       |       |       |       |
| <hr/>  |       |            |        |       |       |       |       |       |       |
| N30656 | 216.9 | 201.3      | 515.2  | 340.0 | 140.0 | 195.0 | 180.0 | 175.0 | 185.0 |
| N30657 | 214.2 | 228.2      | 233.8  | 200.0 | 205.0 | 185.0 | 200.0 | 210.0 | 200.0 |
| N30658 | 223.5 | 234.8      | 177.4  | 200.0 | 205.0 | 175.0 | 190.0 | 195.0 | 170.0 |
| N30659 | 216.4 | 254.1      | 172.7  | 220.0 | 205.0 | 195.0 | 220.0 | 200.0 | 205.0 |
| N30660 | 214.6 | 231.4      | 194.9  | 210.0 | 200.0 | 190.0 | 200.0 | 200.0 | 210.0 |
| Mean   | 217.1 | 230.0      | 258.8  | 234.0 | 191.0 | 188.0 | 198.0 | 196.0 | 192.0 |
| SD     | 3.75  | 18.93      | 145.33 | 59.83 | 28.59 | 8.37  | 14.83 | 12.94 | 14.40 |
|        |       |            |        |       |       |       |       |       |       |

Group 3

Sex: Male

Recovery animals

|        | -5/-4 | -4/-3      | -3/-2 | -2/-1 | -1/1  | 1/2   | 3/4   | 4/5   | 5/6   |
|--------|-------|------------|-------|-------|-------|-------|-------|-------|-------|
| -- Day | 6/7   | Animal No. |       |       |       |       |       |       |       |
| <hr/>  |       |            |       |       |       |       |       |       |       |
| N30666 | 200.5 | 210.7      | 190.6 | 180.0 | 190.0 | 205.0 | 180.0 | 195.0 | 195.0 |
| N30667 | 217.2 | 234.8      | 176.4 | 190.0 | 185.0 | 170.0 | 180.0 | 200.0 | 185.0 |
| N30668 | 201.3 | 205.0      | 165.7 | 175.0 | 175.0 | 160.0 | 215.0 | 200.0 | 210.0 |
| N30669 | 203.9 | 212.2      | 188.5 | 195.0 | 180.0 | 175.0 | 195.0 | 195.0 | 180.0 |
| N30670 | 206.5 | 236.6      | 204.2 | 220.0 | 205.0 | 195.0 | 205.0 | 225.0 | 200.0 |
| Mean   | 205.9 | 219.9      | 185.1 | 192.0 | 187.0 | 181.0 | 195.0 | 203.0 | 192.0 |
| SD     | 6.75  | 14.72      | 14.65 | 17.54 | 11.51 | 18.51 | 15.41 | 12.55 | 9.08  |
|        |       |            |       |       |       |       |       |       |       |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

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| Day<br>Animal No. | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 | 16/17 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30646            | 215.0 | 200.0 | 195.0 | 180.0 | 200.0 | 180.0 | 315.0 | 190.0 | 180.0 | 185.0 |
| N30647            | 215.0 | 230.0 | 245.0 | 210.0 | 220.0 | 200.0 | 225.0 | 220.0 | 195.0 | 195.0 |
| N30648            | 215.0 | 195.0 | 215.0 | 180.0 | 215.0 | 185.0 | 205.0 | 195.0 | 190.0 | 185.0 |
| N30649            | 230.0 | 230.0 | 230.0 | 205.0 | 230.0 | 205.0 | 235.0 | 235.0 | 215.0 | 205.0 |
| N30650            | 215.0 | 210.0 | 235.0 | 200.0 | 225.0 | 205.0 | 230.0 | 210.0 | 210.0 | 185.0 |
| Mean              | 218.0 | 213.0 | 224.0 | 195.0 | 218.0 | 195.0 | 242.0 | 210.0 | 198.0 | 191.0 |
| SD                | 6.71  | 16.43 | 19.49 | 14.14 | 11.51 | 11.73 | 42.37 | 18.37 | 14.40 | 8.94  |

Group 2

Sex: Male

Recovery animals

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| Day<br>Animal No. | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 | 16/17 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30656            | 220.0 | 200.0 | 210.0 | 175.0 | 225.0 | 160.0 | 230.0 | 225.0 | 180.0 | 175.0 |
| N30657            | 220.0 | 200.0 | 210.0 | 195.0 | 200.0 | 175.0 | 200.0 | 195.0 | 160.0 | 170.0 |
| N30658            | 225.0 | 200.0 | 235.0 | 190.0 | 230.0 | 180.0 | 210.0 | 210.0 | 195.0 | 185.0 |
| N30659            | 230.0 | 205.0 | 240.0 | 200.0 | 235.0 | 200.0 | 255.0 | 150.0 | 215.0 | 200.0 |
| N30660            | 220.0 | 215.0 | 215.0 | 195.0 | 220.0 | 195.0 | 225.0 | 220.0 | 200.0 | 195.0 |
| Mean              | 223.0 | 204.0 | 222.0 | 191.0 | 222.0 | 182.0 | 224.0 | 200.0 | 190.0 | 185.0 |
| SD                | 4.47  | 6.52  | 14.40 | 9.62  | 13.51 | 16.05 | 21.04 | 30.21 | 20.92 | 12.75 |

Group 3

Sex: Male

Recovery animals

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| Day<br>Animal No. | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 | 16/17 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30666            | 215.0 | 205.0 | 215.0 | 185.0 | 225.0 | 185.0 | 205.0 | 210.0 | 165.0 | 165.0 |
| N30667            | 195.0 | 185.0 | 195.0 | 185.0 | 200.0 | 175.0 | 205.0 | 185.0 | 155.0 | 160.0 |
| N30668            | 215.0 | 205.0 | 210.0 | 190.0 | 210.0 | 185.0 | 210.0 | 205.0 | 155.0 | 170.0 |
| N30669            | 215.0 | 180.0 | 215.0 | 180.0 | 215.0 | 170.0 | 210.0 | 185.0 | 130.0 | 145.0 |
| N30670            | 235.0 | 210.0 | 235.0 | 220.0 | 240.0 | 195.0 | 235.0 | 240.0 | 175.0 | 225.0 |
| Mean              | 215.0 | 197.0 | 214.0 | 192.0 | 218.0 | 182.0 | 213.0 | 205.0 | 156.0 | 173.0 |
| SD                | 14.14 | 13.51 | 14.32 | 16.05 | 15.25 | 9.75  | 12.55 | 22.64 | 16.73 | 30.54 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

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| Day<br>Animal No. | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 | 26/27 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30646            | 185.0 | 175.0 | 185.0 | 195.0 | 185.0 | 190.0 | 180.0 | 185.0 | 185.0 | 175.0 |
| N30647            | 210.0 | 210.0 | 220.0 | 215.0 | 190.0 | 220.0 | 190.0 | 185.0 | 205.0 | 210.0 |
| N30648            | 195.0 | 185.0 | 195.0 | 190.0 | 185.0 | 200.0 | 175.0 | 165.0 | 175.0 | 190.0 |
| N30649            | 235.0 | 220.0 | 240.0 | 240.0 | 225.0 | 230.0 | 200.0 | 210.0 | 220.0 | 220.0 |
| N30650            | 210.0 | 195.0 | 215.0 | 215.0 | 210.0 | 210.0 | 205.0 | 205.0 | 220.0 | 230.0 |
| Mean              | 207.0 | 197.0 | 211.0 | 211.0 | 199.0 | 210.0 | 190.0 | 190.0 | 201.0 | 205.0 |
| SD                | 18.91 | 18.23 | 21.62 | 19.81 | 17.82 | 15.81 | 12.75 | 18.03 | 20.43 | 22.36 |

Group 2

Sex: Male

Recovery animals

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| Day<br>Animal No. | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 | 26/27 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30656            | 165.0 | 195.0 | 215.0 | 195.0 | 200.0 | 180.0 | 175.0 | 210.0 | 195.0 | 210.0 |
| N30657            | 180.0 | 170.0 | 185.0 | 195.0 | 190.0 | 185.0 | 180.0 | 175.0 | 190.0 | 175.0 |
| N30658            | 185.0 | 185.0 | 210.0 | 205.0 | 185.0 | 195.0 | 185.0 | 190.0 | 175.0 | 190.0 |
| N30659            | 225.0 | 205.0 | 230.0 | 220.0 | 230.0 | 195.0 | 190.0 | 215.0 | 195.0 | 240.0 |
| N30660            | 195.0 | 175.0 | 190.0 | 180.0 | 175.0 | 185.0 | 175.0 | 195.0 | 200.0 | 200.0 |
| Mean              | 190.0 | 186.0 | 206.0 | 199.0 | 196.0 | 188.0 | 181.0 | 197.0 | 191.0 | 203.0 |
| SD                | 22.36 | 14.32 | 18.51 | 14.75 | 21.04 | 6.71  | 6.52  | 16.05 | 9.62  | 24.39 |

Group 3

Sex: Male

Recovery animals

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| Day<br>Animal No. | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 | 26/27 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30666            | 185.0 | 185.0 | 190.0 | 195.0 | 185.0 | 200.0 | 185.0 | 190.0 | 200.0 | 215.0 |
| N30667            | 175.0 | 160.0 | 160.0 | 170.0 | 165.0 | 175.0 | 155.0 | 175.0 | 170.0 | 175.0 |
| N30668            | 180.0 | 195.0 | 195.0 | 210.0 | 195.0 | 205.0 | 185.0 | 185.0 | 200.0 | 195.0 |
| N30669            | 170.0 | 175.0 | 190.0 | 185.0 | 185.0 | 210.0 | 180.0 | 200.0 | 190.0 | 185.0 |
| N30670            | 225.0 | 225.0 | 230.0 | 235.0 | 235.0 | 225.0 | 225.0 | 225.0 | 220.0 | 220.0 |
| Mean              | 187.0 | 188.0 | 193.0 | 199.0 | 193.0 | 203.0 | 186.0 | 195.0 | 196.0 | 198.0 |
| SD                | 21.97 | 24.39 | 24.90 | 24.85 | 25.88 | 18.23 | 25.10 | 19.04 | 18.17 | 19.24 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

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| Day<br>Animal No. | 27/28 | 28/29 | 29/30 | 30/31 | 31/32 | 32/33 | 33/34 | 34/35 | 35/36 | 36/37 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30646            | 255.0 | 130.0 | 180.0 | 180.0 | 30.0  | 180.0 | 170.0 | 180.0 | 190.0 | 190.0 |
| N30647            | 170.0 | 205.0 | 185.0 | 180.0 | 20.0  | 180.0 | 185.0 | 180.0 | 225.0 | 195.0 |
| N30648            | 185.0 | 185.0 | 160.0 | 190.0 | 25.0  | 200.0 | 190.0 | 175.0 | 200.0 | 200.0 |
| N30649            | 230.0 | 225.0 | 190.0 | 200.0 | 25.0  | 195.0 | 215.0 | 195.0 | 230.0 | 225.0 |
| N30650            | 225.0 | 220.0 | 190.0 | 215.0 | 25.0  | 200.0 | 190.0 | 215.0 | 225.0 | 215.0 |
| Mean              | 213.0 | 193.0 | 181.0 | 193.0 | 25.0  | 191.0 | 190.0 | 189.0 | 214.0 | 205.0 |
| SD                | 34.75 | 38.50 | 12.45 | 14.83 | 3.54  | 10.25 | 16.20 | 16.36 | 17.82 | 14.58 |

Group 2

Sex: Male

Recovery animals

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| Day<br>Animal No. | 27/28 | 28/29 | 29/30 | 30/31 | 31/32 | 32/33 | 33/34 | 34/35 | 35/36 | 36/37 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30656            | 200.0 | 205.0 | 190.0 | 200.0 | 30.0  | 190.0 | 160.0 | 200.0 | 225.0 | 220.0 |
| N30657            | 175.0 | 180.0 | 150.0 | 160.0 | 20.0  | 175.0 | 180.0 | 185.0 | 195.0 | 190.0 |
| N30658            | 180.0 | 190.0 | 165.0 | 175.0 | 25.0  | 170.0 | 185.0 | 160.0 | 175.0 | 175.0 |
| N30659            | 205.0 | 215.0 | 180.0 | 190.0 | 25.0  | 205.0 | 215.0 | 205.0 | 230.0 | 200.0 |
| N30660            | 200.0 | 200.0 | 190.0 | 190.0 | 25.0  | 200.0 | 190.0 | 205.0 | 215.0 | 200.0 |
| Mean              | 192.0 | 198.0 | 175.0 | 183.0 | 25.0  | 188.0 | 186.0 | 191.0 | 208.0 | 197.0 |
| SD                | 13.51 | 13.51 | 17.32 | 15.65 | 3.54  | 15.25 | 19.81 | 19.17 | 22.80 | 16.43 |

Group 3

Sex: Male

Recovery animals

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| Day<br>Animal No. | 27/28 | 28/29 | 29/30 | 30/31 | 31/32 | 32/33 | 33/34 | 34/35 | 35/36 | 36/37 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30666            | 200.0 | 160.0 | 185.0 | 200.0 | 15.0  | 185.0 | 180.0 | 190.0 | 210.0 | 205.0 |
| N30667            | 170.0 | 165.0 | 135.0 | 160.0 | 20.0  | 175.0 | 155.0 | 155.0 | 185.0 | 170.0 |
| N30668            | 200.0 | 205.0 | 160.0 | 175.0 | 5.0   | 200.0 | 195.0 | 190.0 | 215.0 | 205.0 |
| N30669            | 190.0 | 185.0 | 165.0 | 190.0 | 30.0  | 210.0 | 195.0 | 205.0 | 225.0 | 210.0 |
| N30670            | 220.0 | 230.0 | 195.0 | 215.0 | 15.0  | 220.0 | 215.0 | 195.0 | 225.0 | 215.0 |
| Mean              | 196.0 | 189.0 | 168.0 | 188.0 | 17.0  | 198.0 | 188.0 | 187.0 | 212.0 | 201.0 |
| SD                | 18.17 | 29.03 | 23.35 | 21.39 | 9.08  | 18.23 | 22.25 | 18.91 | 16.43 | 17.82 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

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| Day<br>Animal No. | 37/38 | 38/39 | 39/40 | 40/41 | 41/42 | 42/43 | 43/44 | 44/45 | 45/46 | 46/47 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30646            | 180.0 | 205.0 | 180.0 | 195.0 | 190.0 | 175.0 | 195.0 | 190.0 | 190.0 | 190.0 |
| N30647            | 190.0 | 225.0 | 200.0 | 220.0 | 195.0 | 205.0 | 215.0 | 205.0 | 205.0 | 205.0 |
| N30648            | 175.0 | 210.0 | 175.0 | 175.0 | 170.0 | 175.0 | 170.0 | 165.0 | 160.0 | 170.0 |
| N30649            | 200.0 | 240.0 | 205.0 | 240.0 | 220.0 | 225.0 | 230.0 | 235.0 | 225.0 | 210.0 |
| N30650            | 210.0 | 225.0 | 205.0 | 225.0 | 205.0 | 210.0 | 200.0 | 200.0 | 205.0 | 210.0 |
| Mean              | 191.0 | 221.0 | 193.0 | 211.0 | 196.0 | 198.0 | 202.0 | 199.0 | 197.0 | 197.0 |
| SD                | 14.32 | 13.87 | 14.40 | 25.84 | 18.51 | 22.25 | 22.53 | 25.35 | 24.14 | 17.18 |

Group 2

Sex: Male

Recovery animals

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| --<br>Day<br>Animal No. | 37/38 | 38/39 | 39/40 | 40/41 | 41/42 | 42/43 | 43/44 | 44/45 | 45/46 | 46/47 |
|-------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30656                  | 185.0 | 230.0 | 190.0 | 210.0 | 205.0 | 210.0 | 205.0 | 205.0 | 210.0 | 195.0 |
| N30657                  | 180.0 | 175.0 | 180.0 | 180.0 | 185.0 | 170.0 | 170.0 | 195.0 | 155.0 | 175.0 |
| N30658                  | 180.0 | 195.0 | 180.0 | 200.0 | 165.0 | 185.0 | 200.0 | 180.0 | 185.0 | 175.0 |
| N30659                  | 195.0 | 220.0 | 195.0 | 240.0 | 210.0 | 210.0 | 210.0 | 220.0 | 200.0 | 210.0 |
| N30660                  | 205.0 | 215.0 | 195.0 | 205.0 | 200.0 | 215.0 | 215.0 | 215.0 | 210.0 | 215.0 |
| Mean                    | 189.0 | 207.0 | 188.0 | 207.0 | 193.0 | 198.0 | 200.0 | 203.0 | 192.0 | 194.0 |
| SD                      | 10.84 | 21.97 | 7.58  | 21.68 | 18.23 | 19.56 | 17.68 | 16.05 | 23.08 | 18.84 |

Group 3

Sex: Male

Recovery animals

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| --<br>Day<br>Animal No. | 37/38 | 38/39 | 39/40 | 40/41 | 41/42 | 42/43 | 43/44 | 44/45 | 45/46 | 46/47 |
|-------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30666                  | 200.0 | 215.0 | 190.0 | 205.0 | 215.0 | 205.0 | 180.0 | 200.0 | 200.0 | 215.0 |
| N30667                  | 185.0 | 175.0 | 165.0 | 195.0 | 185.0 | 180.0 | 180.0 | 175.0 | 180.0 | 180.0 |
| N30668                  | 195.0 | 200.0 | 180.0 | 195.0 | 200.0 | 185.0 | 195.0 | 175.0 | 195.0 | 200.0 |
| N30669                  | 195.0 | 220.0 | 195.0 | 205.0 | 215.0 | 200.0 | 220.0 | 190.0 | 195.0 | 205.0 |
| N30670                  | 220.0 | 220.0 | 215.0 | 220.0 | 225.0 | 220.0 | 240.0 | 220.0 | 230.0 | 225.0 |
| Mean                    | 199.0 | 206.0 | 189.0 | 204.0 | 208.0 | 198.0 | 203.0 | 192.0 | 200.0 | 205.0 |
| SD                      | 12.94 | 19.17 | 18.51 | 10.25 | 15.65 | 16.05 | 26.36 | 18.91 | 18.37 | 16.96 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item (NaCl)

Sex: Male

Recovery animals

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| Day<br>Animal No. | 47/48 | 48/49 | 49/50 | 50/51 | 51/52 | 52/53 | 53/54 | 54/55 | 55/56 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30646            | 180.0 | 170.0 | 200.0 | 200.0 | 190.0 | 180.0 | 205.0 | 155.0 | 190.0 |
| N30647            | 190.0 | 190.0 | 200.0 | 220.0 | 190.0 | 205.0 | 205.0 | 180.0 | 200.0 |
| N30648            | 175.0 | 190.0 | 200.0 | 190.0 | 175.0 | 180.0 | 195.0 | 140.0 | 170.0 |
| N30649            | 220.0 | 215.0 | 225.0 | 235.0 | 220.0 | 210.0 | 225.0 | 210.0 | 230.0 |
| N30650            | 195.0 | 195.0 | 210.0 | 205.0 | 205.0 | 180.0 | 210.0 | 185.0 | 195.0 |
| Mean              | 192.0 | 192.0 | 207.0 | 210.0 | 196.0 | 191.0 | 208.0 | 174.0 | 197.0 |
| SD                | 17.54 | 16.05 | 10.95 | 17.68 | 17.10 | 15.17 | 10.95 | 27.25 | 21.68 |

Group 2

Sex: Male

Recovery animals

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| Day<br>Animal No. | 47/48 | 48/49 | 49/50 | 50/51 | 51/52 | 52/53 | 53/54 | 54/55 | 55/56 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30656            | 170.0 | 180.0 | 225.0 | 210.0 | 180.0 | 195.0 | 210.0 | 160.0 | 200.0 |
| N30657            | 160.0 | 155.0 | 185.0 | 175.0 | 165.0 | 175.0 | 180.0 | 160.0 | 175.0 |
| N30658            | 180.0 | 150.0 | 205.0 | 205.0 | 175.0 | 185.0 | 180.0 | 150.0 | 180.0 |
| N30659            | 215.0 | 210.0 | 170.0 | 240.0 | 210.0 | 205.0 | 210.0 | 190.0 | 220.0 |
| N30660            | 195.0 | 215.0 | 195.0 | 190.0 | 195.0 | 195.0 | 155.0 | 195.0 | 215.0 |
| Mean              | 184.0 | 182.0 | 196.0 | 204.0 | 185.0 | 191.0 | 187.0 | 171.0 | 198.0 |
| SD                | 21.62 | 30.12 | 20.74 | 24.34 | 17.68 | 11.40 | 23.35 | 20.12 | 20.19 |

Group 3

Sex: Male

Recovery animals

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| Day<br>Animal No. | 47/48 | 48/49 | 49/50 | 50/51 | 51/52 | 52/53 | 53/54 | 54/55 | 55/56 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30666            | 190.0 | 205.0 | 225.0 | 215.0 | 200.0 | 200.0 | 230.0 | 180.0 | 220.0 |
| N30667            | 155.0 | 155.0 | 130.0 | 170.0 | 180.0 | 165.0 | 195.0 | 140.0 | 175.0 |
| N30668            | 190.0 | 180.0 | 205.0 | 200.0 | 200.0 | 185.0 | 190.0 | 175.0 | 195.0 |
| N30669            | 190.0 | 200.0 | 190.0 | 215.0 | 195.0 | 185.0 | 195.0 | 175.0 | 220.0 |
| N30670            | 210.0 | 235.0 | 225.0 | 225.0 | 215.0 | 205.0 | 225.0 | 215.0 | 225.0 |
| Mean              | 187.0 | 195.0 | 195.0 | 205.0 | 198.0 | 188.0 | 207.0 | 177.0 | 207.0 |
| SD                | 19.87 | 29.79 | 39.21 | 21.51 | 12.55 | 15.65 | 18.91 | 26.60 | 21.39 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

|                | -5/-4 | -4/-3 | -3/-2 | -2/-1 | -1/1  | 1/2   | 2/3  | 3/4   | 4/5   |       |
|----------------|-------|-------|-------|-------|-------|-------|------|-------|-------|-------|
| -- Day         |       |       |       |       |       |       |      |       |       |       |
| 5/6 Animal No. |       |       |       |       |       |       |      |       |       |       |
| --             |       |       |       |       |       |       |      |       |       |       |
| N30716         | 225.0 | 235.0 | 250.0 | 265.0 | 260.0 | 250.0 | 40.0 | 265.0 | 245.0 | 250.0 |
| N30717         | 200.0 | 315.0 | 235.0 | 255.0 | 230.0 | 235.0 | 40.0 | 180.0 | 205.0 | 230.0 |
| N30718         | 175.0 | 190.0 | 205.0 | 225.0 | 225.0 | 225.0 | 40.0 | 230.0 | 190.0 | 235.0 |
| N30719         | 200.0 | 205.0 | 220.0 | 230.0 | 240.0 | 225.0 | 30.0 | 215.0 | 200.0 | 220.0 |
| N30720         | 215.0 | 225.0 | 225.0 | 245.0 | 240.0 | 245.0 | 45.0 | 250.0 | 225.0 | 245.0 |
| Mean           | 203.0 | 234.0 | 227.0 | 244.0 | 239.0 | 236.0 | 39.0 | 228.0 | 213.0 | 236.0 |
| SD             | 18.91 | 48.53 | 16.81 | 16.73 | 13.42 | 11.40 | 5.48 | 32.90 | 21.97 | 11.94 |

Group 2

Sex: Female

Recovery animals

|                | -5/-4 | -4/-3 | -3/-2 | -2/-1 | -1/1  | 1/2   | 2/3  | 3/4   | 4/5   |       |
|----------------|-------|-------|-------|-------|-------|-------|------|-------|-------|-------|
| -- Day         |       |       |       |       |       |       |      |       |       |       |
| 5/6 Animal No. |       |       |       |       |       |       |      |       |       |       |
| --             |       |       |       |       |       |       |      |       |       |       |
| N30726         | 200.0 | 195.0 | 195.0 | 220.0 | 210.0 | 215.0 | 40.0 | 240.0 | 205.0 | 230.0 |
| N30727         | 215.0 | 210.0 | 235.0 | 230.0 | 220.0 | 220.0 | 45.0 | 255.0 | 175.0 | 250.0 |
| N30728         | 255.0 | 240.0 | 285.0 | 285.0 | 265.0 | 290.0 | 45.0 | 295.0 | 240.0 | 290.0 |
| N30729         | 200.0 | 200.0 | 215.0 | 240.0 | 215.0 | 215.0 | 65.0 | 155.0 | 160.0 | 240.0 |
| N30730         | 195.0 | 185.0 | 210.0 | 215.0 | 210.0 | 200.0 | 50.0 | 225.0 | 195.0 | 220.0 |
| Mean           | 213.0 | 206.0 | 228.0 | 238.0 | 224.0 | 228.0 | 49.0 | 234.0 | 195.0 | 246.0 |
| SD             | 24.65 | 21.04 | 34.93 | 27.97 | 23.29 | 35.46 | 9.62 | 51.28 | 30.62 | 27.02 |

Group 3

Sex: Female

Recovery animals

|                | -5/-4 | -4/-3 | -3/-2 | -2/-1 | -1/1  | 1/2   | 2/3   | 3/4   | 4/5   |       |
|----------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| -- Day         |       |       |       |       |       |       |       |       |       |       |
| 5/6 Animal No. |       |       |       |       |       |       |       |       |       |       |
| --             |       |       |       |       |       |       |       |       |       |       |
| N30736         | 195.0 | 190.0 | 225.0 | 225.0 | 220.0 | 200.0 | 35.0  | 250.0 | 225.0 | 220.0 |
| N30737         | 210.0 | 200.0 | 225.0 | 235.0 | 195.0 | 225.0 | 30.0  | 245.0 | 215.0 | 245.0 |
| N30738         | 220.0 | 205.0 | 235.0 | 245.0 | 215.0 | 235.0 | 70.0  | 230.0 | 210.0 | 235.0 |
| N30739         | 225.0 | 215.0 | 235.0 | 245.0 | 230.0 | 205.0 | 55.0  | 245.0 | 205.0 | 240.0 |
| N30740         | 230.0 | 230.0 | 220.0 | 260.0 | 215.0 | 235.0 | 50.0  | 260.0 | 205.0 | 255.0 |
| Mean           | 216.0 | 208.0 | 228.0 | 242.0 | 215.0 | 220.0 | 48.0  | 246.0 | 212.0 | 239.0 |
| SD             | 13.87 | 15.25 | 6.71  | 13.04 | 12.75 | 16.58 | 16.05 | 10.84 | 8.37  | 12.94 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

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| Day<br>Animal No. | 6/7   | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30716            | 270.0 | 260.0 | 230.0 | 230.0 | 245.0 | 270.0 | 265.0 | 240.0 | 260.0 | 235.0 |
| N30717            | 245.0 | 245.0 | 210.0 | 210.0 | 215.0 | 225.0 | 225.0 | 225.0 | 220.0 | 215.0 |
| N30718            | 225.0 | 240.0 | 185.0 | 225.0 | 215.0 | 230.0 | 220.0 | 230.0 | 225.0 | 205.0 |
| N30719            | 230.0 | 225.0 | 190.0 | 220.0 | 230.0 | 245.0 | 230.0 | 215.0 | 215.0 | 180.0 |
| N30720            | 235.0 | 235.0 | 205.0 | 210.0 | 205.0 | 220.0 | 230.0 | 245.0 | 215.0 | 220.0 |
| Mean              | 241.0 | 241.0 | 204.0 | 219.0 | 222.0 | 238.0 | 234.0 | 231.0 | 227.0 | 211.0 |
| SD                | 17.82 | 12.94 | 17.82 | 8.94  | 15.65 | 20.19 | 17.82 | 11.94 | 18.91 | 20.43 |

Group 2

Sex: Female

Recovery animals

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| Day<br>Animal No. | 6/7   | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30726            | 240.0 | 225.0 | 195.0 | 210.0 | 210.0 | 230.0 | 210.0 | 225.0 | 210.0 | 210.0 |
| N30727            | 185.0 | 245.0 | 225.0 | 220.0 | 225.0 | 245.0 | 235.0 | 240.0 | 235.0 | 210.0 |
| N30728            | 280.0 | 290.0 | 220.0 | 270.0 | 270.0 | 265.0 | 275.0 | 270.0 | 260.0 | 255.0 |
| N30729            | 220.0 | 220.0 | 200.0 | 225.0 | 215.0 | 230.0 | 215.0 | 220.0 | 210.0 | 105.0 |
| N30730            | 220.0 | 225.0 | 205.0 | 240.0 | 235.0 | 225.0 | 235.0 | 240.0 | 200.0 | 200.0 |
| Mean              | 229.0 | 241.0 | 209.0 | 233.0 | 231.0 | 239.0 | 234.0 | 239.0 | 223.0 | 196.0 |
| SD                | 34.71 | 29.03 | 12.94 | 23.35 | 23.82 | 16.36 | 25.59 | 19.49 | 24.39 | 55.16 |

Group 3

Sex: Female

Recovery animals

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| Day<br>Animal No. | 6/7   | 7/8   | 8/9   | 9/10  | 10/11 | 11/12 | 12/13 | 13/14 | 14/15 | 15/16 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30736            | 225.0 | 240.0 | 205.0 | 225.0 | 220.0 | 235.0 | 240.0 | 220.0 | 220.0 | 195.0 |
| N30737            | 245.0 | 240.0 | 230.0 | 235.0 | 225.0 | 240.0 | 245.0 | 220.0 | 215.0 | 205.0 |
| N30738            | 225.0 | 240.0 | 200.0 | 215.0 | 235.0 | 240.0 | 245.0 | 235.0 | 255.0 | 220.0 |
| N30739            | 235.0 | 270.0 | 225.0 | 255.0 | 245.0 | 255.0 | 260.0 | 250.0 | 240.0 | 200.0 |
| N30740            | 250.0 | 260.0 | 240.0 | 250.0 | 235.0 | 245.0 | 240.0 | 235.0 | 245.0 | 215.0 |
| Mean              | 236.0 | 250.0 | 220.0 | 236.0 | 232.0 | 243.0 | 246.0 | 232.0 | 235.0 | 207.0 |
| SD                | 11.40 | 14.14 | 16.96 | 16.73 | 9.75  | 7.58  | 8.22  | 12.55 | 16.96 | 10.37 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

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| Day<br>Animal No. | 16/17 | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30716            | 235.0 | 225.0 | 250.0 | 250.0 | 240.0 | 220.0 | 250.0 | 230.0 | 230.0 | 210.0 |
| N30717            | 225.0 | 225.0 | 235.0 | 225.0 | 215.0 | 190.0 | 225.0 | 210.0 | 215.0 | 200.0 |
| N30718            | 230.0 | 225.0 | 225.0 | 215.0 | 215.0 | 195.0 | 250.0 | 200.0 | 210.0 | 175.0 |
| N30719            | 225.0 | 205.0 | 220.0 | 205.0 | 220.0 | 210.0 | 225.0 | 195.0 | 205.0 | 180.0 |
| N30720            | 225.0 | 175.0 | 215.0 | 250.0 | 235.0 | 220.0 | 250.0 | 240.0 | 240.0 | 225.0 |
| Mean              | 228.0 | 211.0 | 229.0 | 229.0 | 225.0 | 207.0 | 240.0 | 215.0 | 220.0 | 198.0 |
| SD                | 4.47  | 21.91 | 13.87 | 20.43 | 11.73 | 13.96 | 13.69 | 19.36 | 14.58 | 20.80 |

Group 2

Sex: Female

Recovery animals

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| Day<br>Animal No. | 16/17 | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30726            | 220.0 | 210.0 | 215.0 | 210.0 | 195.0 | 180.0 | 220.0 | 200.0 | 195.0 | 190.0 |
| N30727            | 215.0 | 240.0 | 250.0 | 235.0 | 240.0 | 205.0 | 240.0 | 205.0 | 210.0 | 200.0 |
| N30728            | 255.0 | 270.0 | 285.0 | 255.0 | 260.0 | 245.0 | 300.0 | 265.0 | 245.0 | 225.0 |
| N30729            | 210.0 | 205.0 | 205.0 | 200.0 | 200.0 | 185.0 | 225.0 | 195.0 | 205.0 | 185.0 |
| N30730            | 220.0 | 225.0 | 230.0 | 200.0 | 210.0 | 190.0 | 225.0 | 210.0 | 225.0 | 210.0 |
| Mean              | 224.0 | 230.0 | 237.0 | 220.0 | 221.0 | 201.0 | 242.0 | 215.0 | 216.0 | 202.0 |
| SD                | 17.82 | 26.22 | 31.74 | 24.24 | 27.93 | 26.32 | 33.28 | 28.50 | 19.49 | 16.05 |

Group 3

Sex: Female

Recovery animals

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| Day<br>Animal No. | 16/17 | 17/18 | 18/19 | 19/20 | 20/21 | 21/22 | 22/23 | 23/24 | 24/25 | 25/26 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30736            | 200.0 | 230.0 | 220.0 | 215.0 | 150.0 | 205.0 | 220.0 | 180.0 | 200.0 | 175.0 |
| N30737            | 215.0 | 225.0 | 235.0 | 220.0 | 245.0 | 205.0 | 225.0 | 220.0 | 215.0 | 195.0 |
| N30738            | 235.0 | 240.0 | 225.0 | 235.0 | 220.0 | 230.0 | 235.0 | 225.0 | 225.0 | 210.0 |
| N30739            | 245.0 | 230.0 | 240.0 | 250.0 | 250.0 | 240.0 | 260.0 | 245.0 | 255.0 | 220.0 |
| N30740            | 230.0 | 250.0 | 230.0 | 230.0 | 235.0 | 225.0 | 225.0 | 205.0 | 200.0 | 200.0 |
| Mean              | 225.0 | 235.0 | 230.0 | 230.0 | 220.0 | 221.0 | 233.0 | 215.0 | 219.0 | 200.0 |
| SD                | 17.68 | 10.00 | 7.91  | 13.69 | 40.77 | 15.57 | 16.05 | 24.24 | 22.75 | 16.96 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

| Day<br>Animal No. | 26/27 | 27/28 | 28/29 | 29/30 | 30/31 | 31/32 | 32/33 | 33/34 | 34/35 | 35/36 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30716            | 225.0 | 275.0 | 250.0 | 235.0 | 50.0  | 250.0 | 280.0 | 245.0 | 225.0 | 240.0 |
| N30717            | 205.0 | 225.0 | 200.0 | 200.0 | 40.0  | 205.0 | 225.0 | 205.0 | 200.0 | 205.0 |
| N30718            | 200.0 | 225.0 | 210.0 | 200.0 | 45.0  | 200.0 | 260.0 | 195.0 | /     | 115.0 |
| N30719            | 205.0 | 230.0 | 205.0 | /     | 45.0  | 220.0 | 235.0 | 200.0 | 330.0 | 220.0 |
| N30720            | 235.0 | 260.0 | 235.0 | 210.0 | 50.0  | 230.0 | 245.0 | 225.0 | 245.0 | 235.0 |
| Mean              | 214.0 | 243.0 | 220.0 | 211.3 | 46.0  | 221.0 | 249.0 | 214.0 | 250.0 | 203.0 |
| SD                | 15.17 | 23.08 | 21.51 | 16.52 | 4.18  | 20.12 | 21.62 | 20.74 | 56.42 | 51.06 |

Group 2

Sex: Female

Recovery animals

| Day<br>Animal No. | 26/27 | 27/28 | 28/29 | 29/30 | 30/31 | 31/32 | 32/33 | 33/34 | 34/35 | 35/36 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30726            | 195.0 | 210.0 | 195.0 | 180.0 | 35.0  | 210.0 | 225.0 | 200.0 | 215.0 | 200.0 |
| N30727            | 205.0 | 230.0 | 215.0 | 200.0 | 45.0  | 215.0 | 235.0 | 210.0 | 215.0 | 210.0 |
| N30728            | 255.0 | 280.0 | 260.0 | 235.0 | 60.0  | 265.0 | 300.0 | 250.0 | 255.0 | 255.0 |
| N30729            | 190.0 | 225.0 | 205.0 | 175.0 | 30.0  | 220.0 | 240.0 | 230.0 | 220.0 | 220.0 |
| N30730            | 210.0 | 260.0 | 215.0 | 215.0 | 45.0  | 240.0 | 240.0 | 265.0 | 235.0 | 235.0 |
| Mean              | 211.0 | 241.0 | 218.0 | 201.0 | 43.0  | 230.0 | 248.0 | 231.0 | 228.0 | 224.0 |
| SD                | 25.84 | 28.37 | 24.90 | 24.85 | 11.51 | 22.64 | 29.71 | 27.02 | 17.18 | 21.62 |

Group 3

Sex: Female

Recovery animals

| Day<br>Animal No. | 26/27 | 27/28 | 28/29 | 29/30 | 30/31 | 31/32 | 32/33 | 33/34 | 34/35 | 35/36 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30736            | 205.0 | 220.0 | 210.0 | 205.0 | 45.0  | 215.0 | 240.0 | 230.0 | 220.0 | 225.0 |
| N30737            | 205.0 | 255.0 | 220.0 | 205.0 | 20.0  | 235.0 | 235.0 | 230.0 | 215.0 | 225.0 |
| N30738            | 210.0 | 240.0 | 205.0 | 215.0 | 40.0  | 205.0 | 250.0 | 235.0 | 220.0 | 225.0 |
| N30739            | 220.0 | 265.0 | 250.0 | 240.0 | 35.0  | 245.0 | 260.0 | 245.0 | 235.0 | 250.0 |
| N30740            | 195.0 | 250.0 | 205.0 | 215.0 | 40.0  | 215.0 | 245.0 | 425.0 | /     | 235.0 |
| Mean              | 207.0 | 246.0 | 218.0 | 216.0 | 36.0  | 223.0 | 246.0 | 273.0 | 222.5 | 232.0 |
| SD                | 9.08  | 17.10 | 18.91 | 14.32 | 9.62  | 16.43 | 9.62  | 85.19 | 8.66  | 10.95 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

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| Day<br>Animal No. | 36/37 | 37/38 | 38/39 | 39/40 | 40/41 | 41/42 | 42/43 | 43/44 | 44/45 | 45/46 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30716            | 235.0 | 230.0 | 235.0 | 215.0 | 225.0 | 240.0 | 250.0 | 230.0 | 225.0 | 265.0 |
| N30717            | 200.0 | 210.0 | 210.0 | 190.0 | 205.0 | 205.0 | 155.0 | 145.0 | 155.0 | 195.0 |
| N30718            | 195.0 | 200.0 | 195.0 | 195.0 | 200.0 | 185.0 | 195.0 | 190.0 | 185.0 | 210.0 |
| N30719            | 250.0 | 230.0 | 230.0 | 210.0 | 210.0 | 220.0 | 220.0 | 205.0 | 205.0 | 230.0 |
| N30720            | 255.0 | 240.0 | 235.0 | 215.0 | 230.0 | 235.0 | 230.0 | 230.0 | 210.0 | 230.0 |
| Mean              | 227.0 | 222.0 | 221.0 | 205.0 | 214.0 | 217.0 | 210.0 | 200.0 | 196.0 | 226.0 |
| SD                | 27.97 | 16.43 | 17.82 | 11.73 | 12.94 | 22.53 | 36.57 | 35.18 | 27.02 | 26.32 |

Group 2

Sex: Female

Recovery animals

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| Day<br>Animal No. | 36/37 | 37/38 | 38/39 | 39/40 | 40/41 | 41/42 | 42/43 | 43/44 | 44/45  | 45/46 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|--------|-------|
| N30726            | 210.0 | 205.0 | 205.0 | 195.0 | 200.0 | 170.0 | 225.0 | 215.0 | 200.0  | 220.0 |
| N30727            | 225.0 | 215.0 | 205.0 | 200.0 | 210.0 | 235.0 | 205.0 | 200.0 | 200.0  | 220.0 |
| N30728            | 245.0 | 230.0 | 240.0 | 230.0 | 225.0 | 225.0 | 250.0 | 240.0 | 235.0  | 250.0 |
| N30729            | 215.0 | 210.0 | /     | 210.0 | 205.0 | 230.0 | /     | /     | 675.0  | 40.0  |
| N30730            | 240.0 | 250.0 | 120.0 | 245.0 | 235.0 | 250.0 | 260.0 | 255.0 | 220.0  | 265.0 |
| Mean              | 227.0 | 222.0 | 192.5 | 216.0 | 215.0 | 222.0 | 235.0 | 227.5 | 306.0  | 199.0 |
| SD                | 15.25 | 18.23 | 51.07 | 21.04 | 14.58 | 30.54 | 24.83 | 24.66 | 206.80 | 90.99 |

Group 3

Sex: Female

Recovery animals

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| Day<br>Animal No. | 36/37 | 37/38 | 38/39 | 39/40 | 40/41 | 41/42 | 42/43 | 43/44 | 44/45 | 45/46 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30736            | 220.0 | 230.0 | 225.0 | 205.0 | 215.0 | 220.0 | 215.0 | 215.0 | 225.0 | 230.0 |
| N30737            | 220.0 | 215.0 | 230.0 | 215.0 | 225.0 | 220.0 | 220.0 | 230.0 | 215.0 | 245.0 |
| N30738            | 225.0 | 215.0 | 220.0 | 205.0 | 210.0 | 225.0 | 225.0 | 215.0 | 195.0 | 225.0 |
| N30739            | 245.0 | 255.0 | 250.0 | 240.0 | 255.0 | 255.0 | 270.0 | 240.0 | 230.0 | 250.0 |
| N30740            | 385.0 | 245.0 | 230.0 | 225.0 | /     | /     | 350.0 | /     | 40.0  | 120.0 |
| Mean              | 259.0 | 232.0 | 231.0 | 218.0 | 226.3 | 230.0 | 256.0 | 225.0 | 181.0 | 214.0 |
| SD                | 71.19 | 17.89 | 11.40 | 14.83 | 20.16 | 16.83 | 56.94 | 12.25 | 79.95 | 53.55 |

FOOD CONSUMPTION  
(g/animal/day)

Study No.:

Group 1

Control item(NaCl)

Sex: Female

Recovery animals

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| Day<br>Animal No. | 46/47 | 47/48 | 48/49 | 49/50 | 50/51 | 51/52 | 52/53 | 53/54 | 54/55 | 55/56 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30716            | 210.0 | 240.0 | 230.0 | 235.0 | 220.0 | 220.0 | 240.0 | 215.0 | 235.0 | 215.0 |
| N30717            | 170.0 | 190.0 | 200.0 | 215.0 | 205.0 | 185.0 | 210.0 | 195.0 | 215.0 | 200.0 |
| N30718            | 175.0 | 195.0 | 190.0 | 210.0 | 210.0 | 185.0 | 205.0 | 200.0 | 210.0 | 190.0 |
| N30719            | 175.0 | 210.0 | 215.0 | 215.0 | 195.0 | 210.0 | 210.0 | 215.0 | 210.0 | 240.0 |
| N30720            | 210.0 | 220.0 | 230.0 | 235.0 | 235.0 | 210.0 | 245.0 | 235.0 | 220.0 | 220.0 |
| Mean              | 188.0 | 211.0 | 213.0 | 222.0 | 213.0 | 202.0 | 222.0 | 212.0 | 218.0 | 213.0 |
| SD                | 20.19 | 20.12 | 17.89 | 12.04 | 15.25 | 16.05 | 18.91 | 15.65 | 10.37 | 19.24 |

Group 2

Sex: Female

Recovery animals

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| Day<br>Animal No. | 46/47 | 47/48 | 48/49 | 49/50 | 50/51 | 51/52 | 52/53 | 53/54 | 54/55 | 55/56 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30726            | 175.0 | 220.0 | 195.0 | 210.0 | 195.0 | 195.0 | 200.0 | 190.0 | 200.0 | 195.0 |
| N30727            | 200.0 | 215.0 | 235.0 | 225.0 | 215.0 | 215.0 | 205.0 | 210.0 | 215.0 | 210.0 |
| N30728            | 225.0 | 265.0 | 240.0 | 265.0 | 225.0 | 230.0 | 250.0 | 220.0 | 230.0 | 245.0 |
| N30729            | 75.0  | 165.0 | 200.0 | 210.0 | 205.0 | 225.0 | 220.0 | 210.0 | 410.0 | /     |
| N30730            | 215.0 | 240.0 | 230.0 | 265.0 | 235.0 | 240.0 | 255.0 | 235.0 | 235.0 | 255.0 |
| Mean              | 178.0 | 221.0 | 220.0 | 235.0 | 215.0 | 221.0 | 226.0 | 213.0 | 258.0 | 226.3 |
| SD                | 60.58 | 36.98 | 20.92 | 28.06 | 15.81 | 17.10 | 25.35 | 16.43 | 86.07 | 28.39 |

Group 3

Sex: Female

Recovery animals

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| Day<br>Animal No. | 46/47 | 47/48 | 48/49 | 49/50 | 50/51 | 51/52 | 52/53 | 53/54 | 54/55 | 55/56 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| N30736            | 200.0 | 240.0 | 230.0 | 255.0 | 225.0 | 220.0 | 235.0 | 235.0 | 240.0 | 225.0 |
| N30737            | 215.0 | 230.0 | 220.0 | 250.0 | 220.0 | 215.0 | 230.0 | 210.0 | 240.0 | 215.0 |
| N30738            | 175.0 | 205.0 | 210.0 | 225.0 | 190.0 | 175.0 | 205.0 | 190.0 | 190.0 | 210.0 |
| N30739            | 215.0 | 255.0 | 245.0 | 255.0 | 225.0 | 235.0 | 255.0 | 235.0 | 230.0 | 295.0 |
| N30740            | 150.0 | 190.0 | 210.0 | 255.0 | 220.0 | 215.0 | 240.0 | 230.0 | 225.0 | 220.0 |
| Mean              | 191.0 | 224.0 | 223.0 | 248.0 | 216.0 | 212.0 | 233.0 | 220.0 | 225.0 | 233.0 |
| SD                | 28.15 | 26.32 | 14.83 | 13.04 | 14.75 | 22.25 | 18.23 | 19.69 | 20.62 | 35.11 |

10. Rectal temperature: individual values

AM: ante meridian (in the morning)

BD: before dosing

T+3h: 3 hours after treatment

T+6h: 6 hours after treatment

T+24h: 24 hours after treatment

°C: degree Celcius

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 1

Group 1  
Control item (NaCl)  
Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30641     | 38.9     |
| N30642     | 39.4     |
| N30643     | 38.9     |
| N30644     | 39.3     |
| N30645     | 39.3     |
| N30646     | 39.1     |
| N30647     | 38.1     |
| N30648     | 38.8     |
| N30649     | 39.2     |
| N30650     | 39.2     |
| Mean       | 39.0     |
| SD         | 0.38     |

Group 2

Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30651     | 39.3     |
| N30652     | 39.2     |
| N30653     | 39.0     |
| N30654     | 39.6     |
| N30655     | 39.1     |
| N30656     | 39.0     |
| N30657     | 37.9     |
| N30658     | 39.3     |
| N30659     | 38.9     |
| N30660     | 38.9     |
| Mean       | 39.0     |
| SD         | 0.45     |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 1

Group 3

Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30661     | 39.0     |
| N30662     | 39.2     |
| N30663     | 39.1     |
| N30664     | 39.5     |
| N30665     | 38.8     |
| N30666     | 38.9     |
| N30667     | 38.8     |
| N30668     | 38.8     |
| N30669     | 38.9     |
| N30670     | 38.8     |
| Mean       | 39.0     |
| SD         | 0.23     |

## RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 2

Group 1  
Control item (NaCl)  
Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30641     | 38.7     |
| N30642     | 39.6     |
| N30643     | 38.9     |
| N30644     | 39.7     |
| N30645     | 38.8     |
| N30646     | 39.3     |
| N30647     | 38.5     |
| N30648     | 39.4     |
| N30649     | 39.3     |
| N30650     | 39.0     |
| Mean       | 39.1     |
| SD         | 0.40     |

Group 2

Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30651     | 39.7     |
| N30652     | 39.2     |
| N30653     | 39.4     |
| N30654     | 38.5     |
| N30655     | 39.5     |
| N30656     | 37.9     |
| N30657     | 38.4     |
| N30658     | 39.0     |
| N30659     | 39.4     |
| N30660     | 39.3     |
| Mean       | 39.0     |
| SD         | 0.58     |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 2

Group 3

Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30661     | 39.3     |
| N30662     | 39.6     |
| N30663     | 39.6     |
| N30664     | 39.7     |
| N30665     | 39.5     |
| N30666     | 38.1     |
| N30667     | 38.2     |
| N30668     | 39.1     |
| N30669     | 39.2     |
| N30670     | 39.4     |
| Mean       | 39.2     |
| SD         | 0.57     |

## RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 3

Group 1  
Control item (NaCl)  
Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30641     | 38.9     |
| N30642     | 38.8     |
| N30643     | 39.0     |
| N30644     | 38.4     |
| N30645     | 38.6     |
| N30646     | 38.4     |
| N30647     | 38.5     |
| N30648     | 38.3     |
| N30649     | 38.7     |
| N30650     | 38.2     |
| Mean       | 38.6     |
| SD         | 0.27     |

Group 2

Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30651     | 38.9     |
| N30652     | 39.2     |
| N30653     | 39.1     |
| N30654     | 39.1     |
| N30655     | 38.8     |
| N30656     | 38.7     |
| N30657     | 38.6     |
| N30658     | 38.8     |
| N30659     | 38.9     |
| N30660     | 38.6     |
| Mean       | 38.9     |
| SD         | 0.21     |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 3

Group 3

Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30661     | 38.6     |
| N30662     | 39.0     |
| N30663     | 38.6     |
| N30664     | 39.0     |
| N30665     | 38.8     |
| N30666     | 38.4     |
| N30667     | 39.0     |
| N30668     | 38.5     |
| N30669     | 38.7     |
| N30670     | 38.5     |
| Mean       | 38.7     |
| SD         | 0.23     |

## RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 4

Group 1  
Control item (NaCl)  
Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30641     | 39.0     |
| N30642     | 38.9     |
| N30643     | 39.0     |
| N30644     | 39.0     |
| N30645     | 39.3     |
| N30646     | 39.7     |
| N30647     | 39.2     |
| N30648     | 39.8     |
| N30649     | 39.0     |
| N30650     | 38.6     |
| Mean       | 39.2     |
| SD         | 0.37     |

Group 2

Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30651     | 39.2     |
| N30652     | 39.4     |
| N30653     | 39.0     |
| N30654     | 39.2     |
| N30655     | 39.0     |
| N30656     | 39.6     |
| N30657     | 39.1     |
| N30658     | 38.2     |
| N30659     | 39.7     |
| N30660     | 38.4     |
| Mean       | 39.1     |
| SD         | 0.48     |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 4

Group 3

Sex: Male  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30661     | 39.4     |
| N30662     | 39.1     |
| N30663     | 39.5     |
| N30664     | 39.0     |
| N30665     | 39.4     |
| N30666     | 39.8     |
| N30667     | 39.1     |
| N30668     | 39.2     |
| N30669     | 39.0     |
| N30670     | 39.1     |
| Mean       | 39.3     |
| SD         | 0.26     |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 1

Group 1  
Control item (NaCl)  
Sex: Male  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30641     | 38.4     | 38.6        | 38.5        | 38.3         |
| N30642     | 38.4     | 37.9        | 38.1        | 37.9         |
| N30643     | 38.4     | 38.1        | 38.9        | 38.6         |
| N30644     | 38.4     | 38.4        | 39.0        | 38.4         |
| N30645     | 38.5     | 38.4        | 39.2        | 38.4         |
| N30646     | 38.9     | 38.4        | 39.2        | 38.6         |
| N30647     | 38.4     | 37.5        | 38.8        | 38.0         |
| N30648     | 38.5     | 37.7        | 38.6        | 38.7         |
| N30649     | 38.9     | 38.7        | 39.1        | 38.9         |
| N30650     | 38.9     | 38.5        | 39.1        | 38.4         |
| Mean       | 38.6     | 38.2        | 38.9        | 38.4         |
| SD         | 0.23     | 0.40        | 0.36        | 0.30         |

Group 2

Sex: Male  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30651     | 38.1     | 39.2        | 39.4        | 38.4         |
| N30652     | 38.2     | 38.5        | 39.2        | 38.1         |
| N30653     | 38.5     | 38.2        | 39.2        | 38.9         |
| N30654     | 38.7     | 38.7        | 39.2        | 38.4         |
| N30655     | 39.0     | 38.4        | 39.2        | 38.4         |
| N30656     | 38.8     | 38.1        | 38.6        | 38.7         |
| N30657     | 38.5     | 37.7        | 39.1        | 38.4         |
| N30658     | 39.2     | 38.7        | 38.8        | 38.5         |
| N30659     | 39.1     | 38.5        | 39.1        | 38.8         |
| N30660     | 39.1     | 37.9        | 39.0        | 38.5         |
| Mean       | 38.7     | 38.4        | 39.1        | 38.5         |
| SD         | 0.39     | 0.44        | 0.23        | 0.23         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 1

Group 3

Sex: Male  
Principal animals + Recovery animals

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| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30661     | 39.0     | 38.7        | 38.9        | 38.5         |
| N30662     | 39.0     | 39.0        | 39.4        | 39.0         |
| N30663     | 38.5     | 39.1        | 39.1        | 38.2         |
| N30664     | 39.5     | 38.7        | 39.3        | 38.6         |
| N30665     | 39.2     | 39.0        | 39.0        | 38.9         |
| N30666     | 38.8     | 38.5        | 38.7        | 38.4         |
| N30667     | 38.9     | 39.0        | 39.0        | 39.1         |
| N30668     | 39.0     | 38.8        | 39.1        | 38.5         |
| N30669     | 38.8     | 38.5        | 38.9        | 39.0         |
| N30670     | 38.8     | 38.7        | 39.4        | 38.7         |
| Mean       | 39.0     | 38.8        | 39.1        | 38.7         |
| SD         | 0.27     | 0.22        | 0.23        | 0.30         |

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## RECTAL TEMPERATURE

Study No.:  
Time: Week 3

Group 1  
Control item (NaCl)  
Sex: Male  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30641     | 38.6     | 38.5        | 39.0        | 38.8         |
| N30642     | 38.2     | 38.6        | 38.5        | 38.6         |
| N30643     | 38.2     | 38.5        | 38.5        | 38.8         |
| N30644     | 38.1     | 38.3        | 38.8        | 38.7         |
| N30645     | 38.8     | 39.1        | 39.6        | 38.6         |
| N30646     | 38.8     | 39.2        | 38.8        | 38.8         |
| N30647     | 38.8     | 38.6        | 38.5        | 38.6         |
| N30648     | 38.4     | 38.9        | 38.5        | 39.2         |
| N30649     | 38.9     | 38.5        | 38.5        | 38.9         |
| N30650     | 38.4     | 38.8        | 39.0        | 38.7         |
| Mean       | 38.5     | 38.7        | 38.8        | 38.8         |
| SD         | 0.30     | 0.29        | 0.36        | 0.18         |

Group 2

Sex: Male  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30651     | 39.2     | 39.1        | 39.1        | 39.3         |
| N30652     | 39.0     | 39.2        | 38.6        | 39.4         |
| N30653     | 38.3     | 38.6        | 38.2        | 39.0         |
| N30654     | 38.9     | 39.2        | 39.1        | 39.0         |
| N30655     | 39.5     | 38.9        | 38.2        | 40.6         |
| N30656     | 38.6     | 38.5        | 38.4        | 38.6         |
| N30657     | 38.4     | 38.3        | 38.7        | 39.5         |
| N30658     | 39.1     | 38.9        | 38.8        | 38.9         |
| N30659     | 38.7     | 38.6        | 38.9        | 39.0         |
| N30660     | 38.5     | 39.0        | 38.8        | 38.7         |
| Mean       | 38.8     | 38.8        | 38.7        | 39.2         |
| SD         | 0.39     | 0.31        | 0.33        | 0.57         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 3

Group 3

Sex: Male  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30661     | 38.6     | 38.3        | 38.4        | 39.0         |
| N30662     | 38.3     | 39.0        | 38.9        | 39.0         |
| N30663     | 38.6     | 38.6        | 38.6        | 38.9         |
| N30664     | 39.4     | 38.4        | 38.3        | 38.9         |
| N30665     | 38.8     | 38.5        | 38.8        | 38.0         |
| N30666     | 38.9     | 38.1        | 39.5        | 38.6         |
| N30667     | 38.6     | 39.0        | 38.7        | 38.7         |
| N30668     | 38.6     | 38.4        | 38.7        | 38.2         |
| N30669     | 38.7     | 38.7        | 38.8        | 38.3         |
| N30670     | 38.5     | 38.2        | 38.4        | 38.6         |
| Mean       | 38.7     | 38.5        | 38.7        | 38.6         |
| SD         | 0.29     | 0.31        | 0.34        | 0.35         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 5

Group 1  
Control item (NaCl)  
Sex: Male  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30641     | 38.8     | 39.0        | 39.5        | 37.5         |
| N30642     | 39.1     | 38.8        | 38.5        | 37.5         |
| N30643     | 38.6     | 38.9        | 39.5        | 38.2         |
| N30644     | 39.7     | 39.0        | 39.5        | 38.1         |
| N30645     | 38.8     | 38.9        | 39.2        | 37.7         |
| N30646     | 38.8     | 38.8        | 38.5        | 38.6         |
| N30647     | 39.2     | 38.6        | 39.4        | 38.4         |
| N30648     | 39.2     | 39.0        | 38.6        | 38.0         |
| N30649     | 38.7     | 39.2        | 39.1        | 38.7         |
| N30650     | 39.2     | 39.2        | 39.0        | 38.3         |
| Mean       | 39.0     | 38.9        | 39.1        | 38.1         |
| SD         | 0.33     | 0.18        | 0.42        | 0.43         |

Group 2

Sex: Male  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30651     | 39.0     | 39.1        | 39.7        | 38.3         |
| N30652     | 38.8     | 39.2        | 39.1        | 38.2         |
| N30653     | 38.9     | 39.0        | 39.2        | 37.8         |
| N30654     | 39.2     | 39.0        | 39.8        | 38.6         |
| N30655     | 39.5     | 39.0        | 39.3        | 38.4         |
| N30656     | 39.3     | 38.9        | 39.1        | 38.4         |
| N30657     | 39.0     | 38.6        | 39.1        | 38.2         |
| N30658     | 39.8     | 38.7        | 39.5        | 38.4         |
| N30659     | 39.2     | 39.3        | 39.6        | 38.8         |
| N30660     | 38.9     | 39.0        | 39.1        | 38.2         |
| Mean       | 39.2     | 39.0        | 39.4        | 38.3         |
| SD         | 0.31     | 0.21        | 0.28        | 0.27         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 5

## Group 3

Sex: Male  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30661     | 39.2     | 39.4        | 39.4        | 38.1         |
| N30662     | 38.9     | 39.5        | 39.4        | 38.6         |
| N30663     | 39.0     | 39.2        | 38.9        | 38.0         |
| N30664     | 39.0     | 39.6        | 39.0        | 38.8         |
| N30665     | 39.3     | 39.0        | 38.8        | 38.3         |
| N30666     | 38.7     | 39.3        | 39.1        | 38.0         |
| N30667     | 39.0     | 39.1        | 39.0        | 38.0         |
| N30668     | 39.5     | 38.7        | 39.2        | 38.3         |
| N30669     | 39.0     | 38.8        | 39.2        | 38.7         |
| N30670     | 39.1     | 39.1        | 39.3        | 38.5         |
| Mean       | 39.1     | 39.2        | 39.1        | 38.3         |
| SD         | 0.22     | 0.29        | 0.21        | 0.31         |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 1

Group 1  
Control item(NaCl)  
Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30711     | 38.7     |
| N30712     | 38.9     |
| N30713     | 38.8     |
| N30714     | 39.1     |
| N30715     | 38.7     |
| N30716     | 39.3     |
| N30717     | 39.2     |
| N30718     | 39.2     |
| N30719     | 38.9     |
| N30720     | 38.9     |
| Mean       | 39.0     |
| SD         | 0.22     |

Group 2

Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30721     | 39.0     |
| N30722     | 38.8     |
| N30723     | 38.5     |
| N30724     | 38.5     |
| N30725     | 38.6     |
| N30726     | 39.0     |
| N30727     | 39.2     |
| N30728     | 39.2     |
| N30729     | 38.7     |
| N30730     | 39.1     |
| Mean       | 38.9     |
| SD         | 0.28     |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 1

Group 3

Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30731     | 38.9     |
| N30732     | 38.9     |
| N30733     | 38.9     |
| N30734     | 39.0     |
| N30735     | 38.9     |
| N30736     | 38.7     |
| N30737     | 38.8     |
| N30738     | 39.0     |
| N30739     | 38.8     |
| N30740     | 39.2     |
| Mean       | 38.9     |
| SD         | 0.14     |

## RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 2

Group 1  
Control item(NaCl)  
Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30711     | 38.4     |
| N30712     | 39.3     |
| N30713     | 39.2     |
| N30714     | 38.9     |
| N30715     | 39.0     |
| N30716     | 38.1     |
| N30717     | 38.3     |
| N30718     | 38.9     |
| N30719     | 38.2     |
| N30720     | 38.4     |
| Mean       | 38.7     |
| SD         | 0.44     |

Group 2

Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30721     | 39.5     |
| N30722     | 39.0     |
| N30723     | 39.2     |
| N30724     | 39.2     |
| N30725     | 39.4     |
| N30726     | 38.1     |
| N30727     | 38.5     |
| N30728     | 38.5     |
| N30729     | 38.5     |
| N30730     | 38.7     |
| Mean       | 38.9     |
| SD         | 0.46     |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 2

Group 3

Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30731     | 39.2     |
| N30732     | 38.9     |
| N30733     | 38.9     |
| N30734     | 39.1     |
| N30735     | 39.0     |
| N30736     | 38.8     |
| N30737     | 38.6     |
| N30738     | 38.6     |
| N30739     | 38.5     |
| N30740     | 38.4     |
| Mean       | 38.8     |
| SD         | 0.27     |

## RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 3

Group 1  
Control item(NaCl)  
Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30711     | 38.4     |
| N30712     | 38.9     |
| N30713     | 38.9     |
| N30714     | 38.9     |
| N30715     | 38.6     |
| N30716     | 38.2     |
| N30717     | 38.7     |
| N30718     | 39.0     |
| N30719     | 38.5     |
| N30720     | 38.6     |
| Mean       | 38.7     |
| SD         | 0.26     |

## Group 2

Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30721     | 38.9     |
| N30722     | 38.8     |
| N30723     | 39.0     |
| N30724     | 38.8     |
| N30725     | 39.1     |
| N30726     | 39.0     |
| N30727     | 39.2     |
| N30728     | 38.6     |
| N30729     | 39.2     |
| N30730     | 39.8     |
| Mean       | 39.0     |
| SD         | 0.33     |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 3

Group 3

Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30731     | 39.4     |
| N30732     | 39.2     |
| N30733     | 39.2     |
| N30734     | 39.2     |
| N30735     | 38.7     |
| N30736     | 38.5     |
| N30737     | 38.6     |
| N30738     | 38.2     |
| N30739     | 39.2     |
| N30740     | 38.6     |
| Mean       | 38.9     |
| SD         | 0.40     |

## RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 4

Group 1  
Control item(NaCl)  
Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30711     | 39.2     |
| N30712     | 39.1     |
| N30713     | 38.9     |
| N30714     | 38.8     |
| N30715     | 39.0     |
| N30716     | 39.2     |
| N30717     | 38.5     |
| N30718     | 39.3     |
| N30719     | 38.9     |
| N30720     | 38.7     |
| Mean       | 39.0     |
| SD         | 0.25     |

Group 2

Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30721     | 38.9     |
| N30722     | 38.9     |
| N30723     | 38.8     |
| N30724     | 38.8     |
| N30725     | 39.1     |
| N30726     | 38.8     |
| N30727     | 39.0     |
| N30728     | 38.4     |
| N30729     | 38.7     |
| N30730     | 38.8     |
| Mean       | 38.8     |
| SD         | 0.19     |

RECTAL TEMPERATURE - AM

Study No.:  
Time: Predose 4

Group 3

Sex: Female  
Principal animals + Recovery animals

| Animal No. | AM<br>°C |
|------------|----------|
| N30731     | 39.2     |
| N30732     | 39.1     |
| N30733     | 39.1     |
| N30734     | 39.3     |
| N30735     | 39.2     |
| N30736     | 38.6     |
| N30737     | 38.5     |
| N30738     | 39.0     |
| N30739     | 38.2     |
| N30740     | 38.7     |
| Mean       | 38.9     |
| SD         | 0.37     |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 1

Group 1  
Control item(NaCl)  
Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30711     | 38.7     | 38.9        | 39.3        | 38.1         |
| N30712     | 38.1     | 38.9        | 39.4        | 38.7         |
| N30713     | 39.0     | 38.7        | 39.0        | 38.4         |
| N30714     | 38.3     | 39.1        | 39.0        | 38.5         |
| N30715     | 38.2     | 39.2        | 39.2        | 38.6         |
| N30716     | 38.8     | 39.2        | 39.2        | 38.5         |
| N30717     | 38.5     | 38.6        | 39.3        | 38.2         |
| N30718     | 39.2     | 39.1        | 39.3        | 38.6         |
| N30719     | 38.7     | 38.9        | 38.9        | 38.7         |
| N30720     | 39.1     | 38.3        | 39.5        | 39.0         |
| Mean       | 38.7     | 38.9        | 39.2        | 38.5         |
| SD         | 0.38     | 0.29        | 0.19        | 0.26         |

Group 2

Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30721     | 38.8     | 38.9        | 39.4        | 38.3         |
| N30722     | 38.5     | 39.0        | 39.4        | 38.9         |
| N30723     | 38.1     | 39.3        | 38.8        | 38.9         |
| N30724     | 37.7     | 39.0        | 39.0        | 38.7         |
| N30725     | 38.6     | 39.2        | 39.1        | 39.2         |
| N30726     | 38.6     | 38.8        | 39.0        | 38.4         |
| N30727     | 39.3     | 38.5        | 39.3        | 38.8         |
| N30728     | 39.2     | 38.9        | 39.3        | 38.6         |
| N30729     | 39.3     | 38.6        | 39.3        | 38.3         |
| N30730     | 38.9     | 38.8        | 39.4        | 38.7         |
| Mean       | 38.7     | 38.9        | 39.2        | 38.7         |
| SD         | 0.52     | 0.24        | 0.21        | 0.29         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 1

## Group 3

Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30731     | 39.4     | 38.8        | 39.2        | 39.0         |
| N30732     | 38.2     | 38.7        | 38.8        | 38.1         |
| N30733     | 39.0     | 38.7        | 39.1        | 38.8         |
| N30734     | 39.0     | 39.3        | 39.3        | 38.1         |
| N30735     | 38.9     | 39.2        | 39.1        | 38.7         |
| N30736     | 39.0     | 38.8        | 39.1        | 39.0         |
| N30737     | 38.4     | 38.7        | 39.0        | 38.6         |
| N30738     | 38.6     | 38.7        | 39.2        | 38.7         |
| N30739     | 38.9     | 38.7        | 39.3        | 38.5         |
| N30740     | 38.9     | 39.1        | 39.3        | 38.2         |
| Mean       | 38.8     | 38.9        | 39.1        | 38.6         |
| SD         | 0.34     | 0.24        | 0.16        | 0.34         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 3

Group 1  
Control item(NaCl)  
Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30711     | 39.3     | 39.0        | 39.3        | 37.5         |
| N30712     | 38.7     | 38.7        | 39.2        | 38.3         |
| N30713     | 39.2     | 38.6        | 39.4        | 37.7         |
| N30714     | 38.4     | 39.2        | 39.4        | 39.3         |
| N30715     | 39.1     | 39.3        | 39.5        | 37.7         |
| N30716     | 39.5     | 38.9        | 39.5        | 38.4         |
| N30717     | 38.3     | 39.1        | 39.1        | 38.2         |
| N30718     | 38.7     | 39.0        | 39.5        | 38.0         |
| N30719     | 38.7     | 38.9        | 39.1        | 38.4         |
| N30720     | 38.9     | 39.1        | 39.2        | 38.9         |
| Mean       | 38.9     | 39.0        | 39.3        | 38.2         |
| SD         | 0.39     | 0.21        | 0.16        | 0.56         |

Group 2

Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30721     | 39.6     | 38.7        | 39.7        | 37.5         |
| N30722     | 39.3     | 39.1        | 39.1        | 38.8         |
| N30723     | 39.2     | 38.6        | 39.3        | 38.9         |
| N30724     | 39.4     | 39.1        | 39.3        | 38.8         |
| N30725     | 38.7     | 39.1        | 39.3        | 38.7         |
| N30726     | 39.4     | 39.5        | 39.2        | 39.0         |
| N30727     | 39.6     | 39.1        | 39.3        | 38.6         |
| N30728     | 38.6     | 39.0        | 39.2        | 38.9         |
| N30729     | 38.9     | 39.1        | 39.4        | 38.5         |
| N30730     | 38.4     | 38.9        | 39.1        | 38.4         |
| Mean       | 39.1     | 39.0        | 39.3        | 38.6         |
| SD         | 0.43     | 0.25        | 0.17        | 0.43         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 3

Group 3

Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30731     | 39.3     | 39.0        | 39.5        | 38.0         |
| N30732     | 38.8     | 39.1        | 39.0        | 38.2         |
| N30733     | 39.4     | 38.3        | 38.9        | 38.0         |
| N30734     | 39.2     | 39.3        | 39.4        | 39.0         |
| N30735     | 39.6     | 39.1        | 39.1        | 38.3         |
| N30736     | 38.3     | 39.0        | 39.6        | 39.3         |
| N30737     | 39.0     | 38.8        | 39.1        | 39.0         |
| N30738     | 38.7     | 38.9        | 39.2        | 38.6         |
| N30739     | 39.2     | 39.0        | 39.2        | 38.8         |
| N30740     | 38.5     | 39.0        | 39.5        | 38.7         |
| Mean       | 39.0     | 39.0        | 39.3        | 38.6         |
| SD         | 0.42     | 0.26        | 0.24        | 0.45         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 5

Group 1  
Control item(NaCl)  
Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30711     | 39.5     | 39.0        | 38.7        | 39.0         |
| N30712     | 39.3     | 38.9        | 39.0        | 38.4         |
| N30713     | 39.1     | 38.9        | 38.9        | 38.7         |
| N30714     | 39.3     | 38.9        | 39.3        | 39.2         |
| N30715     | 39.1     | 39.0        | 39.2        | 38.2         |
| N30716     | 39.0     | 39.3        | 39.0        | 39.3         |
| N30717     | 38.9     | 39.2        | 38.7        | 38.7         |
| N30718     | 39.4     | 39.3        | 39.2        | 38.9         |
| N30719     | 39.1     | 38.8        | 39.2        | 38.1         |
| N30720     | 39.4     | 39.1        | 39.4        | 39.3         |
| Mean       | 39.2     | 39.0        | 39.1        | 38.8         |
| SD         | 0.20     | 0.18        | 0.24        | 0.44         |

Group 2

Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30721     | 39.3     | 39.2        | 39.2        | 39.2         |
| N30722     | 39.5     | 39.1        | 39.2        | 38.7         |
| N30723     | 39.3     | 39.0        | 38.8        | 39.5         |
| N30724     | 39.3     | 39.0        | 39.3        | 38.5         |
| N30725     | 39.6     | 39.1        | 38.9        | 38.8         |
| N30726     | 39.2     | 38.9        | 39.0        | 38.7         |
| N30727     | 39.5     | 38.9        | 39.2        | 39.1         |
| N30728     | 39.2     | 39.0        | 39.2        | 38.9         |
| N30729     | 39.5     | 38.6        | 39.2        | 38.4         |
| N30730     | 39.1     | 39.0        | 38.9        | 39.0         |
| Mean       | 39.4     | 39.0        | 39.1        | 38.9         |
| SD         | 0.16     | 0.16        | 0.17        | 0.33         |

## RECTAL TEMPERATURE

Study No.:  
Time: Week 5

## Group 3

Sex: Female  
Principal animals + Recovery animals

| Animal No. | BD<br>°C | T+3 h<br>°C | T+6 h<br>°C | T+24 h<br>°C |
|------------|----------|-------------|-------------|--------------|
| N30731     | 39.6     | 38.9        | 38.9        | 38.1         |
| N30732     | 39.2     | 39.0        | 38.9        | 39.3         |
| N30733     | 39.0     | 39.1        | 39.5        | 38.6         |
| N30734     | 39.5     | 39.1        | 39.0        | 39.9         |
| N30735     | 39.5     | 39.2        | 39.4        | 38.5         |
| N30736     | 39.0     | 39.0        | 39.3        | 38.6         |
| N30737     | 38.9     | 39.0        | 38.8        | 39.0         |
| N30738     | 39.2     | 38.9        | 38.9        | 39.2         |
| N30739     | 39.2     | 38.8        | 38.9        | 39.0         |
| N30740     | 39.2     | 39.3        | 39.0        | 39.6         |
| Mean       | 39.2     | 39.0        | 39.1        | 39.0         |
| SD         | 0.24     | 0.15        | 0.25        | 0.55         |

11. Ophthalmology: individual findings

## OPHTHALMOLOGY

Study No.:

Sex: Male

Group 1

Control item (NaCl)

Principal animals

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Animal

No.      Observation

Day  
-4            3            31

RE   LE      RE   LE      RE   LE

|        |                             |   |   |   |   |   |   |
|--------|-----------------------------|---|---|---|---|---|---|
| N30641 | Abnormalities (reflex)      | N | N | N | N | N | N |
|        | Abnormalities (observation) | N | N | N | N | N | N |
| N30642 | Abnormalities (reflex)      | N | N | N | N | N | N |
|        | Abnormalities (observation) | N | N | N | N | N | N |
| N30643 | Abnormalities (reflex)      | N | N | N | N | N | N |
|        | Abnormalities (observation) | N | N | N | N | N | N |
| N30644 | Abnormalities (reflex)      | N | N | N | N | N | N |
|        | Abnormalities (observation) | N | N | N | N | N | N |
| N30645 | Abnormalities (reflex)      | N | N | N | N | N | N |
|        | Abnormalities (observation) | N | N | N | N | N | N |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Male  
 Group 2

## Principal animals

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| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 31 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30651        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30652        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30653        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30654        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30655        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Male  
 Group 3

## Principal animals

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| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 31 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30661        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30662        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30663        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30664        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30665        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Female  
 Group 1  
 Control item(NaCl)  
 Principal animals

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## Animal

No. Observation

Day  
-4      3      31

RE LE    RE LE    RE LE

N30711 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

N30712 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

N30713 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

N30714 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

N30715 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Female  
 Group 2

## Principal animals

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| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 31 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30721        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30722        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30723        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30724        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30725        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Female  
 Group 3

## Principal animals

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| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 31 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30731        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30732        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30733        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30734        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30735        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:

Sex: Male

Group 1

Control item (NaCl)

Recovery animals

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| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 57 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30646        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30647        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30648        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30649        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30650        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Male  
 Group 2

Recovery animals

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| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 57 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30656        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30657        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30658        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30659        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30660        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Male  
 Group 3

Recovery animals

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| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 57 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30666        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30667        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30668        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30669        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30670        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Female  
 Group 1  
 Control item(NaCl)  
 Recovery animals

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## Animal

No. Observation

Day  
-4      3      57

RE LE    RE LE    RE LE

N30716 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

N30717 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

N30718 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

N30719 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

N30720 Abnormalities (reflex)  
 Abnormalities (observation)

N N    N N    N N  
 N N    N N    N N

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Female  
 Group 2

Recovery animals

--

| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 57 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30726        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30727        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30728        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30729        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30730        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

## OPHTHALMOLOGY

Study No.:  
 Sex: Female  
 Group 3

Recovery animals

--

| Animal<br>No. | Observation                 | Day |    |    |    |    |    |
|---------------|-----------------------------|-----|----|----|----|----|----|
|               |                             | -4  |    | 3  |    | 57 |    |
|               |                             | RE  | LE | RE | LE | RE | LE |
| N30736        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30737        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30738        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30739        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |
| N30740        | Abnormalities (reflex)      | N   | N  | N  | N  | N  | N  |
|               | Abnormalities (observation) | N   | N  | N  | N  | N  | N  |

Legend: RE=Right Eye, LE=Left Eye, N=None

12. Immunogenicity phase report

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## PRINCIPAL INVESTIGATOR STATEMENT OF COMPLIANCE

The work related to the study phase and performed at the Test Site was performed in accordance with the OECD Principles of Good Laboratory Practice as required by the:

- Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004.
- Bonnes Pratiques de Laboratoire, Ministère de l'Emploi et de la Solidarité Française, no. 2000/5bis, arrêté du 14/03/2000 (JO 23/03/2000).

OECD Principles of Good Laboratory Practice are accepted by Regulatory Authorities throughout the European Union, United States of America (FDA and EPA) and Japan (MHLW, MAFF and METI) and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

This is a multisite study. The study phase was performed according to the OECD GLP consensus document 13 on "the application of the OECD principles of GLP to the organisation and management of multi-site studies", ENV/JM/MONO (2002)9, 25 June 2002.

Deviations from the above regulations are listed below:

- No expiration dates were provided by the supplier for the reference item and for the control item. However the stability of the reference item and the control item were confirmed by the standard response and the control response measured for each run. In consequence these deviations were considered not to have affected the validity and reliability of the data.

This report is a true and accurate record of the results obtained.

DocuSigned by:



Signer Name: Dominique Favre  
Signing Reason: I approve this document  
Signing Time: 30-Jan-19 | 11:40 CET  
0E0208E1270E477589D03A1E10B24255

Dominique Favre, Higher Diploma in Applied Biology  
Principal Investigator

## TEST SITE QUALITY ASSURANCE STATEMENT

(Charles River Lyon)

Delegated phase title: Immunogenicity.

This phase report was inspected by the Charles River Lyon, Quality Assurance Unit (QAU) according to the Standard Operating Procedure(s).

The reported method and procedures were found to describe those used and the phase report reflects the raw data.

During the on-site process inspections, procedures applicable to this type of study phase were inspected.

The dates of Quality Assurance inspections are given below.

### Delegated phase No. AB22661

| Type of Inspections | Description                        | Start Inspection date | End Inspection date | Reporting date |
|---------------------|------------------------------------|-----------------------|---------------------|----------------|
| Study               | Study Plan and amendments 01 to 02 | 16-Oct-2018           | 16-Oct-2018         | 16-Oct-2018    |
|                     | Study Plan Amendment 3             | 31-Oct-2018           | 31-Oct-2018         | 31-Oct-2018    |
|                     | Study Plan Amendment 4             | 26-Nov-2018           | 26-Nov-2018         | 26-Nov-2018    |
|                     | Phase report review final          | 03-Dec-2018           | 06-Dec-2018         | 06-Dec-2018    |
| Process             | Analysis by Elisa method           | 06-Nov-2018           | 06-Nov-2018         | 06-Nov-2018    |

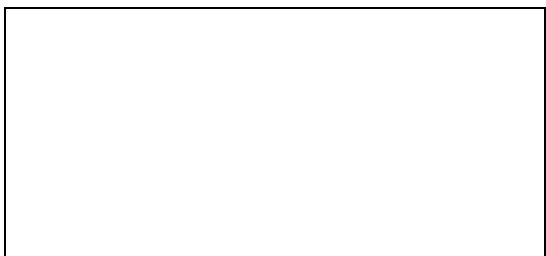
Final Immunogenicity Phase  
Report Test Site Study No.

Page 6  
Test Facility Study No.

Facility inspection program is conducted in accordance with Standard Operating Procedure.

RABBITV1

The review of the final phase report was completed on the date of signing this QA statement.



QA Auditor

## ABBREVIATIONS

|       |                                   |
|-------|-----------------------------------|
| AT    | Ambient Temperature               |
| BLQ   | Below Limit of Quantitation       |
| °C    | Degree Celsius                    |
| ELISA | Enzyme-Linked Immunosorbent Assay |
| EU    | ELISA Unit                        |
| GLP   | Good Laboratory Practices         |
| h     | Hour                              |
| HRP   | Horse Radish Peroxidase           |
| L     | Liter                             |
| LLOQ  | Lower Limit of Quantification     |
| µg    | Microgram                         |
| µL    | Microliter                        |
| min   | Minute                            |
| mg    | Milligram                         |
| mL    | Milliliter                        |
| NEG   | Negative Serum                    |
| NS    | No Sample                         |
| OD    | Optical Density                   |
| PBS   | Phosphate Buffer Saline           |
| QC    | Quality Control                   |
| sd    | Standard Deviation                |
| STD   | Standard                          |
| TMB   | 3,3',5,5'-Tetramethylbenzidine    |

## 1. SUMMARY

The aim of the immunogenicity phase was to confirm the exposure of animals given SENDVACC10 vaccine or VACC99 vaccine in the repeat dose toxicology study (Test Facility Study no. RABBITV1).

Samples were collected on pretest, 2 days after the third injection (Day 31 and after a 4-week observation period (Day 57 from all animals immunized either with SENDVACC10 (Group 2 or VACC99 (Group 3 vaccine or with saline control (Group 1. The specific IgG against xxxx were measured by an Enzyme-Linked Immunosorbent Assay (ELISA; Test Facility Validation Study completed in study no.

No quantifiable or low levels of specific IgG were observed in control animals as well as in test item-treated animals at pretest. These levels were close to the Lower Limit of Quantification (LLOQ) and considered as background. All vaccinated animals showed very high levels of specific IgG on Days 31 and 57. The titers were generally higher in animals given VACC99 vaccine as compared to those given SENDVACC10 vaccine.

In conclusion, the present immunogenicity phase confirmed the exposure of all vaccinated rabbits to SENDVACC10 and AVACC99 vaccines as sustained specific IgG ELISA humoral responses were induced by these vaccines.

## **2. INTRODUCTION**

### **2.1. Location and participating parties**

#### **Test Facility**

Sponsor Director:

Lead QA Contact:

#### **Immunogenicity Test Site**

Principal Investigator (PI):

PI Test site Management:

PI Test Site Quality Assurance (QA):

#### **Sponsor**

Sponsor Representative:

## 2.2. Study schedule

Signature of Acceptance Form date: 13 August 2018.

Sample shipment date: 29 October 2018.

Sample receipt date: 30 October 2018.

Experimental starting date: 05 November 2018 (first preparation).

End of experimentation date: 14 November 2018 (last analysis).

## 2.3. Electronic systems for data acquisition

The following validated proprietary systems were used for data reporting and storage:

| System name       | Software version | Description                   |
|-------------------|------------------|-------------------------------|
| SOFTMAX Pro (SMP) | 7.0.2            | Data acquisition/analysis     |
| PROVANTIS         | 9                | Data acquisition (Dispensary) |
| GTC MOZART 21     | 3.1              | Environmental data recording  |

Microsoft Excel® 2010 was employed to present the results and perform associated calculations.

## 3. ARCHIVES

All study-specific data, documentation, copy of study plan, retained samples and final phase report will be archived at the time of the final phase report issue. All materials generated by Charles River from this phase will be transferred to Charles River archive unit for a period of 5 years following the date of issue of the final phase report.

Records to be maintained will include, but will not be limited to, documentation and data for the following:

- Copies of the study plan, study plan amendments, and deviations.
- Study schedule.
- Study-related correspondence.
- A sample of the reference item, control item and coating protein from each batch used.
- Original final phase report.

Provantis data will be maintained at the Charles River Wilmington (USA) data center.

#### 4. MATERIALS AND METHODS

##### 4.1. Materials

###### 4.1.1. Coating protein

The quality environment (GLP, GMP or other) in which the characterization of the coating protein has been performed is unknown.

Denomination:

Supplier:

Batch number: 14 Dec 2018 (1 year from date of receipt).

Expiry date: 752 µg/mL.

Nominal concentration:

Storage: 2-8°C.

The analytical documentation provided by the supplier is presented in [Addendum 1](#).

###### 4.1.2. Reference item (Standard)

Denomination:

1361966 EU equivalents to 6.13 log<sub>10</sub> EU (as determined in the validation study no. .

Supplier:

Titer: Not defined. No expiration date was provided for the reference item by the supplier. However the stability of the reference item was confirmed by the standard sample response measured for each run.

Retest date: Storage: -70°C/-90°C.

The certificate of analysis provided by the supplier is presented in [Addendum 2](#).

###### 4.1.3. Control item (Quality Control)

Denomination:

1285485 EU equivalents to 6.11 log<sub>10</sub> EU (as determined in the validation study no. .

Supplier:

Titer:

Retest date:

Not defined. No expiration date was provided for the control item by the supplier. However the stability of the control item was confirmed by the control response measured for each run.

Storage:

-70°C/-90°C.

The certificate of analysis provided by the supplier is presented in [Addendum 3](#).

#### **4.1.4. Reagents**

- Phosphate Buffer Saline (PBS) without Ca++, Mg++ (Lonza BE #17-516).
- Tween-20 (Sigma #P1379).
- Skimmed milk powder (Difco #232100).
- Carbonate-Bicarbonate Buffer (Sigma #C3041).
- Conjugate HRP for antibody detection: Anti-Rabbit IgG peroxidase-conjugated, (HRP; Jackson ImmunoResearch Laboratories, Inc #111-036-046).
- Hydrochloric acid (Merck #1.09970.0001).
- 3,3',5,5'-Tetramethylbenzidine (TMB) substrate (Tebu-Bio #TMBW1000).
- Sterile water (Aguettant #600500).
- ELISA plates: 96-Well Microplates, Polystyrene (Greiner Bio-One # 655061).

### **4.2. Solution and buffer preparation**

#### **4.2.1. Wash buffer**

Washing buffer (PBS 1X +0.05% Tween-20) was prepared by adding 10% Tween-20 solution in PBS 1X. The solution was used within the day of preparation at ambient temperature (AT).

10% Tween-20 solution was prepared by performing a 1/10 dilution of Tween-20 in sterile water. This solution was stored for up to 3 months at 2-8°C.

#### **4.2.2. Coating buffer**

One cap of Carbonate-Bicarbonate was dissolved in 100 mL of sterile water and mixed to obtain a Carbonate-Bicarbonate Buffer pH 9.6 and used within the day of preparation at AT.

#### **4.2.3. Assay diluent (also used as blocking buffer)**

Assay diluent (PBS 1X + 0.05% Tween-20 + 1% skimmed milk) was prepared by adding skimmed milk in Wash buffer and used within the day of preparation at AT.

#### **4.2.4. Coating solution**

The coating solution was prepared by diluting the coating protein at 1 µg/mL in coating buffer. The coating solution was used within the day of preparation at AT.

#### **4.2.5. Detection antibody solution**

HRP-conjugated was diluted in assay diluent at 1/20000 dilution and used within the day of preparation at AT.

#### **4.2.6. Stop solution**

The content of one vial of "Hydrochloric acid" was diluted with sterile water in a final volume of 1000 mL to obtain Hydrochloric acid 1N (stop solution). The stop solution was stored for up to 1 month at AT.

### **4.3. Standard, quality control, negative and study sample preparation**

For all of the following items, intermediate dilutions were performed in polypropylene tubes, while final dilutions were prepared in a polystyrene 96-well plate ("dilution plate"). The desired volumes were transferred from each well to the ELISA plate at the antigen capture step.

#### **4.3.1. Standard (STD) samples for calibration curve**

STD was diluted by a 1/10000 factor to obtain an intermediate dilution, which was further diluted (by a 2 fold serial dilution) to obtain the 12 points of the calibration curve (STD1 to STD12). STD1 to 12 were characterized by dilutions ranging from 1/20000 for STD1 to 1/40960000 for STD12. All dilutions were performed in assay diluent at AT the day of use. Only STD5 to STD10 were used for the calculation of the calibration curve.

#### **4.3.2. Quality Control (QC) samples**

QC were diluted by a 1/150000 factor to obtain an intermediate dilutions, which was further diluted (by a 2 fold serial dilution) to obtain QC1 to 6. Dilutions were performed in assay diluent at AT, on the day of use.

#### **4.3.3. Negative serum (NEG) samples**

NEG was obtained from drug naïve rabbits. Aliquots of pooled serum samples were stored at -70 to -90°C for one year. NEG was diluted by a 1/50 to obtain an intermediate dilution, which was further diluted by two fold, at 1/100 in assay diluent at AT, on the day of use.

#### **4.3.4. Blank**

Assay diluent was used as Blank.

#### **4.3.5. Study sample preparation**

Study samples at the test site were stored at -70 to -90°C and analyzed within 120 days (which is the stability period demonstrated in the validation study no. AB22056). Study samples were diluted by a 1/50 factor for low responders or 1/5000 for high responders. These dilutions were further diluted (by 2 fold serial dilutions) to obtain:

- 3 dilutions 1/100, 1/200 and 1/400 for the evaluation of the Pretest study samples and for the evaluation of the Day 31 and Day 57 study samples for Group 1 (control).
- 12 dilutions which ranged from 1/10000 to 1/20480000 for the evaluation of the Day 31 and Day 57 study samples for Groups 2 and 3.

All dilutions were performed in assay diluent at AT the day of use.

The remaining of the serum samples at the test site will be stored frozen (between -70 to -90°C) until the issue of the final phase report and will then be discarded after approval by the Study Sponsor and Study Director.

Note: samples N30649 Pretest, N30654 Pretest and N30719 Pretest were re-analyzed as the OD response of the serial dilutions was not consistent (some wells presented an OD greater than the OD of the previous well). Only the results of the re-analysis were reported.

#### 4.4. ELISA assay, data analysis and acceptance criteria

##### 4.4.1. ELISA

ELISA plates were coated with 100 µL of coating solution and incubated for 10 to 24h at 2-8°C. After removing the coating solution, 150 µL of blocking buffer were added to each well and plates were incubated for minimum of 1h at 37°C ± 2°C.

Following removal of the blocking buffer, 100 µL of standards, controls and study samples were added to wells and incubated for 1h30 minutes (min) ± 10 min at 37°C ± 2°C. After washing the plate, 100 µL of detection antibody solution were added to each well and plates were incubated for 1h30 min ± 10 min at 37°C ± 2°C. Plates were washed before adding 100 µL of TMB substrate to each well and incubating for 30 min ± 1 min at AT protected from light. After adding 100 µL/well of stop solution, absorbance at 450-650 nm was measured within 1h by using the microplate reader SpectraMax M3, Molecular Devices.

##### 4.4.2. Data analysis

Data analysis was performed with the SOFTMAX Pro (SMP) 7.0.2 software.

OD mean for the assay diluent was subtracted from that of the wells of the plate. The Standard calibration curve was calculated from the OD of the Standards (STD5 to STD10) using the 4-parameters Logistic type.

$$F(x) = d + \frac{a - d}{1 + \left(\frac{x}{c}\right)^b}$$

x: concentration (EU); F(x): response value (e.g. absorbance, OD, response value);

a: minimum asymptote; b: Hill slope; c: inflection point; d: maximum asymptote.

For study samples, only wells displaying OD values ranging between 0.200 and 3.000 were retained. For all selected wells, the OD values were plotted on the standard curve to calculate the corresponding x-axis value. The so-obtained x-axis values were multiplied by the relative dilution factors, to obtain the titers (expressed in EU).

The titer of a study sample was obtained as the mean of titers measured for all the retained dilutions of that sample. The titer for samples below limit of quantification (BLQ; equal to 20 EU and corresponding to 1.301 log<sub>10</sub> EU) was reported BLQ and an arbitrary titer of 1.000 log<sub>10</sub> EU was assigned.

##### 4.4.3. Run acceptance criteria

Analytical runs were accepted if the following conditions were met:

- At least two-thirds of Blank and NEG samples were free of interference (<0.2 OD).
- The experimental OD at x-axis = 1 on the calibration curve giving a titer of 1361966 for the Standard serum was within 1.0 ± 50%.
- The correlation coefficient of the calibration curve was ≥0.99.
- The back-calculated EU values of STD5 to STD10 were within 75% to 125% of the nominal EU value.
- At least five of the six standards STD5 to STD10 met the above criteria.
- At least two-thirds of the back-calculated titer of the 6 QC samples (QC1 to QC6) were within ± 0.3 log<sub>10</sub> of the nominal titer expressed as log<sub>10</sub>.

## 5. DEVIATIONS

### 5.1. Adhesion to Study Plan

The study phase was conducted in accordance with the agreed study plan and amendments except the following deviation:

- Due to some prolonged door opening, the storage temperature for the reference item and QC sample in the Laboratory of Biological Evaluation Department was above the -70°C target range on several occasion and for up to a maximum of 4 hours 10 minutes on 27 July 2018 (max temperature: -53.7°C). Taking into account the short duration of this event and the slight drop in temperature, it was considered that there was not impact on the study objectives.

And the following study plan deviation (which was communicated by the study director) occurred in the study:

- The following samples were not centrifuged in 30 to 60 min after blood collection:

| Animal | Occasion | Time between blood collection and centrifugation (min) |
|--------|----------|--|
| N30733 | Pretest  | 27   |
| N30734 | Pretest  | 28   |
| N30735 | Pretest  | 21   |
| N30712 | Day 31   | 27   |
| N30713 | Day 31   | 20   |
| N30714 | Day 31   | 19   |
| N30715 | Day 31   | 14   |

The centrifugation step for serum preparation is performed within 60 min ±10 min after blood collection at Test Site for this ELISA method. In consequence this deviation was considered not to have affected the validity and reliability of the data.

### 5.2. Deviation to the validated analytical method

During the blood collection, the pretest samples were centrifuged at 3000 g instead of 1800 g (which is the setup in the validated ELISA method) as for the other occasions Day 31 and Day 57. The titers of Pretest samples were close to the LLOQ and comparable to the titers observed at Day 31 and Day 57 for Group 1 animals. This deviation did not impact the outcome of the study.

## 6. RESULTS

*Influenza*-specific IgG response was detected in all samples from animals given three intramuscular injections of one human dose of SENDVACC10 or VACC99 vaccine at 2 week intervals (more than 4 log<sub>10</sub> increase in mean log<sub>10</sub> titers in vaccinated groups as compared to pretest). The titers were generally higher in animals given VACC99 vaccine as compared to those given SENDVACC10 vaccine. This demonstrates the exposure of all rabbits to SENDVACC10 and VACC99 vaccines.

No quantifiable or low levels of IgG specific to hemagglutinin from xxxx (xxxx strain) were observed in control animals as well as in test item-treated animals at pretest. Quantifiable low titers of specific IgG were observed in some Group 1 (control animals: 7/20 with titers ≤1.949 log<sub>10</sub> EU at pretest, 12/20 with titers ≤2.375 log<sub>10</sub> EU at Day 31 and 6/10 with titers ≤2.097 log<sub>10</sub> EU at Day 57. In addition, 4/20 animals from Groups 2 and 3 displayed low titers of antigen-specific antibody at pretest (titers ≤2.415 log<sub>10</sub> EU and ≤2.021 log<sub>10</sub> EU, respectively. These titers were considered as background and individual variability since the levels were low, close to the LLOQ and observed in 15/60 animals at pretest.

Results are summarized in the [text-table](#) below.

**Text table 1. Mean anti-xxxx IgG titers (log<sub>10</sub> EU ± sd)**

| Time point | Group 1<br>Control<br>(NaCl 0.9%) | Group 2<br>SENDVACC10 Vaccine | Group 3<br>VACC99      |
|------------|-----------------------------------|-------------------------------|------------------------|
| Pretest    | 1.181 ± 0.283                     | 1.161 ± 0.376                 | 1.1                    |
| Day 31     | 1.381 ± 0.400<br>+0.2*            | 5.372 ± 0.086<br>+4.2*        | 5.853 ± 0.119<br>+4.7* |
| Day 57     | 1.529 ± 0.485<br>+0.3*            | 5.417 ± 0.150<br>+4.3*        | 5.677 ± 0.139<br>+4.6* |

\*: Log<sub>10</sub> increase of mean titers as compared to respective pretest mean value.

## **7. CONCLUSION**

In conclusion, the present immunogenicity phase confirmed the exposure of all rabbits to vaccines as sustained specific IgG ELISA humoral responses were induced by these vaccines.

**8. TABLES**

**Table 1**  
**Summary of analytical runs**

| Plate no. | Assay Date       | Status   | Description  | Comment |
|-----------|------------------|----------|--|---------|
| 1         | 06 November 2018 | Accepted | Pretest ( animals N30641 to N30654 and N30711 to N30720)   | Conform |
| 2         | 06 November 2018 | Accepted | Pretest ( animals N30655 to N30668 and N30721 to N30730)   | Conform |
| 3         | 06 November 2018 | Accepted | Pretest ( animals N30669, N30670 and N30731 to N30740),<br>Day 31 (animals N30651, N30661) and day 57 (N30656) | Conform |
| 4         | 06 November 2018 | Accepted | Day 31 ( animals N30641 to N30650, N30711 to N30720 and<br>N30652)   | Conform |
| 5         | 07 November 2018 | Accepted | Day 31 ( animals N30653 to N30658)   | Conform |
| 6         | 07 November 2018 | Accepted | Day 31 ( animals N30659, N30660 and N30721 to N30724)  | Conform |
| 7         | 07 November 2018 | Accepted | Day 31 ( animals N30725 to N30730)   | Conform |
| 8         | 07 November 2018 | Accepted | Day 31 ( animals N30662 to N30667)   | Conform |
| 9         | 07 November 2018 | Accepted | Day 31 ( animals N30668 to N30670 and N30731 to N30733)  | Conform |
| 10        | 07 November 2018 | Accepted | Day 31 ( animals N30734 to N30739)   | Conform |
| 11        | 08 November 2018 | Accepted | Day 31 ( animal N30740) and Day 57 (animals N30646 to<br>N30650, N30716 to N30720, N30657 and N30658)          | Conform |
| 12        | 08 November 2018 | Accepted | Day 57 ( animals N30659, N30660 and N30726 to N30729)  | Conform |
| 13        | 08 November 2018 | Accepted | Day 57 ( animals N30730 and N30666 to N30670)  | Conform |
| 14        | 08 November 2018 | Accepted | Day 57 ( animals N30736 to N30740) and retest Pretest<br>(animals N30649 and N30654)                           | Conform |
| 15        | 14 November 2018 | Accepted | retest Pretest (animal N30719)   | Conform |

**Table 2**

**Titers of antigen-specific antibodies in study samples**

|                 |                          | Occasion:     | Pretest                         | Occasion:     | Day 31                          | Occasion:     | Day 57                          |
|-----------------|--------------------------|---------------|---------------------------------|---------------|---------------------------------|---------------|---------------------------------|
| Group-Treatment | AnimalID<br>(Sex/Number) | Titer<br>(EU) | Titer<br>(log <sub>10</sub> EU) | Titer<br>(EU) | Titer<br>(log <sub>10</sub> EU) | Titer<br>(EU) | Titer<br>(log <sub>10</sub> EU) |
| 1- NaCl 10.9%   | Male/N30641              | BLQ           | 1000                            | 28            | 1447                            | -             | -                               |
|                 | Male/N30642              | 22            | 1342                            | 237           | 2.375                           | -             | -                               |
|                 | Male/N30643              | BLQ           | 1000                            | BLQ           | 1000                            | -             | -                               |
|                 | Male/N30644              | 89            | 1949                            | 28            | 1447                            | -             | -                               |
|                 | Male/N30645              | 33            | 1.519                           | 47            | 1.672                           | -             | -                               |
|                 | Male/N30646              | BLQ           | 1000                            | BLQ           | 1000                            | BLQ           | 1000                            |
|                 | Male/N30647              | BLQ           | 1000                            | 84            | 1924                            | 123           | 2.090                           |
|                 | Male/N30648              | BLQ           | 1000                            | BLQ           | 1000                            | BLQ           | 1000                            |
|                 | Male/N30649              | 24            | 1.380                           | 35            | 1.544                           | 40            | 1.602                           |
|                 | Male/N30650              | BLQ           | 1000                            | BLQ           | 1000                            | BLQ           | 1000                            |
|                 | Female/N30711            | BLQ           | 1000                            | BLQ           | 1000                            | -             | -                               |
|                 | Female/N30712            | BLQ           | 1000                            | 18            | 1255                            | -             | -                               |
|                 | Female/N30713            | BLQ           | 1000                            | BLQ           | 1000                            | -             | -                               |
|                 | Female/N30714            | 20            | 1.301                           | 36            | 1.556                           | -             | -                               |
|                 | Female/N30715            | BLQ           | 1000                            | BLQ           | 1000                            | -             | -                               |
|                 | Female/N30716            | 45            | 1.653                           | 22            | 1.342                           | 40            | 1.602                           |
|                 | Female/N30717            | BLQ           | 1000                            | 24            | 1.380                           | 89            | 1.949                           |
|                 | Female/N30718            | BLQ           | 1000                            | BLQ           | 1000                            | BLQ           | 1000                            |
|                 | Female/N30719            | BLQ           | 1000                            | 57            | 1.756                           | 89            | 1.949                           |
|                 | Female/N30720            | 30            | 1.477                           | 83            | 1.919                           | 125           | 2.097                           |
| <b>Mean</b>     |                          | <b>1.181</b>  |                                 | <b>1.381</b>  |                                 | <b>1.529</b>  |                                 |
| <b>s d</b>      |                          | <b>0.283</b>  |                                 | <b>0.400</b>  |                                 | <b>0.485</b>  |                                 |
| VACC 10         | Male/N30651              | BLQ           | 1000                            | 219738        | 5.342                           | -             | -                               |
|                 | Male/N30652              | BLQ           | 1000                            | 208778        | 5.320                           | -             | -                               |
|                 | Male/N30653              | BLQ           | 1000                            | 223275        | 5.349                           | -             | -                               |
|                 | Male/N30654              | BLQ           | 1000                            | 298668        | 5.475                           | -             | -                               |
|                 | Male/N30655              | BLQ           | 1000                            | 225262        | 5.353                           | -             | -                               |
|                 | Male/N30656              | BLQ           | 1000                            | 169776        | 5.230                           | 134637        | 5.129                           |
|                 | Male/N30657              | BLQ           | 1000                            | 212267        | 5.327                           | 180031        | 5.255                           |
|                 | Male/N30658              | 56            | 1.748                           | 370353        | 5.569                           | 252633        | 5.402                           |
|                 | Male/N30659              | BLQ           | 1000                            | 239999        | 5.380                           | 256315        | 5.409                           |
|                 | Male/N30660              | BLQ           | 1000                            | 321523        | 5.507                           | 299620        | 5.477                           |
|                 | Female/N30721            | 260           | 2.415                           | 252152        | 5.402                           | -             | -                               |
|                 | Female/N30722            | BLQ           | 1000                            | 196227        | 5.293                           | -             | -                               |
|                 | Female/N30723            | BLQ           | 1000                            | 282219        | 5.451                           | -             | -                               |
|                 | Female/N30724            | BLQ           | 1000                            | 212455        | 5.327                           | -             | -                               |
|                 | Female/N30725            | BLQ           | 1000                            | 281127        | 5.449                           | -             | -                               |
|                 | Female/N30726            | BLQ           | 1000                            | 238439        | 5.377                           | 239997        | 5.380                           |
|                 | Female/N30727            | 53            | 1.724                           | 249870        | 5.398                           | 497913        | 5.697                           |
|                 | Female/N30728            | 22            | 1.342                           | 233453        | 5.368                           | 293832        | 5.468                           |
|                 | Female/N30729            | BLQ           | 1000                            | 187843        | 5.274                           | 283939        | 5.453                           |
|                 | Female/N30730            | BLQ           | 1000                            | 176801        | 5.247                           | 313331        | 5.496                           |
| <b>Mean</b>     |                          | <b>1.161</b>  |                                 | <b>5.372</b>  |                                 | <b>5.417</b>  |                                 |
| <b>s d</b>      |                          | <b>0.376</b>  |                                 | <b>0.086</b>  |                                 | <b>0.150</b>  |                                 |
| VACC 99         | Male/N30661              | 37            | 1.568                           | 635374        | 5.803                           | -             | -                               |
|                 | Male/N30662              | BLQ           | 1000                            | 638501        | 5.805                           | -             | -                               |
|                 | Male/N30663              | BLQ           | 1000                            | 564442        | 5.752                           | -             | -                               |
|                 | Male/N30664              | 105           | 2.021                           | 534649        | 5.728                           | -             | -                               |
|                 | Male/N30665              | BLQ           | 1000                            | 574222        | 5.759                           | -             | -                               |
|                 | Male/N30666              | BLQ           | 1000                            | 553473        | 5.743                           | 324957        | 5.512                           |
|                 | Male/N30667              | BLQ           | 1000                            | 591086        | 5.772                           | 644924        | 5.810                           |
|                 | Male/N30668              | BLQ           | 1000                            | 457902        | 5.661                           | 312234        | 5.494                           |
|                 | Male/N30669              | BLQ           | 1000                            | 1028607       | 6.012                           | 579292        | 5.763                           |
|                 | Male/N30670              | 39            | 1.591                           | 693210        | 5.841                           | 369590        | 5.568                           |
|                 | Female/N30731            | BLQ           | 1000                            | 931047        | 5.969                           | -             | -                               |
|                 | Female/N30732            | BLQ           | 1000                            | 1271203       | 6.104                           | -             | -                               |
|                 | Female/N30733            | BLQ           | 1000                            | 621651        | 5.794                           | -             | -                               |
|                 | Female/N30734            | BLQ           | 1000                            | 709605        | 5.851                           | -             | -                               |
|                 | Female/N30735            | BLQ           | 1000                            | 815709        | 5.912                           | -             | -                               |
|                 | Female/N30736            | BLQ           | 1000                            | 883382        | 5.946                           | 556304        | 5.745                           |
|                 | Female/N30737            | BLQ           | 1000                            | 859893        | 5.934                           | 550845        | 5.741                           |
|                 | Female/N30738            | BLQ           | 1000                            | 705044        | 5.848                           | 428043        | 5.631                           |
|                 | Female/N30739            | BLQ           | 1000                            | 1152038       | 6.061                           | 824003        | 5.916                           |
|                 | Female/N30740            | 20            | 1.301                           | 578215        | 5.762                           | 391530        | 5.593                           |
| <b>Mean</b>     |                          | <b>1.124</b>  |                                 | <b>5.853</b>  |                                 | <b>5.677</b>  |                                 |
| <b>s d</b>      |                          | <b>0.281</b>  |                                 | <b>0.119</b>  |                                 | <b>0.139</b>  |                                 |

BLQ: Below Limit of Quantification; EU: ELISA Unit.

For samples BLQ, titer was expressed as BLQ and the arbitrary titer of 1.000 log<sub>10</sub> EU was assigned.

**9. ADDENDA**

**Addendum 1**

**Certificate of analysis of the coating protein**

**Addendum 2**

**Certificate of analysis of the reference item (STD)**

**Addendum 3**

**Certificate of analysis of the Control item**

13. Hematology parameters: individual values

## **KEY TO ABBREVIATIONS USED FOR HEMATOLOGY**

### **ABBREVIATIONS**

|      |   |
|------|---|
| RBC  | : erythrocytes                          |
| MCV  | : mean cell volume                      |
| PCV  | : packed cell volume                    |
| HB   | : hemoglobin                            |
| MCHC | : mean cell hemoglobin concentration    |
| MCH  | : mean cell hemoglobin                  |
| PLT  | : thrombocytes                          |
| WBC  | : leucocytes                            |
| RTC  | : reticulocytes                         |
| N    | : neutrophils                           |
| E    | : eosinophils                           |
| B    | : basophils                             |
| L    | : lymphocytes                           |
| LUC  | : large unstained cells                 |
| M    | : monocytes                             |
| PT   | : prothrombin time                      |
| FIB  | : fibrinogen                            |
| APTT | : activated partial thromboplastin time |

### **EXPLANATION FOR MISSING VALUE**

|      |                                 |
|------|---------------------------------|
| -    | : dead animal                   |
| ns   | : not sampled                   |
| na   | : not applicable                |
| blq* | : below limit of quantification |
| alq  | : above limit of quantification |
| u    | : unreadable slide              |
| nc   | : not coagulable                |
| m    | : missing value                 |
| cg   | : coagulated sample             |
| i    | : insufficient sample           |
| np   | : not performed                 |
| a    | : aberrant value                |
| t    | : technical problem             |

\*: for calculation of the group mean, "blq" was considered to be equal to zero

### **UNITS**

|    |                          |
|----|--------------------------|
| T  | : tera: $10^{e12}$       |
| G  | : giga: $10^{e9}$        |
| L  | : liter                  |
| g  | : gram                   |
| fL | : femtoliter: $10^{-15}$ |
| pg | : picogram: $10^{-12}$   |
| dL | : deciliter              |
| s  | : second                 |

HEMATOLOGY

Study No.:  
Time: Predose

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30641     | 7.10       | 6.48       | 13.0       | 0.39       | 60.9      | 20.0      | 32.9         | 477        | 3.22     | 0.21       |
| N30642     | 13.39      | 7.00       | 14.5       | 0.43       | 61.6      | 20.7      | 33.6         | 406        | 2.42     | 0.17       |
| N30643     | 8.83       | 6.95       | 14.7       | 0.45       | 64.1      | 21.2      | 33.0         | 435        | 2.85     | 0.20       |
| N30644     | 7.52       | 6.45       | 13.2       | 0.41       | 62.9      | 20.4      | 32.5         | 337        | 3.22     | 0.21       |
| N30645     | 6.71       | 6.41       | 13.6       | 0.41       | 63.6      | 21.2      | 33.3         | 344        | 3.87     | 0.25       |
| N30646     | 3.01       | 6.93       | 14.4       | 0.43       | 61.8      | 20.8      | 33.6         | 330        | 3.12     | 0.22       |
| N30647     | 11.65      | 7.08       | 14.5       | 0.43       | 61.4      | 20.5      | 33.4         | 395        | 3.52     | 0.25       |
| N30648     | 4.70       | 5.94       | 13.1       | 0.39       | 65.6      | 22.0      | 33.5         | 401        | 3.24     | 0.19       |
| N30649     | 6.79       | 6.88       | 13.5       | 0.41       | 59.3      | 19.6      | 33.1         | 373        | 2.78     | 0.19       |
| N30650     | 6.25       | 6.32       | 13.4       | 0.40       | 63.8      | 21.2      | 33.2         | 422        | 2.64     | 0.17       |
| Mean       | 7.60       | 6.64       | 13.8       | 0.42       | 62.5      | 20.8      | 33.2         | 392        | 3.09     | 0.21       |
| SD         | 3.063      | 0.375      | 0.66       | 0.020      | 1.84      | 0.69      | 0.35         | 46.9       | 0.429    | 0.028      |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30651     | 7.78       | 6.70       | 14.0       | 0.42       | 63.3      | 20.9      | 33.0         | 351        | 2.52     | 0.17       |
| N30652     | 6.06       | 6.48       | 13.7       | 0.42       | 65.0      | 21.1      | 32.4         | 385        | 4.16     | 0.27       |
| N30653     | 7.26       | 7.24       | 15.1       | 0.46       | 64.1      | 20.8      | 32.5         | 567        | 2.58     | 0.19       |
| N30654     | 6.33       | 6.63       | 14.3       | 0.44       | 65.8      | 21.5      | 32.7         | 282        | 3.27     | 0.22       |
| N30655     | 7.15       | 6.73       | 14.1       | 0.43       | 64.1      | 21.0      | 32.7         | 442        | 4.19     | 0.28       |
| N30656     | 6.06       | 6.70       | 14.0       | 0.43       | 63.8      | 20.8      | 32.7         | 404        | 3.20     | 0.21       |
| N30657     | 4.42       | 6.38       | 13.6       | 0.41       | 63.9      | 21.2      | 33.2         | 346        | 1.27     | 0.08       |
| N30658     | 5.78       | 6.67       | 13.5       | 0.43       | 64.2      | 20.3      | 31.6         | 356        | 3.32     | 0.22       |
| N30659     | 7.29       | 6.53       | 13.7       | 0.42       | 64.9      | 21.0      | 32.4         | 472        | 2.65     | 0.17       |
| N30660     | 6.51       | 6.60       | 13.6       | 0.41       | 62.4      | 20.5      | 32.9         | 398        | 3.17     | 0.21       |
| Mean       | 6.46       | 6.67       | 14.0       | 0.43       | 64.2      | 20.9      | 32.6         | 400        | 3.03     | 0.20       |
| SD         | 0.972      | 0.230      | 0.48       | 0.015      | 0.94      | 0.34      | 0.44         | 79.1       | 0.851    | 0.056      |

## HEMATOLOGY

Study No.:  
Time: Predose

Group 3

Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30661     | 14.18      | 6.96       | 14.8       | 0.44       | 63.8      | 21.3      | 33.3         | 436        | 3.06     | 0.21       |
| N30662     | 5.31       | 6.89       | 14.4       | 0.43       | 62.1      | 20.8      | 33.5         | 428        | 1.79     | 0.12       |
| N30663     | 6.69       | 7.41       | 14.8       | 0.45       | 60.1      | 20.0      | 33.3         | 420        | 2.96     | 0.22       |
| N30664     | 5.74       | 6.86       | 14.4       | 0.43       | 62.5      | 21.1      | 33.7         | 485        | 2.78     | 0.19       |
| N30665     | 6.73       | 6.86       | 14.1       | 0.43       | 62.7      | 20.6      | 32.9         | 348        | 3.65     | 0.25       |
| N30666     | 6.32       | 6.89       | 14.2       | 0.44       | 63.5      | 20.6      | 32.4         | 323        | 2.39     | 0.16       |
| N30667     | 7.50       | 6.88       | 14.5       | 0.44       | 64.2      | 21.1      | 32.9         | 407        | 3.01     | 0.21       |
| N30668     | 6.46       | 6.72       | 13.6       | 0.42       | 62.0      | 20.3      | 32.7         | 512        | 2.39     | 0.16       |
| N30669     | 9.05       | 6.48       | 13.6       | 0.41       | 63.8      | 20.9      | 32.8         | 339        | 2.94     | 0.19       |
| N30670     | 7.31       | 6.95       | 14.6       | 0.45       | 64.3      | 21.0      | 32.7         | 567        | 2.82     | 0.20       |
| Mean       | 7.53       | 6.89       | 14.3       | 0.43       | 62.9      | 20.8      | 33.0         | 427        | 2.78     | 0.19       |
| SD         | 2.553      | 0.230      | 0.43       | 0.013      | 1.30      | 0.40      | 0.41         | 78.5       | 0.498    | 0.037      |

## HEMATOLOGY

Study No.:  
Time: Predose

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30641     | 2.99     | 0.11     | 0.21     | 3.57     | 0.03       | 0.19     |
| N30642     | 6.12     | 0.19     | 0.31     | 6.07     | 0.03       | 0.66     |
| N30643     | 3.67     | 0.07     | 0.34     | 4.28     | 0.02       | 0.44     |
| N30644     | 3.94     | 0.06     | 0.23     | 3.14     | 0.01       | 0.15     |
| N30645     | 2.53     | 0.06     | 0.20     | 3.64     | 0.01       | 0.27     |
| N30646     | 0.54     | 0.03     | 0.15     | 2.16     | 0.01       | 0.12     |
| N30647     | 4.86     | 0.15     | 0.42     | 5.52     | 0.03       | 0.67     |
| N30648     | 1.50     | 0.06     | 0.19     | 2.66     | 0.01       | 0.28     |
| N30649     | 3.04     | 0.10     | 0.23     | 3.00     | 0.01       | 0.41     |
| N30650     | 2.63     | 0.07     | 0.28     | 3.04     | 0.03       | 0.19     |
| Mean       | 3.18     | 0.09     | 0.26     | 3.71     | 0.02       | 0.34     |
| SD         | 1.594    | 0.049    | 0.081    | 1.246    | 0.010      | 0.201    |

Group 2

Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30651     | 3.30     | 0.09     | 0.24     | 4.01     | 0.01       | 0.12     |
| N30652     | 2.10     | 0.03     | 0.22     | 3.41     | 0.01       | 0.30     |
| N30653     | 3.32     | 0.09     | 0.23     | 3.25     | 0.07       | 0.30     |
| N30654     | 2.98     | 0.07     | 0.18     | 2.78     | 0.01       | 0.31     |
| N30655     | 3.61     | 0.08     | 0.27     | 3.04     | 0.02       | 0.13     |
| N30656     | 2.51     | 0.07     | 0.28     | 3.05     | 0.02       | 0.14     |
| N30657     | 2.37     | 0.06     | 0.25     | 1.54     | 0.01       | 0.19     |
| N30658     | 2.64     | 0.05     | 0.14     | 2.62     | 0.01       | 0.33     |
| N30659     | 3.30     | 0.07     | 0.22     | 3.25     | 0.02       | 0.42     |
| N30660     | 2.85     | 0.06     | 0.29     | 3.04     | 0.02       | 0.26     |
| Mean       | 2.90     | 0.07     | 0.23     | 3.00     | 0.02       | 0.25     |
| SD         | 0.489    | 0.018    | 0.046    | 0.636    | 0.018      | 0.101    |

## HEMATOLOGY

Study No.:  
Time: Predose

Group 3

Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30661     | 9.54     | 0.12     | 0.56     | 3.09     | 0.05       | 0.83     |
| N30662     | 2.14     | 0.07     | 0.25     | 2.47     | 0.01       | 0.37     |
| N30663     | 2.69     | 0.06     | 0.21     | 3.31     | 0.03       | 0.38     |
| N30664     | 2.35     | 0.07     | 0.40     | 2.63     | 0.01       | 0.27     |
| N30665     | 3.06     | 0.07     | 0.20     | 3.08     | 0.01       | 0.30     |
| N30666     | 2.57     | 0.06     | 0.24     | 3.04     | 0.02       | 0.39     |
| N30667     | 2.82     | 0.09     | 0.19     | 3.93     | 0.02       | 0.45     |
| N30668     | 3.60     | 0.03     | 0.17     | 2.17     | 0.01       | 0.47     |
| N30669     | 5.21     | 0.10     | 0.32     | 2.87     | 0.02       | 0.52     |
| N30670     | 3.61     | 0.09     | 0.31     | 2.83     | 0.02       | 0.45     |
| Mean       | 3.76     | 0.08     | 0.29     | 2.94     | 0.02       | 0.44     |
| SD         | 2.214    | 0.025    | 0.120    | 0.483    | 0.012      | 0.156    |

## HEMATOLOGY

Study No.:  
Time: Predose

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30641(1)  | 6.7     | 3.06       | 13.6      |
| N30642     | 7.6     | 3.54       | 13.2      |
| N30643     | 7.5     | 3.03       | 13.1      |
| N30644     | 8.3     | 3.69       | 13.9      |
| N30645(1)  | 6.6     | 2.96       | 13.6      |
| N30646     | 7.8     | 4.35       | 13.2      |
| N30647     | 7.0     | 3.60       | 13.7      |
| N30648     | 7.7     | 3.52       | 12.7      |
| N30649     | 7.4     | 3.50       | 13.8      |
| N30650     | 7.0     | 3.46       | 14.1      |
| Mean       | 7.4     | 3.47       | 13.5      |
| SD         | 0.53    | 0.404      | 0.43      |

Group 2

Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30651     | 7.0     | 3.38       | 15.4      |
| N30652(1)  | 6.6     | 3.47       | 13.7      |
| N30653     | 7.1     | 3.60       | 13.4      |
| N30654     | 7.1     | 4.25       | 14.1      |
| N30655     | 7.3     | 2.69       | 14.1      |
| N30656     | 7.0     | 4.90       | 13.9      |
| N30657(1)  | 6.7     | 3.33       | 14.9      |
| N30658(1)  | 6.7     | 3.57       | 10.9      |
| N30659     | 7.7     | 2.86       | 13.0      |
| N30660     | 7.5     | 3.16       | 13.8      |
| Mean       | 7.1     | 3.52       | 13.7      |
| SD         | 0.36    | 0.646      | 1.21      |

(1) PT : value under validated range.

## HEMATOLOGY

Study No.:  
Time: Predose

Group 3

Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30661     | 7.7     | 3.94       | 13.9      |
| N30662     | 7.4     | 4.08       | 15.2      |
| N30663     | 7.1     | 4.26       | 13.8      |
| N30664(1)  | 6.7     | 4.35       | 13.7      |
| N30665     | 7.8     | 3.49       | 13.8      |
| N30666(1)  | 6.7     | 3.41       | 14.3      |
| N30667     | 7.7     | 3.54       | 13.9      |
| N30668     | 7.0     | 3.73       | 14.1      |
| N30669     | 7.9     | 4.47       | 14.2      |
| N30670(1)  | 6.7     | 3.52       | 14.1      |
| Mean       | 7.3     | 3.88       | 14.1      |
| SD         | 0.49    | 0.394      | 0.43      |

(1) PT : value under validated range.

HEMATOLOGY

Study No.:  
Time: Predose

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30711     | 4.88       | 6.94       | 14.8       | 0.46       | 66.1      | 21.3      | 32.2         | 449        | 3.00     | 0.21       |
| N30712     | 5.50       | 6.28       | 12.8       | 0.40       | 63.6      | 20.3      | 31.9         | 519        | 3.58     | 0.22       |
| N30713     | 8.24       | 6.77       | 13.9       | 0.41       | 61.1      | 20.5      | 33.6         | 545        | 2.50     | 0.17       |
| N30714     | 5.69       | 6.66       | 13.9       | 0.44       | 65.9      | 20.9      | 31.7         | 385        | 3.24     | 0.22       |
| N30715     | 6.35       | 6.23       | 13.1       | 0.40       | 63.5      | 21.0      | 33.0         | 432        | 3.71     | 0.23       |
| N30716     | 6.90       | 6.36       | 13.0       | 0.40       | 63.5      | 20.4      | 32.1         | 363        | 4.18     | 0.27       |
| N30717     | 5.13       | 6.10       | 13.6       | 0.41       | 67.3      | 22.2      | 33.0         | 365        | 3.30     | 0.20       |
| N30718     | 4.66       | 6.14       | 13.5       | 0.41       | 67.4      | 21.9      | 32.5         | 355        | 3.69     | 0.23       |
| N30719     | 8.13       | 6.03       | 12.7       | 0.39       | 63.9      | 21.1      | 33.0         | 523        | 3.37     | 0.20       |
| N30720     | 6.94       | 6.00       | 12.7       | 0.39       | 65.4      | 21.2      | 32.4         | 402        | 3.35     | 0.20       |
| Mean       | 6.24       | 6.35       | 13.4       | 0.41       | 64.8      | 21.1      | 32.5         | 434        | 3.39     | 0.22       |
| SD         | 1.288      | 0.329      | 0.67       | 0.022      | 1.99      | 0.62      | 0.60         | 72.4       | 0.451    | 0.026      |

Group 2

Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30721     | 6.11       | 6.80       | 14.0       | 0.44       | 64.1      | 20.6      | 32.1         | 503        | 2.11     | 0.14       |
| N30722     | 8.11       | 6.57       | 13.5       | 0.42       | 63.3      | 20.6      | 32.6         | 322        | 3.32     | 0.22       |
| N30723     | 7.31       | 6.33       | 13.4       | 0.41       | 64.0      | 21.2      | 33.1         | 389        | 3.03     | 0.19       |
| N30724     | 7.59       | 6.52       | 13.7       | 0.43       | 65.8      | 21.0      | 32.0         | 420        | 5.88     | 0.38       |
| N30725     | 5.67       | 7.23       | 14.3       | 0.44       | 60.9      | 19.8      | 32.5         | 398        | 2.39     | 0.17       |
| N30726     | 5.43       | 6.15       | 13.2       | 0.41       | 66.5      | 21.4      | 32.2         | 344        | 3.33     | 0.20       |
| N30727     | 6.02       | 5.98       | 12.8       | 0.39       | 65.4      | 21.5      | 32.9         | 445        | 3.78     | 0.23       |
| N30728     | 6.07       | 5.95       | 13.0       | 0.40       | 66.7      | 21.9      | 32.8         | 541        | 4.81     | 0.29       |
| N30729     | 7.07       | 6.11       | 13.4       | 0.41       | 67.2      | 21.9      | 32.6         | 378        | 3.06     | 0.19       |
| N30730     | 9.42       | 6.07       | 13.0       | 0.40       | 66.6      | 21.4      | 32.1         | 471        | 3.03     | 0.18       |
| Mean       | 6.88       | 6.37       | 13.4       | 0.42       | 65.1      | 21.1      | 32.5         | 421        | 3.47     | 0.22       |
| SD         | 1.258      | 0.411      | 0.47       | 0.017      | 1.97      | 0.65      | 0.38         | 69.4       | 1.121    | 0.069      |

## HEMATOLOGY

Study No.:  
Time: Predose

Group 3

Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30731     | 7.23       | 6.55       | 14.1       | 0.43       | 65.2      | 21.5      | 32.9         | 481        | 2.19     | 0.14       |
| N30732     | 8.75       | 6.48       | 13.7       | 0.42       | 65.2      | 21.2      | 32.5         | 380        | 2.76     | 0.18       |
| N30733     | 6.64       | 6.49       | 13.4       | 0.42       | 64.2      | 20.6      | 32.1         | 430        | 3.58     | 0.23       |
| N30734     | 8.69       | 6.79       | 13.8       | 0.44       | 64.1      | 20.4      | 31.7         | 389        | 3.50     | 0.24       |
| N30735     | 7.17       | 6.78       | 13.8       | 0.43       | 62.8      | 20.4      | 32.4         | 371        | 2.28     | 0.15       |
| N30736     | 6.36       | 6.31       | 13.5       | 0.42       | 65.9      | 21.4      | 32.5         | 455        | 3.21     | 0.20       |
| N30737     | 5.42       | 6.09       | 12.7       | 0.39       | 63.9      | 20.9      | 32.7         | 465        | 3.27     | 0.20       |
| N30738     | 3.90       | 5.95       | 12.7       | 0.39       | 66.0      | 21.3      | 32.2         | 663        | 3.01     | 0.18       |
| N30739     | 6.18       | 6.05       | 12.5       | 0.39       | 64.3      | 20.7      | 32.3         | 518        | 3.29     | 0.20       |
| N30740     | 6.42       | 6.57       | 13.2       | 0.41       | 62.9      | 20.0      | 31.8         | 423        | 2.03     | 0.13       |
| Mean       | 6.68       | 6.41       | 13.3       | 0.41       | 64.5      | 20.8      | 32.3         | 458        | 2.91     | 0.19       |
| SD         | 1.438      | 0.297      | 0.55       | 0.018      | 1.12      | 0.50      | 0.38         | 86.0       | 0.566    | 0.037      |

## HEMATOLOGY

Study No.:  
Time: Predose

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30711     | 1.83     | 0.07     | 0.28     | 2.39     | 0.01       | 0.30     |
| N30712     | 1.80     | 0.06     | 0.37     | 2.87     | 0.02       | 0.39     |
| N30713     | 3.87     | 0.09     | 0.40     | 3.33     | 0.01       | 0.54     |
| N30714     | 1.97     | 0.06     | 0.28     | 3.04     | 0.01       | 0.32     |
| N30715     | 3.09     | 0.06     | 0.31     | 2.56     | 0.05       | 0.29     |
| N30716     | 2.16     | 0.09     | 0.45     | 3.76     | 0.06       | 0.38     |
| N30717     | 2.17     | 0.04     | 0.18     | 2.54     | 0.01       | 0.19     |
| N30718     | 1.64     | 0.04     | 0.24     | 2.65     | 0.01       | 0.08     |
| N30719     | 3.27     | 0.09     | 0.31     | 3.95     | 0.04       | 0.46     |
| N30720     | 2.24     | 0.05     | 0.41     | 3.82     | 0.03       | 0.39     |
| Mean       | 2.40     | 0.07     | 0.32     | 3.09     | 0.03       | 0.33     |
| SD         | 0.744    | 0.020    | 0.084    | 0.587    | 0.019      | 0.131    |

Group 2

Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30721     | 1.69     | 0.06     | 0.34     | 3.67     | 0.02       | 0.34     |
| N30722     | 4.87     | 0.08     | 0.34     | 2.66     | 0.00       | 0.15     |
| N30723     | 2.81     | 0.12     | 0.25     | 3.74     | 0.01       | 0.38     |
| N30724     | 3.05     | 0.05     | 0.19     | 3.96     | 0.01       | 0.34     |
| N30725     | 2.26     | 0.08     | 0.18     | 2.99     | 0.01       | 0.14     |
| N30726     | 1.90     | 0.07     | 0.27     | 2.66     | 0.02       | 0.51     |
| N30727     | 1.91     | 0.05     | 0.23     | 3.70     | 0.01       | 0.12     |
| N30728     | 1.93     | 0.05     | 0.20     | 3.51     | 0.02       | 0.37     |
| N30729     | 2.47     | 0.06     | 0.30     | 3.88     | 0.02       | 0.35     |
| N30730     | 5.27     | 0.08     | 0.23     | 3.23     | 0.03       | 0.58     |
| Mean       | 2.82     | 0.07     | 0.25     | 3.40     | 0.02       | 0.33     |
| SD         | 1.267    | 0.022    | 0.059    | 0.486    | 0.008      | 0.154    |

## HEMATOLOGY

Study No.:  
Time: Predose

Group 3

Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30731     | 2.51     | 0.08     | 0.35     | 3.77     | 0.03       | 0.49     |
| N30732     | 3.41     | 0.10     | 0.40     | 4.63     | 0.02       | 0.19     |
| N30733     | 2.55     | 0.09     | 0.26     | 3.35     | 0.03       | 0.36     |
| N30734     | 3.47     | 0.13     | 0.43     | 4.37     | 0.03       | 0.25     |
| N30735     | 3.34     | 0.07     | 0.57     | 2.81     | 0.02       | 0.36     |
| N30736     | 2.58     | 0.07     | 0.30     | 3.26     | 0.02       | 0.13     |
| N30737     | 2.44     | 0.05     | 0.28     | 2.39     | 0.02       | 0.24     |
| N30738     | 1.30     | 0.04     | 0.11     | 2.17     | 0.01       | 0.27     |
| N30739     | 1.63     | 0.09     | 0.30     | 3.71     | 0.04       | 0.41     |
| N30740     | 1.66     | 0.05     | 0.25     | 4.08     | 0.01       | 0.36     |
| Mean       | 2.49     | 0.08     | 0.33     | 3.45     | 0.02       | 0.31     |
| SD         | 0.774    | 0.027    | 0.123    | 0.818    | 0.009      | 0.109    |

## HEMATOLOGY

Study No.:  
Time: Predose

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30711     | 7.4     | 2.47       | 13.6      |
| N30712     | 7.2     | 2.51       | 14.0      |
| N30713     | 6.9     | 2.46       | 15.1      |
| N30714     | 7.4     | 3.01       | 13.9      |
| N30715     | 7.0     | 2.65       | 14.9      |
| N30716(1)  | 6.8     | 3.64       | 14.5      |
| N30717(1)  | 6.4     | 1.99       | 13.3      |
| N30718     | 6.9     | 2.29       | 13.9      |
| N30719     | 7.1     | 2.29       | 14.0      |
| N30720(1)  | 6.6     | 2.77       | 11.9      |
| Mean       | 7.0     | 2.61       | 13.9      |
| SD         | 0.32    | 0.458      | 0.90      |

Group 2

Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30721     | 7.2     | 2.71       | 14.5      |
| N30722     | 7.2     | 2.95       | 13.5      |
| N30723     | 6.9     | 3.11       | 13.2      |
| N30724     | 7.3     | 2.71       | 13.7      |
| N30725     | 6.9     | 3.76       | 15.2      |
| N30726     | 6.9     | 2.75       | 12.4      |
| N30727(1)  | 6.3     | 2.33       | 14.1      |
| N30728(1)  | 6.5     | 2.16       | 14.1      |
| N30729(1)  | 6.5     | 2.51       | 14.2      |
| N30730     | 7.5     | 2.01       | 16.2      |
| Mean       | 6.9     | 2.70       | 14.1      |
| SD         | 0.39    | 0.505      | 1.05      |

(1) PT : value under validated range.

## HEMATOLOGY

Study No.:  
Time: Predose

Group 3

Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30731     | 7.3     | 2.46       | 14.1      |
| N30732     | 7.2     | 3.24       | 15.1      |
| N30733     | 5.8     | 2.58       | 13.0      |
| N30734(1)  | 6.7     | 2.95       | 13.1      |
| N30735     | 7.2     | 3.12       | 14.5      |
| N30736     | 7.7     | 2.49       | 14.8      |
| N30737     | 7.5     | 2.34       | 13.4      |
| N30738     | 7.1     | 2.38       | 14.3      |
| N30739(1)  | 6.2     | 2.78       | 13.4      |
| N30740(1)  | 6.4     | 2.41       | 13.9      |
| Mean       | 6.9     | 2.68       | 14.0      |
| SD         | 0.61    | 0.327      | 0.72      |

(1) PT : value under validated range.

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30641     | 5.72       | 6.77       | 13.8       | 0.44       | 64.4      | 20.5      | 31.7         | 547        | 5.17     | 0.35       |
| N30642     | 11.08      | 7.49       | 15.9       | 0.48       | 64.4      | 21.2      | 33.0         | 461        | 4.08     | 0.31       |
| N30643     | 10.11      | 7.21       | 14.8       | 0.46       | 63.6      | 20.5      | 32.3         | 547        | 3.89     | 0.28       |
| N30644     | 5.59       | 7.16       | 14.7       | 0.46       | 63.8      | 20.5      | 32.2         | 384        | 4.05     | 0.29       |
| N30645     | 9.81       | 6.32       | 13.5       | 0.41       | 64.9      | 21.4      | 33.0         | 359        | 4.30     | 0.27       |
| N30646     | 5.57       | 7.28       | 15.3       | 0.45       | 62.0      | 21.0      | 33.9         | 453        | 3.63     | 0.26       |
| N30647     | 10.18      | 7.49       | 15.3       | 0.46       | 61.5      | 20.4      | 33.2         | 398        | 4.42     | 0.33       |
| N30648     | 4.00       | 6.30       | 13.9       | 0.42       | 66.0      | 22.1      | 33.4         | 362        | 3.94     | 0.25       |
| N30649     | 7.18       | 7.05       | 13.9       | 0.43       | 61.0      | 19.7      | 32.2         | 400        | 4.66     | 0.33       |
| N30650     | 6.43       | 6.73       | 14.5       | 0.44       | 66.0      | 21.6      | 32.7         | 477        | 5.17     | 0.35       |
| Mean       | 7.57       | 6.98       | 14.6       | 0.45       | 63.8      | 20.9      | 32.8         | 439        | 4.33     | 0.30       |
| SD         | 2.498      | 0.435      | 0.78       | 0.021      | 1.76      | 0.70      | 0.67         | 69.9       | 0.528    | 0.037      |

Group 2

Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30651     | 7.55       | 7.04       | 15.0       | 0.46       | 64.9      | 21.3      | 32.8         | 427        | 3.92     | 0.28       |
| N30652     | 7.20       | 6.79       | 14.3       | 0.44       | 65.4      | 21.1      | 32.2         | 372        | 3.72     | 0.25       |
| N30653     | 6.92       | 7.15       | 14.7       | 0.45       | 63.3      | 20.6      | 32.6         | 481        | 3.65     | 0.26       |
| N30654     | 4.21       | 6.71       | 14.3       | 0.44       | 65.3      | 21.2      | 32.5         | 107        | 4.34     | 0.29       |
| N30655     | 6.68       | 6.72       | 14.0       | 0.44       | 64.8      | 20.9      | 32.2         | 455        | 3.70     | 0.25       |
| N30656     | 8.35       | 6.92       | 14.5       | 0.45       | 65.0      | 21.0      | 32.3         | 299        | 4.39     | 0.30       |
| N30657     | 3.63       | 6.50       | 13.8       | 0.43       | 65.8      | 21.2      | 32.3         | 386        | 4.39     | 0.29       |
| N30658     | 6.24       | 6.86       | 14.0       | 0.45       | 65.7      | 20.5      | 31.2         | 449        | 3.82     | 0.26       |
| N30659     | 5.58       | 6.81       | 14.2       | 0.45       | 65.8      | 20.8      | 31.7         | 460        | 3.49     | 0.24       |
| N30660     | 5.32       | 6.72       | 13.8       | 0.43       | 63.7      | 20.5      | 32.2         | 375        | 4.45     | 0.30       |
| Mean       | 6.17       | 6.82       | 14.3       | 0.44       | 65.0      | 20.9      | 32.2         | 381        | 3.99     | 0.27       |
| SD         | 1.487      | 0.184      | 0.39       | 0.010      | 0.86      | 0.30      | 0.46         | 110.8      | 0.367    | 0.023      |

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 3

Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30661     | 10.18      | 7.42       | 15.5       | 0.47       | 63.1      | 20.9      | 33.2         | 355        | 3.31     | 0.25       |
| N30662     | 6.00       | 6.77       | 14.0       | 0.42       | 62.5      | 20.7      | 33.1         | 410        | 2.63     | 0.18       |
| N30663     | 6.23       | 7.37       | 14.7       | 0.45       | 60.5      | 20.0      | 33.0         | 279        | 3.55     | 0.26       |
| N30664     | 5.11       | 7.27       | 15.0       | 0.45       | 62.5      | 20.7      | 33.1         | 490        | 4.17     | 0.30       |
| N30665     | 5.76       | 7.40       | 15.0       | 0.46       | 62.1      | 20.3      | 32.7         | 279        | 3.75     | 0.28       |
| N30666     | 6.79       | 7.23       | 14.8       | 0.47       | 64.9      | 20.4      | 31.5         | 314        | 3.68     | 0.27       |
| N30667     | 7.61       | 6.70       | 14.5       | 0.43       | 64.3      | 21.6      | 33.6         | 438        | 4.04     | 0.27       |
| N30668     | 5.49       | 6.82       | 13.9       | 0.42       | 61.7      | 20.3      | 33.0         | 533        | 3.75     | 0.26       |
| N30669     | 5.85       | 6.72       | 14.0       | 0.44       | 65.6      | 20.8      | 31.7         | 335        | 4.12     | 0.28       |
| N30670     | 7.62       | 6.96       | 14.6       | 0.44       | 63.9      | 21.0      | 32.8         | 519        | 4.02     | 0.28       |
| Mean       | 6.66       | 7.07       | 14.6       | 0.45       | 63.1      | 20.7      | 32.8         | 395        | 3.70     | 0.26       |
| SD         | 1.494      | 0.300      | 0.52       | 0.018      | 1.56      | 0.45      | 0.66         | 96.7       | 0.464    | 0.032      |

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30641     | 2.55     | 0.07     | 0.25     | 2.65     | 0.03       | 0.17     |
| N30642     | 4.13     | 0.15     | 0.42     | 5.72     | 0.03       | 0.62     |
| N30643     | 5.16     | 0.07     | 0.36     | 4.05     | 0.01       | 0.45     |
| N30644     | 2.44     | 0.06     | 0.17     | 2.76     | 0.00       | 0.16     |
| N30645     | 6.53     | 0.04     | 0.21     | 2.63     | 0.02       | 0.38     |
| N30646     | 2.43     | 0.04     | 0.22     | 2.73     | 0.01       | 0.13     |
| N30647     | 4.89     | 0.08     | 0.43     | 3.98     | 0.02       | 0.78     |
| N30648     | 1.46     | 0.04     | 0.24     | 2.17     | 0.01       | 0.09     |
| N30649     | 3.33     | 0.08     | 0.25     | 3.13     | 0.02       | 0.38     |
| N30650     | 3.04     | 0.09     | 0.23     | 2.71     | 0.01       | 0.35     |
| Mean       | 3.60     | 0.07     | 0.28     | 3.25     | 0.02       | 0.35     |
| SD         | 1.554    | 0.033    | 0.091    | 1.054    | 0.010      | 0.225    |

Group 2

Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30651     | 2.83     | 0.06     | 0.24     | 4.25     | 0.01       | 0.16     |
| N30652     | 3.11     | 0.04     | 0.28     | 3.15     | 0.03       | 0.58     |
| N30653     | 3.28     | 0.08     | 0.33     | 2.80     | 0.01       | 0.43     |
| N30654     | 0.94     | 0.03     | 0.21     | 2.77     | 0.01       | 0.25     |
| N30655     | 2.12     | 0.05     | 0.32     | 3.83     | 0.02       | 0.34     |
| N30656     | 4.27     | 0.07     | 0.26     | 3.03     | 0.02       | 0.70     |
| N30657     | 1.52     | 0.05     | 0.14     | 1.77     | 0.01       | 0.14     |
| N30658     | 2.26     | 0.03     | 0.18     | 3.21     | 0.02       | 0.54     |
| N30659     | 2.16     | 0.03     | 0.17     | 3.05     | 0.02       | 0.17     |
| N30660     | 1.29     | 0.02     | 0.26     | 3.44     | 0.01       | 0.29     |
| Mean       | 2.38     | 0.05     | 0.24     | 3.13     | 0.02       | 0.36     |
| SD         | 1.014    | 0.020    | 0.063    | 0.663    | 0.007      | 0.195    |

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 3  
VACC99  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30661     | 5.42     | 0.09     | 0.52     | 3.88     | 0.03       | 0.25     |
| N30662     | 2.22     | 0.05     | 0.28     | 3.18     | 0.04       | 0.23     |
| N30663(1)  | 3.18     | 0.12     | 0.06     | 2.43     | 0.00       | 0.44     |
| N30664     | 2.39     | 0.04     | 0.30     | 2.23     | 0.01       | 0.14     |
| N30665     | 2.32     | 0.05     | 0.23     | 2.96     | 0.01       | 0.18     |
| N30666     | 2.16     | 0.04     | 0.24     | 3.89     | 0.02       | 0.45     |
| N30667     | 2.97     | 0.06     | 0.19     | 4.19     | 0.01       | 0.19     |
| N30668     | 2.20     | 0.04     | 0.24     | 2.58     | 0.02       | 0.42     |
| N30669     | 2.57     | 0.05     | 0.24     | 2.75     | 0.00       | 0.24     |
| N30670     | 3.58     | 0.08     | 0.38     | 2.98     | 0.03       | 0.57     |
| Mean       | 2.90     | 0.06     | 0.27     | 3.11     | 0.02       | 0.31     |
| SD         | 1.006    | 0.027    | 0.120    | 0.672    | 0.013      | 0.146    |

(1) Microscopic examination.

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30641     | 6.9     | 2.48       | 13.7      |
| N30642(1)  | 6.6     | 3.30       | 13.3      |
| N30643     | 7.4     | 2.89       | 13.7      |
| N30644     | 7.3     | 3.81       | 13.7      |
| N30645     | 7.0     | 3.68       | 13.1      |
| N30646(1)  | 6.4     | 3.94       | 12.2      |
| N30647     | 7.2     | 3.58       | 13.1      |
| N30648     | 6.9     | 3.42       | 12.8      |
| N30649(1)  | 6.1     | 3.32       | 12.5      |
| N30650(1)  | 6.2     | 2.99       | 13.0      |
| Mean       | 6.8     | 3.34       | 13.1      |
| SD         | 0.46    | 0.451      | 0.52      |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30651(1)  | 6.8     | 4.38       | 13.4      |
| N30652(2)  | 5.9     | 5.23       | 12.5      |
| N30653(3)  | 7.0     | 5.59       | 12.8      |
| N30654     | 7.2     | 4.58       | 12.4      |
| N30655(3)  | 7.5     | 5.43       | 13.7      |
| N30656(2)  | 6.3     | 5.20       | 12.8      |
| N30657(1)  | 6.8     | 4.18       | 11.2      |
| N30658(1)  | 6.1     | 4.05       | 12.6      |
| N30659(1)  | 6.3     | 3.68       | 12.1      |
| N30660(2)  | 6.2     | 4.77       | 13.0      |
| Mean       | 6.6     | 4.71       | 12.7      |
| SD         | 0.53    | 0.642      | 0.69      |

(1) PT : value under validated range.

(2) PT : value under validated range. FIB : value above validated range.

(3) FIB : value above validated range.

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 3  
VACC99  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30661(1)  | 6.6     | 5.02       | 13.5      |
| N30662(2)  | 6.4     | 4.00       | 14.0      |
| N30663(1)  | 6.1     | 6.35       | 13.7      |
| N30664(1)  | 6.1     | 4.74       | 12.6      |
| N30665(1)  | 6.5     | 5.54       | 12.6      |
| N30666(2)  | 6.1     | 4.61       | 13.8      |
| N30667(3)  | 7.6     | 5.30       | 12.5      |
| N30668(1)  | 6.2     | 6.51       | 12.3      |
| N30669(1)  | 6.5     | 5.02       | 13.7      |
| N30670     | 7.3     | 4.14       | 13.7      |
| Mean       | 6.5     | 5.12       | 13.2      |
| SD         | 0.52    | 0.836      | 0.65      |

(1) PT : value under validated range. FIB : value above validated range.

(2) PT : value under validated range.

(3) FIB : value above validated range.

HEMATOLOGY

Study No.:  
Time: Week 1

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30711     | 5.84       | 6.50       | 14.3       | 0.44       | 67.8      | 22.0      | 32.5         | 411        | 4.35     | 0.28       |
| N30712     | 6.50       | 6.09       | 12.9       | 0.41       | 66.9      | 21.3      | 31.8         | 504        | 4.80     | 0.29       |
| N30713     | 7.67       | 6.69       | 13.9       | 0.42       | 62.8      | 20.8      | 33.2         | 408        | 4.79     | 0.32       |
| N30714     | 5.81       | 6.56       | 14.2       | 0.44       | 67.2      | 21.6      | 32.2         | 358        | 4.15     | 0.27       |
| N30715     | 4.76       | 6.17       | 13.3       | 0.41       | 66.3      | 21.6      | 32.6         | 340        | 5.54     | 0.34       |
| N30716     | 5.79       | 6.81       | 14.1       | 0.44       | 64.7      | 20.7      | 32.1         | 432        | 4.93     | 0.34       |
| N30717     | 4.88       | 6.11       | 13.6       | 0.42       | 68.5      | 22.3      | 32.5         | 341        | 4.96     | 0.30       |
| N30718     | 5.32       | 6.31       | 14.1       | 0.43       | 67.6      | 22.4      | 33.1         | 383        | 5.10     | 0.32       |
| N30719     | 6.49       | 6.33       | 13.4       | 0.41       | 65.1      | 21.2      | 32.6         | 511        | 4.79     | 0.30       |
| N30720     | 5.62       | 6.25       | 13.3       | 0.41       | 65.5      | 21.3      | 32.6         | 455        | 4.35     | 0.27       |
| Mean       | 5.87       | 6.38       | 13.7       | 0.42       | 66.2      | 21.5      | 32.5         | 414        | 4.78     | 0.30       |
| SD         | 0.857      | 0.248      | 0.47       | 0.013      | 1.73      | 0.58      | 0.42         | 61.9       | 0.409    | 0.026      |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30721     | 6.75       | 6.22       | 13.3       | 0.41       | 66.3      | 21.4      | 32.3         | 375        | 3.58     | 0.22       |
| N30722     | 5.48       | 6.85       | 14.2       | 0.46       | 66.6      | 20.7      | 31.1         | 382        | 4.74     | 0.32       |
| N30723     | 6.39       | 6.21       | 13.3       | 0.41       | 65.7      | 21.5      | 32.7         | 357        | 4.92     | 0.31       |
| N30724     | 7.60       | 6.50       | 14.2       | 0.44       | 67.8      | 21.8      | 32.2         | 475        | 4.87     | 0.32       |
| N30725     | 5.91       | 6.63       | 13.6       | 0.41       | 62.4      | 20.5      | 32.9         | 457        | 4.41     | 0.29       |
| N30726     | 4.58       | 6.38       | 14.0       | 0.43       | 66.8      | 22.0      | 32.9         | 320        | 4.10     | 0.26       |
| N30727     | 5.82       | 6.00       | 13.0       | 0.40       | 67.2      | 21.7      | 32.3         | 494        | 4.87     | 0.29       |
| N30728     | 6.37       | 6.56       | 14.3       | 0.44       | 67.2      | 21.9      | 32.6         | 496        | 5.17     | 0.34       |
| N30729     | 4.34       | 6.11       | 13.6       | 0.42       | 68.5      | 22.3      | 32.5         | 302        | 4.64     | 0.28       |
| N30730     | 5.79       | 5.80       | 12.7       | 0.38       | 66.2      | 21.8      | 33.0         | 444        | 3.78     | 0.22       |
| Mean       | 5.90       | 6.33       | 13.6       | 0.42       | 66.5      | 21.6      | 32.5         | 410        | 4.51     | 0.29       |
| SD         | 0.969      | 0.318      | 0.55       | 0.023      | 1.64      | 0.57      | 0.55         | 72.0       | 0.528    | 0.041      |

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 3  
VACC99  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30731     | 5.66       | 6.39       | 13.8       | 0.42       | 66.3      | 21.6      | 32.6         | 374        | 3.28     | 0.21       |
| N30732     | 6.98       | 6.24       | 13.4       | 0.41       | 65.7      | 21.4      | 32.6         | 361        | 3.73     | 0.23       |
| N30733     | 4.57       | 6.90       | 14.1       | 0.45       | 65.4      | 20.5      | 31.4         | 451        | 4.39     | 0.30       |
| N30734     | 6.50       | 6.56       | 13.4       | 0.43       | 64.9      | 20.4      | 31.4         | 386        | 5.26     | 0.35       |
| N30735     | 5.64       | 7.03       | 14.3       | 0.45       | 63.8      | 20.3      | 31.8         | 379        | 3.50     | 0.25       |
| N30736     | 6.24       | 6.11       | 13.3       | 0.42       | 68.0      | 21.7      | 32.0         | 417        | 5.56     | 0.34       |
| N30737     | 4.39       | 6.35       | 13.6       | 0.42       | 65.9      | 21.4      | 32.5         | 389        | 4.18     | 0.27       |
| N30738     | 4.40       | 5.91       | 12.9       | 0.39       | 66.5      | 21.8      | 32.7         | 674        | 4.64     | 0.27       |
| N30739     | 5.53       | 5.89       | 12.4       | 0.39       | 66.2      | 21.0      | 31.7         | 462        | 4.11     | 0.24       |
| N30740     | 6.52       | 6.23       | 12.7       | 0.40       | 63.5      | 20.4      | 32.1         | 448        | 5.13     | 0.32       |
| Mean       | 5.64       | 6.36       | 13.4       | 0.42       | 65.6      | 21.1      | 32.1         | 434        | 4.38     | 0.28       |
| SD         | 0.938      | 0.380      | 0.60       | 0.021      | 1.32      | 0.60      | 0.50         | 91.6       | 0.769    | 0.048      |

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30711     | 2.30     | 0.10     | 0.24     | 2.77     | 0.01       | 0.42     |
| N30712     | 2.44     | 0.08     | 0.28     | 3.21     | 0.01       | 0.47     |
| N30713     | 2.99     | 0.08     | 0.32     | 3.81     | 0.03       | 0.46     |
| N30714     | 1.99     | 0.09     | 0.37     | 3.01     | 0.02       | 0.34     |
| N30715     | 1.88     | 0.05     | 0.22     | 2.38     | 0.04       | 0.19     |
| N30716     | 2.69     | 0.10     | 0.39     | 2.37     | 0.03       | 0.23     |
| N30717     | 2.14     | 0.04     | 0.18     | 2.28     | 0.01       | 0.23     |
| N30718     | 1.94     | 0.04     | 0.26     | 2.95     | 0.01       | 0.11     |
| N30719     | 2.50     | 0.09     | 0.27     | 3.24     | 0.02       | 0.37     |
| N30720     | 1.97     | 0.08     | 0.35     | 2.96     | 0.02       | 0.24     |
| Mean       | 2.28     | 0.08     | 0.29     | 2.90     | 0.02       | 0.31     |
| SD         | 0.368    | 0.023    | 0.068    | 0.473    | 0.011      | 0.123    |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30721     | 2.05     | 0.10     | 0.25     | 3.77     | 0.02       | 0.56     |
| N30722     | 2.92     | 0.04     | 0.18     | 2.18     | 0.01       | 0.14     |
| N30723     | 2.19     | 0.08     | 0.30     | 3.38     | 0.02       | 0.41     |
| N30724     | 2.97     | 0.06     | 0.16     | 3.83     | 0.02       | 0.57     |
| N30725     | 2.06     | 0.07     | 0.24     | 2.93     | 0.04       | 0.57     |
| N30726     | 1.15     | 0.05     | 0.34     | 2.61     | 0.01       | 0.41     |
| N30727     | 1.98     | 0.03     | 0.19     | 3.33     | 0.02       | 0.28     |
| N30728     | 2.26     | 0.05     | 0.24     | 3.35     | 0.03       | 0.46     |
| N30729     | 0.66     | 0.03     | 0.25     | 3.25     | 0.02       | 0.13     |
| N30730     | 2.72     | 0.07     | 0.26     | 2.26     | 0.02       | 0.47     |
| Mean       | 2.10     | 0.06     | 0.24     | 3.09     | 0.02       | 0.40     |
| SD         | 0.733    | 0.023    | 0.054    | 0.579    | 0.009      | 0.166    |

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 3  
VACC99  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30731     | 1.96     | 0.05     | 0.28     | 3.08     | 0.04       | 0.24     |
| N30732     | 1.85     | 0.05     | 0.35     | 4.55     | 0.02       | 0.16     |
| N30733     | 2.02     | 0.04     | 0.23     | 1.91     | 0.01       | 0.36     |
| N30734     | 2.28     | 0.07     | 0.34     | 3.38     | 0.05       | 0.38     |
| N30735     | 1.56     | 0.05     | 0.53     | 3.17     | 0.03       | 0.30     |
| N30736     | 2.67     | 0.05     | 0.29     | 2.83     | 0.02       | 0.39     |
| N30737     | 1.60     | 0.03     | 0.27     | 2.17     | 0.01       | 0.30     |
| N30738     | 1.38     | 0.04     | 0.15     | 2.59     | 0.04       | 0.19     |
| N30739     | 1.03     | 0.04     | 0.36     | 3.75     | 0.04       | 0.31     |
| N30740     | 1.89     | 0.05     | 0.21     | 3.91     | 0.02       | 0.44     |
| Mean       | 1.82     | 0.05     | 0.30     | 3.13     | 0.03       | 0.31     |
| SD         | 0.463    | 0.011    | 0.104    | 0.807    | 0.014      | 0.090    |

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30711     | 7.4     | 2.18       | 13.2      |
| N30712     | 6.9     | 2.48       | 13.1      |
| N30713(1)  | 6.8     | 2.18       | 13.3      |
| N30714     | 7.4     | 3.16       | 13.7      |
| N30715(1)  | 6.7     | 2.51       | 14.2      |
| N30716     | 7.3     | 2.88       | 15.4      |
| N30717     | 7.7     | 2.19       | 11.3      |
| N30718     | 7.3     | 2.16       | 12.9      |
| N30719     | 7.2     | 2.24       | 13.8      |
| N30720     | 7.1     | 2.55       | 12.4      |
| Mean       | 7.2     | 2.45       | 13.3      |
| SD         | 0.31    | 0.341      | 1.09      |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30721     | 7.4     | 3.10       | 14.0      |
| N30722(1)  | 6.8     | 4.23       | 13.4      |
| N30723(1)  | 6.7     | 4.10       | 13.5      |
| N30724(1)  | 6.7     | 2.88       | 14.1      |
| N30725     | 7.7     | 4.36       | 14.8      |
| N30726(1)  | 6.2     | 4.34       | 12.7      |
| N30727(2)  | 6.0     | 4.66       | 13.5      |
| N30728(1)  | 6.5     | 2.98       | 14.4      |
| N30729(3)  | 7.7     | 4.73       | 14.6      |
| N30730(1)  | 6.2     | 3.84       | 14.1      |
| Mean       | 6.8     | 3.92       | 13.9      |
| SD         | 0.62    | 0.695      | 0.64      |

(1) PT : value under validated range.

(2) PT : value under validated range. FIB : value above validated range.

(3) FIB : value above validated range.

## HEMATOLOGY

Study No.:  
Time: Week 1

Group 3  
VACC99  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30731(1)  | 6.4     | 4.30       | 13.4      |
| N30732     | 6.9     | 4.62       | 13.1      |
| N30733     | 7.0     | 4.41       | 12.5      |
| N30734(1)  | 6.6     | 3.97       | 12.9      |
| N30735(2)  | 6.4     | 4.66       | 14.8      |
| N30736(1)  | 6.4     | 4.43       | 14.2      |
| N30737(1)  | 6.5     | 3.35       | 13.9      |
| N30738     | 6.9     | 3.68       | 15.9      |
| N30739(2)  | 6.8     | 5.01       | 11.7      |
| N30740(1)  | 5.6     | 4.03       | 12.2      |
| Mean       | 6.6     | 4.25       | 13.5      |
| SD         | 0.41    | 0.495      | 1.27      |

(1) PT : value under validated range.

(2) PT : value under validated range. FIB : value above validated range.

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30641     | 5.48       | 7.13       | 15.0       | 0.46       | 64.9      | 21.1      | 32.5         | 383        | 2.85     | 0.20       |
| N30642     | 8.29       | 7.32       | 16.1       | 0.48       | 65.8      | 22.0      | 33.4         | 312        | 3.06     | 0.22       |
| N30643     | 6.07       | 7.49       | 15.7       | 0.47       | 63.1      | 20.9      | 33.2         | 409        | 2.46     | 0.18       |
| N30644     | 3.81       | 7.55       | 15.1       | 0.47       | 62.7      | 20.1      | 32.0         | 346        | 1.87     | 0.14       |
| N30645     | 4.86       | 7.02       | 15.5       | 0.46       | 64.9      | 22.0      | 34.0         | 276        | 2.32     | 0.16       |
| N30646     | 5.63       | 7.12       | 14.7       | 0.43       | 60.9      | 20.6      | 33.9         | 398        | 2.31     | 0.16       |
| N30647     | 8.95       | 7.63       | 16.0       | 0.47       | 61.9      | 20.9      | 33.8         | 354        | 2.98     | 0.23       |
| N30648     | 3.65       | 6.22       | 13.8       | 0.40       | 65.0      | 22.3      | 34.2         | 320        | 2.26     | 0.14       |
| N30649     | 6.59       | 7.00       | 14.0       | 0.43       | 61.5      | 20.0      | 32.6         | 356        | 3.31     | 0.23       |
| N30650     | 6.60       | 6.88       | 15.2       | 0.46       | 67.4      | 22.0      | 32.7         | 336        | 3.02     | 0.21       |
| Mean       | 5.99       | 7.14       | 15.1       | 0.45       | 63.8      | 21.2      | 33.2         | 349        | 2.64     | 0.19       |
| SD         | 1.722      | 0.410      | 0.78       | 0.025      | 2.10      | 0.84      | 0.75         | 40.8       | 0.461    | 0.036      |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30651     | 5.55       | 7.42       | 15.8       | 0.48       | 64.6      | 21.2      | 32.9         | 342        | 2.12     | 0.16       |
| N30652     | 4.84       | 7.06       | 15.2       | 0.46       | 64.9      | 21.5      | 33.2         | 223        | 2.84     | 0.20       |
| N30653     | 5.44       | 7.76       | 15.9       | 0.49       | 63.0      | 20.5      | 32.6         | 426        | 2.10     | 0.16       |
| N30654     | 6.27       | 7.34       | 15.2       | 0.47       | 63.9      | 20.7      | 32.4         | 219        | 1.91     | 0.14       |
| N30655     | 6.18       | 7.01       | 14.9       | 0.45       | 63.9      | 21.3      | 33.3         | 278        | 2.46     | 0.17       |
| N30656     | 6.20       | 6.94       | 14.8       | 0.44       | 63.7      | 21.3      | 33.4         | 276        | 2.33     | 0.16       |
| N30657     | 4.18       | 6.73       | 14.7       | 0.45       | 66.3      | 21.8      | 33.0         | 286        | 2.33     | 0.16       |
| N30658     | 6.62       | 6.48       | 13.6       | 0.42       | 64.3      | 21.0      | 32.6         | 369        | 2.42     | 0.16       |
| N30659     | 5.63       | 6.99       | 14.7       | 0.45       | 64.9      | 21.1      | 32.5         | 387        | 2.34     | 0.16       |
| N30660     | 5.48       | 7.02       | 14.2       | 0.43       | 61.9      | 20.3      | 32.7         | 340        | 2.83     | 0.20       |
| Mean       | 5.64       | 7.08       | 14.9       | 0.45       | 64.1      | 21.1      | 32.9         | 315        | 2.37     | 0.17       |
| SD         | 0.731      | 0.360      | 0.69       | 0.022      | 1.19      | 0.46      | 0.35         | 69.3       | 0.297    | 0.019      |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 3  
VACC99  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30661     | 8.94       | 7.65       | 16.1       | 0.48       | 62.9      | 21.0      | 33.4         | 387        | 2.25     | 0.17       |
| N30662     | 4.81       | 6.88       | 14.7       | 0.45       | 64.9      | 21.4      | 33.0         | 424        | 2.77     | 0.19       |
| N30663     | 4.04       | 7.53       | 15.0       | 0.44       | 58.7      | 19.9      | 33.9         | 298        | 1.66     | 0.12       |
| N30664     | 3.33       | 7.03       | 15.1       | 0.45       | 64.0      | 21.4      | 33.5         | 339        | 3.44     | 0.24       |
| N30665     | 5.13       | 7.80       | 15.9       | 0.48       | 61.7      | 20.3      | 33.0         | 300        | 2.14     | 0.17       |
| N30666     | 9.05       | 7.30       | 15.2       | 0.47       | 64.3      | 20.8      | 32.3         | 245        | 2.33     | 0.17       |
| N30667     | 5.22       | 6.89       | 14.8       | 0.45       | 65.7      | 21.5      | 32.7         | 482        | 3.06     | 0.21       |
| N30668     | 5.74       | 6.62       | 13.7       | 0.41       | 61.5      | 20.7      | 33.6         | 409        | 2.28     | 0.15       |
| N30669     | 5.56       | 6.45       | 13.7       | 0.41       | 63.8      | 21.2      | 33.2         | 328        | 2.44     | 0.16       |
| N30670     | 8.49       | 6.89       | 14.5       | 0.44       | 63.4      | 21.0      | 33.1         | 352        | 2.20     | 0.15       |
| Mean       | 6.03       | 7.10       | 14.9       | 0.45       | 63.1      | 20.9      | 33.2         | 356        | 2.46     | 0.17       |
| SD         | 2.059      | 0.449      | 0.79       | 0.025      | 2.02      | 0.51      | 0.46         | 70.1       | 0.508    | 0.034      |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30641     | 2.24     | 0.09     | 0.30     | 2.49     | 0.01       | 0.34     |
| N30642     | 2.19     | 0.11     | 0.38     | 5.38     | 0.03       | 0.19     |
| N30643     | 2.66     | 0.06     | 0.33     | 2.61     | 0.02       | 0.39     |
| N30644     | 1.41     | 0.05     | 0.23     | 2.00     | 0.01       | 0.12     |
| N30645     | 1.90     | 0.04     | 0.13     | 2.62     | 0.02       | 0.15     |
| N30646     | 2.07     | 0.08     | 0.23     | 2.87     | 0.02       | 0.35     |
| N30647     | 2.60     | 0.12     | 0.31     | 5.25     | 0.05       | 0.62     |
| N30648     | 0.75     | 0.06     | 0.20     | 2.57     | 0.01       | 0.07     |
| N30649     | 1.81     | 0.10     | 0.31     | 3.99     | 0.02       | 0.38     |
| N30650     | 2.09     | 0.09     | 0.21     | 3.72     | 0.03       | 0.46     |
| Mean       | 1.97     | 0.08     | 0.26     | 3.35     | 0.02       | 0.31     |
| SD         | 0.563    | 0.027    | 0.075    | 1.191    | 0.012      | 0.172    |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30651     | 1.99     | 0.03     | 0.19     | 3.04     | 0.04       | 0.26     |
| N30652     | 1.51     | 0.02     | 0.21     | 2.86     | 0.02       | 0.22     |
| N30653     | 2.01     | 0.03     | 0.32     | 2.75     | 0.03       | 0.30     |
| N30654     | 1.52     | 0.02     | 0.27     | 4.08     | 0.04       | 0.33     |
| N30655     | 1.94     | 0.03     | 0.37     | 3.46     | 0.03       | 0.35     |
| N30656     | 2.49     | 0.04     | 0.37     | 2.86     | 0.11       | 0.32     |
| N30657     | 1.40     | 0.03     | 0.29     | 2.10     | 0.03       | 0.33     |
| N30658     | 1.86     | 0.03     | 0.19     | 4.21     | 0.05       | 0.27     |
| N30659     | 1.59     | 0.04     | 0.21     | 3.42     | 0.11       | 0.26     |
| N30660     | 1.25     | 0.03     | 0.33     | 3.50     | 0.04       | 0.34     |
| Mean       | 1.76     | 0.03     | 0.28     | 3.23     | 0.05       | 0.30     |
| SD         | 0.370    | 0.007    | 0.072    | 0.638    | 0.033      | 0.043    |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 3  
VACC99  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30661     | 4.77     | 0.05     | 0.46     | 3.10     | 0.04       | 0.52     |
| N30662     | 1.50     | 0.03     | 0.21     | 2.78     | 0.02       | 0.26     |
| N30663     | 1.21     | 0.06     | 0.24     | 2.25     | 0.02       | 0.27     |
| N30664     | 1.46     | 0.03     | 0.22     | 1.43     | 0.02       | 0.16     |
| N30665     | 2.46     | 0.04     | 0.22     | 2.16     | 0.02       | 0.22     |
| N30666     | 2.20     | 0.05     | 0.39     | 5.69     | 0.07       | 0.65     |
| N30667     | 1.77     | 0.04     | 0.27     | 2.68     | 0.05       | 0.41     |
| N30668     | 1.50     | 0.04     | 0.16     | 3.63     | 0.05       | 0.37     |
| N30669     | 2.06     | 0.04     | 0.26     | 2.86     | 0.08       | 0.27     |
| N30670     | 2.21     | 0.05     | 0.24     | 5.44     | 0.04       | 0.51     |
| Mean       | 2.11     | 0.04     | 0.27     | 3.20     | 0.04       | 0.36     |
| SD         | 1.017    | 0.009    | 0.090    | 1.378    | 0.022      | 0.157    |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30641     | 7.1     | 2.41       | 13.8      |
| N30642     | 7.2     | 2.61       | 12.6      |
| N30643(1)  | 6.8     | 2.61       | 13.4      |
| N30644     | 7.5     | 2.90       | 13.8      |
| N30645(1)  | 6.5     | 2.91       | 12.6      |
| N30646(1)  | 6.8     | 3.50       | 14.4      |
| N30647(1)  | 6.7     | 3.47       | 14.0      |
| N30648     | 7.2     | 2.77       | 14.5      |
| N30649(1)  | 6.8     | 2.40       | 14.2      |
| N30650(1)  | 6.2     | 2.50       | 13.8      |
| Mean       | 6.9     | 2.81       | 13.7      |
| SD         | 0.38    | 0.399      | 0.67      |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30651     | 7.1     | 3.91       | 14.8      |
| N30652(2)  | 6.5     | 4.92       | 13.2      |
| N30653(3)  | 6.9     | 4.63       | 13.1      |
| N30654     | 7.1     | 3.99       | 13.4      |
| N30655(1)  | 6.6     | 3.78       | 13.5      |
| N30656(1)  | 6.8     | 3.57       | 14.9      |
| N30657(1)  | 6.5     | 4.27       | 14.1      |
| N30658(2)  | 6.4     | 4.67       | t         |
| N30659(1)  | 6.6     | 3.35       | 13.2      |
| N30660     | 7.4     | 4.03       | 13.6      |
| Mean       | 6.8     | 4.11       | 13.8      |
| SD         | 0.33    | 0.506      | 0.69      |

(1) PT : value under validated range.

(2) PT : value under validated range. FIB : value above validated range.

(3) FIB : value above validated range.

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 3  
VACC99  
Sex: Male

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| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
|------------|---------|------------|-----------|

|           |     |      |      |
|-----------|-----|------|------|
| N30661    | 7.3 | 4.17 | 14.1 |
| N30662(1) | 6.8 | 3.98 | 13.6 |
| N30663(2) | 6.7 | 5.49 | 13.6 |
| N30664    | 7.4 | 4.40 | 13.1 |
| N30665(1) | 6.8 | 4.36 | 13.5 |
| N30666(1) | 6.8 | 3.42 | 15.1 |
| N30667(1) | 6.5 | 3.95 | 15.8 |
| N30668(1) | 6.7 | 4.12 | 14.0 |
| N30669    | 7.0 | 4.52 | 15.7 |
| N30670(1) | 6.5 | 4.42 | 14.8 |

|      |      |       |      |
|------|------|-------|------|
| Mean | 6.9  | 4.28  | 14.3 |
| SD   | 0.30 | 0.531 | 0.96 |

(1) PT : value under validated range.

(2) PT : value under validated range. FIB : value above validated range.

HEMATOLOGY

Study No.:  
Time: Week 5

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30711     | 4.36       | 6.93       | 15.3       | 0.47       | 67.5      | 22.1      | 32.8         | 351        | 2.84     | 0.20       |
| N30712     | 5.54       | 6.08       | 13.2       | 0.40       | 66.6      | 21.6      | 32.5         | 461        | 3.77     | 0.23       |
| N30713     | 6.86       | 7.17       | 15.2       | 0.45       | 63.4      | 21.2      | 33.5         | 296        | 3.07     | 0.22       |
| N30714     | 5.18       | 6.40       | 13.8       | 0.42       | 65.2      | 21.6      | 33.2         | 350        | 2.99     | 0.19       |
| N30715     | 4.20       | 6.04       | 13.0       | 0.39       | 65.4      | 21.6      | 33.0         | 275        | 4.69     | 0.28       |
| N30716     | 6.37       | 6.97       | 14.4       | 0.45       | 64.1      | 20.7      | 32.3         | 357        | 3.34     | 0.23       |
| N30717     | 4.22       | 6.40       | 14.7       | 0.44       | 69.0      | 22.9      | 33.2         | 227        | 3.58     | 0.23       |
| N30718     | 4.32       | 6.44       | 14.7       | 0.44       | 68.9      | 22.8      | 33.1         | 264        | 2.74     | 0.18       |
| N30719     | 6.15       | 6.63       | 13.8       | 0.42       | 63.9      | 20.8      | 32.6         | 414        | 2.70     | 0.18       |
| N30720     | 5.81       | 6.39       | 13.7       | 0.42       | 65.2      | 21.5      | 33.0         | 426        | 3.66     | 0.23       |
| Mean       | 5.30       | 6.55       | 14.2       | 0.43       | 65.9      | 21.7      | 32.9         | 342        | 3.34     | 0.22       |
| SD         | 0.992      | 0.376      | 0.80       | 0.024      | 2.01      | 0.74      | 0.37         | 76.5       | 0.613    | 0.031      |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30721     | 7.14       | 6.60       | 13.9       | 0.44       | 67.1      | 21.1      | 31.5         | 349        | 3.07     | 0.20       |
| N30722     | 5.14       | 6.90       | 14.7       | 0.45       | 65.6      | 21.3      | 32.6         | 286        | 2.77     | 0.19       |
| N30723     | 7.52       | 6.20       | 13.4       | 0.41       | 65.6      | 21.5      | 32.8         | 322        | 3.17     | 0.20       |
| N30724     | 7.80       | 6.60       | 14.2       | 0.44       | 66.3      | 21.5      | 32.5         | 371        | 4.01     | 0.26       |
| N30725     | 6.03       | 7.04       | 14.3       | 0.45       | 63.4      | 20.4      | 32.1         | 396        | 3.92     | 0.28       |
| N30726     | 5.91       | 6.75       | 14.4       | 0.44       | 65.4      | 21.4      | 32.7         | 282        | 2.46     | 0.17       |
| N30727     | 6.32       | 6.26       | 13.5       | 0.40       | 64.3      | 21.5      | 33.4         | 374        | 3.70     | 0.23       |
| N30728     | 6.05       | 6.48       | 14.2       | 0.43       | 65.6      | 22.0      | 33.5         | 401        | 4.55     | 0.29       |
| N30729     | 6.94       | 6.75       | 14.5       | 0.44       | 64.7      | 21.5      | 33.2         | 293        | 2.09     | 0.14       |
| N30730     | 7.82       | 6.15       | 13.2       | 0.41       | 66.2      | 21.4      | 32.3         | 419        | 2.69     | 0.17       |
| Mean       | 6.67       | 6.57       | 14.0       | 0.43       | 65.4      | 21.4      | 32.7         | 349        | 3.24     | 0.21       |
| SD         | 0.910      | 0.301      | 0.51       | 0.018      | 1.06      | 0.41      | 0.61         | 50.8       | 0.780    | 0.050      |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 3

Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30731     | 4.78       | 6.55       | 14.1       | 0.44       | 66.9      | 21.5      | 32.2         | 394        | 2.84     | 0.19       |
| N30732     | 8.28       | 6.69       | 14.3       | 0.43       | 64.7      | 21.3      | 32.9         | 380        | 2.57     | 0.17       |
| N30733     | 6.55       | 7.05       | 14.4       | 0.44       | 62.7      | 20.5      | 32.6         | 286        | 2.33     | 0.16       |
| N30734     | 5.81       | 6.83       | 14.0       | 0.44       | 64.8      | 20.4      | 31.5         | 313        | 3.91     | 0.27       |
| N30735     | 5.51       | 7.36       | 14.9       | 0.45       | 61.8      | 20.3      | 32.8         | 341        | 2.85     | 0.21       |
| N30736     | 5.56       | 6.58       | 13.9       | 0.43       | 65.6      | 21.2      | 32.3         | 337        | 2.76     | 0.18       |
| N30737     | 4.78       | 6.54       | 14.0       | 0.43       | 65.5      | 21.4      | 32.7         | 324        | 3.14     | 0.21       |
| N30738     | 4.02       | 6.11       | 13.1       | 0.39       | 64.6      | 21.4      | 33.1         | 576        | 2.41     | 0.15       |
| N30739     | 5.24       | 5.97       | 12.7       | 0.39       | 65.2      | 21.3      | 32.6         | 429        | 3.31     | 0.20       |
| N30740     | 7.02       | 6.79       | 13.9       | 0.43       | 63.8      | 20.5      | 32.1         | 421        | 2.66     | 0.18       |
| Mean       | 5.76       | 6.65       | 13.9       | 0.43       | 64.6      | 21.0      | 32.5         | 380        | 2.88     | 0.19       |
| SD         | 1.242      | 0.408      | 0.63       | 0.021      | 1.48      | 0.49      | 0.47         | 83.3       | 0.471    | 0.034      |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30711     | 1.11     | 0.07     | 0.30     | 2.67     | 0.02       | 0.20     |
| N30712     | 1.81     | 0.08     | 0.41     | 3.04     | 0.03       | 0.16     |
| N30713     | 2.29     | 0.06     | 0.30     | 3.81     | 0.02       | 0.37     |
| N30714     | 1.22     | 0.08     | 0.37     | 3.19     | 0.03       | 0.29     |
| N30715     | 1.35     | 0.07     | 0.31     | 2.23     | 0.03       | 0.20     |
| N30716     | 2.28     | 0.09     | 0.34     | 3.10     | 0.05       | 0.52     |
| N30717     | 1.57     | 0.04     | 0.13     | 2.38     | 0.02       | 0.08     |
| N30718     | 1.08     | 0.03     | 0.31     | 2.67     | 0.01       | 0.20     |
| N30719     | 2.52     | 0.09     | 0.16     | 3.12     | 0.08       | 0.19     |
| N30720     | 1.96     | 0.07     | 0.21     | 3.32     | 0.03       | 0.22     |
| Mean       | 1.72     | 0.07     | 0.28     | 2.95     | 0.03       | 0.24     |
| SD         | 0.531    | 0.020    | 0.090    | 0.471    | 0.020      | 0.124    |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30721     | 2.46     | 0.07     | 0.40     | 3.72     | 0.05       | 0.43     |
| N30722     | 1.89     | 0.03     | 0.17     | 2.72     | 0.02       | 0.30     |
| N30723     | 3.01     | 0.06     | 0.32     | 3.56     | 0.06       | 0.51     |
| N30724     | 2.75     | 0.03     | 0.21     | 4.35     | 0.06       | 0.42     |
| N30725     | 2.14     | 0.05     | 0.27     | 2.99     | 0.07       | 0.51     |
| N30726     | 1.45     | 0.04     | 0.44     | 3.57     | 0.04       | 0.37     |
| N30727     | 2.23     | 0.05     | 0.38     | 3.54     | 0.04       | 0.08     |
| N30728     | 2.00     | 0.05     | 0.24     | 3.22     | 0.04       | 0.50     |
| N30729     | 1.60     | 0.02     | 0.29     | 4.70     | 0.08       | 0.25     |
| N30730     | 3.50     | 0.04     | 0.31     | 3.58     | 0.05       | 0.34     |
| Mean       | 2.30     | 0.04     | 0.30     | 3.60     | 0.05       | 0.37     |
| SD         | 0.639    | 0.015    | 0.086    | 0.585    | 0.017      | 0.136    |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 3

Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30731     | 1.48     | 0.04     | 0.29     | 2.79     | 0.04       | 0.13     |
| N30732     | 2.65     | 0.04     | 0.46     | 4.56     | 0.05       | 0.52     |
| N30733     | 2.14     | 0.04     | 0.38     | 3.34     | 0.08       | 0.56     |
| N30734     | 1.62     | 0.03     | 0.34     | 3.51     | 0.03       | 0.28     |
| N30735     | 1.92     | 0.03     | 0.45     | 2.65     | 0.04       | 0.43     |
| N30736     | 2.28     | 0.07     | 0.36     | 2.53     | 0.10       | 0.24     |
| N30737     | 1.94     | 0.02     | 0.19     | 2.18     | 0.03       | 0.41     |
| N30738     | 0.99     | 0.04     | 0.16     | 2.70     | 0.02       | 0.11     |
| N30739     | 1.24     | 0.03     | 0.34     | 3.44     | 0.04       | 0.15     |
| N30740     | 1.79     | 0.05     | 0.44     | 4.23     | 0.05       | 0.46     |
| Mean       | 1.81     | 0.04     | 0.34     | 3.19     | 0.05       | 0.33     |
| SD         | 0.495    | 0.014    | 0.103    | 0.767    | 0.024      | 0.168    |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30711     | 6.6     | 1.70       | 13.0      |
| N30712     | 7.1     | 2.39       | 15.2      |
| N30713     | 6.9     | 1.66       | 14.8      |
| N30714     | 7.2     | 2.55       | 15.5      |
| N30715     | 6.5     | 1.89       | 15.6      |
| N30716     | 6.4     | 2.55       | 15.4      |
| N30717     | 6.3     | 1.81       | 13.6      |
| N30718     | 7.0     | 2.02       | 13.4      |
| N30719     | 6.6     | 2.10       | 15.3      |
| N30720     | 6.7     | 2.20       | 13.0      |
| Mean       | 6.7     | 2.09       | 14.5      |
| SD         | 0.31    | 0.331      | 1.09      |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30721     | 7.7     | 2.53       | 14.1      |
| N30722     | 7.1     | 2.88       | 14.1      |
| N30723     | 6.4     | 3.58       | 13.8      |
| N30724     | 6.7     | 2.35       | 14.7      |
| N30725     | 6.6     | 3.44       | 15.3      |
| N30726     | 6.6     | 2.96       | 12.8      |
| N30727     | 7.0     | 3.22       | 13.7      |
| N30728     | 7.6     | 2.16       | 14.8      |
| N30729     | 6.2     | 3.87       | 15.2      |
| N30730     | 7.1     | 2.89       | 14.4      |
| Mean       | 6.9     | 2.99       | 14.3      |
| SD         | 0.49    | 0.549      | 0.76      |

## HEMATOLOGY

Study No.:  
Time: Week 5

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30731     | 7.0     | 2.59       | 13.9      |
| N30732     | 6.4     | 3.73       | 14.3      |
| N30733     | 6.9     | 3.68       | 13.3      |
| N30734     | 6.5     | 2.73       | 13.4      |
| N30735     | 6.2     | 3.93       | 13.0      |
| N30736     | 6.5     | 3.67       | 14.1      |
| N30737     | 6.9     | 3.45       | 13.6      |
| N30738     | 7.0     | 2.70       | 15.5      |
| N30739     | 6.4     | 3.09       | 14.4      |
| N30740     | 6.5     | 3.04       | 15.7      |
| Mean       | 6.6     | 3.26       | 14.1      |
| SD         | 0.29    | 0.491      | 0.90      |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30646     | 6.77       | 7.16       | 15.1       | 0.45       | 63.2      | 21.1      | 33.4         | 425        | 2.33     | 0.17       |
| N30647     | 9.18       | 7.46       | 15.7       | 0.47       | 63.3      | 21.0      | 33.3         | 295        | 2.60     | 0.19       |
| N30648     | 4.09       | 6.31       | 13.9       | 0.42       | 66.3      | 22.1      | 33.3         | 294        | 2.11     | 0.13       |
| N30649     | 6.35       | 7.06       | 14.9       | 0.44       | 63.0      | 21.1      | 33.5         | 342        | 3.06     | 0.22       |
| N30650     | 7.47       | 6.98       | 15.4       | 0.48       | 68.9      | 22.1      | 32.1         | 354        | 2.71     | 0.19       |
| Mean       | 6.77       | 6.99       | 15.0       | 0.45       | 64.9      | 21.5      | 33.1         | 342        | 2.56     | 0.18       |
| SD         | 1.848      | 0.423      | 0.69       | 0.024      | 2.60      | 0.57      | 0.58         | 53.7       | 0.364    | 0.033      |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30656     | 5.22       | 7.05       | 15.0       | 0.46       | 65.2      | 21.3      | 32.7         | 293        | 2.62     | 0.18       |
| N30657     | 4.15       | 7.09       | 15.3       | 0.46       | 64.5      | 21.6      | 33.4         | 269        | 1.62     | 0.11       |
| N30658     | 5.17       | 6.94       | 14.3       | 0.45       | 64.9      | 20.6      | 31.8         | 377        | 2.28     | 0.16       |
| N30659     | 4.27       | 7.14       | 15.0       | 0.46       | 64.7      | 21.0      | 32.6         | 417        | 2.45     | 0.17       |
| N30660     | 5.93       | 7.30       | 15.1       | 0.45       | 62.3      | 20.8      | 33.3         | 365        | 2.49     | 0.18       |
| Mean       | 4.95       | 7.10       | 14.9       | 0.46       | 64.3      | 21.1      | 32.8         | 344        | 2.29     | 0.16       |
| SD         | 0.739      | 0.132      | 0.38       | 0.005      | 1.16      | 0.40      | 0.64         | 61.4       | 0.395    | 0.029      |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30666     | 7.79       | 7.42       | 15.7       | 0.49       | 65.9      | 21.2      | 32.2         | 292        | 2.17     | 0.16       |
| N30667     | 7.13       | 7.13       | 15.2       | 0.45       | 63.4      | 21.4      | 33.7         | 330        | 2.38     | 0.17       |
| N30668     | 5.04       | 6.93       | 14.6       | 0.43       | 61.9      | 21.0      | 33.9         | 401        | 2.16     | 0.15       |
| N30669     | 4.83       | 6.70       | 14.3       | 0.44       | 65.6      | 21.4      | 32.6         | 354        | 2.42     | 0.16       |
| N30670     | 6.09       | 6.89       | 15.0       | 0.46       | 66.9      | 21.8      | 32.6         | 469        | 3.08     | 0.21       |
| Mean       | 6.18       | 7.01       | 15.0       | 0.45       | 64.7      | 21.4      | 33.0         | 369        | 2.44     | 0.17       |
| SD         | 1.287      | 0.274      | 0.54       | 0.023      | 2.04      | 0.30      | 0.75         | 68.4       | 0.376    | 0.023      |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30646     | 2.23     | 0.08     | 0.27     | 3.76     | 0.02       | 0.41     |
| N30647     | 2.77     | 0.15     | 0.41     | 5.36     | 0.03       | 0.45     |
| N30648     | 0.90     | 0.08     | 0.23     | 2.81     | 0.02       | 0.07     |
| N30649     | 1.75     | 0.08     | 0.31     | 3.96     | 0.03       | 0.23     |
| N30650     | 2.61     | 0.11     | 0.23     | 4.18     | 0.06       | 0.26     |
| Mean       | 2.05     | 0.10     | 0.29     | 4.01     | 0.03       | 0.28     |
| SD         | 0.754    | 0.031    | 0.075    | 0.916    | 0.016      | 0.152    |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30656     | 1.97     | 0.11     | 0.25     | 2.77     | 0.01       | 0.11     |
| N30657     | 1.55     | 0.07     | 0.28     | 2.09     | 0.01       | 0.15     |
| N30658     | 1.22     | 0.08     | 0.20     | 3.36     | 0.01       | 0.31     |
| N30659     | 1.29     | 0.07     | 0.22     | 2.44     | 0.01       | 0.24     |
| N30660     | 1.41     | 0.10     | 0.29     | 3.84     | 0.02       | 0.27     |
| Mean       | 1.49     | 0.09     | 0.25     | 2.90     | 0.01       | 0.22     |
| SD         | 0.297    | 0.018    | 0.038    | 0.704    | 0.004      | 0.084    |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30666     | 2.35     | 0.13     | 0.33     | 4.65     | 0.01       | 0.32     |
| N30667     | 1.91     | 0.09     | 0.16     | 4.84     | 0.02       | 0.11     |
| N30668     | 1.85     | 0.06     | 0.12     | 2.87     | 0.02       | 0.12     |
| N30669     | 1.90     | 0.12     | 0.28     | 2.32     | 0.01       | 0.20     |
| N30670     | 1.62     | 0.13     | 0.26     | 3.76     | 0.03       | 0.29     |
| Mean       | 1.93     | 0.11     | 0.23     | 3.69     | 0.02       | 0.21     |
| SD         | 0.265    | 0.030    | 0.087    | 1.095    | 0.008      | 0.096    |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30646(1)  | 6.6     | 3.33       | 13.3      |
| N30647     | 7.1     | 2.86       | 13.1      |
| N30648     | 7.6     | 2.89       | 13.7      |
| N30649     | 7.0     | 2.51       | 12.9      |
| N30650(1)  | 6.8     | 2.65       | 12.8      |
| Mean       | 7.0     | 2.85       | 13.2      |
| SD         | 0.38    | 0.311      | 0.36      |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30656     | 7.0     | 2.03       | 14.3      |
| N30657     | 6.9     | 2.32       | 13.2      |
| N30658(1)  | 6.8     | 2.98       | 12.1      |
| N30659(1)  | 6.8     | 2.34       | 12.6      |
| N30660(1)  | 6.6     | 2.62       | 12.9      |
| Mean       | 6.8     | 2.46       | 13.0      |
| SD         | 0.15    | 0.359      | 0.82      |

(1) PT : value under validated range.

HEMATOLOGY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30666(1)  | 6.7     | 2.39       | 14.0      |
| N30667     | 7.0     | 3.32       | 13.3      |
| N30668     | 7.3     | 2.86       | 13.6      |
| N30669     | 7.7     | 2.45       | 14.9      |
| N30670(1)  | 6.6     | 2.41       | 14.5      |
| Mean       | 7.1     | 2.69       | 14.1      |
| SD         | 0.45    | 0.404      | 0.65      |

(1) PT : value under validated range.

HEMATOLOGY

Study No.:  
Time: Week 9

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30716     | 6.40       | 7.13       | 14.9       | 0.46       | 64.6      | 20.9      | 32.3         | 381        | 2.66     | 0.19       |
| N30717     | 4.58       | 6.40       | 14.8       | 0.44       | 69.5      | 23.0      | 33.2         | 238        | 3.16     | 0.20       |
| N30718     | 4.38       | 6.22       | 14.1       | 0.43       | 69.7      | 22.7      | 32.6         | 245        | 2.93     | 0.18       |
| N30719     | 5.07       | 6.75       | 14.1       | 0.45       | 66.0      | 20.9      | 31.7         | 377        | 3.02     | 0.20       |
| N30720     | 6.82       | 5.98       | 13.3       | 0.40       | 66.9      | 22.3      | 33.3         | 386        | 3.56     | 0.21       |
| Mean       | 5.45       | 6.50       | 14.2       | 0.44       | 67.3      | 22.0      | 32.6         | 325        | 3.07     | 0.20       |
| SD         | 1.098      | 0.452      | 0.65       | 0.023      | 2.22      | 1.00      | 0.66         | 76.7       | 0.331    | 0.011      |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30726     | 4.61       | 6.52       | 14.1       | 0.44       | 66.8      | 21.7      | 32.4         | 298        | 2.46     | 0.16       |
| N30727     | 6.25       | 6.29       | 13.8       | 0.42       | 67.1      | 21.9      | 32.6         | 341        | 3.58     | 0.23       |
| N30728     | 5.38       | 6.30       | 14.2       | 0.42       | 67.3      | 22.4      | 33.4         | 353        | 4.02     | 0.25       |
| N30729     | 7.35       | 6.26       | 13.9       | 0.42       | 66.4      | 22.2      | 33.4         | 308        | 2.18     | 0.14       |
| N30730     | 4.84       | 6.25       | 13.6       | 0.42       | 66.5      | 21.7      | 32.7         | 381        | 2.13     | 0.13       |
| Mean       | 5.69       | 6.32       | 13.9       | 0.42       | 66.8      | 22.0      | 32.9         | 336        | 2.87     | 0.18       |
| SD         | 1.124      | 0.111      | 0.24       | 0.009      | 0.38      | 0.31      | 0.47         | 33.8       | 0.869    | 0.054      |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | WBC<br>G/L | RBC<br>T/L | HB<br>g/dL | PCV<br>L/L | MCV<br>fL | MCH<br>pg | MCHC<br>g/dL | PLT<br>G/L | RTC<br>% | RTC<br>T/L |
|------------|------------|------------|------------|------------|-----------|-----------|--------------|------------|----------|------------|
| N30736     | 4.07       | 6.69       | 14.2       | 0.45       | 66.9      | 21.3      | 31.7         | 297        | 3.13     | 0.21       |
| N30737     | 3.96       | 6.27       | 13.7       | 0.42       | 67.1      | 21.9      | 32.7         | 324        | 3.61     | 0.23       |
| N30738     | 4.13       | 5.96       | 12.9       | 0.39       | 65.5      | 21.6      | 33.1         | 529        | 1.88     | 0.11       |
| N30739     | 4.26       | 6.10       | 13.2       | 0.41       | 67.1      | 21.6      | 32.3         | 395        | 2.79     | 0.17       |
| N30740     | 5.24       | 7.03       | 14.4       | 0.45       | 64.3      | 20.5      | 31.9         | 346        | 2.45     | 0.17       |
| Mean       | 4.33       | 6.41       | 13.7       | 0.42       | 66.2      | 21.4      | 32.3         | 378        | 2.77     | 0.18       |
| SD         | 0.519      | 0.442      | 0.64       | 0.026      | 1.25      | 0.54      | 0.57         | 91.6       | 0.658    | 0.046      |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30716     | 2.34     | 0.13     | 0.45     | 3.13     | 0.12       | 0.23     |
| N30717     | 1.56     | 0.11     | 0.25     | 2.54     | 0.03       | 0.10     |
| N30718     | 1.05     | 0.12     | 0.31     | 2.66     | 0.03       | 0.23     |
| N30719     | 1.52     | 0.13     | 0.22     | 2.92     | 0.02       | 0.27     |
| N30720     | 1.75     | 0.16     | 0.35     | 4.38     | 0.03       | 0.15     |
| Mean       | 1.64     | 0.13     | 0.32     | 3.13     | 0.05       | 0.20     |
| SD         | 0.467    | 0.019    | 0.090    | 0.737    | 0.042      | 0.069    |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30726     | 0.96     | 0.13     | 0.33     | 3.06     | 0.02       | 0.10     |
| N30727     | 2.01     | 0.13     | 0.35     | 3.45     | 0.03       | 0.29     |
| N30728     | 1.93     | 0.12     | 0.10     | 2.84     | 0.03       | 0.37     |
| N30729     | 2.00     | 0.16     | 0.40     | 4.49     | 0.04       | 0.26     |
| N30730     | 1.99     | 0.14     | 0.19     | 2.30     | 0.06       | 0.16     |
| Mean       | 1.78     | 0.14     | 0.27     | 3.23     | 0.04       | 0.24     |
| SD         | 0.458    | 0.015    | 0.125    | 0.819    | 0.015      | 0.107    |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | N<br>G/L | E<br>G/L | B<br>G/L | L<br>G/L | LUC<br>G/L | M<br>G/L |
|------------|----------|----------|----------|----------|------------|----------|
| N30736     | 1.57     | 0.08     | 0.17     | 2.04     | 0.02       | 0.19     |
| N30737     | 1.54     | 0.10     | 0.29     | 1.88     | 0.03       | 0.12     |
| N30738     | 0.98     | 0.11     | 0.16     | 2.67     | 0.05       | 0.15     |
| N30739     | 1.05     | 0.15     | 0.32     | 2.53     | 0.02       | 0.19     |
| N30740     | 1.98     | 0.14     | 0.33     | 2.65     | 0.02       | 0.12     |
| Mean       | 1.42     | 0.12     | 0.25     | 2.35     | 0.03       | 0.15     |
| SD         | 0.413    | 0.029    | 0.083    | 0.368    | 0.013      | 0.035    |

## HEMATOLOGY

Study No.:  
Time: Week 9

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30716(1)  | 6.7     | 2.52       | 15.1      |
| N30717     | 7.7     | 1.69       | 12.7      |
| N30718     | 7.1     | 1.86       | 13.1      |
| N30719     | 7.3     | 1.87       | 14.7      |
| N30720     | 7.2     | 2.16       | 13.1      |
| Mean       | 7.2     | 2.02       | 13.7      |
| SD         | 0.36    | 0.327      | 1.08      |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30726     | 7.6     | 2.06       | 13.4      |
| N30727     | 7.0     | 1.84       | 14.1      |
| N30728     | 6.9     | 1.76       | 13.8      |
| N30729     | 7.3     | 2.14       | 14.6      |
| N30730     | 7.1     | 1.79       | 14.6      |
| Mean       | 7.2     | 1.92       | 14.1      |
| SD         | 0.28    | 0.171      | 0.52      |

(1) PT : value under validated range.

HEMATOLOGY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | PT<br>s | FIB<br>g/L | APTT<br>s |
|------------|---------|------------|-----------|
| N30736     | 7.2     | 1.96       | 14.1      |
| N30737(1)  | 6.7     | 2.26       | 13.7      |
| N30738     | 7.9     | 1.88       | 16.7      |
| N30739     | 7.5     | 2.01       | 13.8      |
| N30740(1)  | 6.0     | 2.11       | 15.6      |
| Mean       | 7.1     | 2.04       | 14.8      |
| SD         | 0.74    | 0.147      | 1.32      |

(1) PT : value under validated range.

14. Blood biochemistry parameters: individual values

## **KEY TO ABBREVIATIONS USED FOR BLOOD BIOCHEMISTRY**

### **ABBREVIATIONS**

|                  |                              |
|------------------|------------------------------|
| Na <sup>+</sup>  | : sodium                     |
| K <sup>+</sup>   | : potassium                  |
| Cl <sup>-</sup>  | : chloride                   |
| Ca <sup>++</sup> | : calcium                    |
| PHOS             | : inorganic phosphorus       |
| GLUC             | : glucose                    |
| UREA             | : urea                       |
| CREAT            | : creatinine                 |
| TOT.BIL          | : total bilirubin            |
| CHOL             | : total cholesterol          |
| TRIG             | : triglycerides              |
| ALP              | : alkaline phosphatase       |
| ASAT             | : aspartate aminotransferase |
| ALAT             | : alanine aminotransferase   |
| LDH              | : lactate dehydrogenase      |
| CK               | : creatine kinase            |
| CK-L             | : creatine kinase            |
| GGT              | : gamma glutamyltransferase  |
| PROT             | : total proteins             |
| ALB              | : albumin                    |
| A/G              | : albumin/globulin ratio     |
| GLOB             | : globulin                   |

### **EXPLANATION FOR MISSING VALUE**

|      |                                 |
|------|---------------------------------|
| -    | : dead animal                   |
| ns   | : not sampled                   |
| blq* | : below limit of quantification |
| alq  | : above limit of quantification |
| m    | : missing value                 |
| i    | : insufficient sample           |
| np   | : not performed                 |
| a    | : aberrant value                |
| t    | : technical problem             |

\*: for calculation of the group mean, "blq" was considered to be equal to zero

### **UNITS**

|        |                             |
|--------|-----------------------------|
| mmol/L | : millimole/liter           |
| µmol/L | : micromole/liter           |
| g/L    | : gram/liter                |
| U/L    | : international units/liter |

BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | μmol/L |
| N30641     | 142.1  | 4.54   | 104.8  | 3.59   | 2.20   | 7.25   | 6.6    | 79.46  |
| N30642     | 139.6  | 4.02   | 101.9  | 3.50   | 1.93   | 7.27   | 6.5    | 89.00  |
| N30643     | 141.7  | 3.77   | 103.7  | 3.62   | 2.34   | 5.55   | 7.3    | 103.16 |
| N30644     | 139.9  | 3.73   | 102.2  | 3.48   | 2.13   | 7.27   | 8.0    | 90.44  |
| N30645     | 141.4  | 4.56   | 96.1   | 3.48   | 2.25   | 7.37   | 6.9    | 95.27  |
| N30646     | 141.2  | 3.56   | 100.0  | 3.68   | 2.07   | 7.20   | 7.5    | 92.18  |
| N30647     | 142.1  | 3.98   | 99.9   | 3.65   | 2.30   | 7.33   | 6.0    | 91.18  |
| N30648     | 143.3  | 4.18   | 102.8  | 3.48   | 2.54   | 6.56   | 7.7    | 104.52 |
| N30649     | 142.2  | 3.96   | 104.9  | 3.51   | 2.16   | 7.26   | 6.8    | 98.53  |
| N30650     | 142.5  | 4.35   | 106.7  | 3.42   | 2.09   | 6.90   | 7.1    | 96.46  |
| Mean       | 141.6  | 4.07   | 102.3  | 3.54   | 2.20   | 7.00   | 7.0    | 94.02  |
| SD         | 1.14   | 0.340  | 3.06   | 0.087  | 0.169  | 0.564  | 0.60   | 7.327  |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | μmol/L |
| N30651     | 141.0  | 4.06   | 103.2  | 3.54   | 2.25   | 6.87   | 7.4    | 90.60  |
| N30652     | 140.5  | 4.22   | 104.3  | 3.63   | 2.28   | 6.59   | 8.6    | 72.93  |
| N30653     | 142.4  | 5.63   | 101.3  | 3.77   | 2.70   | 6.95   | 10.6   | 99.32  |
| N30654     | 141.7  | 3.64   | 102.7  | 3.55   | 2.45   | 6.80   | 7.4    | 81.60  |
| N30655     | 142.1  | 3.97   | 103.8  | 3.37   | 2.70   | 7.09   | 9.2    | 93.25  |
| N30656     | 141.6  | 4.06   | 105.8  | 3.73   | 2.17   | 5.47   | 8.1    | 101.82 |
| N30657     | 142.0  | 4.02   | 106.2  | 3.53   | 1.80   | 7.22   | 4.5    | 82.89  |
| N30658     | 143.4  | 4.29   | 104.9  | 3.63   | 2.34   | 7.64   | 6.5    | 108.65 |
| N30659     | 143.3  | 4.30   | 98.9   | 3.57   | 2.49   | 8.34   | 8.1    | 113.42 |
| N30660     | 142.8  | 3.89   | 100.8  | 3.37   | 2.38   | 7.05   | 7.7    | 102.80 |
| Mean       | 142.1  | 4.21   | 103.2  | 3.57   | 2.36   | 7.00   | 7.8    | 94.73  |
| SD         | 0.94   | 0.537  | 2.32   | 0.132  | 0.264  | 0.733  | 1.62   | 12.852 |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | Na <sup>+</sup><br>mmol/L | K <sup>+</sup><br>mmol/L | Cl <sup>-</sup><br>mmol/L | Ca <sup>++</sup><br>mmol/L | PHOS<br>mmol/L | GLUC<br>mmol/L | UREA<br>mmol/L | CREAT<br>μmol/L |
|------------|---------------------------|--------------------------|---------------------------|----------------------------|----------------|----------------|----------------|-----------------|
| N30661     | 140.0                     | 4.17                     | 100.5                     | 3.43                       | 2.59           | 6.49           | 8.7            | 108.55          |
| N30662     | 142.4                     | 3.81                     | 98.9                      | 3.55                       | 2.34           | 7.19           | 11.3           | 102.81          |
| N30663     | 141.3                     | 4.00                     | 97.0                      | 3.65                       | 2.32           | 8.06           | 6.1            | 94.94           |
| N30664     | 136.0                     | 3.98                     | 100.7                     | 3.47                       | 2.13           | 6.95           | 7.2            | 80.45           |
| N30665     | 141.1                     | 3.92                     | 104.3                     | 3.56                       | 2.30           | 7.56           | 8.1            | 86.70           |
| N30666     | 140.3                     | 3.60                     | 105.5                     | 3.58                       | 1.98           | 7.23           | 6.3            | 89.28           |
| N30667     | 141.3                     | 4.09                     | 104.5                     | 3.55                       | 2.35           | 6.51           | 9.0            | 99.31           |
| N30668     | 141.6                     | 3.85                     | 104.4                     | 3.65                       | 2.44           | 7.66           | 6.3            | 86.28           |
| N30669     | 141.5                     | 3.77                     | 106.2                     | 3.50                       | 2.16           | 6.69           | 7.6            | 95.42           |
| N30670     | 141.2                     | 4.30                     | 102.0                     | 3.51                       | 2.50           | 7.16           | 8.9            | 100.06          |
| Mean       | 140.7                     | 3.95                     | 102.4                     | 3.55                       | 2.31           | 7.15           | 8.0            | 94.38           |
| SD         | 1.77                      | 0.205                    | 3.06                      | 0.071                      | 0.182          | 0.512          | 1.61           | 8.657           |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30641     | 455        | 60          | 26          | 709       | 203        | 4          |
| N30642     | 448        | 47          | 25          | 664       | 371        | 7          |
| N30643     | 655        | 67          | 31          | 979       | 343        | 5          |
| N30644     | 597        | 42          | 19          | 619       | 254        | 6          |
| N30645     | 387        | 67          | 26          | 985       | 466        | 6          |
| N30646     | 515        | 40          | 19          | 891       | 363        | 7          |
| N30647     | 523        | 47          | 18          | 1092      | 223        | 5          |
| N30648     | 536        | 39          | 21          | 556       | 221        | 10         |
| N30649     | 524        | 31          | 19          | 461       | 152        | 8          |
| N30650     | 297        | 54          | 25          | 623       | 199        | 4          |
| Mean       | 494        | 49          | 23          | 758       | 280        | 6          |
| SD         | 102.4      | 12.3        | 4.3         | 212.8     | 100.0      | 1.9        |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30651     | 546        | 64          | 24          | 515       | 256        | 9          |
| N30652     | 726        | 54          | 19          | 355       | 145        | 6          |
| N30653     | 755        | 49          | 30          | 549       | 196        | 6          |
| N30654     | 555        | 35          | 21          | 1431      | 364        | 7          |
| N30655     | 469        | 53          | 24          | 1256      | 273        | 4          |
| N30656     | 486        | 36          | 18          | 579       | 309        | 5          |
| N30657     | 340        | 37          | 22          | 546       | 241        | 5          |
| N30658     | 363        | 39          | 17          | 662       | 170        | 9          |
| N30659     | 344        | 37          | 20          | 663       | 167        | 8          |
| N30660     | 532        | 55          | 14          | 306       | 74         | 9          |
| Mean       | 512        | 46          | 21          | 686       | 220        | 7          |
| SD         | 145.6      | 10.3        | 4.5         | 367.3     | 85.7       | 1.9        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30661     | 724        | 57          | 14          | 512       | 169        | 5          |
| N30662     | 466        | 39          | 18          | 553       | 248        | 6          |
| N30663     | 655        | 39          | 18          | 694       | 162        | 7          |
| N30664     | 541        | 51          | 18          | 964       | 344        | 6          |
| N30665     | 759        | 56          | 18          | 550       | 106        | 7          |
| N30666     | 328        | 33          | 17          | 802       | 298        | 5          |
| N30667     | 557        | 70          | 19          | 982       | 244        | 8          |
| N30668     | 494        | 36          | 13          | 462       | 150        | 7          |
| N30669     | 655        | 51          | 16          | 516       | 119        | 7          |
| N30670     | 500        | 63          | 25          | 458       | 84         | 5          |
| Mean       | 568        | 50          | 18          | 649       | 192        | 6          |
| SD         | 131.2      | 12.4        | 3.2         | 200.7     | 86.8       | 1.1        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30641     | blq               | 1.88           | 0.97           | 62.0        | 40         | 1.82     | 22          |
| N30642     | blq               | 1.74           | 0.74           | 61.6        | 39         | 1.73     | 23          |
| N30643     | blq               | 1.73           | 0.85           | 63.8        | 41         | 1.80     | 23          |
| N30644     | blq               | 0.97           | 0.56           | 60.7        | 39         | 1.80     | 22          |
| N30645     | blq               | 1.43           | 0.79           | 61.1        | 40         | 1.90     | 21          |
| N30646     | blq               | 1.54           | 0.73           | 68.0        | 43         | 1.72     | 25          |
| N30647     | blq               | 1.59           | 0.92           | 65.0        | 42         | 1.83     | 23          |
| N30648     | blq               | 1.69           | 1.28           | 60.7        | 39         | 1.80     | 22          |
| N30649     | blq               | 1.20           | 0.50           | 62.7        | 41         | 1.89     | 22          |
| N30650     | blq               | 1.55           | 0.56           | m           | 38         | m        | na          |
| Mean       | 0                 | 1.53           | 0.79           | 62.8        | 40         | 1.81     | 23          |
| SD         | 0.0               | 0.273          | 0.233          | 2.42        | 1.5        | 0.061    | 1.1         |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30651     | blq               | 1.26           | 0.55           | 58.5        | 38         | 1.85     | 21          |
| N30652     | blq               | 1.61           | 0.51           | 63.3        | 41         | 1.84     | 22          |
| N30653     | blq               | 2.02           | 1.52           | 67.9        | 44         | 1.84     | 24          |
| N30654     | blq               | 1.73           | 1.11           | 61.4        | 39         | 1.74     | 22          |
| N30655     | blq               | 1.56           | 0.67           | 61.8        | 40         | 1.83     | 22          |
| N30656     | blq               | 0.77           | 0.43           | 63.0        | 40         | 1.74     | 23          |
| N30657     | blq               | 1.30           | 0.56           | 56.8        | 36         | 1.73     | 21          |
| N30658     | blq               | 1.34           | 0.76           | 64.3        | 42         | 1.88     | 22          |
| N30659     | blq               | 1.44           | 0.70           | 61.1        | 39         | 1.76     | 22          |
| N30660     | blq               | 1.39           | 0.80           | 59.9        | 38         | 1.74     | 22          |
| Mean       | 0                 | 1.44           | 0.76           | 61.8        | 40         | 1.80     | 22          |
| SD         | 0.0               | 0.330          | 0.328          | 3.11        | 2.3        | 0.058    | 0.9         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30661     | blq               | 1.79           | 0.88           | 62.8        | 38         | 1.53     | 25          |
| N30662     | blq               | 1.43           | 0.83           | 63.9        | 41         | 1.79     | 23          |
| N30663     | blq               | 1.85           | 1.27           | 66.4        | 41         | 1.61     | 25          |
| N30664     | blq               | 1.39           | 0.45           | 59.5        | 38         | 1.77     | 22          |
| N30665     | blq               | 1.31           | 1.05           | 60.6        | 39         | 1.81     | 22          |
| N30666     | blq               | 1.31           | 0.66           | 60.7        | 40         | 1.93     | 21          |
| N30667     | blq               | 1.65           | 1.51           | 59.9        | 37         | 1.62     | 23          |
| N30668     | blq               | 1.78           | 0.86           | 66.3        | 42         | 1.73     | 24          |
| N30669     | blq               | 1.22           | 0.65           | 60.5        | 38         | 1.69     | 23          |
| N30670     | blq               | 1.46           | 1.02           | 64.3        | 41         | 1.76     | 23          |
| Mean       | 0                 | 1.52           | 0.92           | 62.5        | 40         | 1.72     | 23          |
| SD         | 0.0               | 0.229          | 0.311          | 2.62        | 1.7        | 0.116    | 1.3         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30711     | 139.8      | 3.94      | 104.1      | 3.40        | 2.32        | 6.71        | 8.6         | 87.21        |
| N30712     | 141.1      | 3.64      | 103.7      | 3.47        | 2.27        | 7.38        | 10.1        | 95.28        |
| N30713     | 140.3      | 4.02      | 103.6      | 3.45        | 2.33        | 6.56        | 7.3         | 92.32        |
| N30714     | 141.9      | 3.75      | 106.3      | 3.52        | 2.12        | 7.27        | 8.7         | 85.96        |
| N30715     | 140.1      | 4.20      | 103.3      | 3.67        | 2.12        | 6.45        | 9.5         | 88.31        |
| N30716     | 141.6      | 3.44      | 100.5      | 3.54        | 2.11        | 6.33        | 8.2         | 86.57        |
| N30717     | 142.2      | 3.81      | 105.8      | 3.35        | 2.42        | 6.29        | 10.3        | 94.69        |
| N30718     | 140.0      | 4.08      | 105.4      | 3.40        | 2.24        | 6.26        | 9.3         | 103.69       |
| N30719     | 138.7      | 3.95      | 100.3      | 3.51        | 2.04        | 5.84        | 10.3        | 98.43        |
| N30720     | 138.1      | 3.91      | 100.5      | 3.55        | 2.11        | 6.62        | 9.4         | 97.35        |
| Mean       | 140.4      | 3.87      | 103.4      | 3.49        | 2.21        | 6.57        | 9.2         | 92.98        |
| SD         | 1.34       | 0.222     | 2.24       | 0.093       | 0.125       | 0.465       | 0.98        | 5.941        |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30721     | 142.1      | 3.99      | 100.9      | 3.41        | 2.50        | 7.21        | 9.8         | 110.65       |
| N30722     | 141.2      | 3.67      | 103.8      | 3.33        | 2.27        | 6.75        | 8.1         | 92.94        |
| N30723     | 140.7      | 3.75      | 103.4      | 3.42        | 2.15        | 7.41        | 9.2         | 82.04        |
| N30724     | 140.0      | 3.88      | 102.4      | 3.46        | 2.46        | 6.54        | 8.0         | 79.94        |
| N30725     | 141.0      | 3.72      | 104.1      | 3.45        | 2.22        | 7.10        | 8.9         | 90.75        |
| N30726     | 142.6      | 4.58      | 104.3      | 3.66        | 2.18        | 6.92        | 9.4         | 76.21        |
| N30727     | 139.1      | 4.02      | 102.1      | 3.35        | 2.28        | 6.20        | 8.0         | 96.84        |
| N30728     | 139.9      | 3.57      | 104.6      | 3.44        | 2.18        | 6.52        | 7.7         | 80.11        |
| N30729     | 141.0      | 3.92      | 102.1      | 3.37        | 2.22        | 6.33        | 7.7         | 83.29        |
| N30730     | 140.3      | 4.24      | 102.1      | 3.54        | 2.09        | 6.58        | 9.7         | 81.47        |
| Mean       | 140.8      | 3.93      | 103.0      | 3.44        | 2.26        | 6.76        | 8.7         | 87.42        |
| SD         | 1.04       | 0.299     | 1.22       | 0.097       | 0.131       | 0.395       | 0.84        | 10.469       |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | µmol/L |
| N30731     | 142.2  | 3.74   | 102.9  | 3.32   | 2.34   | 7.11   | 9.1    | 93.12  |
| N30732     | 140.8  | 3.53   | 100.7  | 3.46   | 2.19   | 6.63   | 9.1    | 83.56  |
| N30733     | 141.5  | 3.69   | 104.2  | 3.32   | 2.39   | 6.64   | 11.0   | 107.34 |
| N30734     | 141.7  | 3.60   | 100.2  | 3.44   | 2.13   | 7.36   | 8.5    | 93.75  |
| N30735     | 140.3  | 3.72   | 104.7  | 3.34   | 2.32   | 6.66   | 9.1    | 99.93  |
| N30736     | 141.4  | 3.73   | 103.5  | 3.54   | 2.28   | 6.12   | 9.9    | 84.36  |
| N30737     | 141.8  | 3.99   | 102.4  | 3.44   | 2.22   | 6.18   | 9.2    | 97.05  |
| N30738     | 141.8  | 3.86   | 102.5  | 3.46   | 2.12   | 6.26   | 8.2    | 73.69  |
| N30739     | 140.1  | 4.00   | 102.7  | 3.49   | 2.28   | 6.99   | 10.0   | 97.35  |
| N30740     | 139.6  | 3.92   | 103.8  | 3.41   | 2.22   | 6.33   | 11.6   | 104.13 |
| Mean       | 141.1  | 3.78   | 102.8  | 3.42   | 2.25   | 6.63   | 9.6    | 93.43  |
| SD         | 0.87   | 0.160  | 1.43   | 0.074  | 0.089  | 0.419  | 1.07   | 10.265 |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30711     | 522        | 60          | 16          | 585       | 184        | 4          |
| N30712     | 558        | 65          | 14          | 524       | 173        | 4          |
| N30713     | 609        | 43          | 13          | 415       | 182        | 9          |
| N30714     | 596        | 57          | 18          | 520       | 134        | 7          |
| N30715     | 490        | 28          | 18          | 296       | 66         | 9          |
| N30716     | 451        | 33          | 13          | 543       | 136        | 7          |
| N30717     | 415        | 25          | 12          | 257       | 59         | 8          |
| N30718     | 427        | 48          | 17          | 378       | 135        | 6          |
| N30719     | 450        | 50          | 23          | 722       | 192        | 7          |
| N30720     | 469        | 38          | 17          | 634       | 189        | 7          |
| Mean       | 499        | 45          | 16          | 487       | 145        | 7          |
| SD         | 69.5       | 13.7        | 3.3         | 148.5     | 49.2       | 1.8        |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30721     | 514        | 43          | 14          | 519       | 208        | 4          |
| N30722     | 612        | 40          | 17          | 395       | 156        | 6          |
| N30723     | 494        | 43          | 13          | 522       | 159        | 3          |
| N30724     | 500        | 57          | 19          | 406       | 141        | 6          |
| N30725     | 402        | 46          | 14          | 528       | 111        | 6          |
| N30726     | 513        | 65          | 19          | 536       | 194        | 6          |
| N30727     | 588        | 44          | 15          | 400       | 136        | 5          |
| N30728     | 567        | 49          | 20          | 497       | 148        | 6          |
| N30729     | 464        | 51          | 14          | 1381      | 118        | 4          |
| N30730     | 445        | 62          | 27          | 481       | 119        | 4          |
| Mean       | 510        | 50          | 17          | 567       | 149        | 5          |
| SD         | 65.1       | 8.6         | 4.3         | 291.6     | 32.0       | 1.2        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30731     | 399        | 59          | 15          | 499       | 221        | 7          |
| N30732     | 659        | 55          | 16          | 402       | 206        | 6          |
| N30733     | 585        | 55          | 16          | 435       | 157        | 4          |
| N30734     | 579        | 30          | 15          | 678       | 202        | 8          |
| N30735     | 576        | 29          | 12          | 351       | 114        | 5          |
| N30736     | 514        | 49          | 17          | 462       | 180        | 4          |
| N30737     | 466        | 47          | 17          | 354       | 188        | 5          |
| N30738     | 311        | 56          | 23          | 665       | 184        | 4          |
| N30739     | 560        | 60          | 16          | 751       | 229        | 7          |
| N30740     | 545        | 42          | 17          | 575       | 216        | 4          |
| Mean       | 519        | 48          | 16          | 517       | 190        | 5          |
| SD         | 102.0      | 11.3        | 2.8         | 142.7     | 34.3       | 1.5        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30711     | blq               | 1.68           | 0.73           | 57.8        | 39         | 2.07     | 19          |
| N30712     | blq               | 1.75           | 0.68           | 62.6        | 42         | 2.04     | 21          |
| N30713     | blq               | 1.62           | 0.86           | 58.9        | 40         | 2.12     | 19          |
| N30714     | blq               | 1.59           | 0.63           | 63.8        | 44         | 2.22     | 20          |
| N30715     | blq               | 1.58           | 0.91           | 65.4        | 44         | 2.06     | 21          |
| N30716     | blq               | 1.78           | 0.47           | 63.8        | 42         | 1.93     | 22          |
| N30717     | blq               | 1.62           | 1.08           | 57.1        | 40         | 2.34     | 17          |
| N30718     | blq               | 1.59           | 0.56           | 56.7        | 38         | 2.03     | 19          |
| N30719     | blq               | 1.85           | 0.73           | 58.2        | 40         | 2.20     | 18          |
| N30720     | blq               | 1.75           | 1.06           | 60.1        | 40         | 1.99     | 20          |
| Mean       | 0                 | 1.68           | 0.77           | 60.4        | 41         | 2.10     | 20          |
| SD         | 0.0               | 0.096          | 0.204          | 3.19        | 2.0        | 0.122    | 1.5         |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30721     | blq               | 1.57           | 0.66           | 60.7        | 41         | 2.08     | 20          |
| N30722     | blq               | 1.47           | 1.17           | 60.3        | 40         | 1.97     | 20          |
| N30723     | blq               | 1.63           | 0.78           | 62.5        | 42         | 2.05     | 21          |
| N30724     | blq               | 1.30           | 1.00           | 61.2        | 42         | 2.19     | 19          |
| N30725     | blq               | 2.35           | 0.86           | 61.7        | 40         | 1.84     | 22          |
| N30726     | blq               | 1.39           | 0.74           | 62.8        | 43         | 2.17     | 20          |
| N30727     | blq               | 1.54           | 0.40           | 60.8        | 41         | 2.07     | 20          |
| N30728     | blq               | 1.36           | 0.61           | 59.5        | 40         | 2.05     | 20          |
| N30729     | blq               | 1.26           | 0.49           | 57.6        | 38         | 1.94     | 20          |
| N30730     | blq               | 1.26           | 0.50           | 62.8        | 43         | 2.17     | 20          |
| Mean       | 0                 | 1.51           | 0.72           | 61.0        | 41         | 2.05     | 20          |
| SD         | 0.0               | 0.322          | 0.241          | 1.62        | 1.6        | 0.112    | 0.8         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Predose

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30731     | blq               | 1.38           | 0.85           | 59.1        | 40         | 2.09     | 19          |
| N30732     | blq               | 1.60           | 0.84           | 61.9        | 41         | 1.96     | 21          |
| N30733     | blq               | 2.42           | 1.25           | 62.8        | 42         | 2.02     | 21          |
| N30734     | blq               | 1.88           | 1.09           | 63.0        | 43         | 2.15     | 20          |
| N30735     | blq               | 1.83           | 0.99           | 57.3        | 37         | 1.82     | 20          |
| N30736     | blq               | 1.11           | 0.82           | 57.9        | 40         | 2.23     | 18          |
| N30737     | blq               | 1.48           | 0.67           | 58.7        | 40         | 2.14     | 19          |
| N30738     | blq               | 1.88           | 0.70           | 62.7        | 43         | 2.18     | 20          |
| N30739     | blq               | 1.47           | 0.74           | 59.7        | 41         | 2.19     | 19          |
| N30740     | blq               | 2.05           | 0.68           | 59.0        | 41         | 2.28     | 18          |
| Mean       | 0                 | 1.71           | 0.86           | 60.2        | 41         | 2.11     | 20          |
| SD         | 0.0               | 0.378          | 0.192          | 2.18        | 1.8        | 0.138    | 1.1         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30641     | 140.2      | 3.93      | 107.0      | 3.65        | 1.92        | 6.76        | 7.7         | 81.98        |
| N30642     | 142.5      | 3.67      | 102.4      | 3.59        | 1.82        | 7.05        | 6.2         | 78.82        |
| N30643     | 141.3      | 3.29      | 106.2      | 3.56        | 1.82        | 7.00        | 6.4         | 76.44        |
| N30644     | 140.7      | 3.90      | 104.1      | 3.71        | 1.85        | 7.48        | 6.5         | 82.21        |
| N30645     | 140.9      | 3.77      | 105.9      | 3.51        | 1.58        | 6.89        | 6.2         | 65.81        |
| N30646     | 140.8      | 3.37      | 103.9      | 3.71        | 1.83        | 6.25        | 7.2         | 81.49        |
| N30647     | 141.3      | 3.37      | 104.6      | 3.55        | 1.87        | 6.56        | 5.7         | 71.06        |
| N30648     | 142.2      | 3.58      | 106.1      | 3.46        | 1.98        | 6.02        | 7.0         | 81.68        |
| N30649     | 142.5      | 3.40      | 105.9      | 3.55        | 1.85        | 6.57        | 6.0         | 74.98        |
| N30650     | 141.1      | 3.58      | 105.2      | 3.54        | 1.72        | 6.49        | 7.7         | 91.97        |
| Mean       | 141.4      | 3.59      | 105.1      | 3.58        | 1.82        | 6.71        | 6.7         | 78.64        |
| SD         | 0.79       | 0.229     | 1.38       | 0.083       | 0.109       | 0.422       | 0.70        | 7.144        |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30651     | 142.7      | 3.40      | 108.0      | 3.49        | 1.74        | 6.51        | 6.9         | 78.59        |
| N30652     | 138.6      | 3.81      | 107.1      | 3.49        | 1.81        | 6.73        | 7.0         | 73.82        |
| N30653     | 140.8      | 3.58      | 106.6      | 3.64        | 1.97        | 6.32        | 7.2         | 88.48        |
| N30654     | 140.3      | 3.40      | 105.0      | 3.57        | 2.02        | 6.38        | 7.3         | 79.48        |
| N30655     | 139.7      | 4.08      | 106.5      | 3.46        | 1.92        | 6.79        | 7.4         | 75.48        |
| N30656     | 140.7      | 3.67      | 107.1      | 3.55        | 1.84        | 6.84        | 6.1         | 81.81        |
| N30657     | 141.6      | 3.39      | 103.2      | 3.52        | 2.20        | 6.91        | 6.5         | 79.17        |
| N30658     | 140.8      | 3.36      | 103.2      | 3.62        | 1.84        | 7.44        | 6.8         | 86.64        |
| N30659     | 141.2      | 3.23      | 103.8      | 3.58        | 1.97        | 7.68        | 7.0         | 88.29        |
| N30660     | 140.8      | 3.38      | 105.3      | 3.45        | 1.96        | 6.42        | 6.4         | 83.96        |
| Mean       | 140.7      | 3.53      | 105.6      | 3.54        | 1.93        | 6.80        | 6.9         | 81.57        |
| SD         | 1.09       | 0.258     | 1.74       | 0.066       | 0.130       | 0.452       | 0.42        | 5.170        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | Na <sup>+</sup><br>mmol/L | K <sup>+</sup><br>mmol/L | Cl <sup>-</sup><br>mmol/L | Ca <sup>++</sup><br>mmol/L | PHOS<br>mmol/L | GLUC<br>mmol/L | UREA<br>mmol/L | CREAT<br>μmol/L |
|------------|---------------------------|--------------------------|---------------------------|----------------------------|----------------|----------------|----------------|-----------------|
| N30661     | 140.6                     | 4.12                     | 104.8                     | 3.59                       | 2.14           | 6.39           | 8.5            | 101.13          |
| N30662     | 142.5                     | 3.61                     | 105.1                     | 3.51                       | 2.05           | 6.80           | 9.6            | 89.99           |
| N30663     | 141.4                     | 3.36                     | 103.8                     | 3.69                       | 1.85           | 7.05           | 6.8            | 77.47           |
| N30664     | 139.9                     | 3.75                     | 107.0                     | 3.41                       | 1.97           | 6.85           | 8.0            | 78.18           |
| N30665     | 141.0                     | 3.40                     | 106.4                     | 3.53                       | 1.71           | 7.14           | 5.7            | 66.26           |
| N30666     | 140.2                     | 3.15                     | 104.4                     | 3.58                       | 1.77           | 6.88           | 6.0            | 78.65           |
| N30667     | 141.3                     | 3.64                     | 105.3                     | 3.47                       | 2.04           | 5.80           | 7.8            | 94.67           |
| N30668     | 140.8                     | 3.69                     | 105.0                     | 3.54                       | 2.15           | 6.79           | 6.8            | 83.71           |
| N30669     | 141.0                     | 3.17                     | 107.4                     | 3.49                       | 1.86           | 6.56           | 6.3            | 84.60           |
| N30670     | 140.5                     | 3.63                     | 104.8                     | 3.55                       | 1.89           | 7.03           | 7.0            | 84.02           |
| Mean       | 140.9                     | 3.55                     | 105.4                     | 3.54                       | 1.94           | 6.73           | 7.3            | 83.87           |
| SD         | 0.73                      | 0.292                    | 1.16                      | 0.076                      | 0.151          | 0.397          | 1.21           | 9.794           |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30641     | 666        | 80          | 46          | 784       | 298        | 5          |
| N30642     | 521        | 63          | 30          | 486       | 181        | 8          |
| N30643     | 527        | 76          | 29          | 881       | 125        | 6          |
| N30644     | 596        | 43          | 19          | 988       | 271        | 7          |
| N30645     | 392        | 64          | 20          | 660       | 187        | 7          |
| N30646     | 518        | 42          | 18          | 903       | 302        | 6          |
| N30647     | 536        | 53          | 18          | 700       | 222        | 5          |
| N30648     | 576        | 42          | 17          | 577       | 199        | 9          |
| N30649     | 634        | 27          | 16          | 540       | 119        | 7          |
| N30650     | 350        | 87          | 63          | 606       | 250        | 5          |
| Mean       | 532        | 58          | 28          | 713       | 215        | 7          |
| SD         | 98.6       | 19.5        | 15.5        | 169.8     | 65.3       | 1.4        |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30651     | 480        | 62          | 20          | 626       | 163        | 9          |
| N30652     | 519        | 66          | 21          | 603       | 137        | 7          |
| N30653     | 605        | 47          | 21          | 677       | 131        | 5          |
| N30654     | 584        | 32          | 17          | 1236      | 150        | 5          |
| N30655     | 399        | 49          | 17          | 748       | 244        | 4          |
| N30656     | 503        | 43          | 20          | 562       | 153        | 6          |
| N30657     | 512        | 56          | 29          | 484       | 176        | 5          |
| N30658     | 407        | 39          | 17          | 1616      | 220        | 8          |
| N30659     | 421        | 40          | 14          | 782       | 114        | 6          |
| N30660     | 470        | 50          | 15          | 446       | 138        | 9          |
| Mean       | 490        | 48          | 19          | 778       | 163        | 6          |
| SD         | 69.9       | 10.6        | 4.3         | 368.2     | 40.8       | 1.8        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30661     | 709        | 61          | 14          | 496       | 139        | 6          |
| N30662     | 471        | 43          | 16          | 447       | 139        | 5          |
| N30663     | 542        | 46          | 12          | 610       | 105        | 8          |
| N30664     | 516        | 50          | 14          | 899       | 155        | 7          |
| N30665     | 548        | 54          | 14          | 991       | 138        | 7          |
| N30666     | 322        | 38          | 19          | 473       | 127        | 5          |
| N30667     | 475        | 59          | 13          | 803       | 80         | 8          |
| N30668     | 407        | 51          | 10          | 560       | 73         | 8          |
| N30669     | 581        | 66          | 18          | 434       | 97         | 7          |
| N30670     | 464        | 55          | 26          | 474       | 124        | 4          |
| Mean       | 504        | 52          | 16          | 619       | 118        | 7          |
| SD         | 104.1      | 8.5         | 4.5         | 204.3     | 27.6       | 1.4        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30641     | blq               | 1.10           | 0.45           | 62.8        | 44         | 2.34     | 19          |
| N30642     | blq               | 1.23           | 0.55           | 61.6        | 43         | 2.31     | 19          |
| N30643     | blq               | 1.30           | 0.82           | 61.6        | 43         | 2.31     | 19          |
| N30644     | blq               | 0.71           | 0.37           | 64.8        | 45         | 2.27     | 20          |
| N30645     | blq               | 1.21           | 0.65           | 61.8        | 43         | 2.29     | 19          |
| N30646     | blq               | 1.04           | 0.52           | 65.4        | 45         | 2.21     | 20          |
| N30647     | blq               | 1.16           | 0.65           | 64.2        | 44         | 2.18     | 20          |
| N30648     | blq               | 1.06           | 0.57           | 60.3        | 42         | 2.30     | 18          |
| N30649     | blq               | 1.05           | 0.45           | 64.3        | 45         | 2.33     | 19          |
| N30650     | blq               | 1.27           | 0.42           | 62.3        | 44         | 2.40     | 18          |
| Mean       | 0                 | 1.11           | 0.55           | 62.9        | 44         | 2.29     | 19          |
| SD         | 0.0               | 0.170          | 0.135          | 1.67        | 1.0        | 0.063    | 0.7         |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30651     | blq               | 1.14           | 0.38           | 62.4        | 44         | 2.39     | 18          |
| N30652     | blq               | 1.16           | 0.40           | 62.9        | 43         | 2.16     | 20          |
| N30653     | blq               | 1.12           | 0.52           | 62.7        | 43         | 2.18     | 20          |
| N30654     | blq               | 1.51           | 0.73           | 61.5        | 42         | 2.15     | 20          |
| N30655     | blq               | 0.97           | 0.41           | 62.7        | 43         | 2.18     | 20          |
| N30656     | blq               | 0.60           | 0.34           | 61.6        | 42         | 2.14     | 20          |
| N30657     | blq               | 1.13           | 0.65           | 64.7        | 44         | 2.13     | 21          |
| N30658     | blq               | 0.91           | 0.45           | 66.7        | 46         | 2.22     | 21          |
| N30659     | blq               | 0.90           | 0.47           | 63.1        | 44         | 2.30     | 19          |
| N30660     | blq               | 1.03           | 0.40           | 62.0        | 43         | 2.26     | 19          |
| Mean       | 0                 | 1.05           | 0.48           | 63.0        | 43         | 2.21     | 20          |
| SD         | 0.0               | 0.234          | 0.125          | 1.58        | 1.2        | 0.083    | 0.9         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30661     | blq               | 1.17           | 0.51           | 61.2        | 40         | 1.89     | 21          |
| N30662     | blq               | 0.93           | 0.40           | 58.4        | 41         | 2.36     | 17          |
| N30663     | blq               | 1.30           | 0.88           | 68.2        | 46         | 2.07     | 22          |
| N30664     | blq               | 1.24           | 0.43           | 60.7        | 42         | 2.25     | 19          |
| N30665     | blq               | 0.73           | 0.58           | 61.6        | 42         | 2.14     | 20          |
| N30666     | blq               | 0.78           | 0.40           | 63.9        | 44         | 2.21     | 20          |
| N30667     | blq               | 1.24           | 0.84           | 59.8        | 39         | 1.88     | 21          |
| N30668     | blq               | 1.05           | 0.64           | 65.6        | 43         | 1.90     | 23          |
| N30669     | blq               | 0.89           | 0.37           | 62.8        | 43         | 2.17     | 20          |
| N30670     | blq               | 1.05           | 0.53           | 62.1        | 43         | 2.25     | 19          |
| Mean       | 0                 | 1.04           | 0.56           | 62.4        | 42         | 2.11     | 20          |
| SD         | 0.0               | 0.201          | 0.181          | 2.87        | 2.0        | 0.171    | 1.7         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30711     | 141.4      | 3.93      | 108.8      | 3.48        | 1.97        | 6.50        | 8.4         | 83.67        |
| N30712     | 140.3      | 4.03      | 106.4      | 3.63        | 2.07        | 6.94        | 10.3        | 86.24        |
| N30713     | 141.4      | 3.87      | 105.3      | 3.62        | 2.16        | 7.27        | 7.8         | 87.76        |
| N30714     | 141.4      | 3.87      | 107.0      | 3.67        | 1.93        | 7.46        | 8.2         | 74.58        |
| N30715     | 141.8      | 3.79      | 106.0      | 3.61        | 1.91        | 6.76        | 8.4         | 79.88        |
| N30716     | 140.3      | 3.52      | 104.2      | 3.56        | 1.97        | 6.92        | 8.5         | 86.20        |
| N30717     | 141.7      | 3.83      | 107.1      | 3.52        | 2.15        | 6.70        | 7.9         | 86.94        |
| N30718     | 140.1      | 4.01      | 106.8      | 3.43        | 1.87        | 6.56        | 9.7         | 100.84       |
| N30719     | 140.6      | 3.76      | 104.3      | 3.52        | 1.98        | 6.96        | 8.6         | 101.54       |
| N30720     | 139.6      | 3.93      | 104.1      | 3.66        | 2.07        | 6.79        | 9.8         | 101.83       |
| Mean       | 140.9      | 3.85      | 106.0      | 3.57        | 2.01        | 6.89        | 8.8         | 88.95        |
| SD         | 0.77       | 0.146     | 1.53       | 0.081       | 0.100       | 0.298       | 0.86        | 9.444        |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30721     | 142.7      | 3.64      | 107.2      | 3.53        | 1.97        | 6.80        | 9.3         | 91.56        |
| N30722     | 141.3      | 3.47      | 108.5      | 3.51        | 1.89        | 7.90        | 8.1         | 80.89        |
| N30723     | 141.2      | 3.91      | 106.1      | 3.59        | 1.98        | 6.71        | 9.8         | 78.10        |
| N30724     | 141.3      | 3.44      | 102.7      | 3.56        | 2.11        | 7.18        | 7.7         | 75.04        |
| N30725     | 140.0      | 3.71      | 106.6      | 3.53        | 1.94        | 6.69        | 9.2         | 82.45        |
| N30726     | 140.8      | 3.70      | 105.6      | 3.68        | 1.69        | 6.47        | 7.6         | 75.78        |
| N30727     | 139.2      | 3.62      | 105.3      | 3.49        | 2.06        | 6.49        | 8.8         | 96.03        |
| N30728     | 141.2      | 3.44      | 104.5      | 3.61        | 1.84        | 6.62        | 7.2         | 78.54        |
| N30729     | 140.4      | 3.33      | 108.0      | 3.46        | 1.95        | 6.53        | 7.1         | 80.50        |
| N30730     | 139.9      | 3.98      | 101.3      | 3.54        | 1.90        | 6.36        | 8.9         | 83.61        |
| Mean       | 140.8      | 3.62      | 105.6      | 3.55        | 1.93        | 6.78        | 8.4         | 82.25        |
| SD         | 0.98       | 0.211     | 2.27       | 0.064       | 0.116       | 0.456       | 0.95        | 6.735        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | µmol/L |
| N30731     | 141.5  | 3.98   | 108.0  | 3.47   | 2.07   | 6.71   | 9.0    | 79.97  |
| N30732     | 142.2  | 3.63   | 104.9  | 3.54   | 2.05   | 6.43   | 8.6    | 75.24  |
| N30733     | 142.4  | 3.27   | 105.0  | 3.49   | 2.03   | 7.72   | 9.0    | 86.73  |
| N30734     | 142.5  | 3.55   | 107.5  | 3.55   | 1.84   | 6.39   | 8.8    | 84.80  |
| N30735     | 141.7  | 3.95   | 102.1  | 3.54   | 2.25   | 6.68   | 9.7    | 95.95  |
| N30736     | 142.9  | 3.44   | 107.5  | 3.49   | 1.92   | 6.53   | 8.5    | 81.47  |
| N30737     | 141.7  | 3.53   | 103.8  | 3.57   | 2.17   | 7.19   | 8.4    | 93.62  |
| N30738     | 141.7  | 3.71   | 105.7  | 3.56   | 1.92   | 6.71   | 7.9    | 75.63  |
| N30739     | 138.0  | 3.56   | 108.1  | 3.56   | 1.79   | 6.98   | 9.4    | 85.37  |
| N30740     | 141.4  | 3.75   | 106.2  | 3.63   | 1.97   | 7.09   | 8.7    | 94.67  |
| Mean       | 141.6  | 3.64   | 105.9  | 3.54   | 2.00   | 6.84   | 8.8    | 85.35  |
| SD         | 1.36   | 0.219  | 1.98   | 0.047  | 0.143  | 0.409  | 0.51   | 7.532  |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30711     | 624        | 61          | 21          | 701       | 230        | 7          |
| N30712     | 485        | 65          | 23          | 966       | 268        | 8          |
| N30713     | 651        | 58          | 23          | 442       | 154        | 11         |
| N30714     | 589        | 66          | 25          | 694       | 214        | 10         |
| N30715     | 467        | 31          | 19          | 504       | 239        | 11         |
| N30716     | 624        | 35          | 12          | 796       | 199        | 9          |
| N30717     | 399        | 27          | 19          | 417       | 117        | 10         |
| N30718     | 523        | 65          | 24          | 387       | 130        | 9          |
| N30719     | 277        | 45          | 24          | 429       | 163        | 8          |
| N30720     | 548        | 44          | 19          | 584       | 127        | 8          |
| Mean       | 519        | 50          | 21          | 592       | 184        | 9          |
| SD         | 116.5      | 15.2        | 3.9         | 192.4     | 53.0       | 1.4        |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30721     | 555        | 48          | 19          | 516       | 213        | 6          |
| N30722     | 547        | 46          | 21          | 623       | 195        | 9          |
| N30723     | 501        | 53          | 18          | 503       | 161        | 6          |
| N30724     | 634        | 83          | 67          | 556       | 266        | 6          |
| N30725     | 446        | 58          | 23          | 864       | 212        | 7          |
| N30726     | 431        | 72          | 16          | 599       | 199        | 10         |
| N30727     | 559        | 46          | 14          | 1220      | 202        | 6          |
| N30728     | 623        | 64          | 35          | 637       | 215        | 9          |
| N30729     | 427        | 53          | 15          | 498       | 204        | 6          |
| N30730     | 473        | 58          | 17          | 930       | 217        | 6          |
| Mean       | 520        | 58          | 25          | 695       | 208        | 7          |
| SD         | 75.8       | 12.0        | 16.1        | 236.7     | 25.9       | 1.6        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30731     | 444        | 48          | 15          | 340       | 144        | 8          |
| N30732     | 541        | 56          | 17          | 381       | 120        | 8          |
| N30733     | 501        | 81          | 15          | 562       | 99         | 6          |
| N30734     | 531        | 33          | 13          | 420       | 130        | 9          |
| N30735     | 662        | 37          | 16          | 621       | 136        | 7          |
| N30736     | 424        | 49          | 12          | 421       | 98         | 6          |
| N30737     | 388        | 52          | 15          | 301       | 138        | 9          |
| N30738     | 317        | 56          | 31          | 2638      | 202        | 6          |
| N30739     | 461        | 56          | 16          | 970       | 189        | 9          |
| N30740     | 493        | 55          | 19          | 780       | 134        | 8          |
| Mean       | 476        | 52          | 17          | 743       | 139        | 8          |
| SD         | 94.1       | 12.9        | 5.3         | 698.3     | 33.8       | 1.3        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30711     | blq               | 1.22           | 0.36           | 56.3        | 40         | 2.45     | 16          |
| N30712     | blq               | 1.30           | 0.45           | 63.0        | 45         | 2.50     | 18          |
| N30713     | blq               | 1.20           | 0.43           | 60.9        | 44         | 2.60     | 17          |
| N30714     | blq               | 1.66           | 0.43           | 65.2        | 47         | 2.58     | 18          |
| N30715     | blq               | 1.36           | 0.49           | 63.3        | 45         | 2.46     | 18          |
| N30716     | blq               | 1.35           | 0.42           | 63.1        | 44         | 2.30     | 19          |
| N30717     | blq               | 1.57           | 0.50           | 59.4        | 44         | 2.86     | 15          |
| N30718     | blq               | 1.43           | 0.38           | 55.8        | 40         | 2.53     | 16          |
| N30719     | blq               | 1.73           | 0.31           | 58.1        | 42         | 2.61     | 16          |
| N30720     | blq               | 1.39           | 0.61           | 62.8        | 45         | 2.53     | 18          |
| Mean       | 0                 | 1.42           | 0.44           | 60.8        | 44         | 2.54     | 17          |
| SD         | 0.0               | 0.179          | 0.083          | 3.24        | 2.3        | 0.144    | 1.3         |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30721     | blq               | 1.16           | 0.50           | 58.6        | 41         | 2.33     | 18          |
| N30722     | blq               | 1.13           | 0.49           | 62.0        | 44         | 2.44     | 18          |
| N30723     | blq               | 1.03           | 0.45           | 62.4        | 45         | 2.59     | 17          |
| N30724     | blq               | 1.12           | 0.46           | 60.1        | 44         | 2.73     | 16          |
| N30725     | blq               | 1.71           | 0.47           | 61.7        | 42         | 2.13     | 20          |
| N30726     | blq               | 1.09           | 0.40           | 62.5        | 44         | 2.38     | 19          |
| N30727     | blq               | 1.26           | 0.29           | 63.9        | 45         | 2.38     | 19          |
| N30728     | blq               | 1.36           | 0.45           | 63.9        | 45         | 2.38     | 19          |
| N30729     | blq               | 0.96           | 0.27           | 59.0        | 41         | 2.28     | 18          |
| N30730     | blq               | 1.02           | 0.38           | 60.0        | 43         | 2.53     | 17          |
| Mean       | 0                 | 1.18           | 0.42           | 61.4        | 43         | 2.42     | 18          |
| SD         | 0.0               | 0.219          | 0.081          | 1.90        | 1.6        | 0.168    | 1.2         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 1

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30731     | blq               | 1.08           | 0.47           | 56.9        | 40         | 2.37     | 17          |
| N30732     | blq               | 1.18           | 0.58           | 59.9        | 41         | 2.17     | 19          |
| N30733     | blq               | 1.78           | 0.46           | 65.9        | 46         | 2.31     | 20          |
| N30734     | blq               | 1.34           | 0.43           | 61.3        | 43         | 2.35     | 18          |
| N30735     | blq               | 1.35           | 0.67           | 61.0        | 42         | 2.21     | 19          |
| N30736     | blq               | 1.05           | 0.42           | 60.0        | 42         | 2.33     | 18          |
| N30737     | blq               | 1.20           | 0.41           | 58.9        | 42         | 2.49     | 17          |
| N30738     | blq               | 1.47           | 0.44           | 61.8        | 44         | 2.47     | 18          |
| N30739     | blq               | 1.35           | 0.41           | 61.2        | 44         | 2.56     | 17          |
| N30740     | blq               | 1.88           | 0.39           | 64.1        | 46         | 2.54     | 18          |
| Mean       | 0                 | 1.37           | 0.47           | 61.1        | 43         | 2.38     | 18          |
| SD         | 0.0               | 0.277          | 0.089          | 2.53        | 2.0        | 0.133    | 1.0         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | μmol/L |
| N30641     | 142.4  | 3.88   | 106.4  | 3.60   | 1.47   | 7.46   | 7.5    | 86.62  |
| N30642     | 141.9  | 3.90   | 104.6  | 3.52   | 1.45   | 7.55   | 7.4    | 91.16  |
| N30643     | 143.2  | 3.74   | 107.4  | 3.63   | 1.55   | 7.14   | 6.1    | 73.80  |
| N30644     | 142.8  | 3.56   | 107.6  | 3.69   | 1.49   | 7.83   | 7.0    | 86.80  |
| N30645     | 143.8  | 3.99   | 107.7  | 3.39   | 1.38   | 7.93   | 6.3    | 81.52  |
| N30646     | 142.2  | 3.78   | 105.6  | 3.55   | 1.48   | 6.85   | 7.4    | 84.96  |
| N30647     | 142.9  | 3.88   | 104.6  | 3.43   | 1.41   | 7.05   | 5.9    | 73.96  |
| N30648     | 143.5  | 4.04   | 108.2  | 3.41   | 1.55   | 6.35   | 9.1    | 88.52  |
| N30649     | 143.3  | 3.93   | 105.8  | 3.55   | 1.57   | 6.79   | 6.7    | 84.41  |
| N30650     | 142.4  | 4.18   | 107.5  | 3.40   | 1.46   | 6.73   | 8.6    | 101.78 |
| Mean       | 142.8  | 3.89   | 106.5  | 3.52   | 1.48   | 7.17   | 7.2    | 85.35  |
| SD         | 0.61   | 0.171  | 1.33   | 0.106  | 0.062  | 0.513  | 1.04   | 8.140  |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | μmol/L |
| N30651     | 142.1  | 3.57   | 107.9  | 3.53   | 1.45   | 6.99   | 8.4    | 85.97  |
| N30652     | 142.5  | 4.03   | 103.7  | 3.64   | 1.46   | 7.51   | 8.1    | 90.88  |
| N30653     | 143.6  | 3.45   | 104.5  | 3.61   | 1.70   | 7.64   | 8.3    | 112.26 |
| N30654     | 142.5  | 3.68   | 106.6  | 3.45   | 1.70   | 7.67   | 7.5    | 98.09  |
| N30655     | 139.9  | 3.91   | 107.4  | 3.26   | 1.74   | 7.01   | 8.5    | 94.16  |
| N30656     | 140.6  | 4.15   | 108.2  | 3.48   | 1.44   | 7.24   | 5.6    | 82.56  |
| N30657     | 140.7  | 4.23   | 105.9  | 3.39   | 1.63   | 6.62   | 6.1    | 82.10  |
| N30658     | 142.7  | 3.82   | 106.7  | 3.53   | 1.63   | 7.45   | 6.8    | 90.32  |
| N30659     | 140.8  | 4.17   | 107.3  | 3.45   | 1.50   | 7.75   | 6.3    | 89.26  |
| N30660     | 142.1  | 3.85   | 106.7  | 3.39   | 1.66   | 6.94   | 6.6    | 89.70  |
| Mean       | 141.8  | 3.89   | 106.5  | 3.47   | 1.59   | 7.28   | 7.2    | 91.53  |
| SD         | 1.18   | 0.264  | 1.44   | 0.112  | 0.116  | 0.379  | 1.07   | 8.758  |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | Na <sup>+</sup><br>mmol/L | K <sup>+</sup><br>mmol/L | Cl <sup>-</sup><br>mmol/L | Ca <sup>++</sup><br>mmol/L | PHOS<br>mmol/L | GLUC<br>mmol/L | UREA<br>mmol/L | CREAT<br>μmol/L |
|------------|---------------------------|--------------------------|---------------------------|----------------------------|----------------|----------------|----------------|-----------------|
| N30661     | 142.0                     | 3.76                     | 107.3                     | 3.39                       | 1.66           | 6.62           | 9.8            | 108.38          |
| N30662     | 142.9                     | 3.65                     | 107.7                     | 3.41                       | 1.69           | 7.18           | 9.9            | 100.83          |
| N30663     | 143.2                     | 3.38                     | 104.9                     | 3.55                       | 1.55           | 7.33           | 7.2            | 85.24           |
| N30664     | 142.4                     | 2.99                     | 103.8                     | 3.18                       | 1.77           | 7.26           | 9.5            | 99.04           |
| N30665     | 141.6                     | 3.36                     | 107.2                     | 3.39                       | 1.34           | 7.52           | 5.8            | 69.66           |
| N30666     | 142.9                     | 3.77                     | 108.8                     | 3.44                       | 1.49           | 6.24           | 6.0            | 81.89           |
| N30667     | 142.0                     | 4.21                     | 108.8                     | 3.33                       | 1.53           | 6.00           | 8.6            | 102.05          |
| N30668     | 140.9                     | 4.06                     | 108.0                     | 3.48                       | 1.69           | 6.79           | 6.8            | 81.08           |
| N30669     | 141.3                     | 3.97                     | 110.3                     | 3.44                       | 1.53           | 6.43           | 6.7            | 88.09           |
| N30670     | 141.1                     | 3.73                     | 106.9                     | 3.50                       | 1.62           | 6.43           | 7.4            | 82.60           |
| Mean       | 142.0                     | 3.69                     | 107.4                     | 3.41                       | 1.59           | 6.78           | 7.8            | 89.89           |
| SD         | 0.81                      | 0.364                    | 1.89                      | 0.102                      | 0.124          | 0.518          | 1.56           | 12.120          |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30641     | 686        | 56          | 26          | 621       | 164        | 4          |
| N30642     | 623        | 48          | 22          | 466       | 172        | 5          |
| N30643     | 502        | 64          | 33          | 828       | 247        | 2          |
| N30644     | 647        | 38          | 20          | 933       | 190        | 4          |
| N30645     | 398        | 63          | 29          | 399       | 120        | 4          |
| N30646     | 378        | 42          | 24          | 1099      | 289        | 5          |
| N30647     | 467        | 46          | 21          | 1073      | 270        | 4          |
| N30648     | 566        | 35          | 22          | 627       | 177        | 8          |
| N30649     | 548        | 23          | 18          | 657       | 221        | 6          |
| N30650     | 316        | 64          | 31          | 1553      | 248        | 4          |
| Mean       | 513        | 48          | 25          | 826       | 210        | 5          |
| SD         | 123.2      | 13.9        | 5.0         | 349.2     | 53.7       | 1.6        |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30651     | 419        | 57          | 34          | 691       | 275        | 5          |
| N30652     | 375        | 44          | 20          | 533       | 216        | 3          |
| N30653     | 476        | 42          | 26          | 614       | 198        | 4          |
| N30654     | 429        | 30          | 18          | 907       | 153        | 5          |
| N30655     | 339        | 45          | 20          | 461       | 232        | 2          |
| N30656     | 453        | 36          | 25          | 974       | 183        | 5          |
| N30657     | 420        | 46          | 19          | 604       | 136        | 5          |
| N30658     | 256        | 35          | 19          | 809       | 122        | 6          |
| N30659     | 301        | 29          | 17          | 512       | 187        | 5          |
| N30660     | 383        | 46          | 21          | 522       | 154        | 6          |
| Mean       | 385        | 41          | 22          | 663       | 186        | 5          |
| SD         | 69.2       | 8.6         | 5.1         | 177.8     | 46.9       | 1.3        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30661     | 637        | 49          | 19          | 767       | 187        | 3          |
| N30662     | 342        | 42          | 19          | 740       | 313        | 5          |
| N30663     | 475        | 38          | 21          | 629       | 157        | 4          |
| N30664     | 429        | 42          | 17          | 671       | 219        | 4          |
| N30665     | 471        | 46          | 21          | 717       | 190        | 3          |
| N30666     | 256        | 31          | 18          | 2249      | 269        | 5          |
| N30667     | 363        | 65          | 19          | 2029      | 227        | 5          |
| N30668     | 424        | 42          | 15          | 1908      | 178        | 6          |
| N30669     | 550        | 60          | 21          | 2115      | 142        | 5          |
| N30670     | 362        | 46          | 22          | 492       | 118        | 4          |
| Mean       | 431        | 46          | 19          | 1232      | 200        | 4          |
| SD         | 109.6      | 10.0        | 2.1         | 734.5     | 59.0       | 1.0        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30641     | blq               | 0.99           | 0.53           | 61.0        | 43         | 2.39     | 18          |
| N30642     | blq               | 1.20           | 0.58           | 60.4        | 41         | 2.11     | 19          |
| N30643     | blq               | 1.34           | 0.79           | 63.4        | 43         | 2.11     | 20          |
| N30644     | blq               | 0.66           | 0.47           | 63.1        | 44         | 2.30     | 19          |
| N30645     | blq               | 1.05           | 0.76           | 61.9        | 43         | 2.28     | 19          |
| N30646     | blq               | 0.87           | 0.49           | 63.3        | 43         | 2.12     | 20          |
| N30647     | blq               | 0.95           | 0.59           | 62.3        | 43         | 2.23     | 19          |
| N30648     | blq               | 0.73           | 0.44           | 59.1        | 41         | 2.27     | 18          |
| N30649     | blq               | 0.99           | 0.52           | 60.5        | 43         | 2.46     | 18          |
| N30650     | blq               | 1.08           | 0.48           | 60.0        | 42         | 2.33     | 18          |
| Mean       | 0                 | 0.99           | 0.57           | 61.5        | 43         | 2.26     | 19          |
| SD         | 0.0               | 0.203          | 0.120          | 1.52        | 1.0        | 0.120    | 0.8         |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30651     | blq               | 1.00           | 0.51           | 61.0        | 42         | 2.21     | 19          |
| N30652     | blq               | 0.92           | 0.67           | 61.4        | 41         | 2.01     | 20          |
| N30653     | blq               | 0.93           | 0.94           | 62.8        | 42         | 2.02     | 21          |
| N30654     | blq               | 1.13           | 0.53           | 58.5        | 38         | 1.85     | 21          |
| N30655     | blq               | 0.76           | 0.44           | 56.3        | 38         | 2.08     | 18          |
| N30656     | blq               | 0.52           | 0.36           | 58.4        | 40         | 2.17     | 18          |
| N30657     | blq               | 0.66           | 0.42           | 60.4        | 40         | 1.96     | 20          |
| N30658     | blq               | 0.79           | 0.56           | 63.5        | 43         | 2.10     | 21          |
| N30659     | blq               | 0.75           | 0.51           | 62.3        | 42         | 2.07     | 20          |
| N30660     | blq               | 0.81           | 0.45           | 59.5        | 41         | 2.22     | 19          |
| Mean       | 0                 | 0.83           | 0.54           | 60.4        | 41         | 2.07     | 20          |
| SD         | 0.0               | 0.175          | 0.165          | 2.25        | 1.7        | 0.115    | 1.2         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30661     | blq               | 0.89           | 0.60           | 61.8        | 40         | 1.83     | 22          |
| N30662     | blq               | 0.77           | 0.50           | 61.1        | 41         | 2.04     | 20          |
| N30663     | blq               | 1.17           | 0.98           | 65.5        | 43         | 1.91     | 23          |
| N30664     | blq               | 0.96           | 0.69           | 59.8        | 40         | 2.02     | 20          |
| N30665     | blq               | 0.64           | 0.69           | 59.7        | 41         | 2.19     | 19          |
| N30666     | blq               | 0.70           | 0.57           | 58.8        | 40         | 2.13     | 19          |
| N30667     | blq               | 0.79           | 0.45           | 57.0        | 37         | 1.85     | 20          |
| N30668     | blq               | 0.90           | 0.51           | 62.3        | 42         | 2.07     | 20          |
| N30669     | blq               | 0.65           | 0.34           | 60.5        | 41         | 2.10     | 20          |
| N30670     | blq               | 0.92           | 0.45           | 60.8        | 41         | 2.07     | 20          |
| Mean       | 0                 | 0.84           | 0.58           | 60.7        | 41         | 2.02     | 20          |
| SD         | 0.0               | 0.163          | 0.179          | 2.26        | 1.6        | 0.120    | 1.3         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | μmol/L |
| N30711     | 142.7  | 3.62   | 107.8  | 3.46   | 1.74   | 6.78   | 9.7    | 101.81 |
| N30712     | 141.5  | 3.83   | 106.4  | 3.65   | 1.50   | 6.95   | 10.8   | 97.80  |
| N30713     | 141.0  | 3.80   | 108.6  | 3.60   | 1.45   | 7.16   | 7.8    | 97.11  |
| N30714     | 141.1  | 3.71   | 106.4  | 3.64   | 1.49   | 7.48   | 8.6    | 85.13  |
| N30715     | 139.3  | 3.49   | 105.0  | 3.62   | 1.46   | 7.21   | 8.6    | 96.59  |
| N30716     | 141.1  | 3.90   | 105.7  | 3.74   | 1.50   | 6.68   | 11.3   | 114.22 |
| N30717     | 140.6  | 3.68   | 106.8  | 3.67   | 1.44   | 6.22   | 8.4    | 103.30 |
| N30718     | 140.6  | 3.80   | 106.7  | 3.46   | 1.62   | 6.49   | 11.0   | 117.97 |
| N30719     | 140.1  | 3.63   | 105.0  | 3.56   | 1.50   | 6.63   | 9.7    | 116.55 |
| N30720     | 138.8  | 3.76   | 104.8  | 3.72   | 1.63   | 7.03   | 10.0   | 115.60 |
| Mean       | 140.7  | 3.72   | 106.3  | 3.61   | 1.53   | 6.86   | 9.6    | 104.61 |
| SD         | 1.11   | 0.121  | 1.25   | 0.096  | 0.098  | 0.376  | 1.21   | 11.006 |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | μmol/L |
| N30721     | 140.1  | 3.86   | 109.3  | 3.52   | 1.45   | 6.99   | 9.4    | 110.45 |
| N30722     | 141.2  | 3.41   | 106.2  | 3.53   | 1.39   | 7.39   | 8.6    | 109.92 |
| N30723     | 139.9  | 3.88   | 104.4  | 3.57   | 1.53   | 6.47   | 9.2    | 90.43  |
| N30724     | 140.1  | 3.58   | 105.9  | 3.56   | 1.63   | 7.29   | 7.5    | 89.48  |
| N30725     | 140.3  | 3.66   | 107.9  | 3.64   | 1.61   | 7.00   | 11.2   | 109.98 |
| N30726     | 140.0  | 3.41   | 105.0  | 3.61   | 1.48   | 6.48   | 9.5    | 92.66  |
| N30727     | 139.4  | 3.81   | 106.3  | 3.41   | 1.58   | 5.87   | 9.7    | 116.00 |
| N30728     | 139.1  | 3.65   | 102.9  | 3.59   | 1.51   | 6.59   | 8.4    | 98.98  |
| N30729     | 140.1  | 3.45   | 105.2  | 3.36   | 1.60   | 6.08   | 10.7   | 101.53 |
| N30730     | 139.4  | 3.42   | 101.3  | 3.67   | 1.32   | 6.34   | 10.3   | 94.08  |
| Mean       | 140.0  | 3.61   | 105.4  | 3.55   | 1.51   | 6.65   | 9.5    | 101.35 |
| SD         | 0.59   | 0.189  | 2.30   | 0.097  | 0.102  | 0.504  | 1.11   | 9.658  |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | µmol/L |
| N30731     | 140.3  | 3.94   | 110.4  | 3.47   | 1.66   | 7.10   | 9.3    | 98.38  |
| N30732     | 141.1  | 3.64   | 106.0  | 3.54   | 1.62   | 6.45   | 10.3   | 87.36  |
| N30733     | 140.1  | 3.80   | 104.7  | 3.56   | 1.80   | 6.87   | 13.2   | 141.63 |
| N30734     | 139.9  | 3.83   | 109.1  | 3.56   | 1.30   | 6.70   | 8.8    | 96.53  |
| N30735     | 140.4  | 3.91   | 106.7  | 3.54   | 1.63   | 6.92   | 9.4    | 103.06 |
| N30736     | 140.5  | 3.44   | 107.9  | 3.48   | 1.45   | 6.00   | 9.6    | 95.30  |
| N30737     | 141.0  | 3.81   | 104.7  | 3.57   | 1.61   | 6.80   | 11.4   | 115.41 |
| N30738     | 141.6  | 3.66   | 106.3  | 3.53   | 1.40   | 6.47   | 10.3   | 93.67  |
| N30739     | 140.3  | 3.79   | 108.4  | 3.62   | 1.56   | 6.79   | 12.0   | 103.39 |
| N30740     | 140.5  | 3.83   | 106.1  | 3.62   | 1.70   | 6.38   | 11.7   | 116.98 |
| Mean       | 140.6  | 3.77   | 107.0  | 3.55   | 1.57   | 6.65   | 10.6   | 105.17 |
| SD         | 0.51   | 0.148  | 1.88   | 0.050  | 0.150  | 0.323  | 1.42   | 15.808 |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30711     | 479        | 57          | 24          | 1163      | 215        | 7          |
| N30712     | 446        | 61          | 19          | 553       | 158        | 7          |
| N30713     | 503        | 47          | 26          | 367       | 188        | 8          |
| N30714     | 558        | 51          | 24          | 625       | 169        | 9          |
| N30715     | 504        | 24          | 18          | 326       | 80         | 7          |
| N30716     | 499        | 41          | 25          | 1003      | 196        | 8          |
| N30717     | 390        | 20          | 16          | 489       | 184        | 8          |
| N30718     | 456        | 61          | 23          | 508       | 122        | 8          |
| N30719     | 177        | 49          | 33          | 758       | 140        | 8          |
| N30720     | 448        | 42          | 22          | 850       | 91         | 9          |
| Mean       | 446        | 45          | 23          | 664       | 154        | 8          |
| SD         | 104.7      | 14.2        | 4.8         | 274.6     | 45.3       | 0.7        |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30721     | 336        | 37          | 20          | 761       | 301        | 6          |
| N30722     | 433        | 40          | 30          | 563       | 256        | 7          |
| N30723     | 397        | 45          | 26          | 456       | 156        | 7          |
| N30724     | 460        | 70          | 63          | 640       | 247        | 7          |
| N30725     | 320        | 48          | 22          | 771       | 137        | 7          |
| N30726     | 361        | 72          | 21          | 830       | 224        | 9          |
| N30727     | 394        | 40          | 18          | 539       | 161        | 7          |
| N30728     | 534        | 68          | 44          | 759       | 242        | 8          |
| N30729     | 371        | 51          | 20          | 394       | 115        | 6          |
| N30730     | 363        | 51          | 24          | 476       | 111        | 7          |
| Mean       | 397        | 52          | 29          | 619       | 195        | 7          |
| SD         | 64.0       | 13.2        | 14.2        | 154.6     | 66.8       | 0.9        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-----------|------------|------------|
| N30731     | 333        | 60          | 17          | 377       | 218        | 8          |
| N30732     | 319        | 53          | 20          | 383       | 186        | 7          |
| N30733     | 339        | 59          | 20          | 454       | 168        | 7          |
| N30734     | 366        | 30          | 18          | 634       | 207        | 8          |
| N30735     | 539        | 35          | 22          | 487       | 160        | 6          |
| N30736     | 335        | 40          | 16          | 420       | 181        | 7          |
| N30737     | 319        | 52          | 27          | 452       | 198        | 8          |
| N30738     | 210        | 54          | 32          | 1112      | 206        | 7          |
| N30739     | 477        | 65          | 23          | 1423      | 309        | 8          |
| N30740     | 347        | 38          | 17          | 617       | 103        | 7          |
| Mean       | 358        | 49          | 21          | 636       | 194        | 7          |
| SD         | 90.4       | 11.9        | 5.1         | 351.7     | 52.1       | 0.7        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30711     | blq               | 1.17           | 0.34           | 58.6        | 41         | 2.33     | 18          |
| N30712     | blq               | 1.26           | 0.52           | 64.5        | 44         | 2.15     | 21          |
| N30713     | blq               | 1.17           | 0.40           | 59.7        | 43         | 2.57     | 17          |
| N30714     | blq               | 1.66           | 0.46           | 64.1        | 45         | 2.36     | 19          |
| N30715     | blq               | 1.67           | 0.68           | 62.3        | 43         | 2.23     | 19          |
| N30716     | blq               | 1.49           | 0.35           | 65.0        | 45         | 2.25     | 20          |
| N30717     | blq               | 2.02           | 0.50           | 60.3        | 43         | 2.49     | 17          |
| N30718     | blq               | 1.40           | 0.37           | 59.3        | 40         | 2.07     | 19          |
| N30719     | blq               | 1.54           | 0.34           | 57.8        | 41         | 2.44     | 17          |
| N30720     | blq               | 1.45           | 0.46           | 64.8        | 45         | 2.27     | 20          |
| Mean       | 0                 | 1.48           | 0.44           | 61.6        | 43         | 2.32     | 19          |
| SD         | 0.0               | 0.261          | 0.107          | 2.81        | 1.8        | 0.154    | 1.4         |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30721     | blq               | 1.08           | 0.33           | 58.2        | 40         | 2.20     | 18          |
| N30722     | blq               | 1.14           | 0.52           | 60.3        | 41         | 2.12     | 19          |
| N30723     | blq               | 0.93           | 0.40           | 62.4        | 43         | 2.22     | 19          |
| N30724     | blq               | 1.33           | 0.47           | 58.6        | 41         | 2.33     | 18          |
| N30725     | blq               | 1.68           | 0.50           | 62.5        | 41         | 1.91     | 22          |
| N30726     | blq               | 1.03           | 0.47           | 59.6        | 41         | 2.20     | 19          |
| N30727     | blq               | 1.14           | 0.33           | 60.5        | 41         | 2.10     | 20          |
| N30728     | blq               | 1.37           | 0.45           | 61.7        | 42         | 2.13     | 20          |
| N30729     | blq               | 0.80           | 0.35           | 58.7        | 38         | 1.84     | 21          |
| N30730     | blq               | 1.05           | 0.33           | 59.1        | 41         | 2.27     | 18          |
| Mean       | 0                 | 1.16           | 0.42           | 60.2        | 41         | 2.13     | 19          |
| SD         | 0.0               | 0.250          | 0.076          | 1.59        | 1.3        | 0.153    | 1.3         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 5

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30731     | blq               | 0.98           | 0.31           | 56.1        | 38         | 2.10     | 18          |
| N30732     | blq               | 0.87           | 0.35           | 62.5        | 42         | 2.05     | 21          |
| N30733     | blq               | 1.52           | 0.53           | 61.0        | 41         | 2.05     | 20          |
| N30734     | blq               | 1.05           | 0.39           | 57.1        | 39         | 2.15     | 18          |
| N30735     | blq               | 1.22           | 0.43           | 61.9        | 42         | 2.11     | 20          |
| N30736     | blq               | 0.98           | 0.42           | 59.2        | 39         | 1.93     | 20          |
| N30737     | blq               | 1.26           | 0.46           | 60.6        | 41         | 2.09     | 20          |
| N30738     | blq               | 1.88           | 0.48           | 61.4        | 42         | 2.17     | 19          |
| N30739     | blq               | 1.35           | 0.36           | 62.0        | 43         | 2.26     | 19          |
| N30740     | blq               | 1.50           | 0.56           | 60.7        | 42         | 2.25     | 19          |
| Mean       | 0                 | 1.26           | 0.43           | 60.3        | 41         | 2.12     | 19          |
| SD         | 0.0               | 0.311          | 0.080          | 2.14        | 1.7        | 0.098    | 1.0         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30646     | 141.6      | 3.53      | 107.8      | 3.50        | 1.47        | 6.27        | 9.3         | 93.41        |
| N30647     | 141.7      | 3.63      | 105.2      | 3.40        | 1.41        | 6.65        | 6.9         | 86.47        |
| N30648     | 141.9      | 3.94      | 110.5      | 3.34        | 1.43        | 6.20        | 8.8         | 97.66        |
| N30649     | 144.1      | 3.18      | 106.2      | 3.43        | 1.41        | 6.93        | 7.1         | 90.18        |
| N30650     | 145.1      | 3.68      | 106.5      | 3.58        | 1.48        | 6.52        | 11.3        | 122.14       |
| Mean       | 142.9      | 3.59      | 107.2      | 3.45        | 1.44        | 6.51        | 8.7         | 97.97        |
| SD         | 1.61       | 0.276     | 2.05       | 0.093       | 0.033       | 0.296       | 1.80        | 14.125       |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30656     | 142.7      | 3.49      | 109.1      | 3.47        | 1.49        | 5.91        | 8.3         | 99.78        |
| N30657     | 142.6      | 3.87      | 108.1      | 3.39        | 1.48        | 6.55        | 7.8         | 93.86        |
| N30658     | 143.4      | 3.47      | 107.1      | 3.45        | 1.55        | 6.95        | 7.9         | 104.91       |
| N30659     | 142.7      | 3.54      | 108.3      | 3.44        | 1.55        | 7.65        | 7.6         | 103.91       |
| N30660     | 143.8      | 3.47      | 107.5      | 3.47        | 1.67        | 5.27        | 8.6         | 106.61       |
| Mean       | 143.0      | 3.57      | 108.0      | 3.44        | 1.55        | 6.47        | 8.0         | 101.81       |
| SD         | 0.53       | 0.171     | 0.77       | 0.033       | 0.076       | 0.920       | 0.40        | 5.108        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | μmol/L |
| N30666     | 144.7  | 3.24   | 106.4  | 3.52   | 1.72   | 6.58   | 8.5    | 107.86 |
| N30667     | 142.4  | 3.76   | 109.3  | 3.28   | 1.42   | 6.21   | 10.8   | 113.36 |
| N30668     | 142.6  | 3.75   | 106.4  | 3.44   | 1.73   | 6.61   | 8.9    | 95.69  |
| N30669     | 141.7  | 3.32   | 111.1  | 3.42   | 1.37   | 6.50   | 7.6    | 95.86  |
| N30670     | 142.5  | 3.81   | 107.6  | 3.43   | 1.41   | 6.23   | 7.8    | 89.65  |
| Mean       | 142.8  | 3.58   | 108.2  | 3.42   | 1.53   | 6.43   | 8.7    | 100.48 |
| SD         | 1.13   | 0.273  | 2.03   | 0.087  | 0.179  | 0.192  | 1.28   | 9.772  |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK-L<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-------------|------------|------------|
| N30646     | 293        | 43          | 19          | 728         | 232        | 6          |
| N30647     | 372        | 48          | 23          | 646         | 320        | 5          |
| N30648     | 427        | 39          | 20          | 500         | 193        | 10         |
| N30649     | 373        | 23          | 20          | 720         | 262        | 6          |
| N30650     | 220        | 72          | 36          | 752         | 323        | 5          |
| Mean       | 337        | 45          | 24          | 669         | 266        | 6          |
| SD         | 81.0       | 17.8        | 7.1         | 102.5       | 56.3       | 2.1        |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK-L<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-------------|------------|------------|
| N30656     | 379        | 34          | 22          | 699         | 228        | 5          |
| N30657     | 392        | 58          | 22          | 546         | 228        | 6          |
| N30658     | 175        | 33          | 16          | 481         | 153        | 7          |
| N30659     | 231        | 31          | 21          | 661         | 204        | 6          |
| N30660     | 314        | 47          | 20          | 964         | 218        | 6          |
| Mean       | 298        | 41          | 20          | 670         | 206        | 6          |
| SD         | 93.9       | 11.6        | 2.5         | 186.0       | 31.3       | 0.7        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK-L<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-------------|------------|------------|
| N30666     | 217        | 32          | 22          | 818         | 295        | 6          |
| N30667     | 355        | 70          | 20          | 1299        | 199        | 7          |
| N30668     | 338        | 46          | 14          | 713         | 169        | 7          |
| N30669     | 474        | 64          | 22          | 1181        | 82         | 6          |
| N30670     | 292        | 52          | 29          | 384         | 113        | 4          |
| Mean       | 335        | 53          | 21          | 879         | 172        | 6          |
| SD         | 94.2       | 15.0        | 5.4         | 368.7       | 82.8       | 1.2        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30646     | blq               | 0.86           | 0.47           | 64.0        | 44         | 2.20     | 20          |
| N30647     | blq               | 0.91           | 0.56           | 61.1        | 43         | 2.38     | 18          |
| N30648     | blq               | 0.67           | 0.40           | 59.0        | 41         | 2.28     | 18          |
| N30649     | blq               | 1.04           | 0.49           | 61.6        | 45         | 2.71     | 17          |
| N30650     | blq               | 1.17           | 0.55           | 60.6        | 43         | 2.44     | 18          |
| Mean       | 0                 | 0.93           | 0.49           | 61.3        | 43         | 2.40     | 18          |
| SD         | 0.0               | 0.189          | 0.065          | 1.82        | 1.5        | 0.195    | 1.1         |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30656     | blq               | 0.63           | 0.42           | 56.8        | 41         | 2.60     | 16          |
| N30657     | blq               | 0.72           | 0.41           | 59.6        | 41         | 2.20     | 19          |
| N30658     | blq               | 0.84           | 0.87           | 61.0        | 43         | 2.39     | 18          |
| N30659     | blq               | 0.80           | 0.68           | 58.5        | 42         | 2.55     | 17          |
| N30660     | blq               | 0.89           | 0.48           | 60.4        | 43         | 2.47     | 17          |
| Mean       | 0                 | 0.78           | 0.57           | 59.3        | 42         | 2.44     | 17          |
| SD         | 0.0               | 0.103          | 0.199          | 1.66        | 1.0        | 0.157    | 1.1         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Male

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30666     | blq               | 0.85           | 0.70           | 58.4        | 42         | 2.56     | 16          |
| N30667     | blq               | 0.86           | 0.55           | 56.7        | 38         | 2.03     | 19          |
| N30668     | blq               | 0.99           | 0.59           | 62.2        | 44         | 2.42     | 18          |
| N30669     | blq               | 0.77           | 0.40           | 59.0        | 42         | 2.47     | 17          |
| N30670     | blq               | 0.93           | 0.59           | 58.3        | 41         | 2.37     | 17          |
| Mean       | 0                 | 0.88           | 0.57           | 58.9        | 41         | 2.37     | 17          |
| SD         | 0.0               | 0.084          | 0.108          | 2.02        | 2.2        | 0.203    | 1.1         |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30716(1)  | 143.6      | 3.62      | 105.0      | 3.66        | 1.37        | 7.00        | 11.8        | 121.40       |
| N30717     | 143.0      | 3.73      | 109.4      | 3.55        | 1.59        | 6.07        | 8.2         | 113.42       |
| N30718     | 142.6      | 3.73      | 108.6      | 3.29        | 1.57        | 7.04        | 11.7        | 141.91       |
| N30719     | 143.8      | 3.88      | 107.6      | 3.70        | 1.38        | 6.18        | 11.7        | 135.46       |
| N30720(2)  | 141.5      | 3.83      | 105.4      | 3.81        | 1.28        | 6.82        | 10.8        | 133.83       |
| Mean       | 142.9      | 3.76      | 107.2      | 3.60        | 1.44        | 6.62        | 10.8        | 129.20       |
| SD         | 0.92       | 0.101     | 1.94       | 0.198       | 0.136       | 0.463       | 1.53        | 11.533       |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | Na+ mmol/L | K+ mmol/L | Cl- mmol/L | Ca++ mmol/L | PHOS mmol/L | GLUC mmol/L | UREA mmol/L | CREAT µmol/L |
|------------|------------|-----------|------------|-------------|-------------|-------------|-------------|--------------|
| N30726     | 140.5      | 3.59      | 106.4      | 3.56        | 1.36        | 6.80        | 11.0        | 106.83       |
| N30727     | 142.3      | 3.59      | 109.0      | 3.53        | 1.52        | 6.10        | 10.9        | 135.60       |
| N30728     | 140.4      | 3.67      | 106.7      | 3.56        | 1.33        | 7.10        | 8.6         | 112.18       |
| N30729     | 141.6      | 3.51      | 106.7      | 3.41        | 1.33        | 7.31        | 9.3         | 114.39       |
| N30730     | 139.7      | 3.66      | 105.6      | 3.68        | 1.29        | 6.80        | 10.5        | 105.75       |
| Mean       | 140.9      | 3.60      | 106.9      | 3.55        | 1.37        | 6.82        | 10.1        | 114.95       |
| SD         | 1.04       | 0.065     | 1.27       | 0.096       | 0.090       | 0.458       | 1.06        | 12.093       |

(1) Hemolyzed.  
(2) Ca++ : value above limit of quantification.

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | Na+    | K+     | Cl-    | Ca++   | PHOS   | GLUC   | UREA   | CREAT  |
|------------|--------|--------|--------|--------|--------|--------|--------|--------|
|            | mmol/L | μmol/L |
| N30736     | 142.1  | 3.28   | 108.9  | 3.52   | 1.35   | 6.80   | 10.1   | 109.36 |
| N30737     | 141.8  | 3.53   | 107.3  | 3.53   | 1.58   | 7.16   | 10.4   | 121.86 |
| N30738     | 142.9  | 3.49   | 108.4  | 3.41   | 1.40   | 6.86   | 10.3   | 104.58 |
| N30739     | 141.9  | 3.75   | 108.5  | 3.68   | 1.48   | 7.15   | 13.1   | 119.98 |
| N30740     | 141.4  | 3.73   | 110.8  | 3.59   | 1.28   | 6.71   | 11.0   | 121.93 |
| Mean       | 142.0  | 3.56   | 108.8  | 3.55   | 1.42   | 6.94   | 11.0   | 115.54 |
| SD         | 0.55   | 0.193  | 1.28   | 0.099  | 0.116  | 0.207  | 1.23   | 8.044  |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK-L<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-------------|------------|------------|
| N30716(1)  | 227        | 46          | 26          | 703         | 678        | 2          |
| N30717     | 220        | 21          | 13          | 594         | 183        | 6          |
| N30718     | 244        | 69          | 26          | 443         | 135        | 5          |
| N30719     | 151        | 50          | 35          | 371         | 129        | 5          |
| N30720     | 293        | 44          | 23          | 873         | 111        | 4          |
| Mean       | 227        | 46          | 25          | 597         | 247        | 4          |
| SD         | 51.2       | 17.1        | 7.9         | 201.4       | 242.3      | 1.5        |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK-L<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-------------|------------|------------|
| N30726     | 256        | 85          | 24          | 612         | 255        | 7          |
| N30727     | 296        | 44          | 16          | 639         | 176        | 5          |
| N30728     | 377        | 82          | 57          | 675         | 231        | 6          |
| N30729     | 256        | 59          | 18          | 372         | 155        | 2          |
| N30730     | 273        | 69          | 44          | 775         | 181        | 5          |
| Mean       | 292        | 68          | 32          | 615         | 200        | 5          |
| SD         | 50.5       | 16.9        | 17.9        | 149.0       | 41.7       | 1.9        |

(1) Hemolyzed.

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | ALP<br>U/L | ALAT<br>U/L | ASAT<br>U/L | CK-L<br>U/L | LDH<br>U/L | GGT<br>U/L |
|------------|------------|-------------|-------------|-------------|------------|------------|
| N30736     | 333        | 44          | 20          | 479         | 143        | 3          |
| N30737     | 209        | 45          | 25          | 254         | 70         | 5          |
| N30738     | 137        | 63          | 26          | 994         | 67         | 4          |
| N30739     | 300        | 72          | 27          | 563         | 69         | 6          |
| N30740     | 273        | 77          | 21          | 417         | 67         | 3          |
| Mean       | 250        | 60          | 24          | 541         | 83         | 4          |
| SD         | 78.0       | 15.2        | 3.1         | 277.2       | 33.5       | 1.3        |

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30716(1)  | blq               | 1.45           | 0.40           | 64.0        | 45         | 2.37     | 19          |
| N30717     | blq               | 1.85           | 0.50           | 58.1        | 43         | 2.85     | 15          |
| N30718     | blq               | 1.29           | 0.36           | 55.9        | 38         | 2.12     | 18          |
| N30719     | blq               | 1.71           | 0.43           | 58.2        | 41         | 2.38     | 17          |
| N30720     | blq               | 1.60           | 0.55           | 63.0        | 44         | 2.32     | 19          |
| Mean       | 0                 | 1.58           | 0.45           | 59.8        | 42         | 2.41     | 18          |
| SD         | 0.0               | 0.219          | 0.077          | 3.48        | 2.8        | 0.268    | 1.7         |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30726     | blq               | 1.04           | 0.51           | 59.3        | 42         | 2.43     | 17          |
| N30727     | blq               | 1.14           | 0.40           | 61.1        | 43         | 2.38     | 18          |
| N30728     | blq               | 1.33           | 0.47           | 60.2        | 41         | 2.14     | 19          |
| N30729     | blq               | 0.74           | 0.34           | 57.5        | 40         | 2.29     | 18          |
| N30730     | blq               | 1.01           | 0.40           | 59.7        | 42         | 2.37     | 18          |
| Mean       | 0                 | 1.05           | 0.42           | 59.6        | 42         | 2.32     | 18          |
| SD         | 0.0               | 0.215          | 0.067          | 1.33        | 1.1        | 0.113    | 0.7         |

(1) Hemolyzed.

## BLOOD BIOCHEMISTRY

Study No.:  
Time: Week 9

Group 3  
SENDVACC99  
Sex: Female

| Animal No. | TOT.BIL<br>μmol/L | CHOL<br>mmol/L | TRIG<br>mmol/L | PROT<br>g/L | ALB<br>g/L | A/G<br>- | GLOB<br>g/L |
|------------|-------------------|----------------|----------------|-------------|------------|----------|-------------|
| N30736     | blq               | 1.13           | 0.52           | 58.1        | 41         | 2.40     | 17          |
| N30737     | blq               | 1.46           | 0.42           | 58.7        | 41         | 2.32     | 18          |
| N30738     | blq               | 1.66           | 0.42           | 58.5        | 41         | 2.34     | 18          |
| N30739     | blq               | 1.46           | 0.45           | 61.3        | 44         | 2.54     | 17          |
| N30740     | blq               | 1.38           | 0.44           | 61.5        | 44         | 2.51     | 18          |
| Mean       | 0                 | 1.42           | 0.45           | 59.6        | 42         | 2.42     | 18          |
| SD         | 0.0               | 0.191          | 0.041          | 1.64        | 1.6        | 0.099    | 0.5         |

15. C-Reactive Protein report

## **CONTENTS**

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| 1.                               | C-Reactive Protein (CRP)     | 19 to 35 |

## Determination of C-Reactive Protein (CRP) serum level using an ELISA method

The analytical procedure for the determination of C-Reactive Protein (CRP) concentration in rabbit serum by ELISA was validated at xxx. The validation results are summarized in the validation report .

### **Principle of the method**

The assay for the determination of CRP level in rabbit serum is an ELISA based assay (Enzyme Linked ImmunoSorbent Assay). Briefly, purified anti-rabbit CRP antibodies are coated onto the wells of a plate. The CRP of the tested sample bind to the coated antibodies on the plate and are revealed by horseradish peroxidase (HRP) conjugated anti-rabbit CRP antibodies for detection. The observation of the enzymatic reaction is made by using a substrate which is transformed in a colored product. CRP concentration is proportional to the optical density of the test sample. The concentration of the analyte in the tested samples is then determined by interpolation of the sample OD values with a calibration curve.

### **Abbreviations**

|       |                                     |
|-------|-------------------------------------|
| CRP   | : C Reactive Protein                |
| CV    | : Coefficient of Variation (in %)   |
| ELISA | : Enzyme Linked ImmunoSorbent Assay |
| HRP   | : Horseradish Peroxidase            |
| LLOQ  | : Lower Limit Of Quantification     |
| MRD   | : Minimum Required Dilution         |
| NA    | : Not Applicable                    |
| OD    | : Optical Density                   |
| QC    | : Quality Control                   |
| ULOQ  | : Upper Limit Of Quantification     |

## 1. REAGENTS AND EQUIPMENTS

### 1.1 REAGENTS

| Reagents             | Suppliers                           | Reference |
|----------------------|-------------------------------------|-----------|
| Milli-Q water        | Millipore water purification system | NA        |
| Rabbit CRP ELISA Kit | Life Diagnostics                    | CRP-10    |

NA: Not Applicable.

### 1.2 MAIN LABORATORY EQUIPMENT

| Equipment         | Suppliers                     |
|-------------------|-------------------------------|
| Variable pipettes | Biohit                        |
| Refrigerator      | Sanyo Labcool                 |
| Freezer (-20°C)   | RUA and Liebherr Profi Line   |
| Freezer (-80°C)   | Thermo Scientific             |
| Centrifuge Gr4i   | Thermo Scientific             |
| Timer             | Thermo Scientific and Hanhart |

| Equipment                               | Suppliers         |
|---|-------------------|
| Laminar flow hood                       | ADS Laminaire     |
| ELISA microplate reader Varioskan Flash | Thermo Scientific |

### 1.3 SOFTWARE

Main computer systems used in the study are detailed in the following table:

| Software                           | Application function   |
|------------------------------------|--|
| Web portal                         | Web business portal Master schedule sheet (including Study Note) Master schedule sheet - Study event |
| PANORAMA E <sup>2</sup> v2.60.0000 | Acquisition of temperature and humidity in study rooms (study and laboratory rooms, cold chambers)   |
| equipment manager                  | Web business portal Management of the equipments   |
| SkanIt DDE version 2.4.3           | Quantization and microplate reading system associated with the Varioskan Flash                       |
| LIMS                               | Acquisitions and management of pre-clinical in life data   |
| Doc system                         | Report files creation (in word data format) of individual data and summary                           |

## 2. ASSAY OF STUDY SAMPLES

### 2.1 ANALYTICAL BATCH

The study samples were assayed in batches using the ELISA method.

Each batch contained the following freshly prepared samples:

- . a blank sample analyzed in duplicate (1x diluent),
- . a calibration curve composed of six levels (7.81 - 250 ng/mL of CRP) and two anchoring points (3.91 and 500 ng/mL) analysed in duplicates,
- . two sets of three Quality Control (QC) samples levels at low (30.0 ng/mL), mid (74.9 ng/mL) and high (180 ng/mL) analysed in duplicates at the beginning and at the end of the batch,
- . study samples analyzed in duplicate at least at the MRD (minimum required dilution) of 1:25.

A total of 216 serum samples including serum samples from supernumerary animals were analyzed (see [§ Deviations to the study plan](#)). The samples at pre-test were stored at a nominal temperature of -80°C and samples from other time-points were stored at a nominal temperature of -20°C pending analysis (see [§ Deviations to the study plan](#)). The time from first blood collection to last day of analysis was 79 days which is below the 109 days validated during long term stability assessment when a sample is stored at a nominal temperature of -20°C and the 105 days validated during long term stability assessment when a sample is stored at a nominal temperature of -80°C.

## 2.2 BATCH ACCEPTANCE CRITERIA

The acceptance of the batch data depended on the calibration curves and the results of the QC samples.

### Calibration curve:

- . at least 75% of back-calculated calibration standards should be within  $\pm 25\%$  of the nominal values, except for LLOQ and ULOQ levels,  $\pm 30\%$ ,
- . intra-duplicate CV% should be lower than 20% (25% at LLOQ and ULOQ levels).

If not, the entire batch was re-assayed.

### Quality Control:

- . at least 67% of QC samples should be within  $\pm 25\%$  of their respective nominal values with an intra-duplicate CV% lower than 20%. In addition, for each concentration level, at least 50% of the QC samples should be validated.

If not, the entire batch was re-assayed.

## 3. QUANTIFICATION

Spiked dilution buffer containing 3.91, 7.81, 15.6, 31.2, 62.5, 125, 250 and 500 ng/mL of CRP were prepared to perform the calibration curves (eight levels in duplicate) fitted by non-linear regression analysis of OD-blank value vs. nominal concentration of calibration samples. Calibration points at 3.91 and 500 ng/mL were used as anchoring points. A four-parameter logistic regression model (4PL regression) was used for the fitting of calibration curves.

The sample concentrations were determined by interpolation from the calibration curve and the precision and accuracy of the method were also checked by analysis of Quality Control samples (QCs) containing CRP and prepared in dilution buffer at three concentration levels: 30.0; 74.9 and 180 ng/mL.

## 4. STUDY SAMPLE: RESULTS

Details of the analytical batches for the determination of CRP levels in serum samples are presented below.

| Run date    | Analytical batch | Accepted Yes / No | Batch content   | Reason for rejection or comments |
|-------------|------------------|-------------------|---|----------------------------------|
| 24-Aug-2018 | Plate 1          | Yes               | Samples collected at:<br>- pre-treatment (1)  | (2)                              |
| 28-Aug-2018 | Plate 2          | Yes               | Re-analysis of Plate 1  | (2)                              |
| 29-Aug-2018 | Plate 3          | Yes               | Samples collected at:<br>- pre-treatment (1)<br>Sample re-analysis                    | NA                               |
| 25-Sep-2018 | Plate 4          | Yes               | Samples collected at:<br>- Day 3 T48h: Groups 1M, 2M, 3M and 1F<br>Sample re-analysis | NA                               |

NA: Not Applicable.

(1): see § Deviation to study plan.

(2): see § Analytical note.

| Run date    | Analytical batch | Accepted Yes / No | Batch content   | Reason for rejection or comments |
|-------------|------------------|-------------------|---|----------------------------------|
| 25-Sep-2018 | Plate 5          | Yes               | Samples collected at:<br>- Day 3 T48h: Groups 1F, 2F and 3F   | NA                               |
| 01-Oct-2018 | Plate 6          | Yes               | Sample re-analysis  | NA                               |
| 02-Oct-2018 | Plate 7          | Yes               | Samples collected at:<br>- Day 31: Groups 1M, 2M, 3M and 1F   | NA                               |
| 02-Oct-2018 | Plate 8          | Yes               | Samples collected at:<br>- Day 31: Groups 1F, 2F and 3F   | NA                               |
| 25-Oct-2018 | Plate 9          | Yes               | Samples collected at:<br>- Day 31: Group 2F<br>- Day 57: Groups 1M, 2M, 3M and 1F<br>Sample re-analysis | NA                               |
| 25-Oct-2018 | Plate 10         | Yes               | Samples collected at:<br>- Day 57: Groups 2F and 3F   | NA                               |
| 26-Oct-2018 | Plate 11         | Yes               | Sample re-analysis  | NA                               |

NA: Not Applicable.

(1): see § Deviation to study plan.

(2): see § Analytical note.

The final determinations of CRP concentration in serum samples are presented in [Tables 1 to 8](#).

## 5. DEVIATIONS TO THE STUDY PLAN

The analysis of the study samples was performed according to the study plan and its amendment with the following deviations:

- . serum samples from supernumerary animals were analysed, however, on Study Director request, results from these analysis are not presented in the contributing report. This was considered to have no impact on the study because these samples were analyzed in excess,
- . sample analysis at pre-test was performed on an aliquot devoted to Immunogenicity testing. Therefore the analysis was done on an aliquot stored at -80°C unlike the -20°C described in study plan. This deviation is considered to have no impact on the study as long term stability assessment analyzed in validation study () was investigated at -20°C and -80°C and show similar performances.

## 6. ANALYTICAL NOTE

Plate 1 was wrongly rejected in a first place, therefore samples were re-analysed in plate 2. After verification, plate 1 was accepted and therefore results from plate 2 are considered as excess analysis and are therefore not reported.

## TABLES

Tables 1 to 8. CRP (mean values)

CRP  
(mean values)

Table: 1

Study No.:

Sex: Male

Time: Predose

| Group       | 1      | 2     | 3     |
|-------------|--------|-------|-------|
| CRP         | M (1)  | 3.80  | 3.23  |
| µg/mL       | SD (L) | 2.495 | 1.826 |
| n           | n      | 10    | 10    |
| %/1st group |        | -15   | 123   |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

\*\* P<0.01

(1) : DUNNETT TEST

(2) : MANN-WHITNEY TEST

(3) : DUNN TEST

(B) BARTLETT TEST P<0.01

(F) FISHER TEST P<0.01

(K) KOLMOGOROV-LILLIEFORST TEST P<0.01

(L) LOGARITHMIC TRANSFORMATION

- STATISTICS EXCLUDED GROUP

CRP  
(mean values)

Table: 2

Study No.:  
Sex: Female  
Time: Predose

| Group | 1           | 2      | 3      |       |
|-------|-------------|--------|--------|-------|
| CRP   | M (1)       | 12.69  | 14.68  | 11.55 |
| µg/mL | SD (L)      | 16.525 | 13.971 | 7.144 |
|       | n           | 10     | 10     | 10    |
|       | %/1st group |        | 16     | -9    |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

CRP  
(mean values)

Table: 3

Study No.:

Sex: Male

Time: Day 3

| Group | 1           | 2     | 3        |          |
|-------|-------------|-------|----------|----------|
| CRP   | M (1)       | 9.36  | 45.14 ** | 66.58 ** |
| µg/mL | SD (L)      | 7.189 | 28.348   | 55.750   |
|       | n           | 10    | 10       | 10       |
|       | %/1st group |       | 382      | 611      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORNS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

CRP  
(mean values)

Table: 4

Study No.:  
Sex: Female  
Time: Day 3

| Group | 1           | 2     | 3        |          |
|-------|-------------|-------|----------|----------|
| CRP   | M (1)       | 14.33 | 62.80 ** | 67.05 ** |
|       | SD (L)      | 8.853 | 32.251   | 24.191   |
|       | n           | 10    | 10       | 10       |
|       | %/1st group |       | 338      | 368      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

CRP  
(mean values)

Table: 5

Study No.:

Sex: Male

Time: Day 31

| Group | 1           | 2     | 3        |          |
|-------|-------------|-------|----------|----------|
| CRP   | M (1)       | 7.55  | 58.23 ** | 62.61 ** |
| µg/mL | SD (L)      | 8.524 | 32.745   | 36.774   |
|       | n           | 10    | 10       | 10       |
|       | %/1st group |       | 671      | 729      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORNS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

CRP  
(mean values)

Table: 6

Study No.:  
Sex: Female  
Time: Day 31

| Group | 1           | 2     | 3        |          |
|-------|-------------|-------|----------|----------|
| CRP   | M (1)       | 8.49  | 41.99 ** | 40.04 ** |
| µg/mL | SD (L)      | 4.676 | 19.853   | 21.494   |
|       | n           | 10    | 10       | 10       |
|       | %/1st group |       | 395      | 372      |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

CRP  
(mean values)

Table: 7

Study No.:

Sex: Male

Time: Day 57

| Group | 1           | 2     | 3     |       |
|-------|-------------|-------|-------|-------|
| CRP   | M (1)       | 4.30  | 6.00  | 5.29  |
| µg/mL | SD          | 2.782 | 3.710 | 1.770 |
|       | n           | 5     | 5     | 5     |
|       | %/1st group | 40    | 23    |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05

(B) BARTLETT TEST P<0.01

\*\* P<0.01

(F) FISHER TEST P<0.01

(1) : DUNNETT TEST

(K) KOLMOGOROV-LILLIEFORNS TEST P<0.01

(2) : MANN-WHITNEY TEST

(L) LOGARITHMIC TRANSFORMATION

(3) : DUNN TEST

- STATISTICS EXCLUDED GROUP

CRP  
(mean values)

Table: 8

Study No.:  
Sex: Female  
Time: Day 57

| Group       | 1           | 2     | 3     |
|-------------|-------------|-------|-------|
| CRP         | M (1) 11.84 | 6.25  | 9.82  |
| µg/mL       | SD 11.803   | 3.892 | 4.817 |
| n           | 5           | 5     | 5     |
| %/1st group | -47         | -17   |       |

SIGNIFICANCE OF THE DIFFERENCE BETWEEN  
TREATED AND CONTROL GROUPS

SAMPLE DISTRIBUTION-RELATIVE TESTS

\* P<0.05  
\*\* P<0.01  
(1) : DUNNETT TEST  
(2) : MANN-WHITNEY TEST  
(3) : DUNN TEST

(B) BARTLETT TEST P<0.01  
(F) FISHER TEST P<0.01  
(K) KOLMOGOROV-LILLIEFORST TEST P<0.01  
(L) LOGARITHMIC TRANSFORMATION  
- STATISTICS EXCLUDED GROUP

## APPENDIX

1. C-Reactive Protein (CRP)

CRP

Study No.:  
Time: Predose

Group 1  
Control item (NaCl)  
Sex: Male

| CRP        |       |
|------------|-------|
| Animal No. | µg/mL |
| N30641     | 1.50  |
| N30642     | 2.92  |
| N30643     | 3.43  |
| N30644     | 2.08  |
| N30645     | 2.35  |
| N30646     | 8.17  |
| N30647     | 8.60  |
| N30648     | 2.42  |
| N30649     | 2.97  |
| N30650     | 3.57  |
| Mean       | 3.80  |
| SD         | 2.495 |

Group 2  
SENDVACC10  
Sex: Male

| --         |       |
|------------|-------|
| CRP        |       |
| Animal No. | µg/mL |
| N30651     | 1.35  |
| N30652     | 2.13  |
| N30653     | 2.97  |
| N30654     | 3.27  |
| N30655     | 4.34  |
| N30656     | 7.86  |
| N30657     | 3.34  |
| N30658     | 2.62  |
| N30659     | 2.39  |
| N30660     | 2.03  |
| Mean       | 3.23  |
| SD         | 1.826 |

## CRP

Study No.:  
Time: Predose

Group 3  
SENDVACC99  
Sex: Male

--

## CRP

Animal No.  $\mu\text{g/mL}$

|        |       |
|--------|-------|
| N30661 | 6.47  |
| N30662 | 3.81  |
| N30663 | 22.82 |
| N30664 | 14.88 |
| N30665 | 1.20  |
| N30666 | 4.04  |
| N30667 | 0.81  |
| N30668 | 15.15 |
| N30669 | 11.29 |
| N30670 | 4.37  |

|      |       |
|------|-------|
| Mean | 8.48  |
| SD   | 7.252 |

CRP

Study No.:  
Time: Predose

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30711     | 15.28        |
| N30712     | 7.69         |
| N30713     | 10.06        |
| N30714     | 5.54         |
| N30715     | 14.93        |
| N30716     | 57.95        |
| N30717     | 4.22         |
| N30718     | 5.07         |
| N30719     | 2.57         |
| N30720     | 3.63         |
| Mean       | 12.69        |
| SD         | 16.525       |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30721     | 8.71         |
| N30722     | 13.98        |
| N30723     | 12.44        |
| N30724     | 20.98        |
| N30725     | 52.11        |
| N30726     | 11.13        |
| N30727     | 3.83         |
| N30728     | 9.39         |
| N30729     | 6.14         |
| N30730     | 8.07         |
| Mean       | 14.68        |
| SD         | 13.971       |

CRP

Study No.:  
Time: Predose

Group 3  
SENDVACC99  
Sex: Female

--

CRP

Animal No.  $\mu\text{g/mL}$

|        |       |
|--------|-------|
| N30731 | 10.64 |
| N30732 | 7.15  |
| N30733 | 14.91 |
| N30734 | 20.53 |
| N30735 | 8.01  |
| N30736 | 5.11  |
| N30737 | 6.43  |
| N30738 | 26.67 |
| N30739 | 5.42  |
| N30740 | 10.63 |

|      |       |
|------|-------|
| Mean | 11.55 |
| SD   | 7.144 |

## CRP

Study No.:  
Time: Day 3

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30641     | 2.25         |
| N30642     | 2.05         |
| N30643     | 18.30        |
| N30644     | 4.17         |
| N30645     | 21.03        |
| N30646     | 16.51        |
| N30647     | 7.84         |
| N30648     | 4.88         |
| N30649     | 12.89        |
| N30650     | 3.69         |
| Mean       | 9.36         |
| SD         | 7.189        |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30651     | 54.18        |
| N30652     | 24.56        |
| N30653     | 37.29        |
| N30654     | 23.43        |
| N30655     | 104.40       |
| N30656     | 83.28        |
| N30657     | 14.53        |
| N30658     | 34.84        |
| N30659     | 31.68        |
| N30660     | 43.17        |
| Mean       | 45.14        |
| SD         | 28.348       |

## CRP

Study No.:  
Time: Day 3

Group 3  
SENDVACC99  
Sex: Male

--

CRP  
Animal No.  $\mu\text{g/mL}$

N30661 12.47  
N30662 13.84  
N30663 190.11  
N30664 38.19  
N30665 56.91  
N30666 97.20  
N30667 46.85  
N30668 126.29  
N30669 41.58  
N30670 42.35

Mean 66.58  
SD 55.750

CRP

Study No.:  
Time: Day 3

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30711     | 6.09         |
| N30712     | 13.20        |
| N30713     | 10.65        |
| N30714     | 15.13        |
| N30715     | 16.75        |
| N30716     | 34.89        |
| N30717     | 22.25        |
| N30718     | 8.93         |
| N30719     | 5.05         |
| N30720     | 10.40        |
| Mean       | 14.33        |
| SD         | 8.853        |

Group 2  
SENDVACC10  
Sex: Female

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30721     | 19.37        |
| N30722     | 59.80        |
| N30723     | 59.90        |
| N30724     | 58.00        |
| N30725     | 107.33       |
| N30726     | 22.07        |
| N30727     | 39.18        |
| N30728     | 110.03       |
| N30729     | 58.18        |
| N30730     | 94.15        |
| Mean       | 62.80        |
| SD         | 32.251       |

## CRP

Study No.:  
Time: Day 3

Group 3  
SENDVACC99  
Sex: Female

--

## CRP

Animal No.  $\mu\text{g/mL}$

|        |        |
|--------|--------|
| N30731 | 35.30  |
| N30732 | 48.44  |
| N30733 | 82.87  |
| N30734 | 58.42  |
| N30735 | 70.33  |
| N30736 | 104.46 |
| N30737 | 59.80  |
| N30738 | 96.42  |
| N30739 | 34.10  |
| N30740 | 80.34  |

|      |        |
|------|--------|
| Mean | 67.05  |
| SD   | 24.191 |

## CRP

Study No.:  
Time: Day 31

Group 1  
Control item (NaCl)  
Sex: Male

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30641     | 6.23         |
| N30642     | 1.56         |
| N30643     | 30.74        |
| N30644     | 2.72         |
| N30645     | 9.12         |
| N30646     | 8.05         |
| N30647     | 4.54         |
| N30648     | 1.82         |
| N30649     | 4.69         |
| N30650     | 6.01         |
| Mean       | 7.55         |
| SD         | 8.524        |

Group 2  
SENDVACC10  
Sex: Male

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30651     | 109.26       |
| N30652     | 57.00        |
| N30653     | 37.35        |
| N30654     | 17.88        |
| N30655     | 50.18        |
| N30656     | 46.15        |
| N30657     | 33.21        |
| N30658     | 116.57       |
| N30659     | 38.12        |
| N30660     | 76.56        |
| Mean       | 58.23        |
| SD         | 32.745       |

## CRP

Study No.:  
Time: Day 31

Group 3  
SENDVACC99  
Sex: Male

--

CRP  
Animal No. µg/mL

|        |        |
|--------|--------|
| N30661 | 13.80  |
| N30662 | 24.40  |
| N30663 | 146.45 |
| N30664 | 89.70  |
| N30665 | 50.88  |
| N30666 | 54.93  |
| N30667 | 56.00  |
| N30668 | 74.60  |
| N30669 | 65.83  |
| N30670 | 49.54  |
| Mean   | 62.61  |
| SD     | 36.774 |

CRP

Study No.:  
Time: Day 31

Group 1  
Control item(NaCl)  
Sex: Female

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30711     | 4.55         |
| N30712     | 10.00        |
| N30713     | 5.72         |
| N30714     | 6.02         |
| N30715     | 11.29        |
| N30716     | 20.25        |
| N30717     | 7.90         |
| N30718     | 6.81         |
| N30719     | 7.77         |
| N30720     | 4.57         |
| Mean       | 8.49         |
| SD         | 4.676        |

Group 2

Sex: Female

| Animal No. | CRP<br>µg/mL |
|------------|--------------|
| N30721     | 28.45        |
| N30722     | 34.65        |
| N30723     | 69.82        |
| N30724     | 35.80        |
| N30725     | 80.52        |
| N30726     | 12.86        |
| N30727     | 32.68        |
| N30728     | 35.86        |
| N30729     | 41.03        |
| N30730     | 48.22        |
| Mean       | 41.99        |
| SD         | 19.853       |

CRP

Study No.:  
Time: Day 31

Group 3  
SENDVACC99  
Sex: Female

--

CRP

Animal No.  $\mu\text{g/mL}$

|        |       |
|--------|-------|
| N30731 | 13.37 |
| N30732 | 32.37 |
| N30733 | 44.77 |
| N30734 | 17.20 |
| N30735 | 61.16 |
| N30736 | 48.70 |
| N30737 | 82.17 |
| N30738 | 34.62 |
| N30739 | 18.52 |
| N30740 | 47.48 |

|      |        |
|------|--------|
| Mean | 40.04  |
| SD   | 21.494 |

CRP

Study No.:  
Time: Day 57

Group 1  
Control item (NaCl)  
Sex: Male

|        | CRP<br>Animal No. µg/mL |
|--------|-------------------------|
| N30646 | 3.22                    |
| N30647 | 5.65                    |
| N30648 | 1.33                    |
| N30649 | 8.44                    |
| N30650 | 2.88                    |
| Mean   | 4.30                    |
| SD     | 2.782                   |

Group 2  
SENDVACC10  
Sex: Male

|        | CRP<br>Animal No. µg/mL |
|--------|-------------------------|
| N30656 | 4.00                    |
| N30657 | 2.27                    |
| N30658 | 8.21                    |
| N30659 | 4.15                    |
| N30660 | 11.37                   |
| Mean   | 6.00                    |
| SD     | 3.710                   |

CRP

Study No.:  
Time: Day 57

Group 3  
SENDVACC99  
Sex: Male

--

CRP  
Animal No.  $\mu\text{g/mL}$

N30666 7.57  
N30667 4.46  
N30668 6.62  
N30669 4.61  
N30670 3.19

Mean 5.29  
SD 1.770

CRP

Study No.:  
Time: Day 57

Group 1  
Control item(NaCl)  
Sex: Female

CRP  
Animal No. µg/mL

|        |        |
|--------|--------|
| N30716 | 31.93  |
| N30717 | 7.27   |
| N30718 | 4.14   |
| N30719 | 3.30   |
| N30720 | 12.58  |
| Mean   | 11.84  |
| SD     | 11.803 |

Group 2  
SENDVACC10  
Sex: Female

--  
CRP  
Animal No. µg/mL

|        |       |
|--------|-------|
| N30726 | 2.59  |
| N30727 | 3.21  |
| N30728 | 9.90  |
| N30729 | 4.63  |
| N30730 | 10.94 |
| Mean   | 6.25  |
| SD     | 3.892 |

CRP

Study No.:  
Time: Day 57

Group 3  
SENDVACC99  
Sex: Female

--

CRP  
Animal No.  $\mu\text{g/mL}$

N30736 11.94  
N30737 16.96  
N30738 9.16  
N30739 5.51  
N30740 5.54

Mean 9.82  
SD 4.817

16. Pathology report

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**LIST OF ABBREVIATIONS**

## **SUMMARY**

The objective of this study was to evaluate the local tolerance and systemic toxicity of the test items, SENDVACC10 and SENDVACC99, in the New Zealand White rabbit, following three intramuscular injections, two weeks apart. An assessment of any delayed onset toxicity and/or the reversibility of any finding observed on completion of the treatment period was evaluated during a 4-week observation period.

### **SENDVACC10**

At necropsy, there was a test item treatment-related statistically significant increase in absolute and relative (to body and brain) weight of the spleen in males and females correlating with lymphoid hyperplasia at histopathological examination. There was partial recovery in males, and complete recovery in females.

At the macroscopic examination, gelatinous abdominal adipose tissue, correlating with edema at microscopic examination, was present in females. There were no other treatment-related macroscopic findings. There was complete recovery.

At the histopathological examination, test item treatment-related observations consisted of lymphoid hyperplasia and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue (on the right side only). These changes showed partial recovery by the end of the 4-week recovery period.

### **VACC99**

At necropsy, there was an increase in absolute and relative (to body and brain) weight of the spleen in males and females. This was not statistically significant; however it correlated with lymphoid hyperplasia at histopathological examination, and was therefore considered test item treatment-related. There was partial recovery in males, and complete recovery in females.

At the macroscopic examination, enlarged right inguinal lymph node, correlating with lymphoid hyperplasia at microscopic examination, was present in males. Gelatinous abdominal adipose tissue, correlating with edema at microscopic examination, was present in females. There was complete recovery. There were no other test compound-related macroscopic findings.

At the histopathological examination, test item treatment-related observations consisted of lymphoid hyperplasia and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue (on the right side only). These changes showed partial recovery by the end of the 4-week recovery period.

These findings were considered non-adverse and related to the pharmacological activity of the adjuvanted vaccines.

## 1. METHODS

The objective of this study was to evaluate the local tolerance and systemic toxicity of the test items, SENDVACC10 and SENDVACC99, in the New Zealand White rabbit, following three intramuscular injections, two weeks apart. An assessment of any delayed onset toxicity and/or the reversibility of any finding observed on completion of the treatment period was evaluated during a 4-week observation period.

The treatment groups for the present study are detailed in the following table:

| Group | Treatment           | Nominal dose level of adjuvant (mg/dose) | Nominal dose level of hemagglutinin (µg HA/strain/dose) | Number of animals |
|-------|---------------------|--|---|-------------------|
| 1     | Control item (NaCl) | 0  | 0   | 10 males          |
|       |                     |  |   | 10 females        |
| 2     | SENDVACC10          | 12.5                                     | 15  | 10 males          |
|       |                     |  |   | 10 females        |
| 3     | SENDVACC99          | 12.5                                     | 45  | 10 males          |
|       |                     |  |   | 10 females        |

The in life and necropsy phases of the study were performed by Citoxlab France, BP 563, 27005 Evreux, France.

The organs specified in the tissue procedure table of the study report were weighed and macroscopically/microscopically examined. For details concerning the sacrifice, organ weights, macroscopic *post-mortem* examination, preservation of tissues, preparation of histological slides and statistics, see study report.

The tissue sections were examined by light microscopy and findings were recorded on line by the Study Pathologist using computer software

All macroscopic and microscopic findings are given for each animal in text form under "Text of Gross and Microscopic Findings". Organ weights, summary incidence tables of macroscopic and microscopic observations are also included in this report; these tables are created by computer. The microscopic examination was carried out by

Peer review was performed by an external pathologist, to confirm that findings recorded by the Study Pathologist are consistent and accurate. After the first draft of the pathology report was issued, the Sponsor's pathologist The study plan and amendments were sent to the peer review Pathologist.

## 2. STUDY PLAN ADHERENCE

The microscopic examination of the study was performed in accordance with study plan No. RABBITV1 and subsequent amendments, with no deviations from the agreed study plan.

### 3. RESULTS

#### 3.1 MORTALITY

There was no mortality reported during the main and recovery periods of the study.

#### 3.2 ORGAN WEIGHTS

##### 3.2.1 At the end of the treatment period

Relevant changes in mean final body weights and organ weights in test item-treated groups  
(% changes from controls):

| Sex                 | Male       |        | Female     |        |
|---------------------|------------|--------|------------|--------|
|                     | 2          | 3      | 2          | 3      |
| Group               | SENDVACC10 | VACC99 | SENDVACC10 | VACC99 |
| Treatment           |            |        |            |        |
| - Final body weight | -7*        | -5     | +5         | -4     |
| - Spleen            |            |        |            |        |
| . absolute          | +47*       | +26    | +63**      | +22    |
| . relative to body  | +57**      | +32    | +56**      | +27    |
| . relative to brain | +52*       | +27    | +57**      | +23    |

Statistically significant from controls: \*: p<0.05, \*\*:p<0.01.

The significance concerned the organ weights values and not the percentages.

#### SENDVACC10

There was a treatment-related statistically significant increase in absolute and relative (to body and brain) weight of the spleen in males and females (correlating with lymphoid hyperplasia at histopathological examination).

#### SENDVACC99

There was an increase in absolute and relative (to body and brain) weight of the spleen in males and females. This was not statistically significant; however it correlated with lymphoid hyperplasia at histopathological examination, and was therefore considered treatment-related.

##### 3.2.2 At the end of the recovery period

Relevant changes in mean final body weights and organ weights in test item-treated groups  
(% changes from controls):

| Sex                 | Male   |        | Female |        |
|---------------------|--------|--------|--------|--------|
|                     | 2      | 3      | 2      | 3      |
| Group               | VACC10 | VACC99 | VACC10 | VACC99 |
| Treatment           |        |        |        |        |
| - Final body weight | -3     | -2     | -2     | -3     |
| - Spleen            |        |        |        |        |
| . absolute          | +38    | +26    | -1     | -3     |
| . relative to body  | +42    | +29    | 0      | -1     |
| . relative to brain | +37    | +25    | 0      | -2     |

There was a treatment-related increase in absolute and relative (to body and brain) weight of the spleen in males (correlating with lymphoid hyperplasia at histopathological examination). There was partial recovery in males, and complete recovery in females.

There was a treatment-related increase in absolute and relative (to body and brain) weight of the spleen in males (correlating with lymphoid hyperplasia at histopathological examination). There was partial recovery in males, and complete recovery in females.

### **Other findings**

All other variations in absolute/relative organ weights were considered to be incidental and unrelated to treatment with test items.

## **3.3 MACROSCOPIC EXAMINATIONS**

### **3.3.1 At the end of the treatment period**

Incidence and severity of macroscopic findings at the inguinal lymph node right, Adipose tissue at the end of the treatment period (n = 5)

| Sex                               | Male              |                 |             | Female            |                 |             |
|-----------------------------------|-------------------|-----------------|-------------|-------------------|-----------------|-------------|
| Group                             | 1<br>NaCl<br>0.9% | 2<br>SENDVACC10 | 3<br>VACC99 | 1<br>NaCl<br>0.9% | 2<br>SENDVACC10 | 3<br>VACC99 |
| Treatment                         |                   |                 |             |                   |                 |             |
| <b>Inguinal lymph node, right</b> |                   |                 |             |                   |                 |             |
| Enlarged                          | -                 | -               | 3           | -                 | -               | -           |
| <b>Adipose tissue</b>             |                   |                 |             |                   |                 |             |
| Gelatinous                        | -                 | -               | -           | -                 | 4               | 3           |

-: finding not present.

### **SENDVACC10**

Gelatinous abdominal adipose tissue (correlating with edema at microscopic examination) was present in females. There were no other test compound-related macroscopic findings.

### **SENDVACC99**

Enlarged right inguinal lymph node (correlating with lymphoid hyperplasia at microscopic examination) was present in males. Gelatinous abdominal adipose tissue (correlating with edema at microscopic examination) was present in females. There were no other test compound-related macroscopic findings.

### **Other findings**

Red discoloration (correlating with hemorrhage at histopathological examination) at the injection sites of control and treated animals was considered to be due to the injection procedure, and unrelated to the test compounds.

The remaining macroscopic findings were considered to be incidental because they were consistent with spontaneously occurring findings described in the literature, the findings were distributed randomly among groups, or their appearance was similar to findings found in controls.

#### 3.3.2 At the end of the recovery period

##### **SENDVACC10**

There were no treatment-related macroscopic findings.

##### **SENDVACC99**

There were no treatment-related macroscopic findings.

### **3.4 MICROSCOPIC OBSERVATIONS**

#### 3.4.1 At the end of the treatment period

##### **SENDVACC10**

Treatment-related microscopic observations consisted of lymphoid hyperplasia (which was mostly follicular) and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia (mostly follicular) in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue (on the right side only).

##### **SENDVACC99**

Treatment-related microscopic observations consisted of lymphoid hyperplasia (mostly follicular) and granulocyte infiltration in regional lymph nodes, lymphoid hyperplasia (mostly follicular) in the spleen, subacute inflammation at the injection sites, and edema, hemorrhage and inflammation in abdominal adipose tissue (on the right side only).

### **Other findings**

Hemorrhage, minimal to slight focal muscle necrosis, needle tract lesions, and degeneration/regeneration of muscle at the injection sites were considered to be due to the injection procedure, and unrelated to the test compounds.

Incidence and severity of selected microscopic findings at the end of the treatment period (n = 5)

| Sex Group                         | 1 | 2 | Male | 3 | 1 | 2 | Female | 3 |
|-----------------------------------|---|---|------|---|---|---|--------|---|
| Treatment                         |   |   |      |   |   |   |        |   |
| <b>Inguinal lymph node, right</b> |   |   |      |   |   |   |        |   |
| Hyperplasia lymphoid              |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | 3 |      | 3 | 1 | 3 |        | 4 |
| Slight (grade 2)                  | - | - |      | 1 | - | 2 |        | 1 |
| Infiltrate granulocyte            |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | 1 | 2 |      | 2 | 1 | - |        | 3 |
| <b>Inguinal lymph node, left</b>  |   |   |      |   |   |   |        |   |
| Hyperplasia lymphoid              |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | 5 |      | 5 | 2 | 4 |        | 4 |
| Slight (grade 2)                  | - | - |      | - | - | 1 |        | 1 |
| Infiltrate granulocyte            |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | 1 | 3 |      | 4 | 2 | - |        | 1 |
| Slight (grade 2)                  | - | - |      | - | - | - |        | 1 |
| <b>Iliac lymph node, right</b>    |   |   |      |   |   |   |        |   |
| Hyperplasia lymphoid              |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | 3 |      | 2 | - | 2 |        | 2 |
| Slight (grade 2)                  | - | 1 |      | - | - | - |        | 2 |
| Infiltrate granulocyte            |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | 1 |      | 1 | - | - |        | 3 |
| <b>Iliac lymph node, left</b>     |   |   |      |   |   |   |        |   |
| Hyperplasia lymphoid              |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | 2 |      | 4 | - | 2 |        | 2 |
| Infiltrate granulocyte            |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | - |      | 1 | - | - |        | - |
| <b>Sacral lymph node</b>          |   |   |      |   |   |   |        |   |
| Hyperplasia lymphoid              |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | - |      | 1 | - | 1 |        | 3 |
| Infiltrate granulocyte            |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | - |      | - | - | - |        | 1 |
| <b>Spleen</b>                     |   |   |      |   |   |   |        |   |
| Hyperplasia lymphoid              |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | 3 |      | 3 | - | 4 |        | 4 |
| Slight (grade 2)                  | - | - |      | - | - | 1 |        | - |
| <b>Injection site 1</b>           |   |   |      |   |   |   |        |   |
| Inflammation                      |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | 2 |      | 2 | 1 | 2 |        | 2 |
| Slight (grade 2)                  | - | 2 |      | 2 | - | 2 |        | 2 |
| Moderate (grade 3)                | - | 1 |      | - | - | - |        | - |
| <b>Injection site 2</b>           |   |   |      |   |   |   |        |   |
| Inflammation                      |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | 3 |      | 2 | 1 | 2 |        | 4 |
| Slight (grade 2)                  | - | 1 |      | 1 | - | 1 |        | - |
| <b>Injection site 3</b>           |   |   |      |   |   |   |        |   |
| Inflammation                      |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | 1 | - |      | - | 2 | - |        | - |
| Slight (grade 2)                  | - | 3 |      | 5 | - | 5 |        | 5 |
| Moderate (grade 3)                | - | 1 |      | - | - | - |        | - |
| <b>Adipose tissue</b>             |   |   |      |   |   |   |        |   |
| Edema                             |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | - |      | - | - | 1 |        | 1 |
| Slight (grade 2)                  | - | - |      | - | - | 3 |        | 2 |
| Hemorrhage                        |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | - |      | - | - | 3 |        | 2 |
| Slight (grade 2)                  | - | - |      | - | - | 1 |        | - |
| Inflammation                      |   |   |      |   |   |   |        |   |
| Minimal (grade 1)                 | - | - |      | - | - | 1 |        | 1 |
| Slight (grade 2)                  | - | - |      | - | - | 3 |        | 2 |

-: not observed.

The remaining microscopic findings were considered to be incidental because they were consistent with spontaneously occurring findings described in the literature, the findings were distributed randomly among groups, or their appearance was similar to findings found in controls.

### 3.4.2 At the end of the recovery period

#### **SENDVACC10**

The incidence and severity of lymphoid hyperplasia in the spleen and lymph nodes was similar to the treatment period, however the secondary follicles in the spleen of recovery animals were less cellular, consistent with involution. There was partial recovery at the injection sites, as the incidence and severity of subacute inflammation was decreased when compared to the treatment period. There was complete recovery in the abdominal adipose tissue.

#### **SENDVACC99**

The incidence and severity of lymphoid hyperplasia in the spleen and lymph nodes was similar to the treatment period, however the secondary follicles in the spleen of recovery animals were less cellular, consistent with involution. There was partial recovery at the injection sites as the incidence and severity of subacute inflammation was decreased when compared to the treatment period. There was complete recovery in the abdominal adipose tissue.

Incidence and severity of selected microscopic findings at the end of the observation period (n = 5)

| Sex<br>Group                      | 1<br>NaCl | 2 | Male | 3 | 1 | Female | 2 | 3 |
|-----------------------------------|-----------|---|------|---|---|--------|---|---|
| Treatment                         |           |   |      |   |   |        |   |   |
| <b>Inguinal lymph node, right</b> |           |   |      |   |   |        |   |   |
| Hyperplasia lymphoid              |           |   |      |   |   |        |   |   |
| Minimal (grade 1)                 | -         | 3 | 4    | 2 | 4 |        | 4 |   |
| Slight (grade 2)                  | -         | 1 | -    | - | - |        | - |   |
| Infiltrate granulocyte            |           |   |      |   |   |        |   |   |
| Minimal (grade 1)                 | 1         | - | 2    | - | - |        | - |   |
| <b>Inguinal lymph node, left</b>  |           |   |      |   |   |        |   |   |
| Hyperplasia lymphoid              |           |   |      |   |   |        |   |   |
| Minimal (grade 1)                 | 1         | 3 | 3    | 3 | 3 |        | 2 |   |
| Slight (grade 2)                  | -         | 1 | 1    | - | - |        | - |   |
| Infiltrate granulocyte            |           |   |      |   |   |        |   |   |
| Minimal (grade 1)                 | -         | 1 | 3    | - | - |        | - |   |
| <b>Iliac lymph node, right</b>    |           |   |      |   |   |        |   |   |
| Hyperplasia lymphoid              |           |   |      |   |   |        |   |   |
| Minimal (grade 1)                 | -         | 1 | 2    | - | 1 |        | 4 |   |
| Slight (grade 2)                  | -         | 2 | -    | - | - |        | - |   |
| <b>Iliac lymph node, left</b>     |           |   |      |   |   |        |   |   |
| Hyperplasia lymphoid              |           |   |      |   |   |        |   |   |
| Minimal (grade 1)                 | -         | 3 | 3    | - | 1 |        | 2 |   |
| <b>Sacral lymph node</b>          |           |   |      |   |   |        |   |   |
| Hyperplasia lymphoid              |           |   |      |   |   |        |   |   |
| Minimal (grade 1)                 | -         | 1 | 1    | - | 1 |        | 1 |   |
| Slight (grade 2)                  | -         | - | 1    | - | - |        | - |   |
| <b>Spleen</b>                     |           |   |      |   |   |        |   |   |
| Hyperplasia lymphoid              |           |   |      |   |   |        |   |   |
| Minimal (grade 1)                 | 1         | 4 | 4    | 1 | 5 |        | 4 |   |
| Slight (grade 2)                  | -         | 1 | -    | - | - |        | - |   |

-: not observed.

| Sex<br>Group            | 1 | 2 | Male | 3 | 1 | 2 | Female | 3 |
|-------------------------|---|---|------|---|---|---|--------|---|
| Treatment               |   |   |      |   |   |   |        |   |
| <b>Injection site 1</b> |   |   |      |   |   |   |        |   |
| Inflammation            |   |   |      |   |   |   |        |   |
| Minimal (grade 1)       | - | - |      | 1 | - | - |        | 2 |
| Slight (grade 2)        | - | 1 |      | - | - | - |        | - |
| <b>Injection site 2</b> |   |   |      |   |   |   |        |   |
| Inflammation            |   |   |      |   |   |   |        |   |
| Minimal (grade 1)       | - | 1 |      | - | - | - |        | 1 |
| <b>Injection site 3</b> |   |   |      |   |   |   |        |   |
| Inflammation            |   |   |      |   |   |   |        |   |
| Minimal (grade 1)       | - | 3 |      | 2 | 1 | 3 |        | 3 |

-: not observed.

There were no other treatment-related microscopic findings.

#### 4. DISCUSSION

Treatment-related findings with both VACC10 and VACC99 were present in the spleen (increased weight and lymphoid hyperplasia), the regional lymph nodes (lymphoid hyperplasia and granulocyte infiltration) and injection sites (subacute inflammation). The severity was minimal to moderate, with most findings being minimal to slight. There was partial recovery.

The inflammation was characterized by the presence of mixed inflammatory cells, as well as clear spaces with faint eosinophilic or basophilic staining, considered to be exudate and serum proteins. These clear spaces were no longer present after the recovery period.

Injection site 1 was used on Day 1, injection site 2 on Day 15, and injection site 3 on Day 29 of the study. It would be expected that the findings would increase in incidence/severity from injection site 1 (first site, with most time for recovery) to injection site 3 (most recent site, with least time for recovery), however findings at injection site 1 were slightly higher in incidence/severity than at Injection Site 2. Both sites 1 and 3 were on the same side of the animal, and approximately 4 cm apart. There appears to have been some cross-over between the two injection sites due to their proximity and to the liquid nature of the injection. This was not considered to have affected the interpretation of the study. Edema, hemorrhage and inflammation in abdominal adipose tissue was also present on the right side only (*i.e.* the same side as Injection sites 1 and 3), and is likely to have been due to extension downwards (due to gravity) of edema and hemorrhage at the injection sites, rather than a direct effect of the test compounds.

These findings were considered non-adverse and related to the pharmacological activity of the adjuvanted vaccines.

**TABLES**

Table 1. Summary table of body/organ weights and statistics

Table: 1

## SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS

STATUS AT NECROPSY: K0

TREATMENT PERIOD

SEX: MALE

| ORGAN             | DOSE GROUP:  | 1       | 2       | 3 |
|-------------------|--------------|---------|---------|---|
|                   | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>             |              |         |         |   |
| FINAL BODY WEIGHT | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 3200.0       | 2980.0* | 3032.0  |   |
| SD :              | 124.1        | 128.8   | 160.4   |   |
| <hr/>             |              |         |         |   |
| ADRENAL GLANDS    | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 0.19040      | 0.19660 | 0.20200 |   |
| SD :              | 0.060        | 0.017   | 0.055   |   |
| MEAN % BODY :     | 0.00595      | 0.00662 | 0.00666 |   |
| SD :              | 0.002        | 0.001   | 0.002   |   |
| MEAN % BRAIN :    | 1.91         | 2.03    | 2.04    |   |
| SD :              | 0.656        | 0.200   | 0.574   |   |
| <hr/>             |              |         |         |   |
| BRAIN             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 10.03        | 9.72    | 9.93    |   |
| SD :              | 0.291        | 0.357   | 0.312   |   |
| MEAN % BODY :     | 0.31382      | 0.32650 | 0.32797 |   |
| SD :              | 0.011        | 0.018   | 0.009   |   |
| <hr/>             |              |         |         |   |
| EPIDIDYMIDES      | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 2.19         | 1.99    | 2.08    |   |
| SD :              | 0.241        | 0.278   | 0.407   |   |
| MEAN % BODY :     | 0.06835      | 0.06683 | 0.06857 |   |
| SD :              | 0.006        | 0.010   | 0.012   |   |
| MEAN % BRAIN :    | 21.83        | 20.48   | 20.92   |   |
| SD :              | 2.25         | 2.81    | 3.72    |   |
| <hr/>             |              |         |         |   |
| HEART             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 7.91         | 8.30    | 7.70    |   |
| SD :              | 0.930        | 1.53    | 0.621   |   |
| MEAN % BODY :     | 0.24699      | 0.27868 | 0.25375 |   |
| SD :              | 0.024        | 0.050   | 0.014   |   |
| MEAN % BRAIN :    | 78.74        | 85.77   | 77.46   |   |
| SD :              | 7.54         | 17.81   | 5.47    |   |
| <hr/>             |              |         |         |   |

\*/\*\*):DUNNETT'S TEST BASED ON POOLED VARIANCES AT 5% (\*) OR 1% (\*\*) LEVEL  
Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: K0  
 TREATMENT PERIOD  
 SEX: MALE

---

| ORGAN            | DOSE GROUP:  | 1       | 2       | 3 |
|------------------|--------------|---------|---------|---|
|                  | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>            |              |         |         |   |
| KIDNEYS          | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 15.91        | 14.16   | 14.43   |   |
| SD :             | 0.937        | 0.925   | 1.71    |   |
| MEAN % BODY :    | 0.49848      | 0.47510 | 0.47503 |   |
| SD :             | 0.045        | 0.024   | 0.037   |   |
| MEAN % BRAIN :   | 158.8        | 145.9   | 145.1   |   |
| SD :             | 12.35        | 11.54   | 14.64   |   |
| <hr/>            |              |         |         |   |
| LIVER            | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 77.76        | 69.00   | 67.63   |   |
| SD :             | 9.31         | 10.11   | 8.13    |   |
| MEAN % BODY :    | 2.43         | 2.31    | 2.23    |   |
| SD :             | 0.216        | 0.255   | 0.208   |   |
| MEAN % BRAIN :   | 775.5        | 712.3   | 680.0   |   |
| SD :             | 96.19        | 116.4   | 71.55   |   |
| <hr/>            |              |         |         |   |
| LUNGS            | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 10.36        | 11.06   | 11.40   |   |
| SD :             | 0.643        | 2.55    | 2.88    |   |
| MEAN % BODY :    | 0.32368      | 0.36994 | 0.37713 |   |
| SD :             | 0.013        | 0.076   | 0.100   |   |
| MEAN % BRAIN :   | 103.3        | 114.4   | 115.0   |   |
| SD :             | 6.27         | 28.87   | 30.64   |   |
| <hr/>            |              |         |         |   |
| PITUITARY GLAND  | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.02860      | 0.02800 | 0.02940 |   |
| SD :             | 0.003        | 0.009   | 0.005   |   |
| MEAN % BODY :    | 0.00089      | 0.00094 | 0.00097 |   |
| SD :             | 0.000        | 0.000   | 0.000   |   |
| MEAN % BRAIN :   | 0.28473      | 0.28619 | 0.29560 |   |
| SD :             | 0.030        | 0.082   | 0.041   |   |
| <hr/>            |              |         |         |   |

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DUNNETT'S TEST, DUNN'S TEST: No statistically significant weight differences noted between treated groups and controls.  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: K0  
 TREATMENT PERIOD  
 SEX: MALE

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| ORGAN              | DOSE GROUP:<br>NO. ANIMALS: | 1       | 2         | 3       |
|--------------------|-----------------------------|---------|-----------|---------|
|                    |                             | 5       | 5         | 5       |
| <hr/>              |                             |         |           |         |
| PROSTATE+SEMINALES | n:                          | 5       | 5         | 5       |
| MEAN WEIGHT (g):   |                             | 3.98    | 4.03      | 4.66    |
| SD :               |                             | 0.481   | 0.468     | 1.00    |
| MEAN % BODY :      |                             | 0.12438 | 0.13541   | 0.15340 |
| SD :               |                             | 0.014   | 0.018     | 0.029   |
| MEAN % BRAIN :     |                             | 39.68   | 41.49     | 46.92   |
| SD :               |                             | 4.88    | 5.16      | 9.79    |
| <hr/>              |                             |         |           |         |
| SPLEEN             | n:                          | 5       | 5         | 5       |
| MEAN WEIGHT (g):   |                             | 1.09    | 1.60#     | 1.37    |
| SD :               |                             | 0.165   | 0.270     | 0.335   |
| MEAN % BODY :      |                             | 0.03423 | 0.05358** | 0.04532 |
| SD :               |                             | 0.005   | 0.007     | 0.011   |
| MEAN % BRAIN :     |                             | 10.89   | 16.52#    | 13.86   |
| SD :               |                             | 1.55    | 2.84      | 3.53    |
| <hr/>              |                             |         |           |         |
| TESTES             | n:                          | 5       | 5         | 5       |
| MEAN WEIGHT (g):   |                             | 4.28    | 3.89      | 4.19    |
| SD :               |                             | 0.350   | 0.677     | 0.638   |
| MEAN % BODY :      |                             | 0.13388 | 0.13012   | 0.13859 |
| SD :               |                             | 0.011   | 0.019     | 0.023   |
| MEAN % BRAIN :     |                             | 42.63   | 40.01     | 42.20   |
| SD :               |                             | 2.69    | 6.74      | 6.47    |
| <hr/>              |                             |         |           |         |
| THYMUS             | n:                          | 5       | 5         | 5       |
| MEAN WEIGHT (g):   |                             | 5.32    | 5.22      | 4.45    |
| SD :               |                             | 0.660   | 1.20      | 0.762   |
| MEAN % BODY :      |                             | 0.16641 | 0.17482   | 0.14740 |
| SD :               |                             | 0.020   | 0.037     | 0.028   |
| MEAN % BRAIN :     |                             | 52.96   | 53.81     | 44.84   |
| SD :               |                             | 5.48    | 12.92     | 8.00    |
| <hr/>              |                             |         |           |         |

\*/\*\*):DUNNETT'S TEST BASED ON POOLED VARIANCES AT 5% (\*) OR 1% (\*\*) LEVEL

#/#):DUNN'S TEST AT 5% (#) OR 1% (##) LEVEL

Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
STATUS AT NECROPSY: K0  
TREATMENT PERIOD  
SEX: MALE

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| ORGAN            | DOSE GROUP:  | 1       | 2       | 3 |
|------------------|--------------|---------|---------|---|
|                  | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>            |              |         |         |   |
| THYROID GLANDS   | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.33380      | 0.28160 | 0.32640 |   |
| SD :             | 0.040        | 0.034   | 0.074   |   |
| MEAN % BODY :    | 0.01042      | 0.00945 | 0.01077 |   |
| SD :             | 0.001        | 0.001   | 0.002   |   |
| MEAN % BRAIN :   | 3.33         | 2.89    | 3.28    |   |
| SD :             | 0.395        | 0.287   | 0.736   |   |
| <hr/>            |              |         |         |   |

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DUNNETT'S TEST: No statistically significant weight differences noted  
between treated groups and controls.  
Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: K0  
 TREATMENT PERIOD  
 SEX: FEMALE

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| ORGAN             | DOSE GROUP:  | 1       | 2       | 3 |
|-------------------|--------------|---------|---------|---|
|                   | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>             |              |         |         |   |
| FINAL BODY WEIGHT | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 3328.0       | 3480.0  | 3208.0  |   |
| SD :              | 84.38        | 263.1   | 122.1   |   |
| <hr/>             |              |         |         |   |
| ADRENAL GLANDS    | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 0.16700      | 0.16360 | 0.16160 |   |
| SD :              | 0.051        | 0.020   | 0.019   |   |
| MEAN % BODY :     | 0.00503      | 0.00469 | 0.00504 |   |
| SD :              | 0.002        | 0.000   | 0.001   |   |
| MEAN % BRAIN :    | 1.74         | 1.64    | 1.70    |   |
| SD :              | 0.508        | 0.278   | 0.260   |   |
| <hr/>             |              |         |         |   |
| BRAIN             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 9.59         | 10.04   | 9.57    |   |
| SD :              | 0.322        | 0.684   | 0.685   |   |
| MEAN % BODY :     | 0.28824      | 0.29045 | 0.29849 |   |
| SD :              | 0.011        | 0.037   | 0.021   |   |
| <hr/>             |              |         |         |   |
| HEART             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 8.16         | 8.07    | 8.15    |   |
| SD :              | 0.510        | 0.954   | 0.662   |   |
| MEAN % BODY :     | 0.24511      | 0.23195 | 0.25402 |   |
| SD :              | 0.015        | 0.021   | 0.015   |   |
| MEAN % BRAIN :    | 85.22        | 80.58   | 85.34   |   |
| SD :              | 7.56         | 10.11   | 6.35    |   |
| <hr/>             |              |         |         |   |
| KIDNEYS           | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 15.68        | 16.14   | 14.31   |   |
| SD :              | 1.66         | 1.51    | 1.48    |   |
| MEAN % BODY :     | 0.47083      | 0.46675 | 0.44586 |   |
| SD :              | 0.044        | 0.065   | 0.040   |   |
| MEAN % BRAIN :    | 163.4        | 161.1   | 149.4   |   |
| SD :              | 14.89        | 16.35   | 10.55   |   |
| <hr/>             |              |         |         |   |

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DUNNETT'S TEST, DUNN'S TEST: No statistically significant weight differences noted between treated groups and controls.  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: K0  
 TREATMENT PERIOD  
 SEX: FEMALE

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| ORGAN            | DOSE GROUP:  | 1       | 2       | 3 |
|------------------|--------------|---------|---------|---|
|                  | NO. ANIMALS: | 5       | 5       | 5 |
| LIVER            | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 82.98        | 82.77   | 70.21#  |   |
| SD               | : 6.77       | 6.85    | 8.26    |   |
| MEAN % BODY      | : 2.49       | 2.38    | 2.18#   |   |
| SD               | : 0.168      | 0.130   | 0.192   |   |
| MEAN % BRAIN     | : 865.8      | 828.7   | 735.6   |   |
| SD               | : 70.60      | 103.8   | 92.53   |   |
| LUNGS            | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 10.66        | 11.09   | 10.41   |   |
| SD               | : 0.860      | 1.11    | 1.19    |   |
| MEAN % BODY      | : 0.31989    | 0.31948 | 0.32431 |   |
| SD               | : 0.020      | 0.036   | 0.031   |   |
| MEAN % BRAIN     | : 111.1      | 110.8   | 108.9   |   |
| SD               | : 8.11       | 12.64   | 10.62   |   |
| OVARIES          | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.28600      | 0.27240 | 0.38940 |   |
| SD               | : 0.071      | 0.047   | 0.209   |   |
| MEAN % BODY      | : 0.00858    | 0.00780 | 0.01220 |   |
| SD               | : 0.002      | 0.001   | 0.007   |   |
| MEAN % BRAIN     | : 2.97       | 2.74    | 4.17    |   |
| SD               | : 0.674      | 0.631   | 2.43    |   |
| PITUITARY GLAND  | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.03940      | 0.03640 | 0.03400 |   |
| SD               | : 0.006      | 0.007   | 0.006   |   |
| MEAN % BODY      | : 0.00118    | 0.00106 | 0.00107 |   |
| SD               | : 0.000      | 0.000   | 0.000   |   |
| MEAN % BRAIN     | : 0.41141    | 0.36107 | 0.35580 |   |
| SD               | : 0.062      | 0.052   | 0.060   |   |

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#/#/:DUNN'S TEST AT 5% (#) OR 1% (##) LEVEL  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: K0  
 TREATMENT PERIOD  
 SEX: FEMALE

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| ORGAN            | DOSE GROUP:  | 1         | 2       | 3 |
|------------------|--------------|-----------|---------|---|
|                  | NO. ANIMALS: | 5         | 5       | 5 |
| SPLEEN           | n:           | 5         | 5       | 5 |
| MEAN WEIGHT (g): | 1.53         | 2.50**    | 1.87    |   |
| SD :             | 0.446        | 0.450     | 0.146   |   |
| MEAN % BODY :    | 0.04588      | 0.07173** | 0.05823 |   |
| SD :             | 0.013        | 0.011     | 0.003   |   |
| MEAN % BRAIN :   | 15.91        | 24.93**   | 19.61   |   |
| SD :             | 4.36         | 4.45      | 2.01    |   |
| THYMUS           | n:           | 5         | 5       | 5 |
| MEAN WEIGHT (g): | 3.94         | 4.18      | 3.90    |   |
| SD :             | 0.618        | 0.354     | 0.828   |   |
| MEAN % BODY :    | 0.11866      | 0.12087   | 0.12149 |   |
| SD :             | 0.021        | 0.016     | 0.025   |   |
| MEAN % BRAIN :   | 41.18        | 41.63     | 40.70   |   |
| SD :             | 7.20         | 2.00      | 8.20    |   |
| THYROID GLANDS   | n:           | 5         | 5       | 5 |
| MEAN WEIGHT (g): | 0.32580      | 0.36700   | 0.35140 |   |
| SD :             | 0.067        | 0.070     | 0.063   |   |
| MEAN % BODY :    | 0.00982      | 0.01061   | 0.01098 |   |
| SD :             | 0.002        | 0.002     | 0.002   |   |
| MEAN % BRAIN :   | 3.39         | 3.68      | 3.71    |   |
| SD :             | 0.614        | 0.822     | 0.866   |   |
| UTERUS           | n:           | 5         | 5       | 5 |
| MEAN WEIGHT (g): | 7.58         | 8.40      | 7.68    |   |
| SD :             | 1.16         | 2.16      | 2.04    |   |
| MEAN % BODY :    | 0.22826      | 0.24071   | 0.24001 |   |
| SD :             | 0.038        | 0.057     | 0.068   |   |
| MEAN % BRAIN :   | 78.91        | 83.60     | 81.73   |   |
| SD :             | 10.33        | 20.57     | 27.05   |   |

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\*/\*\*):DUNNETT'S TEST BASED ON POOLED VARIANCES AT 5% (\*) OR 1% (\*\*) LEVEL  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: R1  
 TREATMENT-FREE PERIOD  
 SEX: MALE

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| ORGAN             | DOSE GROUP:  | 1       | 2       | 3 |
|-------------------|--------------|---------|---------|---|
|                   | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>             |              |         |         |   |
| FINAL BODY WEIGHT | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 3572.0       | 3464.0  | 3492.0  |   |
| SD :              | 223.4        | 168.8   | 213.4   |   |
| <hr/>             |              |         |         |   |
| ADRENAL GLANDS    | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 0.26020      | 0.19800 | 0.24880 |   |
| SD :              | 0.052        | 0.040   | 0.050   |   |
| MEAN % BODY :     | 0.00738      | 0.00574 | 0.00710 |   |
| SD :              | 0.002        | 0.001   | 0.001   |   |
| MEAN % BRAIN :    | 2.55         | 1.93    | 2.44    |   |
| SD :              | 0.499        | 0.346   | 0.584   |   |
| <hr/>             |              |         |         |   |
| BRAIN             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 10.24        | 10.23   | 10.28   |   |
| SD :              | 0.703        | 0.443   | 0.889   |   |
| MEAN % BODY :     | 0.28803      | 0.29562 | 0.29517 |   |
| SD :              | 0.032        | 0.016   | 0.030   |   |
| <hr/>             |              |         |         |   |
| EPIDIDYMIDES      | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 2.29         | 2.62    | 2.47    |   |
| SD :              | 0.328        | 0.427   | 0.233   |   |
| MEAN % BODY :     | 0.06414      | 0.07562 | 0.07062 |   |
| SD :              | 0.008        | 0.011   | 0.003   |   |
| MEAN % BRAIN :    | 22.49        | 25.66   | 24.16   |   |
| SD :              | 3.78         | 3.96    | 3.05    |   |
| <hr/>             |              |         |         |   |
| HEART             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 8.23         | 9.47    | 8.24    |   |
| SD :              | 0.728        | 3.21    | 0.582   |   |
| MEAN % BODY :     | 0.23017      | 0.27168 | 0.23668 |   |
| SD :              | 0.009        | 0.083   | 0.021   |   |
| MEAN % BRAIN :    | 80.70        | 92.04   | 80.31   |   |
| SD :              | 9.27         | 27.96   | 3.30    |   |
| <hr/>             |              |         |         |   |

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DUNNETT'S TEST, DUNN'S TEST: No statistically significant weight differences noted between treated groups and controls.  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: R1  
 TREATMENT-FREE PERIOD  
 SEX: MALE

| ORGAN            | DOSE GROUP:  | 1       | 2       | 3 |
|------------------|--------------|---------|---------|---|
|                  | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>            |              |         |         |   |
| KIDNEYS          | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 16.97        | 16.08   | 16.42   |   |
| SD :             | 1.18         | 1.38    | 1.80    |   |
| MEAN % BODY :    | 0.47512      | 0.46412 | 0.46936 |   |
| SD :             | 0.016        | 0.032   | 0.030   |   |
| MEAN % BRAIN :   | 166.5        | 157.0   | 160.5   |   |
| SD :             | 17.95        | 7.87    | 20.45   |   |
| <hr/>            |              |         |         |   |
| LIVER            | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 70.63        | 78.17   | 72.66   |   |
| SD :             | 9.49         | 14.68   | 9.55    |   |
| MEAN % BODY :    | 1.98         | 2.25    | 2.08    |   |
| SD :             | 0.203        | 0.322   | 0.205   |   |
| MEAN % BRAIN :   | 694.0        | 763.9   | 714.2   |   |
| SD :             | 116.0        | 133.8   | 135.0   |   |
| <hr/>            |              |         |         |   |
| LUNGS            | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 10.53        | 11.72   | 11.20   |   |
| SD :             | 0.434        | 2.83    | 0.920   |   |
| MEAN % BODY :    | 0.29558      | 0.33706 | 0.32063 |   |
| SD :             | 0.020        | 0.071   | 0.015   |   |
| MEAN % BRAIN :   | 103.3        | 114.1   | 109.6   |   |
| SD :             | 9.51         | 23.62   | 12.78   |   |
| <hr/>            |              |         |         |   |
| PITUITARY GLAND  | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.02780      | 0.02100 | 0.02620 |   |
| SD :             | 0.006        | 0.008   | 0.004   |   |
| MEAN % BODY :    | 0.00078      | 0.00060 | 0.00075 |   |
| SD :             | 0.000        | 0.000   | 0.000   |   |
| MEAN % BRAIN :   | 0.27025      | 0.20411 | 0.25422 |   |
| SD :             | 0.050        | 0.071   | 0.030   |   |
| <hr/>            |              |         |         |   |

DUNNETT'S TEST, DUNN'S TEST: No statistically significant weight differences noted between treated groups and controls.  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: R1  
 TREATMENT-FREE PERIOD  
 SEX: MALE

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| ORGAN              | DOSE GROUP:  | 1       | 2       | 3 |
|--------------------|--------------|---------|---------|---|
|                    | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>              |              |         |         |   |
| PROSTATE+SEMINALES | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):   | 4.48         | 3.62    | 4.61    |   |
| SD :               | 0.811        | 0.465   | 1.24    |   |
| MEAN % BODY :      | 0.12630      | 0.10449 | 0.13261 |   |
| SD :               | 0.029        | 0.013   | 0.036   |   |
| MEAN % BRAIN :     | 43.59        | 35.50   | 44.63   |   |
| SD :               | 6.25         | 5.49    | 9.60    |   |
| <hr/>              |              |         |         |   |
| SPLEEN             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):   | 1.04         | 1.44    | 1.32    |   |
| SD :               | 0.234        | 0.376   | 0.108   |   |
| MEAN % BODY :      | 0.02928      | 0.04159 | 0.03783 |   |
| SD :               | 0.006        | 0.011   | 0.004   |   |
| MEAN % BRAIN :     | 10.30        | 14.17   | 12.85   |   |
| SD :               | 2.69         | 4.08    | 1.25    |   |
| <hr/>              |              |         |         |   |
| TESTES             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):   | 5.27         | 4.00    | 4.95    |   |
| SD :               | 0.932        | 1.64    | 0.632   |   |
| MEAN % BODY :      | 0.14831      | 0.11445 | 0.14179 |   |
| SD :               | 0.029        | 0.046   | 0.016   |   |
| MEAN % BRAIN :     | 51.21        | 38.75   | 48.39   |   |
| SD :               | 6.29         | 15.50   | 6.76    |   |
| <hr/>              |              |         |         |   |
| THYMUS             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):   | 4.39         | 4.75    | 5.68    |   |
| SD :               | 1.02         | 0.848   | 1.21    |   |
| MEAN % BODY :      | 0.12221      | 0.13707 | 0.16194 |   |
| SD :               | 0.023        | 0.024   | 0.028   |   |
| MEAN % BRAIN :     | 43.19        | 46.49   | 55.36   |   |
| SD :               | 11.71        | 8.46    | 12.03   |   |
| <hr/>              |              |         |         |   |

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 DUNNETT'S TEST, DUNN'S TEST: No statistically significant weight differences noted between treated groups and controls.  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
STATUS AT NECROPSY: R1  
TREATMENT-FREE PERIOD  
SEX: MALE

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| ORGAN            | DOSE GROUP:  | 1       | 2       | 3 |
|------------------|--------------|---------|---------|---|
|                  | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>            |              |         |         |   |
| THYROID GLANDS   | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.24640      | 0.24780 | 0.28140 |   |
| SD :             | 0.028        | 0.078   | 0.059   |   |
| MEAN % BODY :    | 0.00690      | 0.00718 | 0.00801 |   |
| SD :             | 0.001        | 0.002   | 0.001   |   |
| MEAN % BRAIN :   | 2.41         | 2.44    | 2.74    |   |
| SD :             | 0.321        | 0.787   | 0.553   |   |
| <hr/>            |              |         |         |   |

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DUNNETT'S TEST: No statistically significant weight differences noted  
between treated groups and controls.  
Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: R1  
 TREATMENT-FREE PERIOD  
 SEX: FEMALE

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| ORGAN             | DOSE GROUP:  | 1       | 2       | 3 |
|-------------------|--------------|---------|---------|---|
|                   | NO. ANIMALS: | 5       | 5       | 5 |
| <hr/>             |              |         |         |   |
| FINAL BODY WEIGHT | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 4016.0       | 3940.0  | 3912.0  |   |
| SD :              | 168.8        | 312.4   | 158.5   |   |
| <hr/>             |              |         |         |   |
| ADRENAL GLANDS    | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 0.21620      | 0.18580 | 0.19560 |   |
| SD :              | 0.023        | 0.018   | 0.037   |   |
| MEAN % BODY :     | 0.00537      | 0.00472 | 0.00499 |   |
| SD :              | 0.000        | 0.000   | 0.001   |   |
| MEAN % BRAIN :    | 2.08         | 1.82    | 1.90    |   |
| SD :              | 0.211        | 0.221   | 0.368   |   |
| <hr/>             |              |         |         |   |
| BRAIN             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 10.40        | 10.26   | 10.29   |   |
| SD :              | 0.519        | 0.430   | 0.411   |   |
| MEAN % BODY :     | 0.25910      | 0.26175 | 0.26322 |   |
| SD :              | 0.013        | 0.022   | 0.008   |   |
| <hr/>             |              |         |         |   |
| HEART             | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 9.00         | 8.74    | 9.15    |   |
| SD :              | 0.379        | 0.669   | 1.20    |   |
| MEAN % BODY :     | 0.22402      | 0.22287 | 0.23418 |   |
| SD :              | 0.004        | 0.024   | 0.031   |   |
| MEAN % BRAIN :    | 86.65        | 85.15   | 88.85   |   |
| SD :              | 4.77         | 6.01    | 10.40   |   |
| <hr/>             |              |         |         |   |
| KIDNEYS           | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g):  | 17.51        | 17.61   | 16.28   |   |
| SD :              | 1.66         | 1.44    | 1.34    |   |
| MEAN % BODY :     | 0.43621      | 0.44746 | 0.41583 |   |
| SD :              | 0.040        | 0.024   | 0.026   |   |
| MEAN % BRAIN :    | 168.3        | 172.0   | 157.9   |   |
| SD :              | 12.34        | 17.30   | 7.25    |   |
| <hr/>             |              |         |         |   |

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DUNNETT'S TEST, DUNN'S TEST: No statistically significant weight differences noted between treated groups and controls.  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: R1  
 TREATMENT-FREE PERIOD  
 SEX: FEMALE

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| ORGAN            | DOSE GROUP:  | 1       | 2       | 3 |
|------------------|--------------|---------|---------|---|
|                  | NO. ANIMALS: | 5       | 5       | 5 |
| LIVER            | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 82.27        | 78.27   | 81.76   |   |
| SD :             | 7.35         | 9.23    | 8.48    |   |
| MEAN % BODY :    | 2.05         | 1.98    | 2.09    |   |
| SD :             | 0.174        | 0.085   | 0.202   |   |
| MEAN % BRAIN :   | 790.9        | 763.2   | 793.8   |   |
| SD :             | 53.06        | 92.45   | 67.82   |   |
| LUNGS            | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 10.89        | 11.35   | 10.59   |   |
| SD :             | 1.14         | 1.21    | 0.259   |   |
| MEAN % BODY :    | 0.27106      | 0.28946 | 0.27082 |   |
| SD :             | 0.023        | 0.038   | 0.007   |   |
| MEAN % BRAIN :   | 105.1        | 110.4   | 102.9   |   |
| SD :             | 13.43        | 7.35    | 2.63    |   |
| OVARIES          | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.41100      | 0.43120 | 0.39740 |   |
| SD :             | 0.086        | 0.175   | 0.171   |   |
| MEAN % BODY :    | 0.01027      | 0.01083 | 0.01026 |   |
| SD :             | 0.002        | 0.004   | 0.005   |   |
| MEAN % BRAIN :   | 3.96         | 4.18    | 3.87    |   |
| SD :             | 0.836        | 1.66    | 1.71    |   |
| PITUITARY GLAND  | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.03520      | 0.03500 | 0.04300 |   |
| SD :             | 0.002        | 0.007   | 0.009   |   |
| MEAN % BODY :    | 0.00088      | 0.00089 | 0.00110 |   |
| SD :             | 0.000        | 0.000   | 0.000   |   |
| MEAN % BRAIN :   | 0.33864      | 0.34162 | 0.41768 |   |
| SD :             | 0.016        | 0.073   | 0.085   |   |

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DUNNETT'S TEST, DUNN'S TEST: No statistically significant weight differences noted between treated groups and controls.  
 Assigned control group(s) : 1.

Table: (continued)

SUMMARY TABLE OF BODY/ORGAN WEIGHTS AND STATISTICS  
 STATUS AT NECROPSY: R1  
 TREATMENT-FREE PERIOD  
 SEX: FEMALE

---

| ORGAN            | DOSE GROUP:  | 1       | 2       | 3 |
|------------------|--------------|---------|---------|---|
|                  | NO. ANIMALS: | 5       | 5       | 5 |
| SPLEEN           | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 1.96         | 1.93    | 1.90    |   |
| SD :             | 0.372        | 0.389   | 0.395   |   |
| MEAN % BODY :    | 0.04898      | 0.04891 | 0.04862 |   |
| SD :             | 0.010        | 0.009   | 0.010   |   |
| MEAN % BRAIN :   | 18.84        | 18.76   | 18.44   |   |
| SD :             | 3.41         | 3.49    | 3.38    |   |
| THYMUS           | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 4.30         | 3.98    | 3.94    |   |
| SD :             | 0.950        | 0.865   | 0.542   |   |
| MEAN % BODY :    | 0.10664      | 0.10143 | 0.10036 |   |
| SD :             | 0.020        | 0.023   | 0.011   |   |
| MEAN % BRAIN :   | 41.43        | 39.06   | 38.22   |   |
| SD :             | 9.18         | 9.57    | 4.83    |   |
| THYROID GLANDS   | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 0.43040      | 0.37560 | 0.37300 |   |
| SD :             | 0.182        | 0.040   | 0.091   |   |
| MEAN % BODY :    | 0.01063      | 0.00952 | 0.00954 |   |
| SD :             | 0.004        | 0.000   | 0.002   |   |
| MEAN % BRAIN :   | 4.16         | 3.67    | 3.62    |   |
| SD :             | 1.79         | 0.436   | 0.878   |   |
| UTERUS           | n:           | 5       | 5       | 5 |
| MEAN WEIGHT (g): | 10.22        | 8.65    | 9.07    |   |
| SD :             | 1.94         | 2.20    | 1.35    |   |
| MEAN % BODY :    | 0.25470      | 0.22110 | 0.23309 |   |
| SD :             | 0.047        | 0.062   | 0.043   |   |
| MEAN % BRAIN :   | 98.59        | 84.18   | 88.49   |   |
| SD :             | 19.46        | 20.13   | 15.33   |   |

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DUNNETT'S TEST, DUNN'S TEST: No statistically significant weight differences noted between treated groups and controls.  
 Assigned control group(s) : 1.

Table 2. Number of animals with necropsy findings by organ/group/sex

Table: 2

| NUMBER OF ANIMALS WITH NECROPSY FINDINGS BY ORGAN/GROUP/SEX |                            |        |        |        |
|---|----------------------------|--------|--------|--------|
| STATUS AT NECROPSY: KO                                      |                            |        |        |        |
| TREATMENT PERIOD  |                            |        |        |        |
| ORGAN/FINDING   | DOSE GROUP:<br>ANIM.EXAM.: | 1<br>5 | 2<br>5 | 3<br>5 |
| ILIAC L.N. LEFT   | :                          |        |        |        |
| - Enlarged  | :                          | 2      | -      | -      |
| INGUINAL L.N. RIGHT   | :                          |        |        |        |
| - Enlarged  | :                          | -      | -      | 3      |
| INJECTION SITE 1  | :                          |        |        |        |
| - Red discoloration   | :                          | 2      | 3      | 3      |
| INJECTION SITE 2  | :                          |        |        |        |
| - Red discoloration   | :                          | 2      | -      | 3      |
| INJECTION SITE 3  | :                          |        |        |        |
| - Red discoloration   | :                          | 1      | 2      | 3      |
| LUNGS   | :                          |        |        |        |
| - Enlarged  | :                          | -      | 1      | 1      |
| - Red discoloration   | :                          | -      | 1      | -      |
| MANDIBUL. LYMPH NODE  | :                          |        |        |        |
| - Enlarged  | :                          | -      | -      | 1      |
| SACRAL LYMPH NODE   | :                          |        |        |        |
| - Enlarged  | :                          | 1      | -      | -      |
| SKIN  | :                          |        |        |        |
| - White discoloration                                       | :                          | 2      | -      | 1      |
| SKIN SITE 3   | :                          |        |        |        |
| - Red discoloration   | :                          | -      | -      | 1      |
| TESTES  | :                          |        |        |        |
| - Cryptorchidism  | :                          | -      | 1      | -      |
| - Reduced in size   | :                          | -      | 1      | -      |

Table: (continued)

| NUMBER OF ANIMALS WITH NECROPSY FINDINGS BY ORGAN/GROUP/SEX |             |       |       |
|---|-------------|-------|-------|
| STATUS AT NECROPSY: K0                                      |             |       |       |
| TREATMENT PERIOD  |             |       |       |
| -----   |             |       |       |
| ORGAN/FINDING   | DOSE GROUP: | 1     | 2     |
|   | ANIM.EXAM.: | 5     | 5     |
| ADIPOSE TISSUE  | :           |       |       |
| - Gelatinous  | :           | -     | 4     |
| ADRENAL GLANDS  | :           |       |       |
| - Agenesis  | :           | 1     | -     |
| INJECTION SITE 1  | :           |       |       |
| - Red discoloration   | :           | -     | 1     |
| INJECTION SITE 2  | :           |       |       |
| - Red discoloration   | :           | -     | 1     |
| INJECTION SITE 3  | :           |       |       |
| - Red discoloration   | :           | 2     | 2     |
| OVIDUCTS  | :           |       |       |
| - Cyst, translucent content                                 | :           | 1     | -     |
| SKIN SITE 3   | :           |       |       |
| - Red discoloration   | :           | -     | 1     |
| .....   | .....       | ..... | ..... |

Table: (continued)

NUMBER OF ANIMALS WITH NECROPSY FINDINGS BY ORGAN/GROUP/SEX  
STATUS AT NECROPSY: R1  
TREATMENT-FREE PERIOD

| ORGAN/FINDING       |             | DOSE GROUP: |   |   | MALE |
|---------------------|-------------|-------------|---|---|------|
|                     |             | 1           | 2 | 3 |      |
|                     | ANIM.EXAM.: | 5           | 5 | 5 |      |
| INJECTION SITE 1    | :           |             |   |   |      |
| - Red discoloration | :           | -           | - | 1 |      |
| LUNGS               | :           |             |   |   |      |
| - Red discoloration | :           | -           | 1 | - |      |
| SKIN SITE 3         | :           |             |   |   |      |
| - Red discoloration | :           | 1           | - | - |      |
| TESTES              | :           |             |   |   |      |
| - Reduced in size   | :           | 1           | 1 | - |      |

Table: (continued)

NUMBER OF ANIMALS WITH NECROPSY FINDINGS BY ORGAN/GROUP/SEX  
STATUS AT NECROPSY: R1 FEMALE  
TREATMENT-FREE PERIOD

---

| ORGAN/FINDING         | DOSE GROUP:<br>ANIM.EXAM.: | 1 | 2 | 3 |
|-----------------------|----------------------------|---|---|---|
| ILIAC L.N. RIGHT      | :                          |   |   |   |
| - Red discoloration   | :                          | - | - | 1 |
| INJECTION SITE 3      | :                          |   |   |   |
| - Red discoloration   | :                          | 1 | - | - |
| SKELETAL MUSCLE       | :                          |   |   |   |
| - Red discoloration   | :                          | - | - | 1 |
| SKIN                  | :                          |   |   |   |
| - Scab                | :                          | - | - | 1 |
| - White discoloration | :                          | - | - | 1 |
| THYROID GLANDS        | :                          |   |   |   |
| - Enlarged            | :                          | 1 | - | - |

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Table 3. Number of animals with microscopic findings by organ/group/sex

34/229

616/813

Table: 3

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0

Main sacrifice

| SEX                     | : | MALE |   |   |
|-------------------------|---|------|---|---|
| DOSE GROUP:             |   | 1    | 2 | 3 |
| NO. ANIMALS:            |   | 5    | 5 | 5 |
| ADRENAL GLANDS          | : | 5    | 5 | 5 |
| - Accessory tissue      | : | 1    | 1 | 2 |
| AORTA                   | : | 5    | 5 | 5 |
| BONE MARROW             | : | 5    | 5 | 5 |
| BRAIN                   | : | 5    | 5 | 5 |
| - Vacuol;choroid plex.: |   | 2    | 1 | 1 |
| Grade 1:                |   | 1    | 1 | 1 |
| Grade 2:                |   | 1    | - | - |
| CECUM                   | : | 5    | 5 | 5 |
| COLON                   | : | 5    | 5 | 5 |
| DIAPHRAGM               | : | 5    | 5 | 5 |
| DUODENUM                | : | 5    | 5 | 5 |
| - Dilat;Brunner's gl    | : | -    | 1 | - |
| Grade 2:                |   | -    | 1 | - |
| EPIDIDYMIDES            | : | 5    | 5 | 5 |
| - Cell debris           | : | 1    | - | 1 |
| Grade 2:                |   | 1    | - | - |
| Grade 3:                |   | -    | - | 1 |
| - Dilatation            | : | -    | 1 | - |
| Grade 2:                |   | -    | 1 | - |
| ESOPHAGUS               | : | 5    | 5 | 5 |
| EYE, LEFT               | : | 5    | 5 | 5 |
| EYE, RIGHT              | : | 5    | 5 | 5 |
| FEMUR                   | : | 5    | 5 | 5 |
| G.A.L.T.                | : | 4    | 5 | 4 |
| - Hyperplasia;lymphoid: |   | 4    | 5 | 4 |
| Grade 1:                |   | 3    | 5 | 3 |
| Grade 2:                |   | 1    | - | 1 |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | MALE |
|-------------------------|---|---|---|------|
| NO. ANIMALS:            | 5 | 5 | 5 |      |
| GALL BLADDER :          | 5 | 5 | 5 |      |
| HARDERIAN GLANDS :      | 5 | 5 | 5 |      |
| - Degen;epithelium :    | - | - | 2 |      |
| Grade 1:                | - | - | 1 |      |
| Grade 2:                | - | - | 1 |      |
| - Infilt;mononuclear :  | 1 | - | - |      |
| Grade 1:                | 1 | - | - |      |
| HEART :                 | 5 | 5 | 5 |      |
| - Infilt;mononuc;myoc : | - | 1 | 1 |      |
| Grade 1:                | - | 1 | 1 |      |
| ILEUM :                 | 5 | 5 | 5 |      |
| ILIAC L.N. LEFT :       | 5 | 4 | 5 |      |
| - Hemorrhage;sinus :    | 2 | 1 | - |      |
| Grade 1:                | - | 1 | - |      |
| Grade 2:                | 2 | - | - |      |
| - Hyperplasia;lymphoid: | - | 2 | 4 |      |
| Grade 1:                | - | 2 | 4 |      |
| - Infilt;granulocyte :  | - | - | 1 |      |
| Grade 1:                | - | - | 1 |      |
| ILIAC L.N. RIGHT :      | 5 | 5 | 4 |      |
| - Hemorrhage;sinus :    | 1 | 4 | 1 |      |
| Grade 1:                | 1 | 4 | 1 |      |
| - Hyperplasia;lymphoid: | - | 4 | 2 |      |
| Grade 1:                | - | 3 | 2 |      |
| Grade 2:                | - | 1 | - |      |
| - Infilt;granulocyte :  | - | 1 | 1 |      |
| Grade 1:                | - | 1 | 1 |      |
| INGUINAL L.N. LEFT :    | 5 | 5 | 5 |      |
| - Hyperplasia;lymphoid: | - | 5 | 5 |      |
| Grade 1:                | - | 5 | 5 |      |
| Grade 2:                | - | - | - |      |
| - Infilt;granulocyte :  | 1 | 3 | 4 |      |
| Grade 1:                | 1 | 3 | 4 |      |
| Grade 2:                | - | - | - |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX :                    | MALE |   |   |
|--------------------------|------|---|---|
| DOSE GROUP:              | 1    | 2 | 3 |
| NO. ANIMALS:             | 5    | 5 | 5 |
| <hr/>                    |      |   |   |
| INGUINAL L.N. RIGHT :    | 5    | 5 | 5 |
| - Hyperplasia; lymphoid: | -    | 3 | 4 |
| Grade 1:                 | -    | 3 | 3 |
| Grade 2:                 | -    | - | 1 |
| - Infilt; granulocyte :  | 1    | 2 | 2 |
| Grade 1:                 | 1    | 2 | 2 |
| <hr/>                    |      |   |   |
| INJECTION SITE 1 :       | 5    | 5 | 5 |
| - Inflamm; subacute :    | -    | 5 | 4 |
| Grade 1:                 | -    | 2 | 2 |
| Grade 2:                 | -    | 2 | 2 |
| Grade 3:                 | -    | 1 | - |
| - Hemorrhage :           | 2    | 3 | 4 |
| Grade 1:                 | 1    | 1 | 3 |
| Grade 2:                 | 1    | 2 | 1 |
| - Necrosis; muscle :     | -    | 1 | - |
| Grade 1:                 | -    | 1 | - |
| <hr/>                    |      |   |   |
| INJECTION SITE 2 :       | 5    | 5 | 5 |
| - Inflamm; subacute :    | -    | 4 | 3 |
| Grade 1:                 | -    | 3 | 2 |
| Grade 2:                 | -    | 1 | 1 |
| - Degen/regen; muscle :  | -    | 1 | - |
| Grade 1:                 | -    | 1 | - |
| - Hemorrhage :           | 2    | 1 | 4 |
| Grade 1:                 | 2    | 1 | 2 |
| Grade 2:                 | -    | - | 2 |
| - Needle tract lesion :  | -    | - | 1 |
| <hr/>                    |      |   |   |
| INJECTION SITE 3 :       | 5    | 5 | 5 |
| - Inflamm; subacute :    | 1    | 4 | 5 |
| Grade 1:                 | 1    | - | - |
| Grade 2:                 | -    | 3 | 5 |
| Grade 3:                 | -    | 1 | - |
| - Hemorrhage :           | 1    | 4 | 5 |
| Grade 1:                 | -    | 1 | 4 |
| Grade 2:                 | 1    | 3 | 1 |
| - Infilt; macrophage :   | 2    | - | - |
| Grade 1:                 | 2    | - | - |
| - Necrosis; muscle :     | 2    | 2 | 1 |
| Grade 1:                 | 2    | 1 | - |
| Grade 2:                 | -    | 1 | 1 |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | MALE |
|-------------------------|---|---|---|------|
| NO. ANIMALS:            | 5 | 5 | 5 |      |
| JEJUNUM :               | 5 | 5 | 5 |      |
| JOINTS :                | 5 | 5 | 5 |      |
| KIDNEYS :               | 5 | 5 | 5 |      |
| - Basophilia;tubule :   | 2 | 2 | 2 |      |
| Grade 1:                | 2 | 2 | 2 |      |
| Grade 2:                | - | - | - |      |
| - Dilatation;tubule :   | 1 | - | 1 |      |
| Grade 1:                | 1 | - | 1 |      |
| - Mineral;cortex :      | 2 | 3 | 3 |      |
| Grade 1:                | 2 | 3 | 3 |      |
| Grade 2:                | - | - | - |      |
| LACRIMAL GLANDS :       | 5 | 5 | 5 |      |
| - Infilt;lymphocyte :   | 3 | 2 | - |      |
| Grade 1:                | 3 | 2 | - |      |
| LARYNX :                | 5 | 5 | 5 |      |
| - Infilt;mixed;subepit: | - | 1 | - |      |
| Grade 1:                | - | 1 | - |      |
| LIVER :                 | 5 | 5 | 5 |      |
| - Hypertrophy;focal :   | - | 1 | - |      |
| Grade 1:                | - | 1 | - |      |
| - Infilt;mixed;focal :  | 2 | 3 | 2 |      |
| Grade 1:                | 2 | 3 | 2 |      |
| LUNGS :                 | 5 | 5 | 5 |      |
| - Hemorrhage;agonal :   | - | 2 | - |      |
| Grade 1:                | - | 1 | - |      |
| Grade 2:                | - | 1 | - |      |
| - Infilt;macro;alveol : | 4 | 5 | 5 |      |
| Grade 1:                | 4 | 4 | 3 |      |
| Grade 2:                | - | 1 | 2 |      |
| - Inflamm;chron;bronch: | - | - | 1 |      |
| Grade 2:                | - | - | 1 |      |
| - Metaplasia;osseous :  | - | - | 1 |      |
| MAMMARY GLANDS AREA :   | 5 | 5 | 5 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS: | 1 | 2 | 3 | MALE |
|--------------------------------------|---|---|---|------|
| MANDIBUL. LYMPH NODE :               | 5 | 5 | 5 |      |
| - Dilatation; sinusoid:              | 1 | 1 | 1 |      |
| Grade 1:                             | 1 | 1 | 1 |      |
| Grade 2:                             | - | - | - |      |
| - Hemorrhage; sinus :                | 2 | - | - |      |
| Grade 1:                             | 2 | - | - |      |
| - Infilt;granulocyte :               | 1 | - | 1 |      |
| Grade 1:                             | 1 | - | 1 |      |
| - Infilt;macrophage :                | 1 | - | 1 |      |
| Grade 1:                             | - | - | 1 |      |
| Grade 3:                             | 1 | - | - |      |
| MANDIBULAR GLANDS :                  | 5 | 5 | 5 |      |
| MESENT. LYMPH NODE :                 | 5 | 5 | 5 |      |
| - Hemorrhage;sinus :                 | - | 1 | - |      |
| Grade 1:                             | - | 1 | - |      |
| - Hyperplasia;lymphoid:              | 4 | 4 | 3 |      |
| Grade 1:                             | 3 | 3 | 2 |      |
| Grade 2:                             | 1 | 1 | 1 |      |
| NASAL CAVITY, ANT.L1 :               | 5 | 5 | 5 |      |
| - Artifact;blood lumen:              | - | - | 1 |      |
| NASAL CAVITY, L2 :                   | 5 | 5 | 5 |      |
| - Artifact;blood lumen:              | 1 | - | 1 |      |
| NASAL CAVITY, L3 :                   | 5 | 5 | 5 |      |
| - Artifact;blood lumen:              | 3 | 2 | 1 |      |
| NASAL CAVITY, POS.L4 :               | 5 | 5 | 5 |      |
| - Artifact;blood lumen:              | 2 | 2 | 2 |      |
| OPTIC NERVE, LEFT :                  | 5 | 5 | 5 |      |
| OPTIC NERVE, RIGHT :                 | 5 | 5 | 5 |      |
| PANCREAS :                           | 5 | 5 | 5 |      |
| - Ectopic tiss;spleen :              | 1 | - | - |      |
| PARATHYROID GLANDS :                 | 5 | 4 | 4 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0

Main sacrifice

| SEX                      | : | MALE |   |   |
|--------------------------|---|------|---|---|
| DOSE GROUP:              | 1 | 2    | 3 |   |
| NO. ANIMALS:             | 5 | 5    | 5 |   |
| PAROTID GLANDS           | : | 5    | 5 | 5 |
| PITUITARY GLAND          | : | 5    | 5 | 5 |
| PROSTATE                 | : | 4    | 5 | 5 |
| RECTUM                   | : | 5    | 5 | 5 |
| SACRAL LYMPH NODE        | : | 4    | 3 | 4 |
| - Hemorrhage; sinus      | : | 1    | - | - |
| Grade 1:                 | - | -    | - |   |
| Grade 3:                 | 1 | -    | - |   |
| - Hyperplasia; lymphoid: | - | -    | 1 |   |
| Grade 1:                 | - | -    | 1 |   |
| SCIATIC NERVE            | : | 5    | 5 | 5 |
| SEMINAL VESICLES         | : | 5    | 5 | 5 |
| SKELETAL MUSCLE          | : | 5    | 5 | 5 |
| SKIN                     | : | 5    | 5 | 5 |
| - Crust                  | : | 2    | - | - |
| Grade 1:                 | 2 | -    | - |   |
| - Inflamm; chronic       | : | 1    | - | - |
| Grade 1:                 | 1 | -    | - |   |
| - Inflamm; panniculus    | : | -    | - | 1 |
| Grade 1:                 | - | -    | 1 |   |
| SKIN SITE 1              | : | 5    | 5 | 5 |
| - Infilt; mixed; subcut  | : | -    | 2 | 1 |
| Grade 1:                 | - | 2    | - |   |
| Grade 2:                 | - | -    | 1 |   |
| - Needle tract lesion    | : | -    | 1 | - |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS:                             | 1 | 2 | 3 | MALE |
|--|---|---|---|------|
| SKIN SITE 2 :<br>- Infilt;mixed;subcut :<br>Grade 1:<br>Grade 2: | 5 | 5 | 5 |      |
| - Inflamm;panniculus :<br>Grade 1:                               | - | - | 1 |      |
| SKIN SITE 3 :<br>- Hemorrhage;subcutis :<br>Grade 1:<br>Grade 2: | 5 | 5 | 5 |      |
| - Infilt;mixed;subcut :<br>Grade 1:<br>Grade 2:                  | - | 1 | 2 |      |
| - Inflamm;panniculus :<br>Grade 1:                               | - | - | 1 |      |
| SPINAL CORD :<br>-   | 5 | 5 | 5 |      |
| SPLEEN :<br>- Hyperplasia;lymphoid:<br>Grade 1:<br>Grade 2:      | 5 | 5 | 5 |      |
| -  | - | 3 | 3 |      |
| STERNUM :<br>-   | 5 | 5 | 5 |      |
| STOMACH :<br>- Mineralization;gland:<br>Grade 1:                 | 5 | 5 | 5 |      |
| -  | - | 1 | - |      |
| SUBLINGUAL GLANDS :<br>-   | 5 | 5 | 5 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | MALE |
|-------------------------|---|---|---|------|
| NO. ANIMALS:            | 5 | 5 | 5 |      |
| TESTES :                | 5 | 5 | 5 |      |
| - Atrophy;tubule :      | 2 | 3 | 5 |      |
| Grade 1:                | 1 | 1 | 3 |      |
| Grade 2:                | 1 | 2 | 1 |      |
| Grade 3:                | - | - | 1 |      |
| - Hypoplasia :          | - | 1 | - |      |
| Grade 4:                | - | 1 | - |      |
| - Multinuc giant cell : | 2 | 5 | 5 |      |
| Grade 1:                | 1 | 4 | 1 |      |
| Grade 2:                | 1 | 1 | 3 |      |
| Grade 3:                | - | - | 1 |      |
| THYMUS :                | 5 | 5 | 5 |      |
| - Hemorrhage;agonal :   | 3 | 2 | 3 |      |
| Grade 1:                | 3 | 2 | 3 |      |
| THYROID GLANDS :        | 5 | 5 | 5 |      |
| TONGUE :                | 5 | 5 | 5 |      |
| TRACHEA :               | 5 | 5 | 5 |      |
| URETERS :               | 5 | 5 | 5 |      |
| URINARY BLADDER :       | 5 | 5 | 5 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX

STATUS AT NECROPSY: K0

Main sacrifice

| SEX                     | : | FEMALE |   |   |
|-------------------------|---|--------|---|---|
| DOSE GROUP:             |   | 1      | 2 | 3 |
| NO. ANIMALS:            |   | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| ADIPOSE TISSUE          | : | -      | 4 | 3 |
| - Edema                 | : | -      | 4 | 3 |
| Grade 1:                |   | -      | 1 | 1 |
| Grade 2:                |   | -      | 3 | 2 |
| - Hemorrhage            | : | -      | 4 | 2 |
| Grade 1:                |   | -      | 3 | 2 |
| Grade 2:                |   | -      | 1 | - |
| - Inflammation          | : | -      | 4 | 3 |
| Grade 1:                |   | -      | 1 | 1 |
| Grade 2:                |   | -      | 3 | 2 |
| <hr/>                   |   |        |   |   |
| ADRENAL GLANDS          | : | 5      | 5 | 5 |
| - Accessory tissue      | : | -      | - | 1 |
| <hr/>                   |   |        |   |   |
| AORTA                   | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| BONE MARROW             | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| BRAIN                   | : | 5      | 5 | 5 |
| - Vacuol;choroid plex.: |   | 1      | 1 | - |
| Grade 1:                |   | 1      | 1 | - |
| Grade 2:                |   | -      | - | - |
| <hr/>                   |   |        |   |   |
| CECUM                   | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| COLON                   | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| DIAPHRAGM               | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| DUODENUM                | : | 5      | 5 | 5 |
| - Dilat;Brunner's gl    | : | -      | 1 | - |
| Grade 2:                |   | -      | 1 | - |
| <hr/>                   |   |        |   |   |
| ESOPHAGUS               | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| EYE, LEFT               | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| EYE, RIGHT              | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |
| FEMUR                   | : | 5      | 5 | 5 |
| <hr/>                   |   |        |   |   |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS:  | 1 | 2 | 3 | FEMALE |
|---|---|---|---|--------|
| G.A.L.T. :<br>- Hyperplasia; lymphoid:<br>Grade 1:<br>Grade 2:  | 5 | 5 | 5 |        |
| GALL BLADDER :<br>HARDERIAN GLANDS :<br>HEART :<br>- Infilt; mononuc;<br>Grade 1:   | 5 | 5 | 5 |        |
| ILEUM :<br>ILIAS L.N. LEFT :<br>- Hemorrhage; sinus:<br>Grade 1:<br>Grade 2:<br>- Hyperplasia; lymphoid:<br>Grade 1:                              | 5 | 5 | 5 |        |
| ILIAS L.N. RIGHT :<br>- Hemorrhage; sinus:<br>Grade 1:<br>- Hyperplasia; lymphoid:<br>Grade 1:<br>Grade 2:<br>- Infilt; granulocyte :<br>Grade 1: | 4 | 4 | 4 |        |
| INGUINAL L.N. LEFT :<br>- Hyperplasia; lymphoid:<br>Grade 1:<br>Grade 2:<br>- Infilt; granulocyte :<br>Grade 1:<br>Grade 2:                       | 4 | 5 | 5 |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | FEMALE |
|-------------------------|---|---|---|--------|
| NO. ANIMALS:            | 5 | 5 | 5 |        |
| INGUINAL L.N. RIGHT :   | 5 | 5 | 5 |        |
| - Dilatation;sinusoid : | - | 1 | - |        |
| Grade 1:                | - | 1 | - |        |
| - Hyperplasia;lymphoid: | 1 | 5 | 5 |        |
| Grade 1:                | 1 | 3 | 4 |        |
| Grade 2:                | - | 2 | 1 |        |
| - Infilt;granulocyte :  | 1 | - | 3 |        |
| Grade 1:                | 1 | - | 3 |        |
| INJECTION SITE 1 :      | 5 | 5 | 5 |        |
| - Inflamm;subacute :    | 1 | 4 | 4 |        |
| Grade 1:                | 1 | 2 | 2 |        |
| Grade 2:                | - | 2 | 2 |        |
| Grade 3:                | - | - | - |        |
| - Hemorrhage :          | - | 3 | 4 |        |
| Grade 1:                | - | 2 | 3 |        |
| Grade 2:                | - | 1 | 1 |        |
| - Necrosis;muscle :     | - | 2 | - |        |
| Grade 1:                | - | 2 | - |        |
| - Needle tract lesion : | 2 | - | - |        |
| INJECTION SITE 2 :      | 5 | 5 | 5 |        |
| - Inflamm;subacute :    | 1 | 3 | 4 |        |
| Grade 1:                | 1 | 2 | 4 |        |
| Grade 2:                | - | 1 | - |        |
| - Degen/regen;muscle :  | - | 1 | 1 |        |
| Grade 1:                | - | 1 | 1 |        |
| - Hemorrhage :          | - | 2 | 1 |        |
| Grade 1:                | - | 2 | 1 |        |
| Grade 2:                | - | - | - |        |
| - Infilt;macrophage :   | - | 2 | 1 |        |
| Grade 1:                | - | 2 | 1 |        |
| - Necrosis;muscle :     | - | - | 1 |        |
| Grade 1:                | - | - | 1 |        |
| - Needle tract lesion : | 1 | - | 1 |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | FEMALE |
|-------------------------|---|---|---|--------|
| NO. ANIMALS:            | 5 | 5 | 5 |        |
| INJECTION SITE 3 :      | 5 | 5 | 5 |        |
| - Inflamm;subacute :    | 2 | 5 | 5 |        |
| Grade 1:                | 2 | - | - |        |
| Grade 2:                | - | 5 | 5 |        |
| Grade 3:                | - | - | - |        |
| - Hemorrhage :          | 2 | 4 | 5 |        |
| Grade 1:                | 2 | 2 | 4 |        |
| Grade 2:                | - | 2 | 1 |        |
| - Necrosis;muscle :     | 1 | 2 | 3 |        |
| Grade 1:                | 1 | 2 | 3 |        |
| Grade 2:                | - | - | - |        |
| - Needle tract lesion : | 2 | 1 | 1 |        |
| JEJUNUM :               | 5 | 5 | 5 |        |
| JOINTS :                | 5 | 5 | 5 |        |
| KIDNEYS :               | 5 | 5 | 5 |        |
| - Basophilia;tubule :   | 3 | 3 | - |        |
| Grade 1:                | 2 | 3 | - |        |
| Grade 2:                | 1 | - | - |        |
| - Cyst;cortex :         | - | 1 | - |        |
| Grade 1:                | - | 1 | - |        |
| - Dilatation;tubule :   | 3 | 2 | 1 |        |
| Grade 1:                | 3 | 2 | 1 |        |
| - Infilt;lymphocyte :   | 2 | - | 1 |        |
| Grade 1:                | 2 | - | 1 |        |
| - Infilt;mixed;fascia : | - | 3 | 2 |        |
| Grade 1:                | - | 3 | 2 |        |
| - Mineral;cortex :      | 3 | 3 | 4 |        |
| Grade 1:                | 2 | 3 | 4 |        |
| Grade 2:                | 1 | - | - |        |
| LACRIMAL GLANDS :       | 5 | 5 | 5 |        |
| - Infilt;lymphocyte :   | 1 | 3 | - |        |
| Grade 1:                | 1 | 3 | - |        |
| LARYNX :                | 5 | 5 | 5 |        |
| - Infilt;mononuc;musc : | 1 | - | - |        |
| Grade 1:                | 1 | - | - |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | FEMALE |
|-------------------------|---|---|---|--------|
| NO. ANIMALS:            | 5 | 5 | 5 |        |
| LIVER :                 | 5 | 5 | 5 |        |
| - Infilt;mixed;focal :  | 3 | 4 | 3 |        |
| Grade 1:                | 3 | 4 | 3 |        |
| LUNGS :                 | 5 | 5 | 5 |        |
| - Hemorrhage;agonal :   | 2 | - | - |        |
| Grade 1:                | 1 | - | - |        |
| Grade 2:                | 1 | - | - |        |
| - Hyperplasia;lymphoid: | 1 | 1 | - |        |
| Grade 1:                | 1 | 1 | - |        |
| - Infilt;macro;alveol : | 5 | 4 | 3 |        |
| Grade 1:                | 3 | 4 | 2 |        |
| Grade 2:                | 2 | - | 1 |        |
| - Infilt;mixed;bronchi: | - | - | 1 |        |
| Grade 2:                | - | - | 1 |        |
| MAMMARY GLANDS AREA :   | 5 | 5 | 5 |        |
| MANDIBUL. LYMPH NODE :  | 5 | 5 | 5 |        |
| - Dilatation; sinusoid: | 3 | 2 | 2 |        |
| Grade 1:                | 2 | 2 | 2 |        |
| Grade 2:                | 1 | - | - |        |
| - Hemorrhage; sinus :   | 1 | 1 | - |        |
| Grade 1:                | 1 | 1 | - |        |
| - Hyperplasia;lymphoid: | 1 | - | 3 |        |
| Grade 1:                | 1 | - | 3 |        |
| MANDIBULAR GLANDS :     | 5 | 5 | 5 |        |
| MESENT. LYMPH NODE :    | 5 | 5 | 5 |        |
| - Hyperplasia;lymphoid: | 2 | 5 | 4 |        |
| Grade 1:                | 2 | 3 | 3 |        |
| Grade 2:                | - | 2 | 1 |        |
| NASAL CAVITY, ANT.L1 :  | 5 | 5 | 5 |        |
| - Inflamm;exudate :     | - | 1 | - |        |
| Grade 1:                | - | 1 | - |        |
| NASAL CAVITY, L2 :      | 5 | 5 | 5 |        |
| - Artifact;blood lumen: | - | - | 1 |        |
| - Inflamm;exudate :     | - | 1 | - |        |
| Grade 2:                | - | 1 | - |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | FEMALE |
|-------------------------|---|---|---|--------|
| NO. ANIMALS:            | 5 | 5 | 5 |        |
| NASAL CAVITY, L3 :      | 5 | 5 | 5 |        |
| - Artifact;blood lumen: | 1 | - | - |        |
| - Inflamm;exudate :     | 1 | - | - |        |
| Grade 1:                | 1 | - | - |        |
| NASAL CAVITY, POS.L4 :  | 5 | 5 | 5 |        |
| - Artifact;blood lumen: | 1 | - | - |        |
| - Inflamm;exudate :     | 1 | - | - |        |
| Grade 1:                | 1 | - | - |        |
| OPTIC NERVE, LEFT :     | 5 | 5 | 5 |        |
| OPTIC NERVE, RIGHT :    | 5 | 5 | 5 |        |
| OVARIES :               | 5 | 5 | 5 |        |
| - Cyst;parovarian :     | 1 | - | 1 |        |
| OVIDUCTS :              | 5 | 5 | 5 |        |
| PANCREAS :              | 5 | 5 | 5 |        |
| - Ectopic tiss;spleen : | 1 | - | - |        |
| - Vacuol;acinar cell :  | - | - | 1 |        |
| Grade 2:                | - | - | 1 |        |
| PARATHYROID GLANDS :    | 4 | 4 | 4 |        |
| PAROTID GLANDS :        | 5 | 5 | 5 |        |
| - Atrophy;focal :       | - | 1 | - |        |
| Grade 1:                | - | 1 | - |        |
| PITUITARY GLAND :       | 5 | 5 | 5 |        |
| RECTUM :                | 5 | 5 | 5 |        |
| - Inflamm;adjace.tiss.: | 1 | - | - |        |
| Grade 2:                | 1 | - | - |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | FEMALE |
|-------------------------|---|---|---|--------|
| NO. ANIMALS:            | 5 | 5 | 5 |        |
| SACRAL LYMPH NODE :     | 5 | 4 | 5 |        |
| - Hemorrhage;sinus :    | 3 | - | - |        |
| Grade 1:                | 3 | - | - |        |
| Grade 3:                | - | - | - |        |
| - Hyperplasia;lymphoid: | - | 1 | 3 |        |
| Grade 1:                | - | 1 | 3 |        |
| - Infilt;granulocyte :  | - | - | 1 |        |
| Grade 1:                | - | - | 1 |        |
| SCIATIC NERVE :         | 5 | 5 | 5 |        |
| SKELETAL MUSCLE :       | 5 | 5 | 5 |        |
| SKIN :                  | 5 | 5 | 5 |        |
| SKIN SITE 1 :           | 5 | 5 | 5 |        |
| - Infilt;mixed;dermis : | - | 2 | - |        |
| Grade 1:                | - | 2 | - |        |
| - Infilt;mixed;subcut : | - | 2 | 1 |        |
| Grade 1:                | - | 2 | 1 |        |
| Grade 2:                | - | - | - |        |
| - Needle tract lesion : | - | 1 | - |        |
| SKIN SITE 2 :           | 5 | 5 | 5 |        |
| - Cyst;pseudocyst :     | - | - | 1 |        |
| Grade 2:                | - | - | 1 |        |
| - Fibroplasia :         | - | - | 1 |        |
| Grade 2:                | - | - | 1 |        |
| - Infilt;mixed;dermis : | - | 1 | - |        |
| Grade 1:                | - | 1 | - |        |
| - Infilt;mixed;subcut : | - | - | 1 |        |
| Grade 1:                | - | - | - |        |
| Grade 2:                | - | - | 1 |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: K0  
 Main sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | FEMALE |
|-------------------------|---|---|---|--------|
| NO. ANIMALS:            | 5 | 5 | 5 |        |
| SKIN SITE 3 :           | 5 | 5 | 5 |        |
| - Hemorrhage;dermis :   | - | - | 1 |        |
| Grade 2:                | - | - | 1 |        |
| - Hemorrhage;subcutis : | - | 1 | 1 |        |
| Grade 1:                | - | 1 | 1 |        |
| Grade 2:                | - | - | - |        |
| - Infilt;mixed;dermis : | - | - | 1 |        |
| Grade 1:                | - | - | 1 |        |
| - Infilt;mixed;subcut : | - | - | 1 |        |
| Grade 1:                | - | - | 1 |        |
| Grade 2:                | - | - | - |        |
| SPINAL CORD :           | 5 | 5 | 5 |        |
| SPLEEN :                | 5 | 5 | 5 |        |
| - Hyperplasia;lymphoid: | - | 5 | 4 |        |
| Grade 1:                | - | 4 | 4 |        |
| Grade 2:                | - | 1 | - |        |
| STERNUM :               | 5 | 5 | 5 |        |
| STOMACH :               | 5 | 5 | 5 |        |
| - Dilatation;gland :    | 1 | - | - |        |
| Grade 1:                | 1 | - | - |        |
| - Infilt;mixed;muscle : | - | - | 1 |        |
| Grade 1:                | - | - | 1 |        |
| SUBLINGUAL GLANDS :     | 5 | 5 | 5 |        |
| THYMUS :                | 5 | 5 | 5 |        |
| - Hemorrhage;agonal :   | - | 1 | 1 |        |
| Grade 1:                | - | 1 | 1 |        |
| THYROID GLANDS :        | 5 | 5 | 5 |        |
| TONGUE :                | 5 | 5 | 5 |        |
| - Infilt;mixed;muscle : | - | 1 | - |        |
| Grade 1:                | - | 1 | - |        |
| TRACHEA :               | 5 | 5 | 5 |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX

STATUS AT NECROPSY: K0

Main sacrifice

| SEX                   | : | FEMALE |   |   |
|-----------------------|---|--------|---|---|
| DOSE GROUP:           |   | 1      | 2 | 3 |
| NO. ANIMALS:          |   | 5      | 5 | 5 |
| <hr/>                 |   |        |   |   |
| URETERS               | : | 5      | 5 | 5 |
| - Infilt;mixed;fascia | : | -      | - | 1 |
| Grade 1:              |   | -      | - | 1 |
| <hr/>                 |   |        |   |   |
| URINARY BLADDER       | : | 5      | 5 | 5 |
| <hr/>                 |   |        |   |   |
| UTERUS                | : | 5      | 5 | 5 |
| <hr/>                 |   |        |   |   |
| VAGINA                | : | 5      | 5 | 5 |
| <hr/>                 |   |        |   |   |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS:  | 1 | 2 | 3 | MALE |
|---|---|---|---|------|
| ADRENAL GLANDS :<br>- Accessory tissue :<br>- Hemorrhage; focal :<br>Grade 1:                         | 5 | 5 | 5 |      |
| AORTA :   | 5 | 5 | 5 |      |
| BONE MARROW :   | 5 | 5 | 5 |      |
| BRAIN :   | 5 | 5 | 5 |      |
| CECUM :   | 5 | 5 | 5 |      |
| COLON :   | 5 | 5 | 5 |      |
| DIAPHRAGM :   | 5 | 5 | 5 |      |
| DUODENUM :  | 5 | 5 | 5 |      |
| EPIDIDYMIDES :<br>- Cell debris :<br>Grade 1:<br>- Sperm decreased :<br>Grade 5:                      | 5 | 1 | - |      |
| ESOPHAGUS :   | 5 | 5 | 5 |      |
| EYE, LEFT :   | 5 | 5 | 5 |      |
| EYE, RIGHT :  | 5 | 5 | 5 |      |
| FEMUR :   | 5 | 5 | 5 |      |
| G.A.L.T. :<br>- Hyperplasia; lymphoid:<br>Grade 1:<br>Grade 2:<br>- Infilt; granulocyte :<br>Grade 1: | 4 | 5 | 5 |      |
| GALL BLADDER :  | 5 | 5 | 5 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | MALE |
|-------------------------|---|---|---|------|
| NO. ANIMALS:            | 5 | 5 | 5 |      |
| HARDERIAN GLANDS :      | 5 | 5 | 5 |      |
| - Degen;epithelium :    | 1 | - | 1 |      |
| Grade 1:                | 1 | - | 1 |      |
| - Infilt;mononuclear :  | 1 | - | 1 |      |
| Grade 1:                | 1 | - | 1 |      |
| HEART :                 | 5 | 5 | 5 |      |
| ILEUM :                 | 5 | 5 | 5 |      |
| ILIAC L.N. LEFT :       | 3 | 5 | 4 |      |
| - Dilatation;sinusoid : | 1 | - | - |      |
| Grade 1:                | 1 | - | - |      |
| - Hyperplasia;lymphoid: | - | 3 | 3 |      |
| Grade 1:                | - | 3 | 3 |      |
| ILIAC L.N. RIGHT :      | 4 | 5 | 4 |      |
| - Hemorrhage;sinus :    | - | - | 2 |      |
| Grade 1:                | - | - | 2 |      |
| Grade 2:                | - | - | - |      |
| - Hyperplasia;lymphoid: | - | 3 | 2 |      |
| Grade 1:                | - | 1 | 2 |      |
| Grade 2:                | - | 2 | - |      |
| INGUINAL L.N. LEFT :    | 5 | 5 | 5 |      |
| - Hyperplasia;lymphoid: | 1 | 4 | 4 |      |
| Grade 1:                | 1 | 3 | 3 |      |
| Grade 2:                | - | 1 | 1 |      |
| - Infilt;granulocyte :  | - | 1 | 3 |      |
| Grade 1:                | - | 1 | 3 |      |
| INGUINAL L.N. RIGHT :   | 5 | 5 | 5 |      |
| - Hyperplasia;lymphoid: | - | 4 | 4 |      |
| Grade 1:                | - | 3 | 4 |      |
| Grade 2:                | - | 1 | - |      |
| - Infilt;granulocyte :  | 1 | - | 2 |      |
| Grade 1:                | 1 | - | 2 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS:   | 1 | 2 | 3 | MALE |
|--|---|---|---|------|
| INJECTION SITE 1 :<br>- Inflamm;subacute :<br>Grade 1:<br>Grade 2:<br>- Hemorrhage :<br>Grade 1:<br>- Infilt;lymphocyte :<br>Grade 1:  | 5 | 5 | 5 |      |
| - Inflamm;subacute :<br>Grade 1:<br>- Infilt;lymphocyte :<br>Grade 1:  | - | 1 | 1 |      |
| -  | - | 1 | - |      |
| -  | - | - | 1 |      |
| -  | - | - | 1 |      |
| -  | - | 1 | 1 |      |
| -  | - | 1 | 1 |      |
| INJECTION SITE 2 :<br>- Inflamm;subacute :<br>Grade 1:<br>- Infilt;lymphocyte :<br>Grade 1:  | 5 | 5 | 5 |      |
| -  | - | 1 | - |      |
| -  | - | 1 | - |      |
| -  | - | 1 | - |      |
| -  | - | 1 | - |      |
| INJECTION SITE 3 :<br>- Inflamm;subacute :<br>Grade 1:<br>- Artifact :<br>- Infilt;lymphocyte :<br>Grade 1:  | 5 | 5 | 5 |      |
| -  | - | 3 | 2 |      |
| -  | - | 3 | 2 |      |
| -  | - | - | 1 |      |
| -  | - | 1 | - |      |
| -  | - | 1 | - |      |
| JEJUNUM :<br>JOINTS :<br>KIDNEYS :<br>- Basophilia;tubule :<br>Grade 1:<br>Grade 2:<br>- Cyst;cortex :<br>Grade 1:<br>- Dilatation;tubule :<br>Grade 1:<br>- Fibrosis :<br>Grade 2:<br>- Infilt;lymphocyte :<br>Grade 1:<br>- Mineral;cortex :<br>Grade 1:<br>Grade 2: | 5 | 5 | 5 |      |
| -  | - | 3 | 1 |      |
| -  | - | 2 | 1 |      |
| -  | - | 1 | - |      |
| -  | - | 1 | - |      |
| -  | 1 | 1 | 2 |      |
| -  | 1 | 1 | 2 |      |
| -  | - | 1 | - |      |
| -  | - | 1 | - |      |
| -  | - | 1 | 1 |      |
| -  | - | 1 | 1 |      |
| -  | 4 | 3 | 1 |      |
| -  | 4 | 3 | 1 |      |
| -  | - | - | - |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX : DOSE GROUP:       | 1 | 2 | 3 | MALE |
|-------------------------|---|---|---|------|
| NO. ANIMALS:            | 5 | 5 | 5 |      |
| LACRIMAL GLANDS :       | 5 | 5 | 5 |      |
| - Atrophy; focal :      | - | 1 | - |      |
| Grade 2:                | - | 1 | - |      |
| - Infilt;lymphocyte :   | 1 | - | - |      |
| Grade 1:                | 1 | - | - |      |
| LARYNX :                | 5 | 5 | 5 |      |
| LIVER :                 | 5 | 5 | 5 |      |
| - Infilt;mixed;focal :  | 3 | 1 | 2 |      |
| Grade 1:                | 3 | 1 | 2 |      |
| LUNGS :                 | 5 | 5 | 5 |      |
| - Hemorrhage;agonal :   | 1 | 1 | 1 |      |
| Grade 1:                | 1 | - | 1 |      |
| Grade 2:                | - | 1 | - |      |
| - Hyperplasia;lymphoid: | - | 3 | - |      |
| Grade 1:                | - | 3 | - |      |
| - Infilt;granul;alveol: | - | - | 1 |      |
| Grade 1:                | - | - | 1 |      |
| - Infilt;macro;alveol : | 4 | 2 | 2 |      |
| Grade 1:                | 3 | 1 | 2 |      |
| Grade 2:                | 1 | 1 | - |      |
| Grade 3:                | - | - | - |      |
| - Metaplasia;osseous :  | - | 1 | 1 |      |
| MAMMARY GLANDS AREA :   | 5 | 5 | 5 |      |
| MANDIBUL. LYMPH NODE :  | 5 | 5 | 5 |      |
| - Dilatation; sinusoid: | 2 | 1 | - |      |
| Grade 1:                | 1 | - | - |      |
| Grade 2:                | 1 | 1 | - |      |
| - Hyperplasia;lymphoid: | 4 | 2 | 1 |      |
| Grade 1:                | 4 | 2 | 1 |      |
| - Infilt;granulocytic : | 1 | - | 1 |      |
| Grade 1:                | 1 | - | 1 |      |
| MANDIBULAR GLANDS :     | 5 | 5 | 5 |      |
| MESENT. LYMPH NODE :    | 5 | 5 | 5 |      |
| - Hyperplasia;lymphoid: | 3 | 4 | 4 |      |
| Grade 1:                | 3 | 4 | 4 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS: | 1 | 2 | 3 | MALE |
|--------------------------------------|---|---|---|------|
| NASAL CAVITY, ANT.L1 :               | 5 | 5 | 5 |      |
| NASAL CAVITY, L2 :                   | 5 | 5 | 5 |      |
| NASAL CAVITY, L3 :                   | 5 | 5 | 5 |      |
| - Artifact;blood lumen:              | 1 | - | 1 |      |
| NASAL CAVITY, POS.L4 :               | 5 | 5 | 5 |      |
| - Artifact;blood lumen:              | 1 | - | 2 |      |
| - Inflamm;exudate :                  | - | - | 1 |      |
| Grade 1:                             | - | - | 1 |      |
| OPTIC NERVE, LEFT :                  | 4 | 5 | 5 |      |
| OPTIC NERVE, RIGHT :                 | 5 | 5 | 5 |      |
| PANCREAS :                           | 5 | 5 | 5 |      |
| - Ectopic tiss;spleen :              | - | 1 | - |      |
| PARATHYROID GLANDS :                 | 5 | 5 | 5 |      |
| PAROTID GLANDS :                     | 5 | 5 | 5 |      |
| PITUITARY GLAND :                    | 5 | 5 | 5 |      |
| PROSTATE :                           | 5 | 5 | 5 |      |
| RECTUM :                             | 5 | 5 | 5 |      |
| SACRAL LYMPH NODE :                  | 5 | 4 | 5 |      |
| - Hemorrhage;sinus :                 | 1 | - | - |      |
| Grade 1:                             | 1 | - | - |      |
| - Hyperplasia;lymphoid:              | - | 1 | 2 |      |
| Grade 1:                             | - | 1 | 1 |      |
| Grade 2:                             | - | - | 1 |      |
| SCIATIC NERVE :                      | 5 | 5 | 5 |      |
| SEMINAL VESICLES :                   | 5 | 5 | 5 |      |
| SKELETAL MUSCLE :                    | 5 | 5 | 5 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX                      | : | MALE |   |   |
|--------------------------|---|------|---|---|
| DOSE GROUP:              | 1 | 2    | 3 |   |
| NO. ANIMALS:             | 5 | 5    | 5 |   |
| SKIN                     | : | 5    | 5 | 5 |
| SKIN SITE 1              | : | 5    | 4 | 5 |
| SKIN SITE 2              | : | 5    | 5 | 5 |
| SKIN SITE 3              | : | 5    | 5 | 5 |
| SPINAL CORD              | : | 5    | 5 | 5 |
| SPLEEN                   | : | 5    | 5 | 5 |
| - Hyperplasia; lymphoid: | 1 | 5    | 4 |   |
| Grade 1:                 | 1 | 4    | 4 |   |
| Grade 2:                 | - | 1    | - |   |
| STERNUM                  | : | 5    | 5 | 5 |
| STOMACH                  | : | 5    | 5 | 5 |
| - Congestion; focal      | : | 1    | - | - |
| Grade 1:                 | 1 | -    | - |   |
| - Dilatation; gland      | : | 1    | - | 1 |
| Grade 1:                 | 1 | -    | 1 |   |
| SUBLINGUAL GLANDS        | : | 5    | 5 | 5 |
| TESTES                   | : | 5    | 5 | 5 |
| - Atrophy; tubule        | : | 2    | 3 | 1 |
| Grade 1:                 | 2 | 1    | 1 |   |
| Grade 2:                 | - | 2    | - |   |
| - Dilatation; tubule     | : | 1    | - | - |
| Grade 3:                 | 1 | -    | - |   |
| - Hypoplasia             | : | -    | 1 | - |
| Grade 4:                 | - | 1    | - |   |
| - Multinuc giant cell    | : | 3    | 3 | 4 |
| Grade 1:                 | 3 | 1    | 4 |   |
| Grade 2:                 | - | 2    | - |   |
| THYMUS                   | : | 5    | 5 | 5 |
| - Hemorrhage; agonal     | : | 2    | 2 | 1 |
| Grade 1:                 | 2 | 2    | 1 |   |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
STATUS AT NECROPSY: R1  
Recovery sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS:  | 1 | 2 | 3 | MALE |
|---|---|---|---|------|
| THYROID GLANDS :<br>TONGUE :<br>TRACHEA :<br>URETERS :<br>URINARY BLADDER : | 5 | 5 | 5 |      |
|   | 5 | 5 | 5 |      |
|   | 5 | 5 | 5 |      |
|   | 5 | 5 | 5 |      |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS:   | 1 | 2 | 3 | FEMALE |
|--|---|---|---|--------|
| ADRENAL GLANDS :<br>- Accessory tissue :   | 5 | 5 | 5 |        |
| AORTA :  | 5 | 5 | 5 |        |
| BONE MARROW :  | 5 | 5 | 5 |        |
| BRAIN :  | 5 | 5 | 5 |        |
| CECUM :  | 5 | 5 | 5 |        |
| COLON :  | 5 | 5 | 5 |        |
| DIAPHRAGM :  | 5 | 5 | 5 |        |
| DUODENUM :   | 5 | 5 | 5 |        |
| ESOPHAGUS :  | 5 | 5 | 5 |        |
| EYE, LEFT :  | 5 | 5 | 5 |        |
| EYE, RIGHT :   | 5 | 5 | 5 |        |
| FEMUR :  | 5 | 5 | 5 |        |
| G.A.L.T. :<br>- Hyperplasia; lymphoid:<br>Grade 1:<br>Grade 2:                                 | 5 | 5 | 5 |        |
| GALL BLADDER :   | 5 | 5 | 5 |        |
| HARDERIAN GLANDS :<br>- Degen; epithelium :<br>Grade 1:<br>- Infilt; mononuclear :<br>Grade 1: | 5 | 5 | 5 |        |
| HEART :  | 5 | 5 | 5 |        |
| ILEUM :  | 5 | 5 | 5 |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX : DOSE GROUP:        | 1 | 2 | 3 | FEMALE |
|--------------------------|---|---|---|--------|
| NO. ANIMALS:             | 5 | 5 | 5 |        |
| ILIAC L.N. LEFT :        | 5 | 4 | 5 |        |
| - Hyperplasia; lymphoid: | - | 1 | 2 |        |
| Grade 1:                 | - | 1 | 2 |        |
| ILIAC L.N. RIGHT :       | 5 | 5 | 5 |        |
| - Hemorrhage; sinus :    | 1 | 1 | 1 |        |
| Grade 1:                 | 1 | 1 | - |        |
| Grade 2:                 | - | - | 1 |        |
| - Hyperplasia; lymphoid: | - | 1 | 4 |        |
| Grade 1:                 | - | 1 | 4 |        |
| Grade 2:                 | - | - | - |        |
| INGUINAL L.N. LEFT :     | 5 | 5 | 5 |        |
| - Hyperplasia; lymphoid: | 3 | 3 | 2 |        |
| Grade 1:                 | 3 | 3 | 2 |        |
| Grade 2:                 | - | - | - |        |
| INGUINAL L.N. RIGHT :    | 5 | 5 | 5 |        |
| - Hyperplasia; lymphoid: | 2 | 4 | 4 |        |
| Grade 1:                 | 2 | 4 | 4 |        |
| Grade 2:                 | - | - | - |        |
| INJECTION SITE 1 :       | 5 | 5 | 5 |        |
| - Inflamm; subacute :    | - | - | 2 |        |
| Grade 1:                 | - | - | 2 |        |
| Grade 2:                 | - | - | - |        |
| - Infilt; macrophage :   | - | 1 | 1 |        |
| Grade 1:                 | - | 1 | 1 |        |
| - Needle tract lesion :  | 1 | - | - |        |
| INJECTION SITE 2 :       | 5 | 5 | 5 |        |
| - Inflamm; subacute :    | - | - | 1 |        |
| Grade 1:                 | - | - | 1 |        |
| - Infilt; lymphocyte :   | - | 2 | - |        |
| Grade 1:                 | - | 2 | - |        |
| - Infilt; macrophage :   | - | - | 1 |        |
| Grade 1:                 | - | - | 1 |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX :<br>DOSE GROUP:<br>NO. ANIMALS:  | 1 | 2 | 3 | FEMALE |
|---|---|---|---|--------|
| INJECTION SITE 3 :<br>- Inflamm;subacute :<br>Grade 1:<br>- Needle tract lesion :   | 5 | 5 | 5 |        |
| JEJUNUM :<br>JOINTS :<br>KIDNEYS :<br>- Basophilia;tubule :<br>Grade 1:<br>Grade 2:<br>- Dilatation;tubule :<br>Grade 1:<br>- Infilt;lymphocyte :<br>Grade 1:<br>- Mineral;cortex :<br>Grade 1:<br>Grade 2: | 5 | 5 | 5 |        |
| LACRIMAL GLANDS :<br>- Infilt;lymphocyte :<br>Grade 1:  | 5 | 5 | 5 |        |
| LARYNX :<br>LIVER :<br>- Infilt;mixed;focal :<br>Grade 1:   | 5 | 5 | 5 |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX : DOSE GROUP:         | 1 | 2 | 3 | FEMALE |
|---------------------------|---|---|---|--------|
| NO. ANIMALS:              | 5 | 5 | 5 |        |
| <hr/>                     |   |   |   |        |
| LUNGS :                   | 5 | 5 | 5 |        |
| - Foreign material :      | - | - | 1 |        |
| - Hemorrhage; agonal :    | - | - | 1 |        |
| Grade 1:                  | - | - | 1 |        |
| Grade 2:                  | - | - | - |        |
| - Hyperplasia; lymphoid:  | 3 | 1 | 1 |        |
| Grade 1:                  | 3 | 1 | 1 |        |
| - Infilt; granul; alveol: | 1 | 1 | - |        |
| Grade 1:                  | 1 | 1 | - |        |
| - Infilt; macro; alveol : | 2 | 2 | 1 |        |
| Grade 1:                  | 1 | 1 | - |        |
| Grade 2:                  | 1 | - | 1 |        |
| Grade 3:                  | - | 1 | - |        |
| <hr/>                     |   |   |   |        |
| MAMMARY GLANDS AREA :     | 5 | 5 | 5 |        |
| <hr/>                     |   |   |   |        |
| MANDIBUL. LYMPH NODE :    | 5 | 5 | 5 |        |
| - Dilatation; sinusoid:   | - | 1 | 3 |        |
| Grade 1:                  | - | 1 | 1 |        |
| Grade 2:                  | - | - | 2 |        |
| - Hemorrhage; sinus :     | 1 | - | - |        |
| Grade 1:                  | 1 | - | - |        |
| - Hyperplasia; lymphoid:  | 1 | - | 2 |        |
| Grade 1:                  | 1 | - | 2 |        |
| <hr/>                     |   |   |   |        |
| MANDIBULAR GLANDS :       | 5 | 5 | 5 |        |
| <hr/>                     |   |   |   |        |
| MESENT. LYMPH NODE :      | 5 | 5 | 5 |        |
| - Hyperplasia; lymphoid:  | 3 | 3 | 5 |        |
| Grade 1:                  | 3 | 3 | 5 |        |
| <hr/>                     |   |   |   |        |
| NASAL CAVITY, ANT.L1 :    | 5 | 5 | 5 |        |
| <hr/>                     |   |   |   |        |
| NASAL CAVITY, L2 :        | 5 | 5 | 5 |        |
| - Artifact; blood lumen:  | 2 | 1 | 1 |        |
| <hr/>                     |   |   |   |        |
| NASAL CAVITY, L3 :        | 5 | 5 | 5 |        |
| - Artifact; blood lumen:  | 1 | 1 | 1 |        |
| <hr/>                     |   |   |   |        |
| NASAL CAVITY, POS.L4 :    | 5 | 5 | 5 |        |
| - Artifact; blood lumen:  | 1 | - | 1 |        |
| <hr/>                     |   |   |   |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX : DOSE GROUP:          | 1 | 2 | 3 | FEMALE |
|----------------------------|---|---|---|--------|
| NO. ANIMALS:               | 5 | 5 | 5 |        |
| OPTIC NERVE, LEFT :        | 5 | 5 | 5 |        |
| OPTIC NERVE, RIGHT :       | 5 | 5 | 5 |        |
| OVARIES :                  | 5 | 5 | 5 |        |
| OVIDUCTS :                 | 5 | 5 | 5 |        |
| PANCREAS :                 | 5 | 5 | 5 |        |
| - Ectopic tissue; spleen : | 1 | - | - |        |
| PARATHYROID GLANDS :       | 3 | 5 | 5 |        |
| PAROTID GLANDS :           | 5 | 5 | 5 |        |
| PITUITARY GLAND :          | 5 | 5 | 5 |        |
| RECTUM :                   | 5 | 5 | 5 |        |
| SACRAL LYMPH NODE :        | 5 | 4 | 5 |        |
| - Dilatation; sinusoid :   | 1 | - | - |        |
| Grade 3:                   | 1 | - | - |        |
| - Hemorrhage; sinus :      | 1 | - | - |        |
| Grade 1:                   | 1 | - | - |        |
| - Hyperplasia; lymphoid:   | - | 1 | 1 |        |
| Grade 1:                   | - | 1 | 1 |        |
| Grade 2:                   | - | - | - |        |
| SCIATIC NERVE :            | 5 | 5 | 5 |        |
| SKELETAL MUSCLE :          | 5 | 5 | 5 |        |
| SKIN :                     | 5 | 5 | 5 |        |
| - Hyperkeratosis :         | - | - | 1 |        |
| Grade 1:                   | - | - | 1 |        |
| - Inflamm; chronic :       | - | - | 1 |        |
| Grade 1:                   | - | - | 1 |        |
| SKIN SITE 1 :              | 5 | 5 | 5 |        |
| SKIN SITE 2 :              | 5 | 5 | 5 |        |

Table: (continued)

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX  
 STATUS AT NECROPSY: R1  
 Recovery sacrifice

| SEX : DOSE GROUP:        | 1 | 2 | 3 | FEMALE |
|--------------------------|---|---|---|--------|
| NO. ANIMALS:             | 5 | 5 | 5 |        |
| SKIN SITE 3 :            | 5 | 5 | 5 |        |
| SPINAL CORD :            | 5 | 5 | 5 |        |
| SPLEEN :                 | 5 | 5 | 5 |        |
| - Hyperplasia; lymphoid: | 1 | 5 | 4 |        |
| Grade 1:                 | 1 | 5 | 4 |        |
| Grade 2:                 | - | - | - |        |
| STERNUM :                | 5 | 5 | 5 |        |
| STOMACH :                | 5 | 5 | 5 |        |
| SUBLINGUAL GLANDS :      | 4 | 5 | 5 |        |
| THYMUS :                 | 5 | 5 | 5 |        |
| - Hemorrhage; agonal :   | - | - | 1 |        |
| Grade 1:                 | - | - | 1 |        |
| THYROID GLANDS :         | 5 | 5 | 5 |        |
| - Degeneration; cystic:  | 1 | - | - |        |
| Grade 3:                 | 1 | - | - |        |
| TONGUE :                 | 5 | 5 | 5 |        |
| TRACHEA :                | 5 | 5 | 5 |        |
| URETERS :                | 5 | 5 | 5 |        |
| URINARY BLADDER :        | 5 | 5 | 5 |        |
| UTERUS :                 | 5 | 5 | 5 |        |
| VAGINA :                 | 5 | 5 | 5 |        |
| - Cyst :                 | - | 1 | - |        |
| Grade 1:                 | - | 1 | - |        |

## **APPENDICES**

1. Organ weights: individual values

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS

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Explanation of Symbols:

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0 = Weight not recorded / Value not calculated  
\* = Tissue/Organ weighed after fixation

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D31  
SEX : MALE

| ANIMAL NUMBER             | :        | N30641    | N30642    | N30643    | N30644    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 31        | 31        | 31        | 31        |
| DATE OF NECROPSY          | :        | 19-SEP-18 | 19-SEP-18 | 19-SEP-18 | 19-SEP-18 |
| DEFND./ACTUAL NECR.STATE: |          | K0/K0     | K0/K0     | K0/K0     | K0/K0     |
| FINAL BODY WEIGHT         | KG:      | 3.3800    | 3.1800    | 3.2400    | 3.1600    |
| ADRENAL GLANDS            | G:       | 0.1570    | 0.1800    | 0.2960    | 0.1630    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.00465   | 0.00566   | 0.00914   | 0.00516   |
| % BRAIN:                  |          | 1.511     | 1.776     | 3.069     | 1.605     |
| BRAIN                     | G:       | 10.3930   | 10.1340   | 9.6450    | 10.1550   |
|                           | % BODY : | 0.30749   | 0.31868   | 0.29769   | 0.32136   |
| EPIDIDYMIDES              | G:       | 2.5770    | 1.9710    | 2.2540    | 2.0320    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.07624   | 0.06198   | 0.06957   | 0.06430   |
| % BRAIN:                  |          | 24.796    | 19.449    | 23.370    | 20.010    |
| HEART                     | G:       | 8.9230    | 7.7110    | 7.3850    | 8.7960    |
|                           | % BODY : | 0.26399   | 0.24248   | 0.22793   | 0.27835   |
|                           | % BRAIN: | 85.856    | 76.090    | 76.568    | 86.617    |
| KIDNEYS                   | G:       | 14.3540   | 15.8660   | 16.1980   | 16.8380   |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.42468   | 0.49893   | 0.49994   | 0.53285   |
| % BRAIN:                  |          | 138.112   | 156.562   | 167.942   | 165.810   |
| LIVER                     | G:       | 88.5620   | 70.7820   | 87.2990   | 71.7670   |
|                           | % BODY : | 2.620     | 2.226     | 2.694     | 2.271     |
|                           | % BRAIN: | 852.131   | 698.461   | 905.122   | 706.716   |
| LUNGS                     | G:       | 10.9340   | 9.8660    | 10.7170   | 10.8000   |
|                           | % BODY : | 0.32349   | 0.31025   | 0.33077   | 0.34177   |
|                           | % BRAIN: | 105.205   | 97.355    | 111.115   | 106.352   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D31  
SEX : MALE

| ANIMAL NUMBER      | :        | N30641  | N30642  | N30643  | N30644  |
|--------------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND    | G:       | 0.0300  | 0.0340  | 0.0260  | 0.0270  |
|                    | % BODY : | 0.00089 | 0.00107 | 0.00080 | 0.00085 |
|                    | % BRAIN: | 0.289   | 0.336   | 0.270   | 0.266   |
| PROSTATE+SEMINALES | G:       | 4.2780  | 3.1720  | 4.1620  | 4.3630  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.12657 | 0.09975 | 0.12846 | 0.13807 |
|                    | % BRAIN: | 41.162  | 31.301  | 43.152  | 42.964  |
| SPLEEN             | G:       | 1.0610  | 1.3810  | 0.9610  | 1.0180  |
|                    | % BODY : | 0.03139 | 0.04343 | 0.02966 | 0.03222 |
|                    | % BRAIN: | 10.209  | 13.627  | 9.964   | 10.025  |
| TESTES             | G:       | 4.5460  | 4.0710  | 3.8600  | 4.7190  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.13450 | 0.12802 | 0.11914 | 0.14934 |
|                    | % BRAIN: | 43.741  | 40.172  | 40.021  | 46.470  |
| THYMUS             | G:       | 5.8280  | 4.9820  | 4.5550  | 6.1730  |
|                    | % BODY : | 0.17243 | 0.15667 | 0.14059 | 0.19535 |
|                    | % BRAIN: | 56.076  | 49.161  | 47.227  | 60.788  |
| THYROID GLANDS     | G:       | 0.3860  | 0.2820  | 0.3480  | 0.3100  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.01142 | 0.00887 | 0.01074 | 0.00981 |
|                    | % BRAIN: | 3.714   | 2.783   | 3.608   | 3.053   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D31  
SEX : MALE

ANIMAL NUMBER : N30645  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-SEP-18  
DEFND./ACTUAL NECR.STATE: K0/K0

FINAL BODY WEIGHT KG: 3.0400

ADRENAL GLANDS G: 0.1560  
LEFT :  
RIGHT:  
% BODY : 0.00513  
% BRAIN: 1.584

BRAIN G: 9.8470  
% BODY : 0.32391

EPIDIDYMIDES G: 2.1180  
LEFT :  
RIGHT:  
% BODY : 0.06967  
% BRAIN: 21.509

HEART G: 6.7540  
% BODY : 0.22217  
% BRAIN: 68.589

KIDNEYS G: 16.2950  
LEFT :  
RIGHT:  
% BODY : 0.53602  
% BRAIN: 165.482

LIVER G: 70.4010  
% BODY : 2.316  
% BRAIN: 714.949

LUNGS G: 9.4890  
% BODY : 0.31214  
% BRAIN: 96.364

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D31  
SEX : MALE

ANIMAL NUMBER : N30645

PITUITARY GLAND G: 0.0260  
% BODY : 0.00086  
% BRAIN: 0.264

PROSTATE+SEMINALES G: 3.9230  
LEFT :  
RIGHT:  
% BODY : 0.12905  
% BRAIN: 39.840

SPLEEN G: 1.0480  
% BODY : 0.03447  
% BRAIN: 10.643

TESTES G: 4.2070  
LEFT :  
RIGHT:  
% BODY : 0.13839  
% BRAIN: 42.724

THYMUS G: 5.0770  
% BODY : 0.16701  
% BRAIN: 51.559

THYROID GLANDS G: 0.3430  
LEFT :  
RIGHT:  
% BODY : 0.01128  
% BRAIN: 3.483

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D31  
SEX : FEMALE

| ANIMAL NUMBER             | :        | N30711    | N30712    | N30713    | N30714    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 31        | 31        | 31        | 31        |
| DATE OF NECROPSY          | :        | 27-SEP-18 | 27-SEP-18 | 27-SEP-18 | 27-SEP-18 |
| DEFND./ACTUAL NECR.STATE: |          | K0/K0     | K0/K0     | K0/K0     | K0/K0     |
| FINAL BODY WEIGHT         | KG:      | 3.2600    | 3.3600    | 3.2200    | 3.3800    |
| ADRENAL GLANDS            | G:       | 0.1740    | 0.0780    | 0.2040    | 0.1890    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.00534   | 0.00232   | 0.00634   | 0.00559   |
|                           | % BRAIN: | 1.902     | 0.834     | 2.065     | 1.947     |
| BRAIN                     | G:       | 9.1490    | 9.3560    | 9.8800    | 9.7090    |
|                           | % BODY : | 0.28064   | 0.27845   | 0.30683   | 0.28725   |
| HEART                     | G:       | 8.1980    | 8.9300    | 7.7060    | 8.2610    |
|                           | % BODY : | 0.25147   | 0.26577   | 0.23932   | 0.24441   |
|                           | % BRAIN: | 89.605    | 95.447    | 77.996    | 85.086    |
| KIDNEYS                   | G:       | 14.4060   | 14.3360   | 14.9700   | 18.2290   |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.44190   | 0.42667   | 0.46491   | 0.53932   |
|                           | % BRAIN: | 157.460   | 153.228   | 151.518   | 187.754   |
| LIVER                     | G:       | 79.6340   | 81.3330   | 76.4720   | 94.2590   |
|                           | % BODY : | 2.443     | 2.421     | 2.375     | 2.789     |
|                           | % BRAIN: | 870.412   | 869.314   | 774.008   | 970.841   |
| LUNGS                     | G:       | 9.5530    | 10.9460   | 10.0170   | 11.6960   |
|                           | % BODY : | 0.29304   | 0.32577   | 0.31109   | 0.34604   |
|                           | % BRAIN: | 104.416   | 116.994   | 101.387   | 120.466   |
| OVARIES                   | G:       | 0.2390    | 0.2640    | 0.2950    | 0.2280    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.00733   | 0.00786   | 0.00916   | 0.00675   |
|                           | % BRAIN: | 2.612     | 2.822     | 2.986     | 2.348     |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D31  
SEX : FEMALE

| ANIMAL NUMBER   | :        | N30711  | N30712  | N30713  | N30714  |
|-----------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND | G:       | 0.0350  | 0.0460  | 0.0320  | 0.0420  |
|                 | % BODY : | 0.00107 | 0.00137 | 0.00099 | 0.00124 |
|                 | % BRAIN: | 0.383   | 0.492   | 0.324   | 0.433   |
| SPLEEN          | G:       | 1.0400  | 1.6590  | 1.5110  | 1.2410  |
|                 | % BODY : | 0.03190 | 0.04938 | 0.04693 | 0.03672 |
|                 | % BRAIN: | 11.367  | 17.732  | 15.294  | 12.782  |
| THYMUS          | G:       | 4.7440  | 3.2790  | 4.0920  | 4.2230  |
|                 | % BODY : | 0.14552 | 0.09759 | 0.12708 | 0.12494 |
|                 | % BRAIN: | 51.853  | 35.047  | 41.417  | 43.496  |
| THYROID GLANDS  | G:       | 0.2750  | 0.2870  | 0.4420  | 0.3050  |
|                 | LEFT :   |         |         |         |         |
|                 | RIGHT:   |         |         |         |         |
|                 | % BODY : | 0.00844 | 0.00854 | 0.01373 | 0.00902 |
|                 | % BRAIN: | 3.006   | 3.068   | 4.474   | 3.141   |
| UTERUS          | G:       | 7.0410  | 6.1090  | 9.1600  | 8.2120  |
|                 | % BODY : | 0.21598 | 0.18182 | 0.28447 | 0.24296 |
|                 | % BRAIN: | 76.959  | 65.295  | 92.713  | 84.581  |

WEIGHING COMMENTS

ANIMAL NUMBER : N30712  
\* ADRENAL GLANDS  
AGENESIS

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D31  
SEX : FEMALE

ANIMAL NUMBER : N30715  
DAYS ON TEST : 31  
DATE OF NECROPSY : 27-SEP-18  
DEFND./ACTUAL NECR.STATE: K0/K0

FINAL BODY WEIGHT KG: 3.4200

ADRENAL GLANDS G: 0.1900  
LEFT :  
RIGHT:  
% BODY : 0.00556  
% BRAIN: 1.929

BRAIN G: 9.8510  
% BODY : 0.28804

HEART G: 7.6800  
% BODY : 0.22456  
% BRAIN: 77.962

KIDNEYS G: 16.4630  
LEFT :  
RIGHT:  
% BODY : 0.48137  
% BRAIN: 167.120

LIVER G: 83.2080  
% BODY : 2.433  
% BRAIN: 844.666

LUNGS G: 11.0650  
% BODY : 0.32354  
% BRAIN: 112.324

OVARIES G: 0.4040  
LEFT :  
RIGHT:  
% BODY : 0.01181  
% BRAIN: 4.101

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D31  
SEX : FEMALE

|                 |          |         |
|-----------------|----------|---------|
| ANIMAL NUMBER   | :        | N30715  |
| .....           |          |         |
| PITUITARY GLAND | G:       | 0.0420  |
|                 | % BODY : | 0.00123 |
|                 | % BRAIN: | 0.426   |
| .....           |          |         |
| SPLEEN          | G:       | 2.2050  |
|                 | % BODY : | 0.06447 |
|                 | % BRAIN: | 22.384  |
| .....           |          |         |
| THYMUS          | G:       | 3.3570  |
|                 | % BODY : | 0.09816 |
|                 | % BRAIN: | 34.078  |
| .....           |          |         |
| THYROID GLANDS  | G:       | 0.3200  |
|                 | LEFT :   |         |
|                 | RIGHT:   |         |
|                 | % BODY : | 0.00936 |
|                 | % BRAIN: | 3.248   |
| .....           |          |         |
| UTERUS          | G:       | 7.3890  |
|                 | % BODY : | 0.21605 |
|                 | % BRAIN: | 75.008  |
| .....           |          |         |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D31  
SEX : MALE

| ANIMAL NUMBER             | :        | N30651    | N30652    | N30653    | N30654    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 31        | 31        | 31        | 31        |
| DATE OF NECROPSY          | :        | 19-SEP-18 | 19-SEP-18 | 19-SEP-18 | 19-SEP-18 |
| DEFND./ACTUAL NECR.STATE: |          | K0/K0     | K0/K0     | K0/K0     | K0/K0     |
| FINAL BODY WEIGHT         | KG:      | 3.0200    | 2.8600    | 2.9600    | 3.1800    |
| ADRENAL GLANDS            | G:       | 0.1870    | 0.2220    | 0.2030    | 0.1790    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.00619   | 0.00776   | 0.00686   | 0.00563   |
| % BRAIN:                  |          | 1.991     | 2.369     | 1.987     | 1.847     |
| BRAIN                     | G:       | 9.3930    | 9.3710    | 10.2170   | 9.6930    |
|                           | % BODY : | 0.31103   | 0.32766   | 0.34517   | 0.30481   |
| EPIDIDYMIDES              | G:       | 2.1880    | 1.5990    | 1.9030    | 1.9430    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.07245   | 0.05591   | 0.06429   | 0.06110   |
| % BRAIN:                  |          | 23.294    | 17.063    | 18.626    | 20.045    |
| HEART                     | G:       | 11.0200   | 7.6660    | 7.8360    | 7.5620    |
|                           | % BODY : | 0.36490   | 0.26804   | 0.26473   | 0.23780   |
|                           | % BRAIN: | 117.321   | 81.806    | 76.696    | 78.015    |
| KIDNEYS                   | G:       | 13.4180   | 14.3480   | 13.5950   | 15.6880   |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.44431   | 0.50168   | 0.45929   | 0.49333   |
| % BRAIN:                  |          | 142.851   | 153.111   | 133.063   | 161.849   |
| LIVER                     | G:       | 71.8140   | 68.6570   | 63.2300   | 84.1120   |
|                           | % BODY : | 2.378     | 2.401     | 2.136     | 2.645     |
|                           | % BRAIN: | 764.548   | 732.654   | 618.871   | 867.760   |
| LUNGS                     | G:       | 14.6650   | 9.2320    | 8.6150    | 12.7100   |
|                           | % BODY : | 0.48560   | 0.32280   | 0.29105   | 0.39969   |
|                           | % BRAIN: | 156.127   | 98.517    | 84.320    | 131.126   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D31  
SEX : MALE

| ANIMAL NUMBER      | :        | N30651  | N30652  | N30653  | N30654  |
|--------------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND    | G:       | 0.0230  | 0.0220  | 0.0440  | 0.0260  |
|                    | % BODY : | 0.00076 | 0.00077 | 0.00149 | 0.00082 |
|                    | % BRAIN: | 0.245   | 0.235   | 0.431   | 0.268   |
| PROSTATE+SEMINALES | G:       | 3.3170  | 4.5660  | 4.0150  | 4.2990  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.10983 | 0.15965 | 0.13564 | 0.13519 |
|                    | % BRAIN: | 35.314  | 48.725  | 39.297  | 44.352  |
| SPLEEN             | G:       | 1.6480  | 1.4280  | 1.6350  | 2.0080  |
|                    | % BODY : | 0.05457 | 0.04993 | 0.05524 | 0.06315 |
|                    | % BRAIN: | 17.545  | 15.239  | 16.003  | 20.716  |
| TESTES             | G:       | 4.2440  | 2.7980  | 4.1710  | 4.5280  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.14053 | 0.09783 | 0.14091 | 0.14239 |
|                    | % BRAIN: | 45.183  | 29.858  | 40.824  | 46.714  |
| THYMUS             | G:       | 3.9010  | 5.8710  | 4.4220  | 6.9340  |
|                    | % BODY : | 0.12917 | 0.20528 | 0.14939 | 0.21805 |
|                    | % BRAIN: | 41.531  | 62.651  | 43.281  | 71.536  |
| THYROID GLANDS     | G:       | 0.2950  | 0.2300  | 0.3220  | 0.2830  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.00977 | 0.00804 | 0.01088 | 0.00890 |
|                    | % BRAIN: | 3.141   | 2.454   | 3.152   | 2.920   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D31  
SEX : MALE

ANIMAL NUMBER : N30655  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-SEP-18  
DEFND./ACTUAL NECR.STATE: K0/K0

FINAL BODY WEIGHT KG: 2.8800

ADRENAL GLANDS G: 0.1920  
LEFT :  
RIGHT:  
% BODY : 0.00667  
% BRAIN: 1.939

BRAIN G: 9.9030  
% BODY : 0.34385

EPIDIDYMIDES G: 2.3160  
LEFT :  
RIGHT:  
% BODY : 0.08042  
% BRAIN: 23.387

HEART G: 7.4290  
% BODY : 0.25795  
% BRAIN: 75.018

KIDNEYS G: 13.7350  
LEFT :  
RIGHT:  
% BODY : 0.47691  
% BRAIN: 138.695

LIVER G: 57.1880  
% BODY : 1.986  
% BRAIN: 577.482

LUNGS G: 10.0960  
% BODY : 0.35056  
% BRAIN: 101.949

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D31  
SEX : MALE

|                    |          |         |
|--------------------|----------|---------|
| ANIMAL NUMBER      | :        | N30655  |
| PITUITARY GLAND    | G:       | 0.0250  |
|                    | % BODY : | 0.00087 |
|                    | % BRAIN: | 0.252   |
| PROSTATE+SEMINALES | G:       | 3.9380  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.13674 |
|                    | % BRAIN: | 39.766  |
| SPLEEN             | G:       | 1.2970  |
|                    | % BODY : | 0.04504 |
|                    | % BRAIN: | 13.097  |
| TESTES             | G:       | 3.7130  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.12892 |
|                    | % BRAIN: | 37.494  |
| THYMUS             | G:       | 4.9590  |
|                    | % BODY : | 0.17219 |
|                    | % BRAIN: | 50.076  |
| THYROID GLANDS     | G:       | 0.2780  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.00965 |
|                    | % BRAIN: | 2.807   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D31  
SEX : FEMALE

| ANIMAL NUMBER             | :        | N30721    | N30722    | N30723    | N30724    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 31        | 31        | 31        | 31        |
| DATE OF NECROPSY          | :        | 27-SEP-18 | 27-SEP-18 | 27-SEP-18 | 27-SEP-18 |
| DEFND./ACTUAL NECR.STATE: |          | K0/K0     | K0/K0     | K0/K0     | K0/K0     |
| FINAL BODY WEIGHT         | KG:      | 3.3400    | 3.3200    | 3.2200    | 3.7000    |
| ADRENAL GLANDS            | G:       | 0.1540    | 0.1510    | 0.1440    | 0.1780    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.00461   | 0.00455   | 0.00447   | 0.00481   |
|                           | % BRAIN: | 1.549     | 1.364     | 1.420     | 1.942     |
| BRAIN                     | G:       | 9.9420    | 11.0710   | 10.1380   | 9.1670    |
|                           | % BODY : | 0.29767   | 0.33346   | 0.31485   | 0.24776   |
| HEART                     | G:       | 7.3700    | 8.3000    | 7.5170    | 7.5160    |
|                           | % BODY : | 0.22066   | 0.25000   | 0.23345   | 0.20314   |
|                           | % BRAIN: | 74.130    | 74.971    | 74.147    | 81.990    |
| KIDNEYS                   | G:       | 14.7000   | 17.7290   | 16.8500   | 17.0460   |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.44012   | 0.53401   | 0.52329   | 0.46070   |
|                           | % BRAIN: | 147.858   | 160.139   | 166.206   | 185.950   |
| LIVER                     | G:       | 78.7530   | 85.3410   | 73.0390   | 90.3360   |
|                           | % BODY : | 2.358     | 2.571     | 2.268     | 2.442     |
|                           | % BRAIN: | 792.124   | 770.852   | 720.448   | 985.448   |
| LUNGS                     | G:       | 9.2740    | 11.2500   | 11.8740   | 10.9380   |
|                           | % BODY : | 0.27767   | 0.33886   | 0.36876   | 0.29562   |
|                           | % BRAIN: | 93.281    | 101.617   | 117.124   | 119.319   |
| OVARIES                   | G:       | 0.2240    | 0.2360    | 0.2630    | 0.3360    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.00671   | 0.00711   | 0.00817   | 0.00908   |
|                           | % BRAIN: | 2.253     | 2.132     | 2.594     | 3.665     |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D31  
SEX : FEMALE

| ANIMAL NUMBER   | :        | N30721  | N30722  | N30723  | N30724  |
|-----------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND | G:       | 0.0320  | 0.0440  | 0.0440  | 0.0310  |
|                 | % BODY : | 0.00096 | 0.00133 | 0.00137 | 0.00084 |
|                 | % BRAIN: | 0.322   | 0.397   | 0.434   | 0.338   |
| SPLEEN          | G:       | 1.8790  | 2.7960  | 2.3200  | 2.4530  |
|                 | % BODY : | 0.05626 | 0.08422 | 0.07205 | 0.06630 |
|                 | % BRAIN: | 18.900  | 25.255  | 22.884  | 26.759  |
| THYMUS          | G:       | 4.4010  | 4.5770  | 4.0040  | 3.6710  |
|                 | % BODY : | 0.13177 | 0.13786 | 0.12435 | 0.09922 |
|                 | % BRAIN: | 44.267  | 41.342  | 39.495  | 40.046  |
| THYROID GLANDS  | G:       | 0.4760  | 0.3340  | 0.3170  | 0.3980  |
|                 | LEFT :   |         |         |         |         |
|                 | RIGHT:   |         |         |         |         |
|                 | % BODY : | 0.01425 | 0.01006 | 0.00985 | 0.01076 |
|                 | % BRAIN: | 4.788   | 3.017   | 3.127   | 4.342   |
| UTERUS          | G:       | 8.8500  | 9.6900  | 5.5120  | 6.9950  |
|                 | % BODY : | 0.26497 | 0.29187 | 0.17118 | 0.18905 |
|                 | % BRAIN: | 89.016  | 87.526  | 54.370  | 76.306  |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D31  
SEX : FEMALE

ANIMAL NUMBER : N30725  
DAYS ON TEST : 31  
DATE OF NECROPSY : 27-SEP-18  
DEFND./ACTUAL NECR.STATE: K0/K0

FINAL BODY WEIGHT KG: 3.8200

ADRENAL GLANDS G: 0.1910  
LEFT :  
RIGHT:  
% BODY : 0.00500  
% BRAIN: 1.934

BRAIN G: 9.8760  
% BODY : 0.25853

HEART G: 9.6460  
% BODY : 0.25251  
% BRAIN: 97.671

KIDNEYS G: 14.3500  
LEFT :  
RIGHT:  
% BODY : 0.37565  
% BRAIN: 145.302

LIVER G: 86.3900  
% BODY : 2.262  
% BRAIN: 874.747

LUNGS G: 12.0910  
% BODY : 0.31652  
% BRAIN: 122.428

OVARIES G: 0.3030  
LEFT :  
RIGHT:  
% BODY : 0.00793  
% BRAIN: 3.068

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D31  
SEX : FEMALE

|                 |          |         |
|-----------------|----------|---------|
| ANIMAL NUMBER   | :        | N30725  |
| PITUITARY GLAND | G:       | 0.0310  |
|                 | % BODY : | 0.00081 |
|                 | % BRAIN: | 0.314   |
| SPLEEN          | G:       | 3.0490  |
|                 | % BODY : | 0.07982 |
|                 | % BRAIN: | 30.873  |
| THYMUS          | G:       | 4.2460  |
|                 | % BODY : | 0.11115 |
|                 | % BRAIN: | 42.993  |
| THYROID GLANDS  | G:       | 0.3100  |
|                 | LEFT :   |         |
|                 | RIGHT:   |         |
|                 | % BODY : | 0.00812 |
|                 | % BRAIN: | 3.139   |
| UTERUS          | G:       | 10.9430 |
|                 | % BODY : | 0.28647 |
|                 | % BRAIN: | 110.804 |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D31  
SEX : MALE

| ANIMAL NUMBER             | :        | N30661    | N30662    | N30663    | N30664    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 31        | 31        | 31        | 31        |
| DATE OF NECROPSY          | :        | 19-SEP-18 | 19-SEP-18 | 19-SEP-18 | 19-SEP-18 |
| DEFND./ACTUAL NECR.STATE: |          | K0/K0     | K0/K0     | K0/K0     | K0/K0     |
| FINAL BODY WEIGHT         | KG:      | 2.9600    | 2.9400    | 2.8600    | 3.2400    |
| ADRENAL GLANDS            | G:       | 0.2910    | 0.1550    | 0.1570    | 0.2010    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.00983   | 0.00527   | 0.00549   | 0.00620   |
| % BRAIN:                  |          | 2.995     | 1.575     | 1.620     | 1.922     |
| BRAIN                     | G:       | 9.7150    | 9.8410    | 9.6930    | 10.4570   |
|                           | % BODY : | 0.32821   | 0.33473   | 0.33892   | 0.32275   |
| EPIDIDYMIDES              | G:       | 1.7140    | 2.5310    | 1.6570    | 2.4600    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.05791   | 0.08609   | 0.05794   | 0.07593   |
| % BRAIN:                  |          | 17.643    | 25.719    | 17.095    | 23.525    |
| HEART                     | G:       | 7.2780    | 7.8930    | 6.9020    | 7.9030    |
|                           | % BODY : | 0.24588   | 0.26847   | 0.24133   | 0.24392   |
|                           | % BRAIN: | 74.915    | 80.205    | 71.206    | 75.576    |
| KIDNEYS                   | G:       | 12.8320   | 13.1640   | 13.6980   | 15.7430   |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.43351   | 0.44776   | 0.47895   | 0.48590   |
| % BRAIN:                  |          | 132.084   | 133.767   | 141.318   | 150.550   |
| LIVER                     | G:       | 55.7880   | 69.2090   | 63.8090   | 72.6340   |
|                           | % BODY : | 1.885     | 2.354     | 2.231     | 2.242     |
|                           | % BRAIN: | 574.246   | 703.272   | 658.300   | 694.597   |
| LUNGS                     | G:       | 16.4790   | 9.7070    | 9.5820    | 10.7410   |
|                           | % BODY : | 0.55672   | 0.33017   | 0.33504   | 0.33151   |
|                           | % BRAIN: | 169.624   | 98.638    | 98.855    | 102.716   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D31  
SEX : MALE

| ANIMAL NUMBER      | :        | N30661  | N30662  | N30663  | N30664  |
|--------------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND    | G:       | 0.0270  | 0.0230  | 0.0300  | 0.0330  |
|                    | % BODY : | 0.00091 | 0.00078 | 0.00105 | 0.00102 |
|                    | % BRAIN: | 0.278   | 0.234   | 0.310   | 0.316   |
| PROSTATE+SEMINALES | G:       | 4.4350  | 3.1460  | 4.7970  | 5.0510  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.14983 | 0.10701 | 0.16773 | 0.15590 |
|                    | % BRAIN: | 45.651  | 31.968  | 49.489  | 48.303  |
| SPLEEN             | G:       | 1.7460  | 1.2770  | 1.0330  | 1.1020  |
|                    | % BODY : | 0.05899 | 0.04344 | 0.03612 | 0.03401 |
|                    | % BRAIN: | 17.972  | 12.976  | 10.657  | 10.538  |
| TESTES             | G:       | 3.1090  | 4.6080  | 4.7090  | 4.2990  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.10503 | 0.15674 | 0.16465 | 0.13269 |
|                    | % BRAIN: | 32.002  | 46.825  | 48.581  | 41.111  |
| THYMUS             | G:       | 5.2320  | 4.9370  | 4.1800  | 4.6160  |
|                    | % BODY : | 0.17676 | 0.16793 | 0.14615 | 0.14247 |
|                    | % BRAIN: | 53.855  | 50.168  | 43.124  | 44.143  |
| THYROID GLANDS     | G:       | 0.2730  | 0.4420  | 0.2530  | 0.3280  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.00922 | 0.01503 | 0.00885 | 0.01012 |
|                    | % BRAIN: | 2.810   | 4.491   | 2.610   | 3.137   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D31  
SEX : MALE

ANIMAL NUMBER : N30665  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-SEP-18  
DEFND./ACTUAL NECR.STATE: K0/K0

FINAL BODY WEIGHT KG: 3.1600

ADRENAL GLANDS G: 0.2060  
LEFT :  
RIGHT:  
% BODY : 0.00652  
% BRAIN: 2.068

BRAIN G: 9.9620  
% BODY : 0.31525

EPIDIDYMIDES G: 2.0530  
LEFT :  
RIGHT:  
% BODY : 0.06497  
% BRAIN: 20.608

HEART G: 8.5060  
% BODY : 0.26918  
% BRAIN: 85.384

KIDNEYS G: 16.7170  
LEFT :  
RIGHT:  
% BODY : 0.52902  
% BRAIN: 167.808

LIVER G: 76.6890  
% BODY : 2.427  
% BRAIN: 769.815

LUNGS G: 10.4980  
% BODY : 0.33222  
% BRAIN: 105.380

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D31  
SEX : MALE

|                    |          |         |
|--------------------|----------|---------|
| ANIMAL NUMBER      | :        | N30665  |
| PITUITARY GLAND    | G:       | 0.0340  |
|                    | % BODY : | 0.00108 |
|                    | % BRAIN: | 0.341   |
| PROSTATE+SEMINALES | G:       | 5.8940  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.18652 |
|                    | % BRAIN: | 59.165  |
| SPLEEN             | G:       | 1.7080  |
|                    | % BODY : | 0.05405 |
|                    | % BRAIN: | 17.145  |
| TESTES             | G:       | 4.2300  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.13386 |
|                    | % BRAIN: | 42.461  |
| THYMUS             | G:       | 3.2770  |
|                    | % BODY : | 0.10370 |
|                    | % BRAIN: | 32.895  |
| THYROID GLANDS     | G:       | 0.3360  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.01063 |
|                    | % BRAIN: | 3.373   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D31  
SEX : FEMALE

| ANIMAL NUMBER             | :        | N30731    | N30732    | N30733    | N30734    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 31        | 31        | 31        | 31        |
| DATE OF NECROPSY          | :        | 27-SEP-18 | 27-SEP-18 | 27-SEP-18 | 27-SEP-18 |
| DEFND./ACTUAL NECR.STATE: |          | K0/K0     | K0/K0     | K0/K0     | K0/K0     |
| FINAL BODY WEIGHT         | KG:      | 3.2000    | 3.1000    | 3.0800    | 3.3000    |
| ADRENAL GLANDS            | G:       | 0.1420    | 0.1440    | 0.1720    | 0.1880    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.00444   | 0.00465   | 0.00558   | 0.00570   |
|                           | % BRAIN: | 1.566     | 1.392     | 1.965     | 1.974     |
| BRAIN                     | G:       | 9.0690    | 10.3450   | 8.7520    | 9.5230    |
|                           | % BODY : | 0.28341   | 0.33371   | 0.28416   | 0.28858   |
| HEART                     | G:       | 8.4700    | 7.9600    | 7.3550    | 7.8820    |
|                           | % BODY : | 0.26469   | 0.25677   | 0.23880   | 0.23885   |
|                           | % BRAIN: | 93.395    | 76.945    | 84.038    | 82.768    |
| KIDNEYS                   | G:       | 14.3120   | 15.2400   | 11.7620   | 15.3420   |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.44725   | 0.49161   | 0.38188   | 0.46491   |
|                           | % BRAIN: | 157.812   | 147.318   | 134.392   | 161.105   |
| LIVER                     | G:       | 75.9250   | 63.1410   | 59.4260   | 76.7400   |
|                           | % BODY : | 2.373     | 2.037     | 1.929     | 2.325     |
|                           | % BRAIN: | 837.193   | 610.353   | 678.999   | 805.838   |
| LUNGS                     | G:       | 10.9480   | 10.2640   | 9.2190    | 9.4700    |
|                           | % BODY : | 0.34213   | 0.33110   | 0.29932   | 0.28697   |
|                           | % BRAIN: | 120.719   | 99.217    | 105.336   | 99.443    |
| OVARIES                   | G:       | 0.7410    | 0.2670    | 0.4100    | 0.3080    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.02316   | 0.00861   | 0.01331   | 0.00933   |
|                           | % BRAIN: | 8.171     | 2.581     | 4.685     | 3.234     |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D31  
SEX : FEMALE

| ANIMAL NUMBER   | :        | N30731  | N30732  | N30733  | N30734  |
|-----------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND | G:       | 0.0320  | 0.0440  | 0.0350  | 0.0310  |
|                 | % BODY : | 0.00100 | 0.00142 | 0.00114 | 0.00094 |
|                 | % BRAIN: | 0.353   | 0.425   | 0.400   | 0.326   |
| SPLEEN          | G:       | 1.8770  | 1.7180  | 1.7510  | 2.0850  |
|                 | % BODY : | 0.05866 | 0.05542 | 0.05685 | 0.06318 |
|                 | % BRAIN: | 20.697  | 16.607  | 20.007  | 21.894  |
| THYMUS          | G:       | 4.7380  | 4.1840  | 2.5520  | 3.7900  |
|                 | % BODY : | 0.14806 | 0.13497 | 0.08286 | 0.11485 |
|                 | % BRAIN: | 52.244  | 40.445  | 29.159  | 39.798  |
| THYROID GLANDS  | G:       | 0.2870  | 0.3160  | 0.4480  | 0.3770  |
|                 | LEFT :   |         |         |         |         |
|                 | RIGHT:   |         |         |         |         |
|                 | % BODY : | 0.00897 | 0.01019 | 0.01455 | 0.01142 |
|                 | % BRAIN: | 3.165   | 3.055   | 5.119   | 3.959   |
| UTERUS          | G:       | 9.4450  | 5.0100  | 9.9890  | 7.1440  |
|                 | % BODY : | 0.29516 | 0.16161 | 0.32432 | 0.21649 |
|                 | % BRAIN: | 104.146 | 48.429  | 114.134 | 75.018  |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D31  
SEX : FEMALE

ANIMAL NUMBER : N30735  
DAYS ON TEST : 31  
DATE OF NECROPSY : 27-SEP-18  
DEFND./ACTUAL NECR.STATE: K0/K0

FINAL BODY WEIGHT KG: 3.3600

ADRENAL GLANDS G: 0.1620  
LEFT :  
RIGHT:  
% BODY : 0.00482  
% BRAIN: 1.593

BRAIN G: 10.1670  
% BODY : 0.30259

HEART G: 9.1050  
% BODY : 0.27098  
% BRAIN: 89.554

KIDNEYS G: 14.9070  
LEFT :  
RIGHT:  
% BODY : 0.44366  
% BRAIN: 146.621

LIVER G: 75.8260  
% BODY : 2.257  
% BRAIN: 745.805

LUNGS G: 12.1640  
% BODY : 0.36202  
% BRAIN: 119.642

OVARIES G: 0.2210  
LEFT :  
RIGHT:  
% BODY : 0.00658  
% BRAIN: 2.174

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D31  
SEX : FEMALE

|                 |          |         |
|-----------------|----------|---------|
| ANIMAL NUMBER   | :        | N30735  |
| .....           |          |         |
| PITUITARY GLAND | G:       | 0.0280  |
|                 | % BODY : | 0.00083 |
|                 | % BRAIN: | 0.275   |
| .....           |          |         |
| SPLEEN          | G:       | 1.9160  |
|                 | % BODY : | 0.05702 |
|                 | % BRAIN: | 18.845  |
| .....           |          |         |
| THYMUS          | G:       | 4.2570  |
|                 | % BODY : | 0.12670 |
|                 | % BRAIN: | 41.871  |
| .....           |          |         |
| THYROID GLANDS  | G:       | 0.3290  |
|                 | LEFT :   |         |
|                 | RIGHT:   |         |
|                 | % BODY : | 0.00979 |
|                 | % BRAIN: | 3.236   |
| .....           |          |         |
| UTERUS          | G:       | 6.8030  |
|                 | % BODY : | 0.20247 |
|                 | % BRAIN: | 66.913  |
| .....           |          |         |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS

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Explanation of Symbols:

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0 = Weight not recorded / Value not calculated  
\* = Tissue/Organ weighed after fixation

RD1811

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D57  
SEX : MALE

| ANIMAL NUMBER             | :        | N30646    | N30647    | N30648    | N30649    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 57        | 57        | 57        | 57        |
| DATE OF NECROPSY          | :        | 15-OCT-18 | 15-OCT-18 | 15-OCT-18 | 15-OCT-18 |
| DEFND./ACTUAL NECR.STATE: |          | R1/R1     | R1/R1     | R1/R1     | R1/R1     |
| FINAL BODY WEIGHT         | KG:      | 3.2400    | 3.4800    | 3.6000    | 3.8000    |
| ADRENAL GLANDS            | G:       | 0.3390    | 0.2850    | 0.2170    | 0.2430    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.01046   | 0.00819   | 0.00603   | 0.00640   |
|                           | % BRAIN: | 3.153     | 2.964     | 1.949     | 2.384     |
| BRAIN                     | G:       | 10.7530   | 9.6150    | 11.1330   | 10.1940   |
|                           | % BODY : | 0.33188   | 0.27629   | 0.30925   | 0.26826   |
| EPIDIDYMIDES              | G:       | 2.0290    | 2.4470    | 2.1550    | 2.7940    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.06262   | 0.07032   | 0.05986   | 0.07353   |
|                           | % BRAIN: | 18.869    | 25.450    | 19.357    | 27.408    |
| HEART                     | G:       | 7.0580    | 8.0070    | 8.7870    | 8.7850    |
|                           | % BODY : | 0.21784   | 0.23009   | 0.24408   | 0.23118   |
|                           | % BRAIN: | 65.637    | 83.276    | 78.928    | 86.178    |
| KIDNEYS                   | G:       | 15.7620   | 16.4240   | 16.5570   | 18.8610   |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.48648   | 0.47195   | 0.45992   | 0.49634   |
|                           | % BRAIN: | 146.582   | 170.816   | 148.720   | 185.021   |
| LIVER                     | G:       | 65.3110   | 68.8550   | 61.6330   | 86.3580   |
|                           | % BODY : | 2.016     | 1.979     | 1.712     | 2.273     |
|                           | % BRAIN: | 607.375   | 716.121   | 553.606   | 847.145   |
| LUNGS                     | G:       | 10.6450   | 10.0940   | 10.0960   | 10.7170   |
|                           | % BODY : | 0.32855   | 0.29006   | 0.28044   | 0.28203   |
|                           | % BRAIN: | 98.996    | 104.982   | 90.685    | 105.130   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D57  
SEX : MALE

| ANIMAL NUMBER      | :        | N30646  | N30647  | N30648  | N30649  |
|--------------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND    | G:       | 0.0250  | 0.0290  | 0.0370  | 0.0280  |
|                    | % BODY : | 0.00077 | 0.00083 | 0.00103 | 0.00074 |
|                    | % BRAIN: | 0.232   | 0.302   | 0.332   | 0.275   |
| PROSTATE+SEMINALES | G:       | 5.6010  | 3.3490  | 4.6200  | 4.5990  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.17287 | 0.09624 | 0.12833 | 0.12103 |
|                    | % BRAIN: | 52.088  | 34.831  | 41.498  | 45.115  |
| SPLEEN             | G:       | 0.9690  | 1.2660  | 0.7490  | 1.3010  |
|                    | % BODY : | 0.02991 | 0.03638 | 0.02081 | 0.03424 |
|                    | % BRAIN: | 9.011   | 13.167  | 6.728   | 12.762  |
| TESTES             | G:       | 5.3580  | 5.1650  | 6.6710  | 5.0860  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.16537 | 0.14842 | 0.18531 | 0.13384 |
|                    | % BRAIN: | 49.828  | 53.718  | 59.921  | 49.892  |
| THYMUS             | G:       | 3.6260  | 3.2910  | 4.3730  | 4.7720  |
|                    | % BODY : | 0.11191 | 0.09457 | 0.12147 | 0.12558 |
|                    | % BRAIN: | 33.721  | 34.228  | 39.280  | 46.812  |
| THYROID GLANDS     | G:       | 0.2380  | 0.2150  | 0.2350  | 0.2890  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.00735 | 0.00618 | 0.00653 | 0.00761 |
|                    | % BRAIN: | 2.213   | 2.236   | 2.111   | 2.835   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D57  
SEX : MALE

ANIMAL NUMBER : N30650  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-OCT-18  
DEFND./ACTUAL NECR.STATE: R1/R1  
.....  
FINAL BODY WEIGHT KG: 3.7400  
.....  
ADRENAL GLANDS G: 0.2170  
LEFT :  
RIGHT:  
% BODY : 0.00580  
% BRAIN: 2.280  
.....  
BRAIN G: 9.5170  
% BODY : 0.25447  
.....  
EPIDIDYMIDES G: 2.0330  
LEFT :  
RIGHT:  
% BODY : 0.05436  
% BRAIN: 21.362  
.....  
HEART G: 8.5140  
% BODY : 0.22765  
% BRAIN: 89.461  
.....  
KIDNEYS G: 17.2370  
LEFT :  
RIGHT:  
% BODY : 0.46088  
% BRAIN: 181.118  
.....  
LIVER G: 70.9800  
% BODY : 1.898  
% BRAIN: 745.823  
.....  
LUNGS G: 11.1010  
% BODY : 0.29682  
% BRAIN: 116.644  
.....

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D57  
SEX : MALE

|                    |          |         |
|--------------------|----------|---------|
| ANIMAL NUMBER      | :        | N30650  |
| PITUITARY GLAND    | G:       | 0.0200  |
|                    | % BODY : | 0.00054 |
|                    | % BRAIN: | 0.210   |
| PROSTATE+SEMINALES | G:       | 4.2270  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.11302 |
|                    | % BRAIN: | 44.415  |
| SPLEEN             | G:       | 0.9380  |
|                    | % BODY : | 0.02508 |
|                    | % BRAIN: | 9.856   |
| TESTES             | G:       | 4.0630  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.10864 |
|                    | % BRAIN: | 42.692  |
| THYMUS             | G:       | 5.8910  |
|                    | % BODY : | 0.15751 |
|                    | % BRAIN: | 61.900  |
| THYROID GLANDS     | G:       | 0.2550  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.00682 |
|                    | % BRAIN: | 2.679   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D57  
SEX : FEMALE

| ANIMAL NUMBER             | :        | N30716    | N30717    | N30718    | N30719    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 57        | 57        | 57        | 57        |
| DATE OF NECROPSY          | :        | 23-OCT-18 | 23-OCT-18 | 23-OCT-18 | 23-OCT-18 |
| DEFND./ACTUAL NECR.STATE: |          | R1/R1     | R1/R1     | R1/R1     | R1/R1     |
| FINAL BODY WEIGHT         | KG:      | 4.1800    | 3.8200    | 3.9800    | 3.9000    |
| ADRENAL GLANDS            | G:       | 0.2440    | 0.1880    | 0.2110    | 0.2040    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.00584   | 0.00492   | 0.00530   | 0.00523   |
| % BRAIN:                  |          | 2.356     | 1.779     | 2.003     | 2.133     |
| BRAIN                     | G:       | 10.3570   | 10.5670   | 10.5350   | 9.5620    |
|                           | % BODY : | 0.24778   | 0.27662   | 0.26470   | 0.24518   |
| HEART                     | G:       | 9.4030    | 8.4640    | 9.1240    | 8.7600    |
|                           | % BODY : | 0.22495   | 0.22157   | 0.22925   | 0.22462   |
|                           | % BRAIN: | 90.789    | 80.098    | 86.607    | 91.613    |
| KIDNEYS                   | G:       | 18.7330   | 17.7470   | 19.0220   | 14.8530   |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.44816   | 0.46458   | 0.47794   | 0.38085   |
| % BRAIN:                  |          | 180.873   | 167.947   | 180.560   | 155.334   |
| LIVER                     | G:       | 83.8960   | 87.3220   | 73.6970   | 75.7150   |
|                           | % BODY : | 2.007     | 2.286     | 1.852     | 1.941     |
|                           | % BRAIN: | 810.042   | 826.365   | 699.544   | 791.832   |
| LUNGS                     | G:       | 12.6520   | 9.4960    | 10.7680   | 11.0330   |
|                           | % BODY : | 0.30268   | 0.24859   | 0.27055   | 0.28290   |
|                           | % BRAIN: | 122.159   | 89.865    | 102.212   | 115.384   |
| OVARIES                   | G:       | 0.4690    | 0.4350    | 0.5010    | 0.3620    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.01122   | 0.01139   | 0.01259   | 0.00928   |
| % BRAIN:                  |          | 4.528     | 4.117     | 4.756     | 3.786     |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D57  
SEX : FEMALE

| ANIMAL NUMBER   | :        | N30716  | N30717  | N30718  | N30719  |
|-----------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND | G:       | 0.0360  | 0.0350  | 0.0380  | 0.0320  |
|                 | % BODY : | 0.00086 | 0.00092 | 0.00096 | 0.00082 |
|                 | % BRAIN: | 0.348   | 0.331   | 0.361   | 0.335   |
| SPLEEN          | G:       | 2.0890  | 2.4440  | 2.0960  | 1.5940  |
|                 | % BODY : | 0.04998 | 0.06398 | 0.05266 | 0.04087 |
|                 | % BRAIN: | 20.170  | 23.129  | 19.896  | 16.670  |
| THYMUS          | G:       | 4.7750  | 3.3480  | 3.2950  | 4.6140  |
|                 | % BODY : | 0.11423 | 0.08764 | 0.08279 | 0.11831 |
|                 | % BRAIN: | 46.104  | 31.684  | 31.277  | 48.254  |
| THYROID GLANDS  | G:       | 0.7210  | 0.2180  | 0.3890  | 0.4240  |
|                 | LEFT :   |         |         |         |         |
|                 | RIGHT:   |         |         |         |         |
|                 | % BODY : | 0.01725 | 0.00571 | 0.00977 | 0.01087 |
|                 | % BRAIN: | 6.961   | 2.063   | 3.692   | 4.434   |
| UTERUS          | G:       | 12.2410 | 9.2890  | 12.2400 | 9.4350  |
|                 | % BODY : | 0.29285 | 0.24317 | 0.30754 | 0.24192 |
|                 | % BRAIN: | 118.191 | 87.906  | 116.184 | 98.672  |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D57  
SEX : FEMALE

ANIMAL NUMBER : N30720  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-OCT-18  
DEFND./ACTUAL NECR.STATE: R1/R1  
.....  
FINAL BODY WEIGHT KG: 4.2000  
.....  
ADRENAL GLANDS G: 0.2340  
LEFT :  
RIGHT:  
% BODY : 0.00557  
% BRAIN: 2.133  
.....  
BRAIN G: 10.9710  
% BODY : 0.26121  
.....  
HEART G: 9.2290  
% BODY : 0.21974  
% BRAIN: 84.122  
.....  
KIDNEYS G: 17.2010  
LEFT :  
RIGHT:  
% BODY : 0.40955  
% BRAIN: 156.786  
.....  
LIVER G: 90.7110  
% BODY : 2.160  
% BRAIN: 826.825  
.....  
LUNGS G: 10.5250  
% BODY : 0.25060  
% BRAIN: 95.935  
.....  
OVARIES G: 0.2880  
LEFT :  
RIGHT:  
% BODY : 0.00686  
% BRAIN: 2.625  
.....

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 1, 0 microg HA/strain/dose D57  
SEX : FEMALE

|                 |          |         |
|-----------------|----------|---------|
| ANIMAL NUMBER   | :        | N30720  |
| PITUITARY GLAND | G:       | 0.0350  |
|                 | % BODY : | 0.00083 |
|                 | % BRAIN: | 0.319   |
| SPLEEN          | G:       | 1.5710  |
|                 | % BODY : | 0.03741 |
|                 | % BRAIN: | 14.320  |
| THYMUS          | G:       | 5.4690  |
|                 | % BODY : | 0.13021 |
|                 | % BRAIN: | 49.850  |
| THYROID GLANDS  | G:       | 0.4000  |
|                 | LEFT :   |         |
|                 | RIGHT:   |         |
|                 | % BODY : | 0.00952 |
|                 | % BRAIN: | 3.646   |
| UTERUS          | G:       | 7.8980  |
|                 | % BODY : | 0.18805 |
|                 | % BRAIN: | 71.990  |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D57  
SEX : MALE

| ANIMAL NUMBER             | :        | N30656    | N30657    | N30658    | N30659    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 57        | 57        | 57        | 57        |
| DATE OF NECROPSY          | :        | 15-OCT-18 | 15-OCT-18 | 15-OCT-18 | 15-OCT-18 |
| DEFND./ACTUAL NECR.STATE: |          | R1/R1     | R1/R1     | R1/R1     | R1/R1     |
| FINAL BODY WEIGHT         | KG:      | 3.4200    | 3.3400    | 3.2800    | 3.6600    |
| ADRENAL GLANDS            | G:       | 0.2630    | 0.1960    | 0.1870    | 0.1520    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.00769   | 0.00587   | 0.00570   | 0.00415   |
| % BRAIN:                  |          | 2.482     | 1.914     | 1.930     | 1.538     |
| BRAIN                     | G:       | 10.5980   | 10.2410   | 9.6900    | 9.8840    |
|                           | % BODY : | 0.30988   | 0.30662   | 0.29543   | 0.27006   |
| EPIDIDYMIDES              | G:       | 2.7980    | 1.9180    | 2.6080    | 2.7440    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.08181   | 0.05743   | 0.07951   | 0.07497   |
| % BRAIN:                  |          | 26.401    | 18.729    | 26.914    | 27.762    |
| HEART                     | G:       | 7.9390    | 8.2870    | 7.3820    | 8.5830    |
|                           | % BODY : | 0.23214   | 0.24811   | 0.22506   | 0.23451   |
|                           | % BRAIN: | 74.910    | 80.920    | 76.182    | 86.837    |
| KIDNEYS                   | G:       | 17.1960   | 15.1400   | 14.5460   | 15.6920   |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.50281   | 0.45329   | 0.44348   | 0.42874   |
| % BRAIN:                  |          | 162.257   | 147.837   | 150.114   | 158.762   |
| LIVER                     | G:       | 69.1660   | 66.7030   | 67.7060   | 88.1220   |
|                           | % BODY : | 2.022     | 1.997     | 2.064     | 2.408     |
|                           | % BRAIN: | 652.633   | 651.333   | 698.720   | 891.562   |
| LUNGS                     | G:       | 10.6930   | 10.9300   | 9.5140    | 10.7790   |
|                           | % BODY : | 0.31266   | 0.32725   | 0.29006   | 0.29451   |
|                           | % BRAIN: | 100.896   | 106.728   | 98.184    | 109.055   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D57  
SEX : MALE

| ANIMAL NUMBER      | :        | N30656  | N30657  | N30658  | N30659  |
|--------------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND    | G:       | 0.0300  | 0.0110  | 0.0150  | 0.0230  |
|                    | % BODY : | 0.00088 | 0.00033 | 0.00046 | 0.00063 |
|                    | % BRAIN: | 0.283   | 0.107   | 0.155   | 0.233   |
| PROSTATE+SEMINALES | G:       | 3.5230  | 2.8720  | 4.0530  | 3.9400  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.10301 | 0.08599 | 0.12357 | 0.10765 |
|                    | % BRAIN: | 33.242  | 28.044  | 41.827  | 39.862  |
| SPLEEN             | G:       | 1.2230  | 0.9180  | 1.8920  | 1.5910  |
|                    | % BODY : | 0.03576 | 0.02749 | 0.05768 | 0.04347 |
|                    | % BRAIN: | 11.540  | 8.964   | 19.525  | 16.097  |
| TESTES             | G:       | 4.3960  | 4.8130  | 1.1020  | 4.5420  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.12854 | 0.14410 | 0.03360 | 0.12410 |
|                    | % BRAIN: | 41.480  | 46.997  | 11.373  | 45.953  |
| THYMUS             | G:       | 5.4650  | 3.2790  | 5.0970  | 4.9610  |
|                    | % BODY : | 0.15980 | 0.09817 | 0.15540 | 0.13555 |
|                    | % BRAIN: | 51.566  | 32.018  | 52.601  | 50.192  |
| THYROID GLANDS     | G:       | 0.2980  | 0.2730  | 0.2290  | 0.3170  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.00871 | 0.00817 | 0.00698 | 0.00866 |
|                    | % BRAIN: | 2.812   | 2.666   | 2.363   | 3.207   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D57  
SEX : MALE

ANIMAL NUMBER : N30660  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-OCT-18  
DEFND./ACTUAL NECR.STATE: R1/R1

FINAL BODY WEIGHT KG: 3.6200

ADRENAL GLANDS G: 0.1920  
LEFT :  
RIGHT:  
% BODY : 0.00530  
% BRAIN: 1.791

BRAIN G: 10.7190  
% BODY : 0.29611

EPIDIDYMIDES G: 3.0550  
LEFT :  
RIGHT:  
% BODY : 0.08439  
% BRAIN: 28.501

HEART G: 15.1520  
% BODY : 0.41856  
% BRAIN: 141.356

KIDNEYS G: 17.8210  
LEFT :  
RIGHT:  
% BODY : 0.49229  
% BRAIN: 166.256

LIVER G: 99.1730  
% BODY : 2.740  
% BRAIN: 925.208

LUNGS G: 16.6820  
% BODY : 0.46083  
% BRAIN: 155.630

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D57  
SEX : MALE

|                    |          |         |
|--------------------|----------|---------|
| ANIMAL NUMBER      | :        | N30660  |
| PITUITARY GLAND    | G:       | 0.0260  |
|                    | % BODY : | 0.00072 |
|                    | % BRAIN: | 0.243   |
| PROSTATE+SEMINALES | G:       | 3.7010  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.10224 |
|                    | % BRAIN: | 34.527  |
| SPLEEN             | G:       | 1.5770  |
|                    | % BODY : | 0.04356 |
|                    | % BRAIN: | 14.712  |
| TESTES             | G:       | 5.1370  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.14191 |
|                    | % BRAIN: | 47.924  |
| THYMUS             | G:       | 4.9390  |
|                    | % BODY : | 0.13644 |
|                    | % BRAIN: | 46.077  |
| THYROID GLANDS     | G:       | 0.1220  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.00337 |
|                    | % BRAIN: | 1.138   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D57  
SEX : FEMALE

| ANIMAL NUMBER             | :        | N30726    | N30727    | N30728    | N30729    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 57        | 57        | 57        | 57        |
| DATE OF NECROPSY          | :        | 23-OCT-18 | 23-OCT-18 | 23-OCT-18 | 23-OCT-18 |
| DEFND./ACTUAL NECR.STATE: |          | R1/R1     | R1/R1     | R1/R1     | R1/R1     |
| FINAL BODY WEIGHT         | KG:      | 3.5800    | 3.8400    | 4.4000    | 3.8000    |
| ADRENAL GLANDS            | G:       | 0.1890    | 0.1670    | 0.2150    | 0.1760    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.00528   | 0.00435   | 0.00489   | 0.00463   |
| % BRAIN:                  |          | 1.937     | 1.619     | 2.129     | 1.609     |
| BRAIN                     | G:       | 9.7590    | 10.3180   | 10.1010   | 10.9360   |
|                           | % BODY : | 0.27260   | 0.26870   | 0.22957   | 0.28779   |
| HEART                     | G:       | 8.5640    | 7.9970    | 8.2580    | 9.3360    |
|                           | % BODY : | 0.23922   | 0.20826   | 0.18768   | 0.24568   |
|                           | % BRAIN: | 87.755    | 77.505    | 81.754    | 85.369    |
| KIDNEYS                   | G:       | 17.1010   | 15.9070   | 19.3680   | 16.8540   |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.47768   | 0.41425   | 0.44018   | 0.44353   |
| % BRAIN:                  |          | 175.233   | 154.167   | 191.743   | 154.115   |
| LIVER                     | G:       | 65.8850   | 76.3300   | 90.6970   | 75.5060   |
|                           | % BODY : | 1.840     | 1.988     | 2.061     | 1.987     |
|                           | % BRAIN: | 675.120   | 739.775   | 897.901   | 690.435   |
| LUNGS                     | G:       | 9.9640    | 11.8680   | 11.0710   | 13.1420   |
|                           | % BODY : | 0.27832   | 0.30906   | 0.25161   | 0.34584   |
|                           | % BRAIN: | 102.101   | 115.022   | 109.603   | 120.172   |
| OVARIES                   | G:       | 0.2770    | 0.3640    | 0.6730    | 0.5550    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.00774   | 0.00948   | 0.01530   | 0.01461   |
| % BRAIN:                  |          | 2.838     | 3.528     | 6.663     | 5.075     |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D57  
SEX : FEMALE

| ANIMAL NUMBER   | :        | N30726  | N30727  | N30728  | N30729  |
|-----------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND | G:       | 0.0350  | 0.0370  | 0.0440  | 0.0350  |
|                 | % BODY : | 0.00098 | 0.00096 | 0.00100 | 0.00092 |
|                 | % BRAIN: | 0.359   | 0.359   | 0.436   | 0.320   |
| SPLEEN          | G:       | 1.4780  | 2.0580  | 2.3540  | 2.1970  |
|                 | % BODY : | 0.04129 | 0.05359 | 0.05350 | 0.05782 |
|                 | % BRAIN: | 15.145  | 19.946  | 23.305  | 20.090  |
| THYMUS          | G:       | 4.6450  | 3.1990  | 4.0400  | 3.0310  |
|                 | % BODY : | 0.12975 | 0.08331 | 0.09182 | 0.07976 |
|                 | % BRAIN: | 47.597  | 31.004  | 39.996  | 27.716  |
| THYROID GLANDS  | G:       | 0.3430  | 0.3660  | 0.4460  | 0.3580  |
|                 | LEFT :   |         |         |         |         |
|                 | RIGHT:   |         |         |         |         |
|                 | % BODY : | 0.00958 | 0.00953 | 0.01014 | 0.00942 |
|                 | % BRAIN: | 3.515   | 3.547   | 4.415   | 3.274   |
| UTERUS          | G:       | 9.3960  | 5.8420  | 9.3420  | 11.5210 |
|                 | % BODY : | 0.26246 | 0.15214 | 0.21232 | 0.30318 |
|                 | % BRAIN: | 96.280  | 56.619  | 92.486  | 105.349 |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D57  
SEX : FEMALE

ANIMAL NUMBER : N30730  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-OCT-18  
DEFND./ACTUAL NECR.STATE: R1/R1  
.....  
FINAL BODY WEIGHT KG: 4.0800  
.....  
ADRENAL GLANDS G: 0.1820  
LEFT :  
RIGHT:  
% BODY : 0.00446  
% BRAIN: 1.784  
.....  
BRAIN G: 10.2030  
% BODY : 0.25007  
.....  
HEART G: 9.5280  
% BODY : 0.23353  
% BRAIN: 93.384  
.....  
KIDNEYS G: 18.8350  
LEFT :  
RIGHT:  
% BODY : 0.46164  
% BRAIN: 184.603  
.....  
LIVER G: 82.9130  
% BODY : 2.032  
% BRAIN: 812.634  
.....  
LUNGS G: 10.7080  
% BODY : 0.26245  
% BRAIN: 104.950  
.....  
OVARIES G: 0.2870  
LEFT :  
RIGHT:  
% BODY : 0.00703  
% BRAIN: 2.813  
.....

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 2, 15 microg HA/strain/dose D57  
SEX : FEMALE

|                 |          |         |
|-----------------|----------|---------|
| ANIMAL NUMBER   | :        | N30730  |
| .....           |          |         |
| PITUITARY GLAND | G:       | 0.0240  |
|                 | % BODY : | 0.00059 |
|                 | % BRAIN: | 0.235   |
| .....           |          |         |
| SPLEEN          | G:       | 1.5640  |
|                 | % BODY : | 0.03833 |
|                 | % BRAIN: | 15.329  |
| .....           |          |         |
| THYMUS          | G:       | 4.9990  |
|                 | % BODY : | 0.12253 |
|                 | % BRAIN: | 48.995  |
| .....           |          |         |
| THYROID GLANDS  | G:       | 0.3650  |
|                 | LEFT :   |         |
|                 | RIGHT:   |         |
|                 | % BODY : | 0.00895 |
|                 | % BRAIN: | 3.577   |
| .....           |          |         |
| UTERUS          | G:       | 7.1570  |
|                 | % BODY : | 0.17542 |
|                 | % BRAIN: | 70.146  |
| .....           |          |         |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D57  
SEX : MALE

| ANIMAL NUMBER             | :        | N30666    | N30667    | N30668    | N30669    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 57        | 57        | 57        | 57        |
| DATE OF NECROPSY          | :        | 15-OCT-18 | 15-OCT-18 | 15-OCT-18 | 15-OCT-18 |
| DEFND./ACTUAL NECR.STATE: |          | R1/R1     | R1/R1     | R1/R1     | R1/R1     |
| FINAL BODY WEIGHT         | KG:      | 3.3000    | 3.2800    | 3.5200    | 3.5600    |
| ADRENAL GLANDS            | G:       | 0.2260    | 0.2380    | 0.2320    | 0.2110    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.00685   | 0.00726   | 0.00659   | 0.00593   |
| % BRAIN:                  |          | 2.533     | 2.202     | 2.091     | 1.967     |
| BRAIN                     | G:       | 8.9210    | 10.8070   | 11.0960   | 10.7260   |
|                           | % BODY : | 0.27033   | 0.32948   | 0.31523   | 0.30129   |
| EPIDIDYMIDES              | G:       | 2.3040    | 2.1920    | 2.5340    | 2.5260    |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.06982   | 0.06683   | 0.07199   | 0.07096   |
| % BRAIN:                  |          | 25.827    | 20.283    | 22.837    | 23.550    |
| HEART                     | G:       | 7.4500    | 8.5550    | 8.3810    | 8.9390    |
|                           | % BODY : | 0.22576   | 0.26082   | 0.23810   | 0.25110   |
|                           | % BRAIN: | 83.511    | 79.162    | 75.532    | 83.340    |
| KIDNEYS                   | G:       | 15.1990   | 14.0210   | 17.9110   | 16.7140   |
| LEFT :                    |          |           |           |           |           |
| RIGHT:                    |          |           |           |           |           |
| % BODY :                  |          | 0.46058   | 0.42747   | 0.50884   | 0.46949   |
| % BRAIN:                  |          | 170.373   | 129.740   | 161.419   | 155.827   |
| LIVER                     | G:       | 75.3000   | 58.5930   | 75.2220   | 69.5380   |
|                           | % BODY : | 2.282     | 1.786     | 2.137     | 1.953     |
|                           | % BRAIN: | 844.076   | 542.176   | 677.920   | 648.313   |
| LUNGS                     | G:       | 10.7900   | 9.8310    | 11.9550   | 11.3710   |
|                           | % BODY : | 0.32697   | 0.29973   | 0.33963   | 0.31941   |
|                           | % BRAIN: | 120.951   | 90.969    | 107.742   | 106.013   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D57  
SEX : MALE

| ANIMAL NUMBER      | :        | N30666  | N30667  | N30668  | N30669  |
|--------------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND    | G:       | 0.0210  | 0.0280  | 0.0320  | 0.0230  |
|                    | % BODY : | 0.00064 | 0.00085 | 0.00091 | 0.00065 |
|                    | % BRAIN: | 0.235   | 0.259   | 0.288   | 0.214   |
| PROSTATE+SEMINALES | G:       | 3.9680  | 4.5420  | 6.7710  | 4.0430  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.12024 | 0.13848 | 0.19236 | 0.11357 |
|                    | % BRAIN: | 44.479  | 42.028  | 61.022  | 37.693  |
| SPLEEN             | G:       | 1.3020  | 1.3160  | 1.3150  | 1.4750  |
|                    | % BODY : | 0.03946 | 0.04012 | 0.03736 | 0.04143 |
|                    | % BRAIN: | 14.595  | 12.177  | 11.851  | 13.752  |
| TESTES             | G:       | 4.7010  | 4.4980  | 5.8300  | 4.3430  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.14246 | 0.13713 | 0.16563 | 0.12199 |
|                    | % BRAIN: | 52.696  | 41.621  | 52.541  | 40.490  |
| THYMUS             | G:       | 4.1850  | 5.8710  | 4.9400  | 6.0060  |
|                    | % BODY : | 0.12682 | 0.17899 | 0.14034 | 0.16871 |
|                    | % BRAIN: | 46.912  | 54.326  | 44.521  | 55.995  |
| THYROID GLANDS     | G:       | 0.2170  | 0.2240  | 0.2880  | 0.3390  |
|                    | LEFT :   |         |         |         |         |
|                    | RIGHT:   |         |         |         |         |
|                    | % BODY : | 0.00658 | 0.00683 | 0.00818 | 0.00952 |
|                    | % BRAIN: | 2.432   | 2.073   | 2.596   | 3.161   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D57  
SEX : MALE

ANIMAL NUMBER : N30670  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-OCT-18  
DEFND./ACTUAL NECR.STATE: R1/R1  
.....  
FINAL BODY WEIGHT KG: 3.8000  
.....  
ADRENAL GLANDS G: 0.3370  
LEFT :  
RIGHT:  
% BODY : 0.00887  
% BRAIN: 3.417  
.....  
BRAIN G: 9.8620  
% BODY : 0.25953  
.....  
EPIDIDYMIDES G: 2.7930  
LEFT :  
RIGHT:  
% BODY : 0.07350  
% BRAIN: 28.321  
.....  
HEART G: 7.8890  
% BODY : 0.20761  
% BRAIN: 79.994  
.....  
KIDNEYS G: 18.2570  
LEFT :  
RIGHT:  
% BODY : 0.48045  
% BRAIN: 185.125  
.....  
LIVER G: 84.6520  
% BODY : 2.228  
% BRAIN: 858.365  
.....  
LUNGS G: 12.0610  
% BODY : 0.31740  
% BRAIN: 122.298  
.....

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D57  
SEX : MALE

|                    |          |         |
|--------------------|----------|---------|
| ANIMAL NUMBER      | :        | N30670  |
| PITUITARY GLAND    | G:       | 0.0270  |
|                    | % BODY : | 0.00071 |
|                    | % BRAIN: | 0.274   |
| PROSTATE+SEMINALES | G:       | 3.7400  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.09842 |
|                    | % BRAIN: | 37.923  |
| SPLEEN             | G:       | 1.1700  |
|                    | % BODY : | 0.03079 |
|                    | % BRAIN: | 11.864  |
| TESTES             | G:       | 5.3860  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.14174 |
|                    | % BRAIN: | 54.614  |
| THYMUS             | G:       | 7.4030  |
|                    | % BODY : | 0.19482 |
|                    | % BRAIN: | 75.066  |
| THYROID GLANDS     | G:       | 0.3390  |
|                    | LEFT :   |         |
|                    | RIGHT:   |         |
|                    | % BODY : | 0.00892 |
|                    | % BRAIN: | 3.437   |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D57  
SEX : FEMALE

| ANIMAL NUMBER             | :        | N30736    | N30737    | N30738    | N30739    |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| DAYS ON TEST              | :        | 57        | 57        | 57        | 57        |
| DATE OF NECROPSY          | :        | 23-OCT-18 | 23-OCT-18 | 23-OCT-18 | 23-OCT-18 |
| DEFND./ACTUAL NECR.STATE: |          | R1/R1     | R1/R1     | R1/R1     | R1/R1     |
| FINAL BODY WEIGHT         | KG:      | 3.8000    | 3.9200    | 4.0000    | 4.1200    |
| ADRENAL GLANDS            | G:       | 0.1810    | 0.1520    | 0.2530    | 0.2040    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.00476   | 0.00388   | 0.00633   | 0.00495   |
|                           | % BRAIN: | 1.860     | 1.437     | 2.470     | 1.890     |
| BRAIN                     | G:       | 9.7330    | 10.5770   | 10.2430   | 10.7930   |
|                           | % BODY : | 0.25613   | 0.26982   | 0.25608   | 0.26197   |
| HEART                     | G:       | 8.9000    | 11.0540   | 7.7810    | 9.3110    |
|                           | % BODY : | 0.23421   | 0.28199   | 0.19453   | 0.22600   |
|                           | % BRAIN: | 91.441    | 104.510   | 75.964    | 86.269    |
| KIDNEYS                   | G:       | 14.8410   | 16.8760   | 15.4720   | 18.2760   |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.39055   | 0.43051   | 0.38680   | 0.44359   |
|                           | % BRAIN: | 152.481   | 159.554   | 151.049   | 169.332   |
| LIVER                     | G:       | 78.5020   | 80.8430   | 71.2790   | 94.5230   |
|                           | % BODY : | 2.066     | 2.062     | 1.782     | 2.294     |
|                           | % BRAIN: | 806.555   | 764.328   | 695.880   | 875.781   |
| LUNGS                     | G:       | 10.4670   | 10.6790   | 10.4370   | 10.9980   |
|                           | % BODY : | 0.27545   | 0.27242   | 0.26093   | 0.26694   |
|                           | % BRAIN: | 107.541   | 100.964   | 101.894   | 101.899   |
| OVARIES                   | G:       | 0.2680    | 0.3400    | 0.3990    | 0.2900    |
|                           | LEFT :   |           |           |           |           |
|                           | RIGHT:   |           |           |           |           |
|                           | % BODY : | 0.00705   | 0.00867   | 0.00998   | 0.00704   |
|                           | % BRAIN: | 2.754     | 3.215     | 3.895     | 2.687     |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D57  
SEX : FEMALE

| ANIMAL NUMBER   | :        | N30736  | N30737  | N30738  | N30739  |
|-----------------|----------|---------|---------|---------|---------|
| PITUITARY GLAND | G:       | 0.0490  | 0.0460  | 0.0300  | 0.0520  |
|                 | % BODY : | 0.00129 | 0.00117 | 0.00075 | 0.00126 |
|                 | % BRAIN: | 0.503   | 0.435   | 0.293   | 0.482   |
| SPLEEN          | G:       | 1.6920  | 2.5660  | 1.6670  | 1.9740  |
|                 | % BODY : | 0.04453 | 0.06546 | 0.04168 | 0.04791 |
|                 | % BRAIN: | 17.384  | 24.260  | 16.275  | 18.290  |
| THYMUS          | G:       | 4.0000  | 3.5700  | 4.1070  | 4.7070  |
|                 | % BODY : | 0.10526 | 0.09107 | 0.10268 | 0.11425 |
|                 | % BRAIN: | 41.097  | 33.752  | 40.096  | 43.612  |
| THYROID GLANDS  | G:       | 0.2390  | 0.3530  | 0.4730  | 0.3580  |
|                 | LEFT :   |         |         |         |         |
|                 | RIGHT:   |         |         |         |         |
|                 | % BODY : | 0.00629 | 0.00901 | 0.01183 | 0.00869 |
|                 | % BRAIN: | 2.456   | 3.337   | 4.618   | 3.317   |
| UTERUS          | G:       | 9.6890  | 7.7040  | 8.1000  | 8.8070  |
|                 | % BODY : | 0.25497 | 0.19653 | 0.20250 | 0.21376 |
|                 | % BRAIN: | 99.548  | 72.837  | 79.078  | 81.599  |

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D57  
SEX : FEMALE

ANIMAL NUMBER : N30740  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-OCT-18  
DEFND./ACTUAL NECR.STATE: R1/R1  
.....  
FINAL BODY WEIGHT KG: 3.7200  
.....  
ADRENAL GLANDS G: 0.1880  
LEFT :  
RIGHT:  
% BODY : 0.00505  
% BRAIN: 1.857  
.....  
BRAIN G: 10.1230  
% BODY : 0.27212  
.....  
HEART G: 8.7120  
% BODY : 0.23419  
% BRAIN: 86.061  
.....  
KIDNEYS G: 15.9110  
LEFT :  
RIGHT:  
% BODY : 0.42772  
% BRAIN: 157.177  
.....  
LIVER G: 83.6470  
% BODY : 2.249  
% BRAIN: 826.306  
.....  
LUNGS G: 10.3550  
% BODY : 0.27836  
% BRAIN: 102.292  
.....  
OVARIES G: 0.6900  
LEFT :  
RIGHT:  
% BODY : 0.01855  
% BRAIN: 6.816  
.....

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS  
TREATMENT-FREE PERIOD

-DOSE GROUP : 3, 45 microg HA/strain/dose D57  
SEX : FEMALE

|                 |          |         |
|-----------------|----------|---------|
| ANIMAL NUMBER   | :        | N30740  |
| .....           |          |         |
| PITUITARY GLAND | G:       | 0.0380  |
|                 | % BODY : | 0.00102 |
|                 | % BRAIN: | 0.375   |
| .....           |          |         |
| SPLEEN          | G:       | 1.6190  |
|                 | % BODY : | 0.04352 |
|                 | % BRAIN: | 15.993  |
| .....           |          |         |
| THYMUS          | G:       | 3.2930  |
|                 | % BODY : | 0.08852 |
|                 | % BRAIN: | 32.530  |
| .....           |          |         |
| THYROID GLANDS  | G:       | 0.4420  |
|                 | LEFT :   |         |
|                 | RIGHT:   |         |
|                 | % BODY : | 0.01188 |
|                 | % BRAIN: | 4.366   |
| .....           |          |         |
| UTERUS          | G:       | 11.0730 |
|                 | % BODY : | 0.29766 |
|                 | % BRAIN: | 109.385 |
| .....           |          |         |

2. Macroscopic and microscopic examinations: individual findings

EXPLANATION OF CODES AND SYMBOLS

---

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

---

M = Male animal  
F = Female animal  
K0 = Terminal sacrifice group  
R1...R9 = Recovery / post-treatment group 1...9

CODES AND SYMBOLS USED AT FINDING LEVEL:

---

GRADE 1 = Minimal / very few / very small  
GRADE 2 = Slight / few / small  
GRADE 3 = Moderate / moderate number / moderate size  
GRADE 4 = Marked / many / large  
GRADE 5 = Severe  
P = Finding present, severity not scored

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

---

ADIPOSE TISSUE

- Edema = Edema
- Hemorrhage = Hemorrhage
- Inflammation = Inflammation

ADRENAL GLANDS

- Accessory tissue = Accessory tissue
- Hemorrhage;focal = Hemorrhage; focal

BRAIN (MEDULLA,PONS,CEREBELLAR,CEREBRAL CORTEX)

- Vacuol;choroid plex. = Vacuolation; choroid plexus

DUODENUM

- Dilat;Brunner's gl = Dilatation; Brunner's gland

EPIDIDYMIDES

- Cell debris = Cell debris
- Dilatation = Dilatation
- Sperm decreased = Sperm decreased number

GUT ASSOCIATED LYMPHOID TISSUE

- Hyperplasia;lymphoid = Hyperplasia; lymphoid

EXPLANATION OF CODES AND SYMBOLS

---

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

---

- Infilt;granulocyte
  - = Infiltrate; granulocyte
- HARDERIAN GLANDS
- Degen;epithelium
  - = Degeneration; epithelium
- Infilt;mononuclear
  - = Infiltrate; mononuclear cell
- HEART
- Infilt;mononuc;myoc
  - = Infiltrate; mononuclear cell; myocardium
- ILIAC LYMPH NODES LEFT
- Dilatation;sinusoid
  - = Dilatation; sinusoid
- Hemorrhage;sinus
  - = Hemorrhage; sinus
- Hyperplasia;lymphoid
  - = Hyperplasia; lymphoid
- Infilt;granulocyte
  - = Infiltrate; granulocyte
- ILIAC LYMPH NODES RIGHT
- Hemorrhage;sinus
  - = Hemorrhage; sinus
- Hyperplasia;lymphoid
  - = Hyperplasia; lymphoid
- Infilt;granulocyte
  - = Infiltrate; granulocyte
- INGUINAL LYMPH NODES LEFT
- Hyperplasia;lymphoid
  - = Hyperplasia; lymphoid
- Infilt;granulocyte
  - = Infiltrate; granulocyte
- INGUINAL LYMPH NODES RIGHT
- Dilatation;sinusoid
  - = Dilatation; sinusoid
- Hyperplasia;lymphoid
  - = Hyperplasia; lymphoid
- Infilt;granulocyte
  - = Infiltrate; granulocyte
- INJECTION SITE 1
- Hemorrhage
  - = Hemorrhage
- Infilt;lymphocyte
  - = Infiltrate; lymphocyte
- Infilt;macrophage

EXPLANATION OF CODES AND SYMBOLS

---

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

---

- = Infiltrate; macrophage
- Inflamm;subacute
  - = Inflammation; subacute
- Necrosis;muscle
  - = Necrosis; muscle
- Needle tract lesion
  - = Needle tract lesion
- INJECTION SITE 2
  - Degen/regen;muscle
    - = Degeneration/regeneration; muscle
  - Hemorrhage
    - = Hemorrhage
  - Infilt;lymphocyte
    - = Infiltrate; lymphocyte
  - Infilt;macrophage
    - = Infiltrate; macrophage
  - Inflamm;subacute
    - = Inflammation; subacute
  - Necrosis;muscle
    - = Necrosis; muscle
  - Needle tract lesion
    - = Needle tract lesion
- INJECTION SITE 3
  - Artifact
    - = Artifact
  - Hemorrhage
    - = Hemorrhage
  - Infilt;lymphocyte
    - = Infiltrate; lymphocyte
  - Infilt;macrophage
    - = Infiltrate; macrophage
  - Inflamm;subacute
    - = Inflammation; subacute
  - Necrosis;muscle
    - = Necrosis; muscle
  - Needle tract lesion
    - = Needle tract lesion
- KIDNEYS
  - Basophilia;tubule
    - = Basophilia; tubule
  - Cyst;cortex
    - = Cyst; cortex
  - Dilatation;tubule
    - = Dilatation; tubule

EXPLANATION OF CODES AND SYMBOLS

---

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

---

- Fibrosis
    - = Fibrosis
  - Infilt;lymphocyte
    - = Infiltrate; lymphocyte
  - Infilt;mixed;fascia
    - = Infiltrate; mixed cell; fascia
  - Mineral;cortex
    - = Mineralization; cortex
- LACRIMAL GLANDS
- Atrophy; focal
    - = Atrophy; focal
  - Infilt;lymphocyte
    - = Infiltrate; lymphocyte
- LARYNX
- Infilt;mixed;subepit
    - = Infiltrate; mixed cell; subepithelial
  - Infilt;mononuc;musc
    - = Infiltrate; mononuclear cell; muscle
- LIVER
- Hypertrophy;focal
    - = Hypertrophy; focal
  - Infilt;mixed;focal
    - = Infiltrate; mixed cell; focal
- LUNGS (+ BRONCHI)
- Foreign material
    - = Foreign material
  - Hemorrhage;agonal
    - = Hemorrhage; agonal
  - Hyperplasia;lymphoid
    - = Hyperplasia; lymphoid
  - Infilt;granul;alveol
    - = Infiltrate; granulocyte; alveolus
  - Infilt;macro;alveol
    - = Infiltrate; macrophage; alveolus
  - Infilt;mixed;bronchi
    - = Infiltrate; mixed; bronchial lumen
  - Inflamm;chron;bronch
    - = Inflammation; chronic; bronchus
  - Metaplasia;osseous
    - = Metaplasia; osseous
- MANDIBULAR LYMPH NODES
- Dilatation; sinusoid
    - = Dilatation; sinusoid
  - Hemorrhage; sinus

EXPLANATION OF CODES AND SYMBOLS

---

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

---

- = Hemorrhage; sinus
- Hyperplasia; lymphoid
  - = Hyperplasia; lymphoid
- Infilt;granulocyte
  - = Infiltrate; granulocyte
- Infilt;macrophage
  - = Infiltrate; macrophage
- MESENTERIC LYMPH NODE
  - Hemorrhage;sinus
    - = Hemorrhage; sinus
  - Hyperplasia;lymphoid
    - = Hyperplasia; lymphoid
- NASAL CAVITY (ANTERIOR PART)
  - Artifact;blood lumen
    - = Artifact;blood in lumen
  - Inflamm;exudate
    - = Inflammation; intranasal exudate
- NASAL CAVITY (LEVEL 2)
  - Artifact;blood lumen
    - = Artifact;blood in lumen
  - Inflamm;exudate
    - = Inflammation; intranasal exudate
- NASAL CAVITY (LEVEL 3)
  - Artifact;blood lumen
    - = Artifact;blood in lumen
  - Inflamm;exudate
    - = Inflammation; intranasal exudate
- NASAL CAVITY (POSTERIOR, LEVEL 4)
  - Artifact;blood lumen
    - = Artifact;blood in lumen
  - Inflamm;exudate
    - = Inflammation; intranasal exudate
- OVARIES
  - Cyst;parovarian
    - = Cyst; parovarian
- PANCREAS
  - Ectopic tiss;spleen
    - = Ectopic tissue; spleen
  - Vacuol;acinar cell
    - = Vacuolation; acinar cell
- PAROTID GLANDS
  - Atrophy;focal
    - = Atrophy; focal

EXPLANATION OF CODES AND SYMBOLS

---

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

---

PITUITARY GLAND

- Cyst

= Cyst

RECTUM

- Inflamm;adjace.tiss.

= Inflammation; adjacent tissue

SACRAL LYMPH NODE

- Dilatation;sinusoid

= Dilatation; sinusoid

- Hemorrhage;sinus

= Hemorrhage; sinus

- Hyperplasia;lymphoid

= Hyperplasia; lymphoid

- Infilt;granulocyte

= Infiltrate; granulocyte

SKIN

- Crust

= Crust

- Hyperkeratosis

= Hyperkeratosis

- Inflamm;chronic

= Inflammation; chronic

- Inflamm;panniculus

= Inflammation; panniculus muscle

SKIN SITE 1

- Infilt;mixed;dermis

= Infiltrate; mixed cell; dermis

- Infilt;mixed;subcut

= Infiltrate; mixed; subcutis

- Needle tract lesion

= Needle tract lesion

SKIN SITE 2

- Cyst;pseudocyst

= Cyst; inflammatory pseudocyst

- Fibroplasia

= Fibroplasia

- Infilt;mixed;dermis

= Infiltrate; mixed cell; dermis

- Infilt;mixed;subcut

= Infiltrate; mixed; subcutis

- Inflamm;panniculus

= Inflammation; panniculus muscle

SKIN SITE 3

- Hemorrhage;dermis

EXPLANATION OF CODES AND SYMBOLS

---

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

---

= Hemorrhage; dermis  
- Hemorrhage; subcutis  
= Hemorrhage; subcutis  
- Infilt;mixed;dermis  
= Infiltrate; mixed cell; dermis  
- Infilt;mixed;subcut  
= Infiltrate; mixed; subcutis  
- Inflamm;panniculus  
= Inflammation; panniculus muscle  
SPLEEN  
- Hyperplasia; lymphoid  
= Hyperplasia; lymphoid  
STOMACH  
- Congestion; focal  
= Congestion; focal  
- Dilatation; gland  
= Dilatation; gland  
- Infilt;mixed;muscle  
= Infiltrate; mixed cell; muscle  
- Mineralization; gland  
= Mineralization; gland  
TESTES  
- Atrophy;tubule  
= Atrophy; tubule  
- Dilatation;tubule  
= Dilatation; tubule  
- Hypoplasia  
= Hypoplasia  
- Multinuc giant cell  
= Multinucleated giant cell  
THYMUS  
- Hemorrhage;agonal  
= Hemorrhage; agonal  
THYROID GLANDS  
- Degeneration; cystic  
= Degeneration; cystic  
TONGUE  
- Infilt;mixed;muscle  
= Infiltrate; mixed; muscle  
URETERS  
- Infilt;mixed;fascia  
= Infiltrate; mixed cell; fascia  
VAGINA  
- Cyst

EXPLANATION OF CODES AND SYMBOLS

-----

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

-----

= Cyst

## ANIMAL HEADING DATA

DOSE GROUP : 1, 0 microg HA/strain/dose D31

| ANIMAL<br>NUMBER | SEX<br>M/F | DEFINED AND FINAL<br>STATE OF NECROPSY | TEST<br>DAYS | FIRST AND LAST<br>DAY UNDER TEST | DATE OF<br>NECROPSY |
|------------------|------------|--|--------------|----------------------------------|---------------------|
| N30641           | M          | K0                                     | K0           | 31 20-AUG-18                     | 19-SEP-18           |
| N30642           | M          | K0                                     | K0           | 31 20-AUG-18                     | 19-SEP-18           |
| N30643           | M          | K0                                     | K0           | 31 20-AUG-18                     | 19-SEP-18           |
| N30644           | M          | K0                                     | K0           | 31 20-AUG-18                     | 19-SEP-18           |
| N30645           | M          | K0                                     | K0           | 31 20-AUG-18                     | 19-SEP-18           |
| N30711           | F          | K0                                     | K0           | 31 28-AUG-18                     | 27-SEP-18           |
| N30712           | F          | K0                                     | K0           | 31 28-AUG-18                     | 27-SEP-18           |
| N30713           | F          | K0                                     | K0           | 31 28-AUG-18                     | 27-SEP-18           |
| N30714           | F          | K0                                     | K0           | 31 28-AUG-18                     | 27-SEP-18           |
| N30715           | F          | K0                                     | K0           | 31 28-AUG-18                     | 27-SEP-18           |

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30641 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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| * NECROPSY OBSERVATION                              | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| INJECTION SITE 1                                    |                                   |
| - 01: Red discoloration, approx 3 cm in diameter.   | - Hemorrhage, fascia, grade 2.    |
| INJECTION SITE 2                                    |                                   |
| - 01: Red discoloration, approx 0.8 cm in diameter. | - Hemorrhage, fascia, grade 1.    |
| INJECTION SITE 3                                    |                                   |
| - 01: Red discoloration, approx 3 cm in diameter.   | - Hemorrhage, fascia, grade 2.    |
| NO OTHER NECROPSY OBSERVATIONS NOTED                |                                   |

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:  
-Accessory tissue, unilateral  
BRAIN (MEDULLA,PONS,CEREBELLAR,CEREBRAL CORTEX):  
-Vacuolation; choroid plexus, grade 2  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Hemorrhage, fascia, grade 2  
This finding corresponds to necropsy observation no: 01.  
INJECTION SITE 2:  
-Hemorrhage, fascia, grade 1  
This finding corresponds to necropsy observation no: 01.  
INJECTION SITE 3:  
-Inflammation; subacute, fascia, grade 1  
-Hemorrhage, fascia, grade 2  
This finding corresponds to necropsy observation no: 01.  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30641

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LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 1  
MANDIBULAR LYMPH NODES:  
-Hemorrhage; sinus, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
NASAL CAVITY (LEVEL 2):  
-Artifact; blood in lumen  
NASAL CAVITY (LEVEL 3):  
-Artifact; blood in lumen  
NASAL CAVITY (POSTERIOR, LEVEL 4):  
-Artifact; blood in lumen  
PROSTATE:  
Tissue not present for histologic examination  
SACRAL LYMPH NODE:  
-Hemorrhage; sinus, grade 3  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30642 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

BRAIN (MEDULLA,PONS,CEREBELLAR,CEREBRAL CORTEX):  
-Vacuolation; choroid plexus, grade 1  
GUT ASSOCIATED LYMPHOID TISSUE:  
Tissue not present for histologic examination  
ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 3:  
-Infiltrate; macrophage, muscle, focal, grade 1  
-Necrosis; muscle, focal, grade 1  
KIDNEYS:  
-Mineralization; cortex, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 2  
PARATHYROID GLANDS:  
Only one of paired organs examined/present  
THYMUS:  
-Hemorrhage; agonal, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30643 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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| * NECROPSY OBSERVATION  | CORRESPONDING MICROSCOPIC FINDING        |
|---|--|
| ILIAC LYMPH NODES LEFT  |  |
| - 01: Enlarged.   | - Hemorrhage; sinus, grade 2.            |
| INJECTION SITE 2  |  |
| - 01: Red discoloration, approx 0.4 cm in diameter.   | - Hemorrhage, fascia, grade 1.           |
| SKIN  |  |
| - 01: Dorsal region: white discoloration, approx 0.2 cm in diameter, raised, corresponding to: papulla. | - Inflammation; chronic, focal, grade 1. |
| NO OTHER NECROPSY OBSERVATIONS NOTED  |  |

\* MICROSCOPIC FINDINGS

EPIDIDYMIDES:  
-Cell debris, bilateral, grade 2  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
HARDERIAN GLANDS:  
-Infiltrate; mononuclear cell, unilateral, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hemorrhage; sinus, grade 2  
This finding corresponds to necropsy observation no: 01.  
INGUINAL LYMPH NODES RIGHT:  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 2:  
-Hemorrhage, fascia, grade 1  
This finding corresponds to necropsy observation no: 01.  
INJECTION SITE 3:  
-Infiltrate; macrophage, muscle, focal, grade 1  
-Necrosis; muscle, focal, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30643

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KIDNEYS:

- Dilatation; tubule, bilateral, grade 1
- Mineralization; cortex, bilateral, grade 1

LACRIMAL GLANDS:

- Infiltrate; lymphocyte, unilateral, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1

MANDIBULAR LYMPH NODES:

- Infiltrate; granulocyte, bilateral, grade 1
- Infiltrate; macrophage, bilateral, grade 3

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

NASAL CAVITY (LEVEL 3):

- Artifact; blood in lumen

PANCREAS:

- Ectopic tissue; spleen

PARATHYROID GLANDS:

- Only one of paired organs examined/present

SACRAL LYMPH NODE:

Tissue not present for histologic examination

SKIN:

- Crust, grade 1

- Inflammation; chronic, focal, grade 1

This finding corresponds to necropsy observation no: 01.

TESTES:

- Atrophy; tubule, bilateral, grade 2
- Multinucleated giant cell, bilateral, grade 2

THYMUS:

- Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30644 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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| * NECROPSY OBSERVATION   | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| INJECTION SITE 1   |                                   |
| - 01: Red discoloration, approx 2 cm long, approx 0.5 cm wide. | - Hemorrhage, fascia, grade 1.    |
| NO OTHER NECROPSY OBSERVATIONS NOTED                           |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 2  
ILIIAC LYMPH NODES LEFT:  
-Hemorrhage; sinus, grade 2  
INJECTION SITE 1:  
-Hemorrhage, fascia, grade 1  
This finding corresponds to necropsy observation no: 01.  
KIDNEYS:  
-Basophilia; tubule, unilateral, grade 1  
LACRIMAL GLANDS:  
-Infiltrate; lymphocyte, bilateral, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 1  
MANDIBULAR LYMPH NODES:  
-Dilatation; sinusoid, bilateral, grade 1  
-Hemorrhage; sinus, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
PARATHYROID GLANDS:  
Only one of paired organs examined/present  
URETERS:  
Only one of paired organs examined/present  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30645 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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| * NECROPSY OBSERVATION  | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| ILIACT LYMPH NODES LEFT   |                                   |
| - 01: Enlarged.   | - Nothing abnormal discovered.    |
| SACRAL LYMPH NODE   |                                   |
| - 01: Enlarged.   | - Nothing abnormal discovered.    |
| SKIN  |                                   |
| - 01: Dorsal region, white discoloration, a few, up to 0.2 cm in diameter, raised, corresponding to: papulla. | - Crust, grade 1.                 |
| NO OTHER NECROPSY OBSERVATIONS NOTED  |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIACT LYMPH NODES LEFT:  
Nothing abnormal discovered corresponding to necropsy observation no.01.  
KIDNEYS:  
-Basophilia; tubule, unilateral, grade 1  
LACRIMAL GLANDS:  
-Infiltrate; lymphocyte, unilateral, grade 1  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 1  
NASAL CAVITY (LEVEL 3):  
-Artifact;blood in lumen  
NASAL CAVITY (POSTERIOR, LEVEL 4):  
-Artifact;blood in lumen  
PARATHYROID GLANDS:  
Only one of paired organs examined/present

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30645

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SACRAL LYMPH NODE:

Nothing abnormal discovered corresponding to necropsy observation no.01.

SKIN:

-Crust, grade 1

This finding corresponds to necropsy observation no: 01.

TESTES:

-Atrophy; tubule, bilateral, grade 1

-Multinucleated giant cell, bilateral, grade 1

THYMUS:

-Hemorrhage; agonal, grade 1

URETERS:

Only one of paired organs examined/present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30711 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 27-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 27-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 1  
-Needle tract lesion  
INJECTION SITE 2:  
-Inflammation; subacute, grade 1  
-Needle tract lesion  
KIDNEYS:  
-Basophilia; tubule, bilateral, grade 1  
-Dilatation; tubule, unilateral, grade 1  
-Infiltrate; lymphocyte, bilateral, grade 1  
-Mineralization; cortex, bilateral, grade 2  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Hemorrhage; agonal, grade 1  
-Infiltrate; macrophage; alveolus, grade 2  
MANDIBULAR LYMPH NODES:  
-Dilatation; sinusoid, bilateral, grade 2  
-Hemorrhage; sinus, bilateral, grade 1  
PARATHYROID GLANDS:  
Only one of paired organs examined/present

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30711

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SACRAL LYMPH NODE:  
-Hemorrhage; sinus, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30712                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

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| * NECROPSY OBSERVATION               | CORRESPONDING MICROSCOPIC FINDING |
|--------------------------------------|-----------------------------------|
| ADRENAL GLANDS                       |                                   |
| - 01: Left: agenesis.                | - Not submitted for examination.  |
| NO OTHER NECROPSY OBSERVATIONS NOTED |                                   |

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

Only one of paired organs examined/present  
Tissue with necropsy observation no.01 not submitted for microscopic examination.

BRAIN (MEDULLA,PONS,CEREBELLAR,CEREBRAL CORTEX):

-Vacuolation; choroid plexus, grade 1

HEART:

-Infiltrate; mononuclear cell; myocardium, grade 1

ILIAC LYMPH NODES LEFT:

Tissue not present for histologic examination

INJECTION SITE 3:

-Inflammation; subacute, grade 1

KIDNEYS:

-Basophilia; tubule, bilateral, grade 2

-Dilatation; tubule, bilateral, grade 1

-Infiltrate; lymphocyte, bilateral, grade 1

-Mineralization; cortex, bilateral, grade 1

LIVER:

-Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

-Infiltrate; macrophage; alveolus, grade 1

NASAL CAVITY (LEVEL 3):

-Inflammation; intranasal exudate, grade 1

NASAL CAVITY (POSTERIOR, LEVEL 4):

-Inflammation; intranasal exudate, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30712

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PARATHYROID GLANDS:

Only one of paired organs examined/present

RECTUM:

-Inflammation; adjacent tissue, grade 2

SACRAL LYMPH NODE:

-Hemorrhage; sinus, grade 1

STOMACH:

-Dilatation; gland, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30713 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 27-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 27-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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| * NECROPSY OBSERVATION                            | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| INJECTION SITE 3                                  |                                   |
| - 01: Red discoloration, approx 1 cm in diameter. | - Hemorrhage, grade 1.            |
| NO OTHER NECROPSY OBSERVATIONS NOTED              |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, fascia, grade 1  
-Hemorrhage, grade 1  
This finding corresponds to necropsy observation no: 01.  
-Needle tract lesion  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 2  
MANDIBULAR LYMPH NODES:  
-Dilatation; sinusoid, bilateral, grade 1  
-Hyperplasia; lymphoid, bilateral, grade 1  
PARATHYROID GLANDS:  
Tissue not present for histologic examination  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30714 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 27-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 27-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES RIGHT:

Tissue not present for histologic examination

INGUINAL LYMPH NODES LEFT:

Tissue not present for histologic examination

INGUINAL LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 1

INJECTION SITE 3:

-Needle tract lesion

KIDNEYS:

-Basophilia; tubule, bilateral, grade 1

-Dilatation; tubule, bilateral, grade 1

-Mineralization; cortex, bilateral, grade 1

LUNGS (+ BRONCHI):

-Hemorrhage; agonal, grade 2

-Hyperplasia; lymphoid, grade 1

-Infiltrate; macrophage; alveolus, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30715                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

| * NECROPSY OBSERVATION   | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| INJECTION SITE 3   |                                   |
| - 01: Red discoloration, approx 1.5 cm in diameter.                      | - Hemorrhage, grade 1.            |
| OVARIES  |                                   |
| Finding 01 in OVIDUCTS   | - Cyst; parovarian, unilateral.   |
| OVIDUCTS   |                                   |
| - 01: Right: cyst, translucent content, a few, up to 0.5 cm in diameter. | - SEE UNDER: OVARIES.             |
| NO OTHER NECROPSY OBSERVATIONS NOTED                                     |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1

INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

INJECTION SITE 1:  
-Needle tract lesion

INJECTION SITE 3:  
-Hemorrhage, grade 1  
This finding corresponds to necropsy observation no: 01.  
-Necrosis; muscle, focal, grade 1

LACRIMAL GLANDS:  
-Infiltrate; lymphocyte, unilateral, grade 1

LARYNX:  
-Infiltrate; mononuclear cell; muscle, grade 1

LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30715

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MANDIBULAR LYMPH NODES:

-Dilatation; sinusoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

NASAL CAVITY (LEVEL 3):

-Artifact; blood in lumen

NASAL CAVITY (POSTERIOR, LEVEL 4):

-Artifact; blood in lumen

OVARIES:

-Cyst; parovarian, unilateral

This finding corresponds to necropsy observation no.: 01  
in the OVIDUCTS.

OVIDUCTS:

For diagnosis of necropsy observation no. 01 see under: OVARIES.

PANCREAS:

-Ectopic tissue; spleen

PARATHYROID GLANDS:

Only one of paired organs examined/present

SACRAL LYMPH NODE:

-Hemorrhage; sinus, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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## ANIMAL HEADING DATA

DOSE GROUP : 2, 15 microg HA/strain/dose D31

| ANIMAL<br>NUMBER | SEX<br>M/F | DEFINED AND FINAL<br>STATE OF NECROPSY | TEST<br>DAYS | FIRST AND LAST<br>DAY UNDER TEST | DATE OF<br>NECROPSY |
|------------------|------------|--|--------------|----------------------------------|---------------------|
| N30651           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30652           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30653           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30654           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30655           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30721           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |
| N30722           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |
| N30723           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |
| N30724           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |
| N30725           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30651 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

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| * NECROPSY OBSERVATION                         | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| INJECTION SITE 3                               |                                   |
| - 01: Red discoloration, a few,<br>punctiform. | - Hemorrhage, grade 2.            |
| LUNGS (+ BRONCHI)                              |                                   |
| - 01: Enlarged.                                | - Hemorrhage; agonal, grade 2.    |
| - 02: Red discoloration, many,<br>punctiform.  | - Hemorrhage; agonal, grade 2.    |
| NO OTHER NECROPSY OBSERVATIONS NOTED           |                                   |

\* MICROSCOPIC FINDINGS

BRAIN (MEDULLA,PONS,CEREBELLAR,CEREBRAL CORTEX):  
-Vacuolation; choroid plexus, grade 1  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, focal, grade 1  
INJECTION SITE 2:  
-Inflammation; subacute, grade 1  
-Degeneration/regeneration; muscle, focal, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Necrosis; muscle, focal, grade 2

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30651

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KIDNEYS:

-Mineralization; cortex, unilateral, grade 1

LACRIMAL GLANDS:

-Infiltrate; lymphocyte, unilateral, grade 1

LUNGS (+ BRONCHI):

-Hemorrhage; agonal, grade 2

This finding corresponds to necropsy observations nos: 01,02.

-Infiltrate; macrophage; alveolus, grade 2

MANDIBULAR LYMPH NODES:

-Dilatation; sinusoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:

Tissue not present for histologic examination

SACRAL LYMPH NODE:

Tissue not present for histologic examination

SKIN SITE 2:

-Infiltrate; mixed; subcutis, grade 1

SPLEEN:

-Hyperplasia; lymphoid, grade 1

TESTES:

-Atrophy; tubule, unilateral, grade 2

-Multinucleated giant cell, bilateral, grade 1

THYMUS:

-Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30652 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

| * NECROPSY OBSERVATION               | CORRESPONDING MICROSCOPIC FINDING  |
|--------------------------------------|------------------------------------|
| INJECTION SITE 1                     |                                    |
| - 01: Red discoloration, diffuse.    | - Hemorrhage, grade 2.             |
| INJECTION SITE 3                     |                                    |
| - 01: Red discoloration, diffuse.    | - Hemorrhage, grade 2.             |
| TESTES                               |                                    |
| - 01: Left: cryptorchidism.          | - Hypoplasia, unilateral, grade 4. |
| - 02: Left: reduced in size, soft.   | - Hypoplasia, unilateral, grade 4. |
| NO OTHER NECROPSY OBSERVATIONS NOTED |                                    |

\* MICROSCOPIC FINDINGS

EPIDIDYMIDES:  
-Dilatation, unilateral, grade 2  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
HEART:  
-Infiltrate; mononuclear cell; myocardium, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 2  
This finding corresponds to necropsy observation no: 01.  
INJECTION SITE 2:  
-Inflammation; subacute, fascia, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30652

---

INJECTION SITE 3:

- Inflammation; subacute, grade 3
- Hemorrhage, grade 2

This finding corresponds to necropsy observation no: 01.

KIDNEYS:

- Basophilia; tubule, unilateral, grade 1
- Mineralization; cortex, unilateral, grade 1

LACRIMAL GLANDS:

- Infiltrate; lymphocyte, bilateral, grade 1

LIVER:

- Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1
- with focal chronic inflammation

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 2

NASAL CAVITY (LEVEL 3):

- Artifact;blood in lumen

NASAL CAVITY (POSTERIOR, LEVEL 4):

- Artifact;blood in lumen

PARATHYROID GLANDS:

Only one of paired organs examined/present

SKIN SITE 1:

- Infiltrate; mixed; subcutis, grade 1

SKIN SITE 2:

- Infiltrate; mixed; subcutis, grade 2

SKIN SITE 3:

- Infiltrate; mixed; subcutis, grade 1

SPLEEN:

- Hyperplasia; lymphoid, grade 1

TESTES:

- Atrophy; tubule, unilateral, grade 2

- Hypoplasia, unilateral, grade 4

This finding corresponds to necropsy observations nos: 01,02.

- Multinucleated giant cell, unilateral, grade 1

THYMUS:

- Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

---

\* ANIMAL NUMBER : N30653 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

| * NECROPSY OBSERVATION                              | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| INJECTION SITE 1                                    |                                   |
| - 01: Red discoloration, approx 0.5 cm in diameter. | - Hemorrhage, grade 2.            |
| NO OTHER NECROPSY OBSERVATIONS NOTED                |                                   |

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:  
-Accessory tissue, unilateral  
DUODENUM:  
-Dilatation; Brunner's gland, grade 2  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
(mostly follicular in all animals)  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 3  
-Hemorrhage, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Necrosis; muscle, focal, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 2

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30653

---

KIDNEYS:

- Basophilia; tubule, unilateral, grade 1
- Mineralization; cortex, unilateral, grade 1

LARYNX:

- Infiltrate; mixed cell; subepithelial, grade 1

LIVER:

- Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

NASAL CAVITY (LEVEL 3):

- Artifact; blood in lumen

NASAL CAVITY (POSTERIOR, LEVEL 4):

- Artifact; blood in lumen

STOMACH:

- Mineralization; gland, grade 1

TESTES:

- Multinucleated giant cell, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30654 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

| * NECROPSY OBSERVATION                     | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| INJECTION SITE 1                           |                                   |
| - 01: Red discoloration, many, punctiform. | - Hemorrhage, fascia, grade 1.    |
| NO OTHER NECROPSY OBSERVATIONS NOTED       |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIIAC LYMPH NODES LEFT:  
Tissue not present for histologic examination  
ILIIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 2  
(mostly follicular in all animals)  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 2  
-Hemorrhage, fascia, grade 1  
This finding corresponds to necropsy observation no: 01.  
INJECTION SITE 2:  
-Inflammation; subacute, fascia, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 1  
LUNGS (+ BRONCHI):  
-Hemorrhage; agonal, grade 1  
-Infiltrate; macrophage; alveolus, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30654

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PARATHYROID GLANDS:

Only one of paired organs examined/present

SACRAL LYMPH NODE:

Tissue not present for histologic examination

SPLEEN:

-Hyperplasia; lymphoid, grade 1

TESTES:

-Atrophy; tubule, bilateral, grade 1

-Multinucleated giant cell, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30655 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIIAC LYMPH NODES LEFT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 1  
ILIIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 1  
INJECTION SITE 2:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 1  
INJECTION SITE 3:  
-Necrosis; muscle, focal, grade 1  
LIVER:  
-Hypertrophy; focal, grade 1  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 1  
MESENTERIC LYMPH NODE:  
-Hemorrhage; sinus, grade 1  
PARATHYROID GLANDS:  
Only one of paired organs examined/present

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30655

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SKIN SITE 1:  
-Infiltrate; mixed; subcutis, grade 1  
-Needle tract lesion

TESTES:  
-Multinucleated giant cell, bilateral, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30721                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

---

| * NECROPSY OBSERVATION               | CORRESPONDING MICROSCOPIC FINDING |
|--------------------------------------|-----------------------------------|
| INJECTION SITE 3                     |                                   |
| - 01: Red discoloration, diffuse.    | - Hemorrhage, grade 2.            |
| NO OTHER NECROPSY OBSERVATIONS NOTED |                                   |

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:  
Medulla missing

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES LEFT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1

INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 2  
(mostly follicular in all animals)

INJECTION SITE 1:  
-Inflammation; subacute, grade 1  
-Hemorrhage, fascia, grade 1

INJECTION SITE 2:  
-Inflammation; subacute, grade 1  
-Degeneration/regeneration; muscle, grade 1

INJECTION SITE 3:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 2  
This finding corresponds to necropsy observation no: 01.

KIDNEYS:  
-Cyst; cortex, unilateral, grade 1  
-Mineralization; cortex, bilateral, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30721

---

LACRIMAL GLANDS:

-Infiltrate; lymphocyte, bilateral, grade 1

LIVER:

-Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

-Hyperplasia; lymphoid, grade 1

-Infiltrate; macrophage; alveolus, grade 1

MANDIBULAR LYMPH NODES:

-Dilatation; sinusoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

NASAL CAVITY (ANTERIOR PART):

-Inflammation; intranasal exudate, grade 1

NASAL CAVITY (LEVEL 2):

-Inflammation; intranasal exudate, grade 2

PARATHYROID GLANDS:

Only one of paired organs examined/present

SACRAL LYMPH NODE:

Tissue not present for histologic examination

SKIN SITE 1:

-Infiltrate; mixed cell; dermis, grade 1

SKIN SITE 2:

-Infiltrate; mixed cell; dermis, grade 1

SPLEEN:

-Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30722                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

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| * NECROPSY OBSERVATION                        | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| ADIPOSE TISSUE                                |                                   |
| - 01: Abdominal region, right,<br>gelatinous. | - Edema, grade 2.                 |
| NO OTHER NECROPSY OBSERVATIONS NOTED          |                                   |

\* MICROSCOPIC FINDINGS

ADIPOSE TISSUE:  
-Edema, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Hemorrhage, grade 1  
-Inflammation, grade 1  
BRAIN (MEDULLA,PONS,CEREBELLAR,CEREBRAL CORTEX):  
-Vacuolation; choroid plexus, grade 1  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, fascia, grade 1  
INJECTION SITE 2:  
-Inflammation; subacute, grade 2  
-Hemorrhage, fascia, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 1  
-Necrosis; muscle, focal, grade 1  
-Needle tract lesion

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30722

---

KIDNEYS:

- Basophilia; tubule, unilateral, grade 1
- Dilatation; tubule, unilateral, grade 1
- Infiltrate; mixed cell; fascia, unilateral, grade 1
- Mineralization; cortex, unilateral, grade 1

LACRIMAL GLANDS:

- Infiltrate; lymphocyte, bilateral, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1

MANDIBULAR LYMPH NODES:

- Dilatation; sinusoid, bilateral, grade 1
- Hemorrhage; sinus, bilateral, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present

PAROTID GLANDS:

- Atrophy; focal, bilateral, grade 1

PITUITARY GLAND:

No pars nervosa present

SPLEEN:

- Hyperplasia; lymphoid, grade 1

THYMUS:

- Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30723                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

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| * NECROPSY OBSERVATION                                      | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| ADIPOSE TISSUE  |                                   |
| - 01: Abdominal region, right,<br>gelatinous.               | - Edema, grade 1.                 |
| INJECTION SITE 1  |                                   |
| - 01: Red discoloration, many, up<br>to 0.2 cm in diameter. | - Hemorrhage, grade 2.            |
| INJECTION SITE 2  |                                   |
| - 01: Red discoloration, many,<br>punctiform.               | - Hemorrhage, fascia, grade 1.    |
| NO OTHER NECROPSY OBSERVATIONS NOTED                        |                                   |

\* MICROSCOPIC FINDINGS

ADIPOSE TISSUE:  
-Edema, grade 1  
This finding corresponds to necropsy observation no: 01.  
-Hemorrhage, grade 2  
-Inflammation, grade 2  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 2  
INJECTION SITE 1:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Necrosis; muscle, focal, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30723

---

INJECTION SITE 2:

- Inflammation; subacute, fascia, grade 1
  - Hemorrhage, fascia, grade 1
- This finding corresponds to necropsy observation no: 01.

INJECTION SITE 3:

- Inflammation; subacute, grade 2
- Hemorrhage, fascia, grade 1

KIDNEYS:

- Basophilia; tubule, unilateral, grade 1
- Dilatation; tubule, unilateral, grade 1
- Infiltrate; mixed cell; fascia, unilateral, grade 1
- Mineralization; cortex, bilateral, grade 1

LACRIMAL GLANDS:

- Infiltrate; lymphocyte, unilateral, grade 1

LIVER:

- Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 2

PARATHYROID GLANDS:

Tissue not present for histologic examination

SKIN SITE 1:

- Infiltrate; mixed; subcutis, grade 1

SPLEEN:

- Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30724                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

---

| * NECROPSY OBSERVATION  | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| ADIPOSE TISSUE  |                                   |
| - 01: Abdominal region, right,<br>gelatinous.                       | - Edema, grade 2.                 |
| INJECTION SITE 3  |                                   |
| - 01: Red discoloration, approx 1.5<br>cm long, approx 0.5 cm wide. | - Hemorrhage, grade 2.            |
| SKIN SITE 3   |                                   |
| - 01: Subcutaneous tissue, red<br>discoloration, diffuse.           | - Hemorrhage; subcutis, grade 1.  |
| NO OTHER NECROPSY OBSERVATIONS NOTED                                |                                   |

\* MICROSCOPIC FINDINGS

ADIPOSE TISSUE:  
-Edema, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Hemorrhage, grade 1  
-Inflammation, grade 2  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES LEFT:  
Tissue not present for histologic examination  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 2  
(mostly follicular in all animals)  
INGUINAL LYMPH NODES RIGHT:  
-Dilatation; sinusoid, grade 1  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 2:  
-Infiltrate; macrophage, muscle, focal, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30724

---

INJECTION SITE 3:

- Inflammation; subacute, grade 2
  - Hemorrhage, grade 2
- This finding corresponds to necropsy observation no: 01.
- Necrosis; muscle, focal, grade 1

KIDNEYS:

- Infiltrate; mixed cell; fascia, unilateral, grade 1

LIVER:

- Infiltrate; mixed cell; focal, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 2

SACRAL LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

SKIN SITE 3:

- Hemorrhage; subcutis, grade 1

This finding corresponds to necropsy observation no: 01.

SPLEEN:

- Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30725                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

---

| * NECROPSY OBSERVATION                        | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| ADIPOSE TISSUE                                |                                   |
| - 01: Abdominal region, right,<br>gelatinous. | - Edema, grade 2.                 |
| NO OTHER NECROPSY OBSERVATIONS NOTED          |                                   |

\* MICROSCOPIC FINDINGS

ADIPOSE TISSUE:  
-Edema, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Hemorrhage, grade 1  
-Inflammation, grade 2

DUODENUM:  
-Dilatation; Brunner's gland, grade 2

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1

INJECTION SITE 1:  
-Inflammation; subacute, grade 2  
-Hemorrhage, fascia, grade 1  
-Necrosis; muscle, focal, grade 1

INJECTION SITE 2:  
-Infiltrate; macrophage, muscle, focal, grade 1

INJECTION SITE 3:  
-Inflammation; subacute, grade 2

KIDNEYS:  
-Basophilia; tubule, bilateral, grade 1

LIVER:  
-Infiltrate; mixed cell; focal, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D31

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CONT./FF. ANIMAL NO. : N30725

---

LUNGS (+ BRONCHI):

-Infiltrate; macrophage; alveolus, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present  
SKIN SITE 1:

-Infiltrate; mixed cell; dermis, grade 1

-Infiltrate; mixed; subcutis, grade 1

-Needle tract lesion

SPLEEN:

-Hyperplasia; lymphoid, grade 2

(mostly follicular in all animals)

TONGUE:

-Infiltrate; mixed; muscle, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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## ANIMAL HEADING DATA

DOSE GROUP : 3, 45 microg HA/strain/dose D31

| ANIMAL<br>NUMBER | SEX<br>M/F | DEFINED AND FINAL<br>STATE OF NECROPSY | TEST<br>DAYS | FIRST AND LAST<br>DAY UNDER TEST | DATE OF<br>NECROPSY |
|------------------|------------|--|--------------|----------------------------------|---------------------|
| N30661           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30662           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30663           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30664           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30665           | M          | K0                                     | K0           | 31                               | 20-AUG-18 19-SEP-18 |
| N30731           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |
| N30732           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |
| N30733           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |
| N30734           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |
| N30735           | F          | K0                                     | K0           | 31                               | 28-AUG-18 27-SEP-18 |

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30661 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

| * NECROPSY OBSERVATION            | CORRESPONDING MICROSCOPIC FINDING            |
|-----------------------------------|--|
| INJECTION SITE 1                  |  |
| - 01: Red discoloration, diffuse. | - Hemorrhage, fascia, grade 1.               |
| INJECTION SITE 2                  |  |
| - 01: Red discoloration, diffuse. | - Hemorrhage, fascia, grade 2.               |
| INJECTION SITE 3                  |  |
| - 01: Red discoloration, diffuse. | - Hemorrhage, grade 1.                       |
| LUNGS (+ BRONCHI)                 |  |
| - 01: Enlarged.                   | - Infiltrate; macrophage; alveolus, grade 2. |

NO OTHER NECROPSY OBSERVATIONS NOTED

\* MICROSCOPIC FINDINGS

EPIDIDYMIDES:  
-Cell debris, bilateral, grade 3  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
(mostly follicular in all animals)  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 1  
-Hemorrhage, fascia, grade 1  
This finding corresponds to necropsy observation no: 01.  
INJECTION SITE 2:  
-Inflammation; subacute, fascia, grade 2  
-Hemorrhage, fascia, grade 2  
This finding corresponds to necropsy observation no: 01.  
INJECTION SITE 3:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30661

---

This finding corresponds to necropsy observation no: 01.

KIDNEYS:

-Mineralization; cortex, unilateral, grade 1

LUNGS (+ BRONCHI):

-Infiltrate; macrophage; alveolus, grade 2

This finding corresponds to necropsy observation no: 01.

-Inflammation; chronic; bronchus, grade 2

SPLEEN:

-Hyperplasia; lymphoid, grade 1

(mostly follicular in all animals)

TESTES:

-Atrophy; tubule, bilateral, grade 3

-Multinucleated giant cell, bilateral, grade 3

THYMUS:

-Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

\* ANIMAL NUMBER : N30662 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

- Hyperplasia; lymphoid, grade 2
- present on slide number
- 11

HARDERIAN GLANDS:

- Degeneration; epithelium, bilateral, grade 2

HEART:

- Infiltrate; mononuclear cell; myocardium, grade 1
- at septal/ventricular junction

ILIAC LYMPH NODES LEFT:

- Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES RIGHT:

Tissue not present for histologic examination

INGUINAL LYMPH NODES LEFT:

- Hyperplasia; lymphoid, grade 1
- Infiltrate; granulocyte, grade 1

INGUINAL LYMPH NODES RIGHT:

- Hyperplasia; lymphoid, grade 1
- Infiltrate; granulocyte, grade 1

INJECTION SITE 1:

- Inflammation; subacute, grade 2
- Hemorrhage, grade 1

INJECTION SITE 3:

- Inflammation; subacute, grade 2
- Hemorrhage, grade 1

KIDNEYS:

- Basophilia; tubule, bilateral, grade 1
- Dilatation; tubule, bilateral, grade 1
- Mineralization; cortex, bilateral, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30662

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LIVER:

-Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

-Infiltrate; macrophage; alveolus, grade 1

MANDIBULAR LYMPH NODES:

-Dilatation; sinusoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

NASAL CAVITY (POSTERIOR, LEVEL 4):

-Artifact; blood in lumen

SACRAL LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

(mostly follicular in all animals)

TESTES:

-Atrophy; tubule, bilateral, grade 2

-Multinucleated giant cell, bilateral, grade 2

THYMUS:

-Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

\* ANIMAL NUMBER : N30663 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

| * NECROPSY OBSERVATION                            | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| INGUINAL LYMPH NODES RIGHT                        |                                   |
| - 01: Enlarged.                                   | - Hyperplasia; lymphoid, grade 1. |
| INJECTION SITE 3                                  |                                   |
| - 01: Red discoloration, approx 1 cm in diameter. | - Hemorrhage, grade 1.            |
| NO OTHER NECROPSY OBSERVATIONS NOTED              |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
Tissue not present for histologic examination

HARDERIAN GLANDS:  
-Degeneration; epithelium, bilateral, grade 1

ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1

INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
This finding corresponds to necropsy observation no: 01.

INJECTION SITE 2:  
-Inflammation; subacute, with fibrosis, grade 1  
-Hemorrhage, fascia, grade 1

INJECTION SITE 3:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 1  
This finding corresponds to necropsy observation no: 01.  
-Necrosis; muscle, focal, grade 2

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30663

---

KIDNEYS:

- Basophilia; tubule, unilateral, grade 1
- Mineralization; cortex, unilateral, grade 1

LIVER:

- Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1
- Metaplasia; osseous

PARATHYROID GLANDS:

- Only one of paired organs examined/present

SKIN:

- Inflammation; panniculus muscle, grade 1

SKIN SITE 3:

- Infiltrate; mixed; subcutis, grade 2

SPLEEN:

- Hyperplasia; lymphoid, grade 1

TESTES:

- Atrophy; tubule, bilateral, grade 1
- Multinucleated giant cell, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

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\* ANIMAL NUMBER : N30664 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

| * NECROPSY OBSERVATION   | CORRESPONDING MICROSCOPIC FINDING             |
|--|---|
| INGUINAL LYMPH NODES RIGHT   |   |
| - 01: Enlarged.  | - Hyperplasia; lymphoid, grade 2.             |
| INJECTION SITE 1   |   |
| - 01: Red discoloration, diffuse.                                      | - Hemorrhage, fascia, grade 2.                |
| INJECTION SITE 2   |   |
| - 01: Red discoloration, diffuse.                                      | - Hemorrhage, fascia, grade 2.                |
| MANDIBULAR LYMPH NODES   |   |
| - 01: Enlarged.  | - Infiltrate; macrophage, bilateral, grade 1. |
| SKIN SITE 3  |   |
| - 01: Subcutaneous tissue, red discoloration, approx 2 cm in diameter. | - Hemorrhage; subcutis, grade 2.              |

NO OTHER NECROPSY OBSERVATIONS NOTED

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Accessory tissue, unilateral

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

-Infiltrate; granulocyte, grade 1

ILIAC LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 1

-Infiltrate; granulocyte, grade 1

INGUINAL LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

-Infiltrate; granulocyte, grade 1

INGUINAL LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 2

This finding corresponds to necropsy observation no: 01.

-Infiltrate; granulocyte, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30664

---

INJECTION SITE 1:

- Inflammation; subacute, grade 2
  - Hemorrhage, fascia, grade 2
- This finding corresponds to necropsy observation no: 01.

INJECTION SITE 2:

- Inflammation; subacute, grade 1
  - Hemorrhage, fascia, grade 2
- This finding corresponds to necropsy observation no: 01.

-Needle tract lesion

INJECTION SITE 3:

- Inflammation; subacute, grade 2
- Hemorrhage, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 2

MANDIBULAR LYMPH NODES:

- Infiltrate; granulocyte, bilateral, grade 1
  - Infiltrate; macrophage, bilateral, grade 1
- This finding corresponds to necropsy observation no: 01.

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 2

SKIN SITE 1:

- Infiltrate; mixed; subcutis, grade 2

SKIN SITE 2:

- Inflammation; panniculus muscle, grade 1

SKIN SITE 3:

- Hemorrhage; subcutis, grade 2
- This finding corresponds to necropsy observation no: 01.
- Infiltrate; mixed; subcutis, grade 2
  - Inflammation; panniculus muscle, grade 1

TESTES:

- Atrophy; tubule, bilateral, grade 1
- Multinucleated giant cell, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

\* ANIMAL NUMBER : N30665 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 19-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 19-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

| * NECROPSY OBSERVATION   | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| INGUINAL LYMPH NODES RIGHT   |                                   |
| - 01: Enlarged.  | - Hyperplasia; lymphoid, grade 1. |
| INJECTION SITE 1   |                                   |
| - 01: Red discoloration, many,<br>punctiform.  | - Hemorrhage, grade 1.            |
| INJECTION SITE 2   |                                   |
| - 01: Red discoloration, many,<br>punctiform.  | - Hemorrhage, fascia, grade 1.    |
| INJECTION SITE 3   |                                   |
| - 01: Red discoloration, approx 0.5<br>cm in diameter.   | - Hemorrhage, grade 2.            |
| SKIN   |                                   |
| - 01: Dorsal region, white<br>discoloration, approx 0.2 cm<br>in diameter, raised,<br>corresponding to: papulla. | - Nothing abnormal discovered.    |

NO OTHER NECROPSY OBSERVATIONS NOTED

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:  
-Accessory tissue, unilateral  
BRAIN (MEDULLA,PONS,CEREBELLAR,CEREBRAL CORTEX):  
-Vacuolation; choroid plexus, grade 1  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
This finding corresponds to necropsy observation no: 01.

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30665

---

INJECTION SITE 1:

- Inflammation; subacute, grade 1
- Hemorrhage, grade 1

This finding corresponds to necropsy observation no: 01.

INJECTION SITE 2:

- Hemorrhage, fascia, grade 1

This finding corresponds to necropsy observation no: 01.

INJECTION SITE 3:

- Inflammation; subacute, grade 2
- Hemorrhage, grade 2

This finding corresponds to necropsy observation no: 01.

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

NASAL CAVITY (ANTERIOR PART):

- Artifact;blood in lumen

NASAL CAVITY (LEVEL 2):

- Artifact;blood in lumen

NASAL CAVITY (LEVEL 3):

- Artifact;blood in lumen

NASAL CAVITY (POSTERIOR, LEVEL 4):

- Artifact;blood in lumen

PARATHYROID GLANDS:

Tissue not present for histologic examination

SACRAL LYMPH NODE:

Tissue not present for histologic examination

SKIN:

Nothing abnormal discovered corresponding to necropsy observation no.01.

SPLEEN:

- Hyperplasia; lymphoid, grade 1

TESTES:

- Atrophy; tubule, bilateral, grade 1
- Multinucleated giant cell, bilateral, grade 2

THYMUS:

- Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

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|  |   |                                   |       |        |
|--|---|-----------------------------------|-------|--------|
| * ANIMAL NUMBER  | : | N30731                            | SEX : | FEMALE |
| FIRST DAY ON TEST                                      | : | 28-Aug-18                         |       |        |
| LAST DAY ON TEST                                       | : | 27-Sep-18                         |       |        |
| DAYS ON TEST   | : | 31                                |       |        |
| DATE OF NECROPSY                                       | : | 27-Sep-18                         |       |        |
| DEFINED SACR.GROUP                                     | : | TERMINAL SACRIFICE GROUP          |       |        |
| STATUS AT NECROPSY                                     | : | TERMINAL SACRIFICE GROUP          |       |        |
| .....  |   |                                   |       |        |
| * NECROPSY OBSERVATION                                 |   | CORRESPONDING MICROSCOPIC FINDING |       |        |
| INJECTION SITE 1                                       |   |                                   |       |        |
| - 01: Red discoloration, many, punctiform.             |   | - Hemorrhage, fascia, grade 1.    |       |        |
| INJECTION SITE 2                                       |   |                                   |       |        |
| - 01: Red discoloration, many, punctiform.             |   | - Hemorrhage, fascia, grade 1.    |       |        |
| INJECTION SITE 3                                       |   |                                   |       |        |
| - 01: Red discoloration, many, punctiform.             |   | - Hemorrhage, grade 1.            |       |        |
| SKIN SITE 3  |   |                                   |       |        |
| - 01: Subcutaneous tissue, red discoloration, diffuse. |   | - Hemorrhage; dermis, grade 2.    |       |        |
| NO OTHER NECROPSY OBSERVATIONS NOTED                   |   |                                   |       |        |

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:  
Only one of paired organs examined/present

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES LEFT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1

INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30731

---

INJECTION SITE 1:

- Hemorrhage, fascia, grade 1
- This finding corresponds to necropsy observation no: 01.

INJECTION SITE 2:

- Inflammation; subacute, focal, grade 1
- Hemorrhage, fascia, grade 1
- This finding corresponds to necropsy observation no: 01.

INJECTION SITE 3:

- Inflammation; subacute, grade 2
- Hemorrhage, grade 1
- This finding corresponds to necropsy observation no: 01.

KIDNEYS:

- Infiltrate; mixed cell; fascia, unilateral, grade 1
- Mineralization; cortex, unilateral, grade 1

LIVER:

- Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 2

MANDIBULAR LYMPH NODES:

- Hyperplasia; lymphoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

NASAL CAVITY (LEVEL 2):

- Artifact; blood in lumen

PANCREAS:

- Vacuolation; acinar cell, grade 2

PARATHYROID GLANDS:

Only one of paired organs examined/present  
SACRAL LYMPH NODE:

- Infiltrate; granulocyte, grade 1

SKIN SITE 3:

- Hemorrhage; dermis, grade 2
- This finding corresponds to necropsy observation no: 01.

- Hemorrhage; subcutis, grade 1

- Infiltrate; mixed cell; dermis, grade 1

- Infiltrate; mixed; subcutis, grade 1

SPLEEN:

- Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30732                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

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| * NECROPSY OBSERVATION                               | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| ADIPOSE TISSUE                                       |                                   |
| - 01: Abdominal region, right,<br>gelatinous.        | - Edema, grade 1.                 |
| INJECTION SITE 3                                     |                                   |
| - 01: Red discoloration, approx 1<br>cm in diameter. | - Hemorrhage, grade 1.            |
| NO OTHER NECROPSY OBSERVATIONS NOTED                 |                                   |

\* MICROSCOPIC FINDINGS

ADIPPOSE TISSUE:  
-Edema, grade 1  
This finding corresponds to necropsy observation no: 01.  
-Inflammation, grade 2

ADRENAL GLANDS:  
-Accessory tissue, unilateral

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 2  
(mostly follicular in all animals)

INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1

INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 2  
(mostly follicular in all animals)  
-Infiltrate; granulocyte, grade 1

INJECTION SITE 1:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30732

---

INJECTION SITE 2:

- Inflammation; subacute, focal, grade 1
- Infiltrate; macrophage, muscle, focal, grade 1
- Necrosis; muscle, focal, grade 1

INJECTION SITE 3:

- Inflammation; subacute, grade 2
  - Hemorrhage, grade 1
- This finding corresponds to necropsy observation no: 01.
- Necrosis; muscle, focal, grade 1

KIDNEYS:

- Infiltrate; lymphocyte, bilateral, grade 1
- Mineralization; cortex, bilateral, grade 1

LIVER:

- Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1

MANDIBULAR LYMPH NODES:

- Hyperplasia; lymphoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present  
SACRAL LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

SKIN SITE 1:

- Infiltrate; mixed; subcutis, grade 1

URETERS:

- Infiltrate; mixed cell; fascia, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30733                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

| * NECROPSY OBSERVATION   | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| INJECTION SITE 1   |                                   |
| - 01: Red discoloration, approx 1.2 cm long, approx 0.2 cm wide. | - Hemorrhage, grade 1.            |
| INJECTION SITE 2   |                                   |
| - 01: Red discoloration, approx 0.8 cm long, approx 0.1 cm wide. | - Nothing abnormal discovered.    |
| INJECTION SITE 3   |                                   |
| - 01: Red discoloration, a few, punctiform.                      | - Hemorrhage, grade 1.            |
| NO OTHER NECROPSY OBSERVATIONS NOTED                             |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES LEFT:  
Tissue not present for histologic examination

ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1

INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1

INJECTION SITE 1:  
-Inflammation; subacute, grade 2  
-Hemorrhage, grade 1  
This finding corresponds to necropsy observation no: 01.

INJECTION SITE 2:  
Nothing abnormal discovered corresponding to necropsy observation no.01.  
-Inflammation; subacute, grade 1  
-Degeneration/regeneration; muscle, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30733

---

INJECTION SITE 3:

- Inflammation; subacute, grade 2
  - Hemorrhage, grade 1
- This finding corresponds to necropsy observation no: 01.
- Necrosis; muscle, focal, grade 1

KIDNEYS:

- Mineralization; cortex, bilateral, grade 1

MANDIBULAR LYMPH NODES:

- Dilatation; sinusoid, bilateral, grade 1
- Hyperplasia; lymphoid, bilateral, grade 1

PARATHYROID GLANDS:

Tissue not present for histologic examination

SPLEEN:

- Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

\* ANIMAL NUMBER : N30734 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 27-Sep-18  
DAYS ON TEST : 31  
DATE OF NECROPSY : 27-Sep-18  
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP  
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP

---

| * NECROPSY OBSERVATION  | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| ADIPOSE TISSUE  |                                   |
| - 01: Abdominal region, right,<br>gelatinous.                     | - Edema, grade 2.                 |
| INJECTION SITE 3  |                                   |
| - 01: Red discoloration, approx 3<br>cm long, approx 0.5 cm wide. | - Hemorrhage, grade 2.            |
| NO OTHER NECROPSY OBSERVATIONS NOTED                              |                                   |

\* MICROSCOPIC FINDINGS

ADIPOSE TISSUE:  
-Edema, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Hemorrhage, grade 1  
-Inflammation, grade 2  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 2  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 2  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 2  
(mostly follicular in all animals)  
-Infiltrate; granulocyte, grade 2  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 1  
INJECTION SITE 2:  
-Inflammation; subacute, focal, grade 1  
-Needle tract lesion

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30734

---

INJECTION SITE 3:

- Inflammation; subacute, grade 2
  - Hemorrhage, grade 2
- This finding corresponds to necropsy observation no: 01.
- Necrosis; muscle, focal, grade 1
  - Needle tract lesion

KIDNEYS:

- Infiltrate; mixed cell; fascia, unilateral, grade 1
- Mineralization; cortex, unilateral, grade 1

LUNGS (+ BRONCHI):

- Infiltrate; macrophage; alveolus, grade 1
- Infiltrate; mixed; bronchial lumen, grade 2

MANDIBULAR LYMPH NODES:

- Dilatation; sinusoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 2

PARATHYROID GLANDS:

- Only one of paired organs examined/present

SACRAL LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

SKIN SITE 2:

- Cyst; inflammatory pseudocyst, grade 2
- containing necrotic debris and intercellular spaces
- consistent with injection of fluid
- Fibroplasia, grade 2
- Infiltrate; mixed; subcutis, grade 2

SPLEEN:

- Hyperplasia; lymphoid, grade 1

STOMACH:

- Infiltrate; mixed cell; muscle, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

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|                    |   |                          |       |        |
|--------------------|---|--------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30735                   | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                |       |        |
| LAST DAY ON TEST   | : | 27-Sep-18                |       |        |
| DAYS ON TEST       | : | 31                       |       |        |
| DATE OF NECROPSY   | : | 27-Sep-18                |       |        |
| DEFINED SACR.GROUP | : | TERMINAL SACRIFICE GROUP |       |        |
| STATUS AT NECROPSY | : | TERMINAL SACRIFICE GROUP |       |        |

---

| * NECROPSY OBSERVATION  | CORRESPONDING MICROSCOPIC FINDING |
|---|-----------------------------------|
| ADIPOSE TISSUE  |                                   |
| - 01: Abdominal region, right,<br>gelatinous.                           | - Edema, grade 2.                 |
| INJECTION SITE 1  |                                   |
| - 01: Red discoloration, approx 1<br>cm in diameter.                    | - Hemorrhage, fascia, grade 2.    |
| OVARIES   |                                   |
| Finding 01 in OVIDUCTS  | - Cyst; parovarian, unilateral.   |
| OVIDUCTS  |                                   |
| - 01: Left: cyst, translucent<br>content, approx 0.4 cm in<br>diameter. | - SEE UNDER: OVARIES.             |
| NO OTHER NECROPSY OBSERVATIONS NOTED                                    |                                   |

\* MICROSCOPIC FINDINGS

ADIPOSE TISSUE:  
-Edema, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Hemorrhage, grade 1  
-Inflammation, grade 1  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 1  
-Hemorrhage, fascia, grade 2  
This finding corresponds to necropsy observation no: 01.

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D31

---

CONT./FF. ANIMAL NO. : N30735

---

INJECTION SITE 3:

- Inflammation; subacute, grade 2
- Hemorrhage, grade 1

KIDNEYS:

- Dilatation; tubule, unilateral, grade 1

LIVER:

- Infiltrate; mixed cell; focal, grade 1

MESENTERIC LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

OVARIES:

- Cyst; parovarian, unilateral

This finding corresponds to necropsy observation no.: 01  
in the OVIDUCTS.

OVIDUCTS:

For diagnosis of necropsy observation no. 01 see under: OVARIES.

PARATHYROID GLANDS:

Only one of paired organs examined/present

SACRAL LYMPH NODE:

- Hyperplasia; lymphoid, grade 1

SPLEEN:

- Hyperplasia; lymphoid, grade 1

THYMUS:

- Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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## ANIMAL HEADING DATA

DOSE GROUP : 1, 0 microg HA/strain/dose D57

| ANIMAL<br>NUMBER | SEX<br>M/F | DEFINED AND FINAL<br>STATE OF NECROPSY | TEST<br>DAYS | FIRST AND LAST<br>DAY UNDER TEST | DATE OF<br>NECROPSY |
|------------------|------------|--|--------------|----------------------------------|---------------------|
| N30646           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30647           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30648           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30649           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30650           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| .....            |            |  |              |                                  |                     |
| N30716           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| N30717           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| N30718           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| N30719           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| N30720           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| .....            |            |  |              |                                  |                     |

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30646 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Accessory tissue, unilateral

GUT ASSOCIATED LYMPHOID TISSUE:

Tissue not present for histologic examination

KIDNEYS:

-Dilatation; tubule, bilateral, grade 1

-Mineralization; cortex, unilateral, grade 1

LUNGS (+ BRONCHI):

-Infiltrate; macrophage; alveolus, grade 2

MANDIBULAR LYMPH NODES:

-Hyperplasia; lymphoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present  
SPLEEN:

-Hyperplasia; lymphoid, grade 1

STOMACH:

-Congestion; focal, grade 1

TESTES:

-Atrophy; tubule, bilateral, grade 1

-Multinucleated giant cell, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30647 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Infiltrate; granulocyte, grade 1  
LACRIMAL GLANDS:  
-Infiltrate; lymphocyte, unilateral, grade 1  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Hemorrhage; agonal, grade 1  
-Infiltrate; macrophage; alveolus, grade 1  
MANDIBULAR LYMPH NODES:  
-Dilatation; sinusoid, bilateral, grade 2  
-Hyperplasia; lymphoid, bilateral, grade 1  
-Infiltrate; granulocyte, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
PARATHYROID GLANDS:  
Only one of paired organs examined/present  
TESTES:  
-Multinucleated giant cell, unilateral, grade 1  
THYMUS:  
-Hemorrhage; agonal, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30648 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY OBSERVATION CORRESPONDING MICROSCOPIC FINDING  
  
TESTES  
- 01: Right: reduced in size. - Atrophy; tubule, bilateral,  
grade 1.

NO OTHER NECROPSY OBSERVATIONS NOTED

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Accessory tissue, unilateral

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

HARDERIAN GLANDS:

-Degeneration; epithelium, unilateral, grade 1

-Infiltrate; mononuclear cell, bilateral, grade 1

ILIAC LYMPH NODES LEFT:

Tissue not present for histologic examination

KIDNEYS:

-Mineralization; cortex, unilateral, grade 1

LIVER:

-Infiltrate; mixed cell; focal, grade 1

LUNGS (+ BRONCHI):

-Infiltrate; macrophage; alveolus, grade 1

MANDIBULAR LYMPH NODES:

-Hyperplasia; lymphoid, bilateral, grade 1

NASAL CAVITY (POSTERIOR, LEVEL 4):

-Artifact; blood in lumen

TESTES:

-Atrophy; tubule, bilateral, grade 1

This finding corresponds to necropsy observation no: 01.

-Dilatation; tubule, unilateral, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30649 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

| * NECROPSY OBSERVATION                                    | CORRESPONDING MICROSCOPIC FINDING  |
|---|------------------------------------|
| GENERAL OBSERVATION                                       |                                    |
| - 01: Clinical observations not seen at necropsy, papula. | - This necropsy finding was noted. |
| NO OTHER NECROPSY OBSERVATIONS NOTED.                     |                                    |

\* MICROSCOPIC FINDINGS

GENERAL OBSERVATION:

This necropsy finding was noted. Microscopic evaluation was not applicable.

ADRENAL GLANDS:

-Hemorrhage; focal, unilateral, grade 1

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES LEFT:

Tissue not present for histologic examination

ILIAC LYMPH NODES RIGHT:

Tissue not present for histologic examination

INGUINAL LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

KIDNEYS:

-Mineralization; cortex, bilateral, grade 1

MANDIBULAR LYMPH NODES:

-Dilatation; sinusoid, bilateral, grade 1

-Hyperplasia; lymphoid, bilateral, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

NASAL CAVITY (LEVEL 3):

-Artifact; blood in lumen

OPTIC NERVE (LEFT):

Tissue not present for histologic examination

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

CONT./FF. ANIMAL NO. : N30649

---

PARATHYROID GLANDS:

Only one of paired organs examined/present

STOMACH:

-Dilatation; gland, grade 1

TESTES:

-Multinucleated giant cell, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30650 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

| * NECROPSY OBSERVATION   | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| SKIN SITE 3  |                                   |
| - 01: Subcutaneous tissue, red discoloration, approx 0.4 cm in diameter. | - Nothing abnormal discovered.    |
| NO OTHER NECROPSY OBSERVATIONS NOTED                                     |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Infiltrate; granulocyte, grade 1  
ILIAC LYMPH NODES LEFT:  
-Dilatation; sinusoid, grade 1  
KIDNEYS:  
-Mineralization; cortex, bilateral, grade 1  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 1  
PARATHYROID GLANDS:  
Only one of paired organs examined/present  
SACRAL LYMPH NODE:  
-Hemorrhage; sinus, grade 1  
SKIN SITE 3:  
Nothing abnormal discovered corresponding to necropsy observation no.01.  
THYMUS:  
-Hemorrhage; agonal, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

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|                    |   |                                 |       |        |
|--------------------|---|---------------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30716                          | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                       |       |        |
| LAST DAY ON TEST   | : | 23-Oct-18                       |       |        |
| DAYS ON TEST       | : | 57                              |       |        |
| DATE OF NECROPSY   | : | 23-Oct-18                       |       |        |
| DEFINED SACR.GROUP | : | RECOVERY / POST-TREATMENT GROUP |       |        |
| STATUS AT NECROPSY | : | RECOVERY / POST-TREATMENT GROUP |       |        |

---

| * NECROPSY OBSERVATION        | CORRESPONDING MICROSCOPIC FINDING               |
|-------------------------------|---|
| THYROID GLANDS                |   |
| - 01: Left: enlarged, marked. | - Degeneration; cystic, unilateral,<br>grade 3. |

NO OTHER NECROPSY OBSERVATIONS NOTED

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
KIDNEYS:  
-Basophilia; tubule, bilateral, grade 1  
-Dilatation; tubule, bilateral, grade 1  
-Mineralization; cortex, bilateral, grade 2  
LUNGS (+ BRONCHI):  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte; alveolus, grade 1  
-Infiltrate; macrophage; alveolus, grade 2  
MANDIBULAR LYMPH NODES:  
-Hyperplasia; lymphoid, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
NASAL CAVITY (LEVEL 2):  
-Artifact; blood in lumen  
NASAL CAVITY (LEVEL 3):  
-Artifact; blood in lumen  
NASAL CAVITY (POSTERIOR, LEVEL 4):  
-Artifact; blood in lumen

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

CONT./FF. ANIMAL NO. : N30716

---

PARATHYROID GLANDS:

Tissue not present for histologic examination

SACRAL LYMPH NODE:

-Dilatation; sinusoid, grade 3

SPLEEN:

-Hyperplasia; lymphoid, grade 1

THYROID GLANDS:

-Degeneration; cystic, unilateral, grade 3

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30717 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

LUNGS (+ BRONCHI):

-Hyperplasia; lymphoid, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

PANCREAS:

-Ectopic tissue; spleen

PARATHYROID GLANDS:

Only one of paired organs examined/present

SUBLINGUAL GLANDS:

Tissue not present for histologic examination

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30718 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
KIDNEYS:  
-Dilatation; tubule, bilateral, grade 1  
-Mineralization; cortex, bilateral, grade 1  
NASAL CAVITY (LEVEL 2):  
-Artifact; blood in lumen, nasolacrimal gland  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30719 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

INJECTION SITE 1:

-Needle tract lesion

INJECTION SITE 3:

-Needle tract lesion, with focal macrophages

LUNGS (+ BRONCHI):

-Hyperplasia; lymphoid, grade 1

-Infiltrate; macrophage; alveolus, grade 1

MANDIBULAR LYMPH NODES:

-Hemorrhage; sinus, bilateral, grade 1

PARATHYROID GLANDS:

Tissue not present for histologic examination

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 1, 0 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30720 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY OBSERVATION CORRESPONDING MICROSCOPIC FINDING  
  
INJECTION SITE 3  
- 01: Red discoloration, many, punctiform. - Nothing abnormal discovered.  
NO OTHER NECROPSY OBSERVATIONS NOTED

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIIAC LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 3:  
Nothing abnormal discovered corresponding to necropsy observation no.01.  
-Inflammation; subacute, focal, grade 1  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
PARATHYROID GLANDS:  
Only one of paired organs examined/present  
SACRAL LYMPH NODE:  
-Hemorrhage; sinus, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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## ANIMAL HEADING DATA

DOSE GROUP : 2, 15 microg HA/strain/dose D57

| ANIMAL<br>NUMBER | SEX<br>M/F | DEFINED AND FINAL<br>STATE OF NECROPSY | TEST<br>DAYS | FIRST AND LAST<br>DAY UNDER TEST | DATE OF<br>NECROPSY |
|------------------|------------|--|--------------|----------------------------------|---------------------|
| N30656           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30657           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30658           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30659           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30660           | M          | R1                                     | R1           | 57 20-AUG-18                     | 15-OCT-18           |
| N30726           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| N30727           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| N30728           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| N30729           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |
| N30730           | F          | R1                                     | R1           | 57 28-AUG-18                     | 23-OCT-18           |

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30656 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, fascia, grade 1  
KIDNEYS:  
-Mineralization; cortex, bilateral, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 2  
with minimal chronic inflammation of septa, multifocal  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
SACRAL LYMPH NODE:  
Tissue not present for histologic examination  
SPLEEN:  
-Hyperplasia; lymphoid, grade 1  
TESTES:  
-Atrophy; tubule, bilateral, grade 2  
-Multinucleated giant cell, bilateral, grade 2  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30657 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

ILIAc LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

ILIAc LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

INJECTION SITE 2:

-Infiltrate; lymphocyte, fascia, grade 1

INJECTION SITE 3:

-Infiltrate; lymphocyte, focal, grade 1

KIDNEYS:

-Basophilia; tubule, unilateral, grade 1

LUNGS (+ BRONCHI):

-Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present

SACRAL LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

SPLEEN:

-Hyperplasia; lymphoid, grade 1

TESTES:

-Atrophy; tubule, bilateral, grade 1

-Multinucleated giant cell, bilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30658 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

| * NECROPSY OBSERVATION               | CORRESPONDING MICROSCOPIC FINDING |
|--------------------------------------|-----------------------------------|
| TESTES                               |                                   |
| - 01: Reduced in size, soft.         | - Hypoplasia, bilateral, grade 4. |
| NO OTHER NECROPSY OBSERVATIONS NOTED |                                   |

\* MICROSCOPIC FINDINGS

EPIDIDYMIDES:  
-Sperm decreased number, bilateral, grade 5  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 2  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 2  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 2  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 2  
KIDNEYS:  
-Basophilia; tubule, focal, unilateral, grade 2  
-Cyst; cortex, unilateral, grade 1  
-Fibrosis, focal, unilateral, grade 2  
LACRIMAL GLANDS:  
-Atrophy; focal, unilateral, grade 2  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Metaplasia; osseous  
MANDIBULAR LYMPH NODES:  
-Dilatation; sinusoid, bilateral, grade 2  
-Hyperplasia; lymphoid, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

CONT./FF. ANIMAL NO. : N30658

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PARATHYROID GLANDS:

Only one of paired organs examined/present

SKIN SITE 1:

Tissue not present for histologic examination

SPLEEN:

-Hyperplasia; lymphoid, grade 1

TESTES:

-Hypoplasia, bilateral, grade 4

This finding corresponds to necropsy observation no: 01.

THYMUS:

-Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30659 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 1

INJECTION SITE 1:

-Inflammation; subacute, grade 2

mainly lymphocytes

-Infiltrate; lymphocyte, fascia, grade 1

INJECTION SITE 2:

-Inflammation; subacute, fascia, grade 1

mainly lymphocytes

INJECTION SITE 3:

-Inflammation; subacute, grade 1

mainly lymphocytes

KIDNEYS:

-Infiltrate; lymphocyte, bilateral, grade 1

-Mineralization; cortex, bilateral, grade 1

LUNGS (+ BRONCHI):

-Hyperplasia; lymphoid, grade 1

-Infiltrate; macrophage; alveolus, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

SPLEEN:

-Hyperplasia; lymphoid, grade 2

Spleen in recovery group animals has less cellular secondary follicles, consistent with involution

THYMUS:

-Hemorrhage; agonal, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

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CONT./FF. ANIMAL NO. : N30659

.....

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30660 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY OBSERVATION CORRESPONDING MICROSCOPIC FINDING  
  
LUNGS (+ BRONCHI)  
- 01: Red discoloration, many, punctiform.  
- Hemorrhage; agonal, grade 2.  
NO OTHER NECROPSY OBSERVATIONS NOTED

\* MICROSCOPIC FINDINGS

EPIDIDYMIDES:  
-Cell debris, bilateral, grade 1  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 2  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, grade 1  
KIDNEYS:  
-Basophilia; tubule, unilateral, grade 1  
-Dilatation; tubule, unilateral, grade 1  
-Mineralization; cortex, bilateral, grade 1  
LUNGS (+ BRONCHI):  
-Hemorrhage; agonal, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Hyperplasia; lymphoid, grade 1  
MANDIBULAR LYMPH NODES:  
-Hyperplasia; lymphoid, bilateral, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

CONT./FF. ANIMAL NO. : N30660

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MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

PANCREAS:

-Ectopic tissue; spleen

PARATHYROID GLANDS:

Only one of paired organs examined/present  
SPLEEN:

-Hyperplasia; lymphoid, grade 1

TESTES:

-Atrophy; tubule, bilateral, grade 2

-Multinucleated giant cell, bilateral, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30726 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 1

INJECTION SITE 1:

-Infiltrate; macrophage, muscle, focal, grade 1

INJECTION SITE 3:

-Inflammation; subacute, focal, grade 1

KIDNEYS:

-Infiltrate; lymphocyte, unilateral, grade 1

-Mineralization; cortex, unilateral, grade 1

LUNGS (+ BRONCHI):

-Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present  
SACRAL LYMPH NODE:

Tissue not present for histologic examination

SPLEEN:

-Hyperplasia; lymphoid, grade 1

VAGINA:

-Cyst, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30727 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAc LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
ILIAc LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, grade 1  
mainly lymphocytes  
KIDNEYS:  
-Mineralization; cortex, unilateral, grade 1  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; granulocyte; alveolus, grade 1  
-Infiltrate; macrophage; alveolus, grade 3  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
SPLEEN:  
-Hyperplasia; lymphoid, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30728 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 1

KIDNEYS:

-Dilatation; tubule, bilateral, grade 1

-Mineralization; cortex, bilateral, grade 1

LIVER:

-Infiltrate; mixed cell; focal, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

NASAL CAVITY (LEVEL 3):

-Artifact; blood in lumen, nasolacrimal duct

PARATHYROID GLANDS:

Only one of paired organs examined/present  
SACRAL LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

SPLEEN:

-Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

---

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

---

\* ANIMAL NUMBER : N30729 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

ILIAC LYMPH NODES LEFT:

Tissue not present for histologic examination

INJECTION SITE 2:

-Infiltrate; lymphocyte, focal, grade 1

KIDNEYS:

-Basophilia; tubule, unilateral, grade 1

-Dilatation; tubule, bilateral, grade 1

-Mineralization; cortex, bilateral, grade 1

MANDIBULAR LYMPH NODES:

-Dilatation; sinusoid, bilateral, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present  
SPLEEN:

-Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 2, 15 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30730 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

---

\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

HARDERIAN GLANDS:

-Degeneration; epithelium, focal, unilateral, grade 1  
-Infiltrate; mononuclear cell, unilateral, grade 1

ILIAC LYMPH NODES RIGHT:

-Hemorrhage; sinus, grade 1

INGUINAL LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 1

INJECTION SITE 2:

-Infiltrate; lymphocyte, focal, grade 1

INJECTION SITE 3:

-Inflammation; subacute, grade 1  
mainly lymphocytes

LUNGS (+ BRONCHI):

-Infiltrate; macrophage; alveolus, grade 1

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

NASAL CAVITY (LEVEL 2):

-Artifact; blood in lumen

PARATHYROID GLANDS:

Only one of paired organs examined/present

SPLEEN:

-Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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## ANIMAL HEADING DATA

DOSE GROUP : 3, 45 microg HA/strain/dose D57

| ANIMAL<br>NUMBER | SEX<br>M/F | DEFINED AND FINAL<br>STATE OF NECROPSY | TEST<br>DAYS | FIRST AND LAST<br>DAY UNDER TEST | DATE OF<br>NECROPSY |
|------------------|------------|--|--------------|----------------------------------|---------------------|
| N30666           | M          | R1                                     | R1           | 57                               | 20-AUG-18 15-OCT-18 |
| N30667           | M          | R1                                     | R1           | 57                               | 20-AUG-18 15-OCT-18 |
| N30668           | M          | R1                                     | R1           | 57                               | 20-AUG-18 15-OCT-18 |
| N30669           | M          | R1                                     | R1           | 57                               | 20-AUG-18 15-OCT-18 |
| N30670           | M          | R1                                     | R1           | 57                               | 20-AUG-18 15-OCT-18 |
| .....            |            |  |              |                                  |                     |
| N30736           | F          | R1                                     | R1           | 57                               | 28-AUG-18 23-OCT-18 |
| N30737           | F          | R1                                     | R1           | 57                               | 28-AUG-18 23-OCT-18 |
| N30738           | F          | R1                                     | R1           | 57                               | 28-AUG-18 23-OCT-18 |
| N30739           | F          | R1                                     | R1           | 57                               | 28-AUG-18 23-OCT-18 |
| N30740           | F          | R1                                     | R1           | 57                               | 28-AUG-18 23-OCT-18 |
| .....            |            |  |              |                                  |                     |

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30666 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

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| * NECROPSY OBSERVATION                     | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| INJECTION SITE 1                           |                                   |
| - 01: Red discoloration, many, punctiform. | - Hemorrhage, fascia, grade 1.    |
| NO OTHER NECROPSY OBSERVATIONS NOTED       |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 2  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, fascia, grade 1  
-Hemorrhage, fascia, grade 1  
This finding corresponds to necropsy observation no: 01.  
INJECTION SITE 3:  
-Inflammation; subacute, grade 1  
mainly lymphocytes  
KIDNEYS:  
-Basophilia; tubule, unilateral, grade 1  
-Dilatation; tubule, unilateral, grade 1  
-Infiltrate; lymphocyte, unilateral, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; granulocyte; alveolus, grade 1  
-Infiltrate; macrophage; alveolus, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

---

CONT./FF. ANIMAL NO. : N30666

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MANDIBULAR LYMPH NODES:

-Infiltrate; granulocyte, bilateral, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present

SACRAL LYMPH NODE:

-Hyperplasia; lymphoid, grade 2

SPLEEN:

-Hyperplasia; lymphoid, grade 1

Spleen in recovery group animals has less cellular secondary follicles, consistent with involution

STOMACH:

-Dilatation; gland, grade 1

TESTES:

-Atrophy; tubule, bilateral, grade 1

-Multinucleated giant cell, bilateral, grade 1

URETERS:

Only one of paired organs examined/present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30667 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

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| * NECROPSY OBSERVATION                                    | CORRESPONDING MICROSCOPIC FINDING  |
|---|------------------------------------|
| GENERAL OBSERVATION                                       |                                    |
| - 01: Clinical observations not seen at necropsy, papula. | - This necropsy finding was noted. |
| NO OTHER NECROPSY OBSERVATIONS NOTED.                     |                                    |

\* MICROSCOPIC FINDINGS

GENERAL OBSERVATION:  
This necropsy finding was noted. Microscopic evaluation was not applicable.  
ADRENAL GLANDS:  
-Accessory tissue, bilateral  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
Tissue not present for histologic examination  
INJECTION SITE 3:  
-Inflammation; subacute, grade 1  
KIDNEYS:  
-Dilatation; tubule, unilateral, grade 1  
-Mineralization; cortex, unilateral, grade 1  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
NASAL CAVITY (LEVEL 3):  
-Artifact; blood in lumen  
NASAL CAVITY (POSTERIOR, LEVEL 4):  
-Artifact; blood in lumen

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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CONT./FF. ANIMAL NO. : N30667

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TESTES:

-Multinucleated giant cell, bilateral, grade 1

THYMUS:

-Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30668 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

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\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIACT LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 1  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
-Infiltrate; granulocyte, grade 1  
INJECTION SITE 3:  
-Artifact  
hemorrhage  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
PARATHYROID GLANDS:  
Only one of paired organs examined/present  
SACRAL LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
SPLEEN:  
-Hyperplasia; lymphoid, grade 1  
TESTES:  
-Multinucleated giant cell, unilateral, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30669 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

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\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
HARDERIAN GLANDS:  
-Degeneration; epithelium, unilateral, grade 1  
-Infiltrate; mononuclear cell, unilateral, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Infiltrate; lymphocyte, fascia, grade 1  
LUNGS (+ BRONCHI):  
-Infiltrate; macrophage; alveolus, grade 1  
MANDIBULAR LYMPH NODES:  
-Hyperplasia; lymphoid, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
NASAL CAVITY (POSTERIOR, LEVEL 4):  
-Artifact; blood in lumen  
-Inflammation; intranasal exudate, nasolacrimal duct, grade 1  
SPLEEN:  
-Hyperplasia; lymphoid, grade 1  
TESTES:  
-Multinucleated giant cell, bilateral, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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CONT./FF. ANIMAL NO. : N30669

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ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30670 SEX : MALE  
FIRST DAY ON TEST : 20-Aug-18  
LAST DAY ON TEST : 15-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 15-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

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\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:

-Hyperplasia; lymphoid, grade 1

ILIIAC LYMPH NODES LEFT:

Tissue not present for histologic examination

ILIIAC LYMPH NODES RIGHT:

-Hemorrhage; sinus, grade 1

INGUINAL LYMPH NODES LEFT:

-Hyperplasia; lymphoid, grade 1

-Infiltrate; granulocyte, grade 1

INGUINAL LYMPH NODES RIGHT:

-Hyperplasia; lymphoid, grade 1

LUNGS (+ BRONCHI):

-Hemorrhage; agonal, grade 1

-Metaplasia; osseous

MESENTERIC LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:

Only one of paired organs examined/present

SPLEEN:

-Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30736 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

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\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

ADRENAL GLANDS:  
-Accessory tissue, unilateral  
GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
HARDERIAN GLANDS:  
-Infiltrate; mononuclear cell, unilateral, grade 1  
ILIAC LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, grade 1  
KIDNEYS:  
-Basophilia; tubule, unilateral, grade 1  
-Dilatation; tubule, unilateral, grade 1  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Hemorrhage; agonal, grade 1  
MANDIBULAR LYMPH NODES:  
-Dilatation; sinusoid, bilateral, grade 2  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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CONT./FF. ANIMAL NO. : N30736

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SACRAL LYMPH NODE:

-Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30737 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

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| * NECROPSY OBSERVATION  | CORRESPONDING MICROSCOPIC FINDING                             |
|---|---|
| SKIN  |   |
| - 01: Right, ear: scab, approx 2 cm long, approx 0.3 cm wide. | - Hyperkeratosis, grade 1.<br>Inflammation; chronic, grade 1. |
| NO OTHER NECROPSY OBSERVATIONS NOTED                          |   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Infiltrate; macrophage, muscle, focal, grade 1  
INJECTION SITE 2:  
-Infiltrate; macrophage, muscle, focal, grade 1  
KIDNEYS:  
-Dilatation; tubule, bilateral, grade 1  
-Mineralization; cortex, unilateral, grade 1  
LACRIMAL GLANDS:  
-Infiltrate; lymphocyte, bilateral, grade 1  
MANDIBULAR LYMPH NODES:  
-Hyperplasia; lymphoid, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
PARATHYROID GLANDS:  
Only one of paired organs examined/present  
SKIN:  
-Hyperkeratosis, grade 1  
This finding corresponds to necropsy observation no: 01.  
-Inflammation; chronic, grade 1

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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CONT./FF. ANIMAL NO. : N30737

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This finding corresponds to necropsy observation no: 01.  
SPLEEN:  
-Hyperplasia; lymphoid, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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|                    |   |                                 |       |        |
|--------------------|---|---------------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30738                          | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                       |       |        |
| LAST DAY ON TEST   | : | 23-Oct-18                       |       |        |
| DAYS ON TEST       | : | 57                              |       |        |
| DATE OF NECROPSY   | : | 23-Oct-18                       |       |        |
| DEFINED SACR.GROUP | : | RECOVERY / POST-TREATMENT GROUP |       |        |
| STATUS AT NECROPSY | : | RECOVERY / POST-TREATMENT GROUP |       |        |

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| * NECROPSY OBSERVATION   | CORRESPONDING MICROSCOPIC FINDING |
|--|-----------------------------------|
| SKELETAL MUSCLE  |                                   |
| - 01: Dorsal part, right: red discoloration, many, punctiform.   | - Nothing abnormal discovered.    |
| Skin   |                                   |
| - 01: Dorsal region: white discoloration, a few, up to 0.3 cm in diameter, raised, corresponding to: papula. | - Nothing abnormal discovered.    |
| NO OTHER NECROPSY OBSERVATIONS NOTED   |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
ILIAC LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 1:  
-Inflammation; subacute, focal, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, focal, grade 1  
LUNGS (+ BRONCHI):  
-Hyperplasia; lymphoid, grade 1  
MANDIBULAR LYMPH NODES:  
-Dilatation; sinusoid, bilateral, grade 2  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
NASAL CAVITY (LEVEL 2):  
-Artifact; blood in lumen

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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CONT./FF. ANIMAL NO. : N30738

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NASAL CAVITY (LEVEL 3):

-Artifact; blood in lumen

NASAL CAVITY (POSTERIOR, LEVEL 4):

-Artifact; blood in lumen

PARATHYROID GLANDS:

Only one of paired organs examined/present

SKELETAL MUSCLE:

Nothing abnormal discovered corresponding to necropsy observation no.01.

SKIN:

Nothing abnormal discovered corresponding to necropsy observation no.01.

SPLEEN:

-Hyperplasia; lymphoid, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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|                    |   |                                 |       |        |
|--------------------|---|---------------------------------|-------|--------|
| * ANIMAL NUMBER    | : | N30739                          | SEX : | FEMALE |
| FIRST DAY ON TEST  | : | 28-Aug-18                       |       |        |
| LAST DAY ON TEST   | : | 23-Oct-18                       |       |        |
| DAYS ON TEST       | : | 57                              |       |        |
| DATE OF NECROPSY   | : | 23-Oct-18                       |       |        |
| DEFINED SACR.GROUP | : | RECOVERY / POST-TREATMENT GROUP |       |        |
| STATUS AT NECROPSY | : | RECOVERY / POST-TREATMENT GROUP |       |        |

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| * NECROPSY OBSERVATION               | CORRESPONDING MICROSCOPIC FINDING |
|--------------------------------------|-----------------------------------|
| ILIAc LYMPH NODES RIGHT              |                                   |
| - 01: Red discoloration, diffuse.    | - Hemorrhage; sinus, grade 2.     |
| NO OTHER NECROPSY OBSERVATIONS NOTED |                                   |

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1

ILIAc LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

ILIAc LYMPH NODES RIGHT:  
-Hemorrhage; sinus, grade 2  
This finding corresponds to necropsy observation no: 01.  
-Hyperplasia; lymphoid, grade 1

INGUINAL LYMPH NODES LEFT:  
-Hyperplasia; lymphoid, grade 1

INJECTION SITE 2:  
-Inflammation; subacute, focal, grade 1

KIDNEYS:  
-Basophilia; tubule, unilateral, grade 1  
-Dilatation; tubule, bilateral, grade 1  
-Infiltrate; lymphocyte, bilateral, grade 1  
-Mineralization; cortex, bilateral, grade 1

LACRIMAL GLANDS:  
-Infiltrate; lymphocyte, unilateral, grade 1

MANDIBULAR LYMPH NODES:  
-Dilatation; sinusoid, bilateral, grade 1

MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1

PARATHYROID GLANDS:  
Only one of paired organs examined/present

TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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CONT./FF. ANIMAL NO. : N30739

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SPLEEN:

-Hyperplasia; lymphoid, grade 1

THYMUS:

-Hemorrhage; agonal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEXT OF GROSS AND MICROSCOPIC FINDINGS  
DOSE GROUP : 3, 45 microg HA/strain/dose D57

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\* ANIMAL NUMBER : N30740 SEX : FEMALE  
FIRST DAY ON TEST : 28-Aug-18  
LAST DAY ON TEST : 23-Oct-18  
DAYS ON TEST : 57  
DATE OF NECROPSY : 23-Oct-18  
DEFINED SACR.GROUP : RECOVERY / POST-TREATMENT GROUP  
STATUS AT NECROPSY : RECOVERY / POST-TREATMENT GROUP

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\* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

\* MICROSCOPIC FINDINGS

GUT ASSOCIATED LYMPHOID TISSUE:  
-Hyperplasia; lymphoid, grade 1  
INGUINAL LYMPH NODES RIGHT:  
-Hyperplasia; lymphoid, grade 1  
INJECTION SITE 3:  
-Inflammation; subacute, grade 1  
LIVER:  
-Infiltrate; mixed cell; focal, grade 1  
LUNGS (+ BRONCHI):  
-Foreign material, focal  
-Infiltrate; macrophage; alveolus, focal, grade 2  
MANDIBULAR LYMPH NODE:  
-Hyperplasia; lymphoid, bilateral, grade 1  
MESENTERIC LYMPH NODE:  
-Hyperplasia; lymphoid, grade 1  
SPLEEN:  
-Hyperplasia; lymphoid, grade 1  
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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