# Title Page

| | | |
|---|---|---|
| Function: | **Experimental Toxicology** | **Nonclinical Study Report** |
| | | GLP: No |
| Report ID: | PH-42754 | |
| Test Item: | **BAY 2469430** | |
| Title: | **Non-GLP report version 1**<br>**2-week repeat-dose systemic toxicity study in dogs with once daily oral (gavage) administration** | |
| Study ID: | T103508-7 | |
| Study Director: | Rainer Lewin | |
| DMS-Product Name: | BAY 2469430 | |
| Program Name: | CRM PREP Inh PH_15/PID 463000 | |

**Test Facility**

Bayer AG
Nonclinical Drug Safety
Müllerstraße 178
13353 Berlin
Germany

# 1. Key Study Information

## 1.1 Key Study Data

**Table 1–1: Key Study Data**

| | |
|---|---|
| Test Item | BAY 2469430 |
| Project ID | 463000 |
| Project Description | CRM PREP Inh PH_15 |
| Pharmacological MoA | PREP Inhibitor |
| GLP | No |
| Experimental starting date | 05 Sep 2017 |
| Experimental completion date | 19 Sep2017 |
| Study ID | T103508-7 |
| Animals | 4 male and 4 female dogs |
| Dose levels | 0, 5, 20 and 80 mg/kg |
| Treatment scheme | Once daily for 14 days |
| Route of administration | Oral by gavage |
| Formulation | Solution |
| Vehicle | PEG400 |
| Concentration | 2.5 to 40 mg/mL |
| Volume | 2.0 mL/kg |
| Batch no. | SYFO13623-3-1 |
| NOAEL | 20 mg/kg |

For details on study conduct see Materials and Methods

## 1.2 Dosing Schedule

**Table 1–2: Dosing Schedule**

| Group no. | Test item | Dose [mg/kg] | Concen-tration | Application volume | Number of animals and sex | Time of sacrifice [dosing day] |
|---|---|---|---|---|---|---|
| 1 | - | - | - | 2.0 | 1M/1F | 15 |
| 2 | BAY 2468430 | 5 | 2.5 | 2.0 | 1M/1F | 15 |
| 3 | BAY 2469430 | 20 | 10 | 2.0 | 1M/1F | 15 |
| 4 | BAY 2469430 | 80 | 40 | 2.0 | 1M/1F | 15 |

## 1.3 Investigation

**Table 1–3: Investigation Included into the Study**

| Investigation | Schedule of Investigation |
|---|---|
| Clinical observation | Pre-dosing: once daily<br>Dosing: twice daily |
| Mortality | Twice daily |
| Body weight | Pre-random: once<br>Pre-dosing: once<br>Dosing: day 1, 3 and 7 |
| Food intake | Daily |
| EKG / Blood Pressure | Pre-Dosing: once<br>Dosing: week 2 (prior to and 1-2 h after administration) |
| Hematology / Hemostasis | Predosing: once<br>Dosing week 2 |
| Clinical chemistry | Predosing: once<br>Dosing: day 3 and week 2 |
| Necropsy | Dosing: day 15 |
| Toxicokinetics | Dosing: day 1/2 and week 2 (1, 2, 4, 7 and 24 h after administration) |

# 2. Summary of Results

Potentially test item-related effects are summarized in Table 2–1

**Table 2–1: Noteworthy and Potentially Treatment-related Findings and Lowest Dose of Occurrence**

| Endpoint | Findings | Sex | Dose [mg/kg] |
|---|---|---|---|
| Hematology and Hemostasis | Decrease in thrombocytes | M+F | 80 |

M male
F = Female
M+F = Finding occurred in both sexes at the same dose level
M/F = Finding occurred in both sexes at different dose level

## 2.1 Mortality

No mortality was observed in the study.

## 2.2 Clinical Examination

No test item-related findings were observed.

## 2.3 Electrocardiography and Blood Pressure

No relevant effects of BAY 2469430 on arterial blood pressure, heart rate and ECG intervals (incl. QT/QTc) were observed. In ECG recordings conducted at pre-dosing and in Week 2 no arrhythmias were detected.

## 2.4 Body Weight

No test item-related effect were observed.

### 2.4.1 Food intake

No test item-related effect were observed.

## 2.5 Laboratory Examination

### 2.5.1 Hematology and Hemostasis

At the high dose of 80 mg/kg a decrease in thrombocytes was observed on day 10 in the male and female animal.

### 2.5.2 Clinical Chemistry

No test item-related effects were observed.

## 2.6 Post-mortem Examination

### 2.6.1 Necropsy and Organ Weights

No test item-related findings were observed.

### 2.6.2 Histopathology

No test item-related findings were observed.

Background findings were observed in several organs throughout the dose groups including the control group. A minimal decrease in glycogen content in the liver at the high dose animals compared to the control animals is considered within the range of physiological variation of glycogen content in the liver. The slight tubular atrophy/hypospermatogenesis in the testes of the high dose male dog is also considered within the physiological range for animals at this age, as the testes are not yet fully mature. The male high dose animal also showed minimally decreased cell content in the periarterial sheath of the spleen as a single event.

## 2.7 Toxicokinetic Data

The results of the toxicokinetic evaluation at steady-state are summarized in Table 2-3. The exposure in all plasma samples of the vehicle groups (0 mg/kg) was below the lower limit of quantification (LLOQ = 3 µg/L).

Exposures of BAY 2469430 were generally increased with dose in both genders. Only $C_{max}$ at 80 mg/kg in females and $AUC_{(0-24)}$ at 20 mg/kg in males showed a tendency for subproportional increase with dose. Except from a moderate increase in $AUC_{(0-24)}$ at 20 mg/kg in females, no relevant differences in exposure were observed between the two sexes.

Both genders did not show any relevant accumulation of $C_{max}$ or $AUC_{(0-24)}$ at any of the investigated dose levels.

**Table 2–2: Systemic Exposure at Steady-State (day 8)**

| | | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|---|
| Dose | [mg/kg] | 0 | 5 | 20 | 80 | 0 | 5 | 20 | 80 |

**Table 2–2: Systemic Exposure at Steady-State (day 8)**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $AUC_{(0-24)}$ | [mg·h/L] | − | 44 | 120 | 699 | − | 40 | 171 | 751 |
| $AUC_{(0-24)norm}$ | [kg·h/L] | − | 8.8 | 6.0 | 8.7 | − | 7.9 | 8.6 | 9.4 |
| $C_{max}$ | [mg/L] | − | 4.2 | 17 | 62 | − | 5.2 | 18 | 63 |
| $C_{max,norm}$ | [kg/L] | − | 0.83 | 0.85 | 0.78 | − | 1.0 | 0.88 | 0.79 |
| $C_{(24)}/C_{max}$ | [%] | − | 15 | 3.7 | 15 | − | 4.5 | 10 | 21 |
| $t_{max}$ | [h] | − | 2.0 | 1.0 | 2.0 | − | 1.0 | 1.0 | 2.0 |
| $RA_{AUC}$ | [%] | − | 116 | 110 | 123 | − | 103 | 106 | 124 |
| $RA_{Cmax}$ | [%] | − | 111 | 110 | 117 | − | 100 | 105 | 116 |

$RA_{AUC}$ = Accumulation ratio ($AUC_{(0-24)}$, SS / $AUC_{(0-24)}$, Day 1)
$RA_{Cmax}$ = Accumulation ratio ($C_{max}$, SS / $C_{max}$,Day 1)

# 3. Conclusion

Once daily oral administration (by gavage) of 5, 20 and 80 mg/kg BAY 2469430 to Beagle dogs over a period of 2 weeks was well tolerated without test item-related findings in clinical and postmortem examinations. A decreased thrombocyte count was observed on day 10 in both animals at the high dose of 80 mg/kg.

Toxicokinetic evaluation revealed a dose-dependent increase in exposure, tmax between 1-2 h after administration and no relevant accumulation potential.

# 4. Signature

Valid without signature.

| PATHOLOGY REPORT (FINAL DRAFT) | | PROJECT | :T 103508-7 |
|---|---|---|---|
| TEST ITEM | : BAY 2469430 | PATHOL. NO. | : 13508 GUT |
| TEST SYSTEM | : DOG, 2 weeks, p.o. | DATE | : 08-NOV-17 |
| SPONSOR | : Bayer AG | PathData®System | V6.2e2 |

PREPARED BY: Dr. Katrin Gutberlet
Veterinary Pathologist

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## EXPLANATION OF CODES AND SYMBOLS

### CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male animal
F = Female animal
K0 = Terminal sacrifice group

### CODES AND SYMBOLS USED AT ORGAN LEVEL:

G = Gross observation checked off histologically
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
- = Organ examined, no pathologic findings noted (AOFT only)
( = Only one of paired organs examined/present

### CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / few / small
( = Finding unilateral in paired organs

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NUMBER OF ANIMALS WITH NECROPSY FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

| DOSE GROUP: | 01 | | 02 | | 03 | | 04 | |
|---|---|---|---|---|---|---|---|---|
| SEX: | M | F | M | F | M | F | M | F |
| ORGAN/FINDING ANIM.EXAM.: | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| SPLEEN : | | | | | | | | |
| - Nodule : | - | - | - | - | - | - | - | 1 |

Group 01, vehicle, males: BAY 2469430 (0 mg/kg); females: BAY 2469430 (0 mg/kg)
Group 02, low dose (5 mg/kg), males: BAY 2469430 (5 mg/kg); females: BAY 2469430 (5 mg/kg)
Group 03, mid dose (20 mg/kg), males: BAY 2469430 (20 mg/kg); females: BAY 2469430 (20 mg/kg)
Group 04, high dose (80 mg/kg), males: BAY 2469430 (80 mg/kg); females: BAY 2469430 (80 mg/kg)

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SPONSOR : Bayer AG PathData®System V6.2e2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

| DOSE GROUP: | 01 | | 02 | | 03 | | 04 | |
|---|---|---|---|---|---|---|---|---|
| SEX : | M | F | M | F | M | F | M | F |
| NO.ANIMALS: | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| LIVER : | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Mixed Infl.C.Infilt.: | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Grade 1: | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Glycogen Depletion : | - | - | - | - | - | - | 1 | 1 |
| Grade 1: | - | - | - | - | - | - | 1 | 1 |
| HEART : | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Mixed Infl.C.Infilt.: | 1 | - | - | - | - | - | - | - |
| Grade 1: | 1 | - | - | - | - | - | - | - |
| - Inflammation : | - | - | - | - | - | - | - | 1 |
| Grade 1: | - | - | - | - | - | - | - | 1 |
| KIDNEYS : | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Tubular Vacuolation : | 1 | 1 | - | 1 | 1 | 1 | - | 1 |
| Grade 1: | 1 | 1 | - | 1 | 1 | 1 | - | 1 |
| - Lymphoid C.Infiltr. : | - | - | - | - | - | - | 1 | - |
| Grade 1: | - | - | - | - | - | - | 1 | - |
| - Mineralization : | 1 | 1 | - | - | - | 1 | 1 | 1 |
| Grade 1: | 1 | 1 | - | - | - | 1 | 1 | 1 |
| LUNG : | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Inflammation : | 1 | 1 | 1 | - | - | - | 1 | 1 |
| Grade 1: | 1 | 1 | 1 | - | - | - | 1 | - |
| Grade 2: | - | - | - | - | - | - | - | 1 |
| - Pigment : | - | 1 | - | - | - | - | - | - |
| Grade 1: | - | 1 | - | - | - | - | - | - |
| - Hemorrhage : | - | 1 | - | - | - | - | - | - |
| Grade 1: | - | 1 | - | - | - | - | - | - |
| SPLEEN : | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Lymphoid Depletion : | - | - | - | - | - | - | 1 | - |
| Grade 1: | - | - | - | - | - | - | 1 | - |

Group 01, vehicle, males: BAY 2469430 (0 mg/kg); females: BAY 2469430 (0 mg/kg)
Group 02, low dose (5 mg/kg), males: BAY 2469430 (5 mg/kg); females: BAY 2469430 (5 mg/kg)
Group 03, mid dose (20 mg/kg), males: BAY 2469430 (20 mg/kg); females: BAY 2469430 (20 mg/kg)
Group 04, high dose (80 mg/kg), males: BAY 2469430 (80 mg/kg); females: BAY 2469430 (80 mg/kg)

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

| DOSE GROUP: | 01 | | 02 | | 03 | | 04 | |
|---|---|---|---|---|---|---|---|---|
| SEX : | M | F | M | F | M | F | M | F |
| NO.ANIMALS: | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| THYMUS : | 1 | - | 1 | 1 | 1 | 1 | - | 1 |
| - Involution/Atrophy : | 1 | - | 1 | 1 | 1 | - | - | - |
| Grade 1: | - | - | - | 1 | - | - | - | - |
| Grade 2: | 1 | - | 1 | - | 1 | - | - | - |
| STOMACH : | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Autolysis : | - | - | - | - | - | - | - | 1 |
| Grade 2: | - | - | - | - | - | - | - | 1 |
| ADRENAL GLANDS : | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Hypertrophy : | - | - | - | - | - | - | 1 | - |
| Grade 1: | - | - | - | - | - | - | 1 | - |
| - Access.Cort.Tissue : | 1 | - | - | 1 | - | - | - | - |
| Grade 1: | 1 | - | - | 1 | - | - | - | - |
| THYROID GLAND : | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| - Cyst : | - | - | - | 1 | - | - | - | - |
| Grade 2: | - | - | - | 1 | - | - | - | - |
| PARATHYROID GLANDS : | 1 | 1 | 1 | - | 1 | 1 | 1 | 1 |
| - Cyst : | - | - | - | - | - | - | 1 | - |
| Grade 1: | - | - | - | - | - | - | 1 | - |
| TESTES : | 1 | - | 1 | - | 1 | - | 1 | - |
| - Immaturity : | - | - | - | - | - | - | 1 | - |
| Grade 1: | - | - | - | - | - | - | 1 | - |
| - Tubular Atrophy : | 1 | - | - | - | - | - | 1 | - |
| Grade 1: | 1 | - | - | - | - | - | - | - |
| Grade 2: | - | - | - | - | - | - | 1 | - |
| - Multinucl.Giant C. : | - | - | 1 | - | - | - | 1 | - |
| Grade 1: | - | - | 1 | - | - | - | 1 | - |

Group 01, vehicle, males: BAY 2469430 (0 mg/kg); females: BAY 2469430 (0 mg/kg)
Group 02, low dose (5 mg/kg), males: BAY 2469430 (5 mg/kg); females: BAY 2469430 (5 mg/kg)
Group 03, mid dose (20 mg/kg), males: BAY 2469430 (20 mg/kg); females: BAY 2469430 (20 mg/kg)
Group 04, high dose (80 mg/kg), males: BAY 2469430 (80 mg/kg); females: BAY 2469430 (80 mg/kg)

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NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

| DOSE GROUP: | 01 | | 02 | | 03 | | 04 | |
|---|---|---|---|---|---|---|---|---|
| SEX : | M | F | M | F | M | F | M | F |
| NO.ANIMALS: | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EPIDIDYMIDES : | 1 | - | 1 | - | 1 | - | 1 | - |
| - Cell Debris : | 1 | - | - | - | 1 | - | 1 | - |
| Grade 1: | 1 | - | - | - | 1 | - | 1 | - |

Group 01, vehicle, males: BAY 2469430 (0 mg/kg); females: BAY 2469430 (0 mg/kg)
Group 02, low dose (5 mg/kg), males: BAY 2469430 (5 mg/kg); females: BAY 2469430 (5 mg/kg)
Group 03, mid dose (20 mg/kg), males: BAY 2469430 (20 mg/kg); females: BAY 2469430 (20 mg/kg)
Group 04, high dose (80 mg/kg), males: BAY 2469430 (80 mg/kg); females: BAY 2469430 (80 mg/kg)

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CORRELATION TABLE: NECROPSY - MICROSCOPY DOSE GROUP 04, FEMALE

| NECROPSY OBSERVATION | CORRESPONDING MICROSCOPIC FINDING |
|---|---|
| | ANIMAL NO: 0008 |
| SPLEEN | |
| - 01: Margin: nodule, red, single, approx 1 cm in diameter. | - uneven blood distribution |

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, vehicle

| ANIMAL NUMBER : | 0001 | 0005 |
|---|---|---|
| | MK0 | FK0 |
| LIVER | + | + |
| - Mixed Infl.C.Infilt. | 1. | 1. |
| HEART | + | - |
| - Mixed Infl.C.Infilt. | 1. | . |
| KIDNEYS | + | + |
| - Tubular Vacuolation | ( 1. | ( 1. |
| - Mineralization | 1. | ( 1. |
| LUNG | + | + |
| - Inflammation | 1. | 1. |
| - Pigment | . | 1. |
| - Hemorrhage | . | 1. |
| TRACHEA | - | - |
| LARYNX | - | - |
| SPLEEN | - | - |
| THYMUS | + | 0 |
| - Involution/Atrophy | 2. | . |
| STOMACH | - | - |
| SKELETAL MUSCLE | - | - |
| ADRENAL GLANDS | + | - |
| - Access.Cort.Tissue | ( 1. | . |
| THYROID GLAND | - | - |
| PARATHYROID GLANDS | - | ( - |
| TESTES | + | |
| - Tubular Atrophy | ( 1. | |

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SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, vehicle

| ANIMAL NUMBER : | 0001 | 0005 |
|---|---|---|
| | MK0 | FK0 |
| EPIDIDYMIDES | + | |
| - Cell Debris | 1. | |

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TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, low dose (5 mg/kg)

| ANIMAL NUMBER : | 0002 MK0 | 0006 FK0 |
|---|---|---|
| LIVER | + | + |
| - Mixed Infl.C.Infilt. | 1. | 1. |
| HEART | - | - |
| KIDNEYS | - | + |
| - Tubular Vacuolation | . | 1. |
| LUNG | + | - |
| - Inflammation | 1. | . |
| TRACHEA | - | - |
| LARYNX | - | - |
| SPLEEN | - | - |
| THYMUS | + | + |
| - Involution/Atrophy | 2. | 1. |
| STOMACH | - | - |
| SKELETAL MUSCLE | - | - |
| ADRENAL GLANDS | - | + |
| - Access.Cort.Tissue | . ( | 1. |
| THYROID GLAND | - | + |
| - Cyst | . ( | 2. |
| PARATHYROID GLANDS | - | 0 |
| TESTES | + | |
| - Multinucl.Giant C. | ( 1. | |
| EPIDIDYMIDES | - | |

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SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, mid dose (20 mg/kg)

| ANIMAL NUMBER : | 0003 MK0 | 0007 FK0 |
|---|---|---|
| LIVER | + | + |
| - Mixed Infl.C.Infilt. | 1. | 1. |
| HEART | - | - |
| KIDNEYS | + | + |
| - Tubular Vacuolation | 1. | 1. |
| - Mineralization | . | 1. |
| LUNG | - | - |
| TRACHEA | - | - |
| LARYNX | - | - |
| SPLEEN | - | - |
| THYMUS | + | - |
| - Involution/Atrophy | 2. | . |
| STOMACH | - | - |
| SKELETAL MUSCLE | - | - |
| ADRENAL GLANDS | - | - |
| THYROID GLAND | - | - |
| PARATHYROID GLANDS | - | ( - |
| TESTES | - | |
| EPIDIDYMIDES | + | |
| - Cell Debris | 1. | |

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SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, high dose (80 mg/kg)

| ANIMAL NUMBER : | 0004 MK0 | 0008 FK0 |
|---|---|---|
| LIVER | + | + |
| - Mixed Infl.C.Infilt. | 1. | 1. |
| - Glycogen Depletion | 1. | 1. |
| HEART | - | + |
| - Inflammation | . | 1. |
| KIDNEYS | + | + |
| - Tubular Vacuolation | . | 1. |
| - Lymphoid C.Infiltr. | ( 1. | . |
| - Mineralization | ( 1. | ( 1. |
| LUNG | + | + |
| - Inflammation | 1. | 2. |
| TRACHEA | - | - |
| LARYNX | - | - |
| SPLEEN | + | -G |
| - Lymphoid Depletion | 1. | . |
| THYMUS | 0 | - |
| STOMACH | - | + |
| - Autolysis | . | 2. |
| SKELETAL MUSCLE | - | - |
| ADRENAL GLANDS | + | - |
| - Hypertrophy | ( 1. | . |
| THYROID GLAND | - | - |
| PARATHYROID GLANDS | ( + | ( - |
| - Cyst | ( 1. | . |

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SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, high dose (80 mg/kg)

| ANIMAL NUMBER : | 0004 MK0 | 0008 FK0 |
|---|---|---|
| TESTES | + | |
| - Immaturity | 1. | |
| - Tubular Atrophy | 2. | |
| - Multinucl.Giant C. | 1. | |
| EPIDIDYMIDES | + | |
| - Cell Debris | 1. | |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 13/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

ANIMAL HEADING DATA
DOSE GROUP : 01, vehicle

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | | TEST DAYS | FIRST AND LAST DAY UNDER TEST | | DATE OF NECROPSY |
|---|---|---|---|---|---|---|---|
| 0001 | M | K0 | K0 | 15 | 05-SEP-17 | 19-SEP-17 | 19-SEP-17 |
| 0005 | F | K0 | K0 | 15 | 05-SEP-17 | 19-SEP-17 | 19-SEP-17 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 14/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, vehicle MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 15 * ANIMAL NO. : 0001

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Infiltrate:mixed inflammatory cell, multifocal, grade 1
HEART:
-Infiltrate:mixed inflammatory cell, focal, atrium, grade 1
KIDNEYS:
-Vacuolation:tubular cell, focal, unilateral, grade 1
-Mineralization, caliceal, bilateral, grade 1
LUNG:
-Inflammation, interstitial, grade 1
THYMUS:
-Involution/Atrophy, grade 2
ADRENAL GLANDS:
-Accessory tissue:cortical, single, unilateral, grade 1
TESTES:
-Atrophy:tubule, focal, unilateral, grade 1
EPIDIDYMIDES:
-Cell debris, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 15/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, vehicle FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 15 * ANIMAL NO. : 0005

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Infiltrate:mixed inflammatory cell, multifocal, grade 1
KIDNEYS:
-Vacuolation:tubular cell, focal, unilateral, grade 1
-Mineralization, caliceal, glomerular, unilateral, grade 1
LUNG:
-Inflammation, peribronchial, grade 1
-Pigment, brown, peribronchial, grade 1
-Hemorrhage, acute, grade 1
THYMUS:
Tissue not present for histologic examination
PARATHYROID GLANDS:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 16/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

ANIMAL HEADING DATA
DOSE GROUP : 02, low dose (5 mg/kg)

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | | TEST DAYS | FIRST AND LAST DAY UNDER TEST | | DATE OF NECROPSY |
|---|---|---|---|---|---|---|---|
| 0002 | M | K0 | K0 | 15 | 05-SEP-17 | 19-SEP-17 | 19-SEP-17 |
| 0006 | F | K0 | K0 | 15 | 05-SEP-17 | 19-SEP-17 | 19-SEP-17 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 17/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, low dose (5 mg/kg) MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 15 * ANIMAL NO. : 0002

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Infiltrate:mixed inflammatory cell, focal, grade 1
LUNG:
-Inflammation, interstitial, grade 1
THYMUS:
-Involution/Atrophy, grade 2
TESTES:
-Multinucleated giant cell, focal, unilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 18/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, low dose (5 mg/kg) FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 15 * ANIMAL NO. : 0006

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Infiltrate:mixed inflammatory cell, focal, grade 1
KIDNEYS:
-Vacuolation:tubular cell, focal, bilateral, grade 1
THYMUS:
-Involution/Atrophy, grade 1
ADRENAL GLANDS:
-Accessory tissue:cortical, single, unilateral, grade 1
THYROID GLAND:
-Cyst, single, unilateral, grade 2
PARATHYROID GLANDS:
Tissue not present for histologic examination
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 19/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

ANIMAL HEADING DATA
DOSE GROUP : 03, mid dose (20 mg/kg)

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | | TEST DAYS | FIRST AND LAST DAY UNDER TEST | | DATE OF NECROPSY |
|---|---|---|---|---|---|---|---|
| 0003 | M | K0 | K0 | 15 | 05-SEP-17 | 19-SEP-17 | 19-SEP-17 |
| 0007 | F | K0 | K0 | 15 | 05-SEP-17 | 19-SEP-17 | 19-SEP-17 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 20/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, mid dose (20 mg/kg) MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 15 * ANIMAL NO. : 0003

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Infiltrate:mixed inflammatory cell, multifocal, grade 1
KIDNEYS:
-Vacuolation:tubular cell, multifocal, bilateral, grade 1
THYMUS:
-Involution/Atrophy, grade 2
EPIDIDYMIDES:
-Cell debris, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 21/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, mid dose (20 mg/kg) FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 15 * ANIMAL NO. : 0007

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Infiltrate:mixed inflammatory cell, focal, grade 1
KIDNEYS:
-Vacuolation:tubular cell, focal, bilateral, grade 1
-Mineralization, caliceal, bilateral, grade 1
PARATHYROID GLANDS:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 22/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

ANIMAL HEADING DATA
DOSE GROUP : 04, high dose (80 mg/kg)

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | | TEST DAYS | FIRST AND LAST DAY UNDER TEST | | DATE OF NECROPSY |
|---|---|---|---|---|---|---|---|
| 0004 | M | K0 | K0 | 15 | 05-SEP-17 | 19-SEP-17 | 19-SEP-17 |
| 0008 | F | K0 | K0 | 15 | 05-SEP-17 | 19-SEP-17 | 19-SEP-17 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 23/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, high dose (80 mg/kg) MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 15 * ANIMAL NO. : 0004

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

LIVER:
-Infiltrate:mixed inflammatory cell, multifocal, grade 1
-Depletion:glycogen, grade 1
KIDNEYS:
-Infiltrate:lymphoid cell, focal, unilateral, grade 1
-Mineralization, caliceal, unilateral, grade 1
LUNG:
-Inflammation, chronic,subpleural,bronchi,foreign material, grade 1
SPLEEN:
-Atrophy:lymphoid, grade 1
THYMUS:
Tissue not present for histologic examination
ADRENAL GLANDS:
-Hypertrophy, focal, Z.glomerulosa, unilateral, grade 1
PARATHYROID GLANDS:
Only one of paired organs examined/present
-Cyst, single, unilateral, grade 1
TESTES:
-Immaturity, bilateral, grade 1
-Atrophy:tubule, focal, bilateral, grade 2
-Multinucleated giant cell, focal, bilateral, grade 1
EPIDIDYMIDES:
-Cell debris, bilateral, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 24/ 49
INDIVIDUAL ANIMAL DATA PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 04, high dose (80 mg/kg) FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 15 * ANIMAL NO. : 0008

* NECROPSY FINDINGS

SPLEEN:
01: Margin: nodule, red, single, approx 1 cm in diameter.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

LIVER:
-Infiltrate:mixed inflammatory cell, multifocal, grade 1
-Depletion:glycogen, grade 1
HEART:
-Inflammation, chronic, focal, epicardium, atrium, grade 1
KIDNEYS:
-Vacuolation:tubular cell, focal, bilateral, grade 1
-Mineralization, caliceal, unilateral, grade 1
LUNG:
-Inflammation, chronic, subpleural, grade 2
SPLEEN:
uneven blood distribution
STOMACH:
-Autolysis, grade 2
PARATHYROID GLANDS:
Only one of paired organs examined/present
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 25/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS

Explanation of Symbols:

_ = Excluded from statistical calculations
0 = Weight not recorded / Value not calculated
* = Tissue/Organ weighed after fixation
M = Male
F = Female

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 26/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ABSOLUTE WEIGHTS IN GRAMS

DOSE GROUP : 01, vehicle
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | FINAL BODY WEIGHT | LIVER | HEART | KIDNEYS | SPLEEN |
|---|---|---|---|---|---|---|
| 0001 | M | 5650 | 220.58 | 51.28 | 27.41 | 20.25 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 5650.0 | 220.579 | 51.283 | 27.411 | 20.250 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | THYMUS | ADRENAL GLANDS | TESTES |
|---|---|---|---|---|
| 0001 | M | 1.68 | 1.41 | 10.21 |
| NO.EXAM. | | 1 | 1 | 1 |
| MEAN | | 1.676 | 1.410 | 10.212 |
| STD.DEV. | | 0 | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 27/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ABSOLUTE WEIGHTS IN GRAMS

DOSE GROUP : 01, vehicle
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | FINAL BODY WEIGHT | LIVER | HEART | KIDNEYS | SPLEEN |
|---|---|---|---|---|---|---|
| 0005 | F | 6200 | 242.20 | 57.90 | 25.18 | 17.06 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 6200.0 | 242.204 | 57.896 | 25.177 | 17.055 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | THYMUS | ADRENAL GLANDS |
|---|---|---|---|
| 0005 | F | 2.01 | 3.22 |
| NO.EXAM. | | 1 | 1 |
| MEAN | | 2.014 | 3.218 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 28/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ABSOLUTE WEIGHTS IN GRAMS

DOSE GROUP : 02, low dose (5 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | FINAL BODY WEIGHT | LIVER | HEART | KIDNEYS | SPLEEN |
|---|---|---|---|---|---|---|
| 0002 | M | 7850 | 301.22 | 62.35 | 35.61 | 116.22 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 7850.0 | 301.221 | 62.345 | 35.614 | 116.224 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | THYMUS | ADRENAL GLANDS | TESTES |
|---|---|---|---|---|
| 0002 | M | 4.26 | 1.42 | 12.14 |
| NO.EXAM. | | 1 | 1 | 1 |
| MEAN | | 4.257 | 1.419 | 12.137 |
| STD.DEV. | | 0 | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 29/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ABSOLUTE WEIGHTS IN GRAMS

DOSE GROUP : 02, low dose (5 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | FINAL BODY WEIGHT | LIVER | HEART | KIDNEYS | SPLEEN |
|---|---|---|---|---|---|---|
| 0006 | F | 6350 | 283.87 | 63.43 | 28.39 | 19.38 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 6350.0 | 283.870 | 63.428 | 28.394 | 19.376 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | THYMUS | ADRENAL GLANDS |
|---|---|---|---|
| 0006 | F | 4.84 | 1.10 |
| NO.EXAM. | | 1 | 1 |
| MEAN | | 4.837 | 1.099 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 30/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ABSOLUTE WEIGHTS IN GRAMS

DOSE GROUP : 03, mid dose (20 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | FINAL BODY WEIGHT | LIVER | HEART | KIDNEYS | SPLEEN |
|---|---|---|---|---|---|---|
| 0003 | M | 6450 | 236.52 | 64.11 | 34.47 | 18.24 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 6450.0 | 236.524 | 64.105 | 34.469 | 18.235 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | THYMUS | ADRENAL GLANDS | TESTES |
|---|---|---|---|---|
| 0003 | M | 5.71 | 1.11 | 9.66 |
| NO.EXAM. | | 1 | 1 | 1 |
| MEAN | | 5.714 | 1.109 | 9.657 |
| STD.DEV. | | 0 | 0 | 0 |

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BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ABSOLUTE WEIGHTS IN GRAMS

DOSE GROUP : 03, mid dose (20 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | FINAL BODY WEIGHT | LIVER | HEART | KIDNEYS | SPLEEN |
|---|---|---|---|---|---|---|
| 0007 | F | 6250 | 266.62 | 59.24 | 27.16 | 17.70 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 6250.0 | 266.618 | 59.243 | 27.158 | 17.698 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | THYMUS | ADRENAL GLANDS |
|---|---|---|---|
| 0007 | F | 3.71 | 1.34 |
| NO.EXAM. | | 1 | 1 |
| MEAN | | 3.707 | 1.338 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 32/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ABSOLUTE WEIGHTS IN GRAMS

DOSE GROUP : 04, high dose (80 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | FINAL BODY WEIGHT | LIVER | HEART | KIDNEYS | SPLEEN |
|---|---|---|---|---|---|---|
| 0004 | M | 7600 | 265.86 | 65.75 | 43.61 | 50.95 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 7600.0 | 265.860 | 65.754 | 43.609 | 50.945 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | THYMUS | ADRENAL GLANDS | TESTES |
|---|---|---|---|---|
| 0004 | M | 4.22 | 1.42 | 10.38 |
| NO.EXAM. | | 1 | 1 | 1 |
| MEAN | | 4.217 | 1.421 | 10.381 |
| STD.DEV. | | 0 | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 33/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ABSOLUTE WEIGHTS IN GRAMS

DOSE GROUP : 04, high dose (80 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | FINAL BODY WEIGHT | LIVER | HEART | KIDNEYS | SPLEEN |
|---|---|---|---|---|---|---|
| 0008 | F | 6950 | 280.77 | 68.36 | 32.32 | 38.91 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 6950.0 | 280.772 | 68.358 | 32.320 | 38.914 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | THYMUS | ADRENAL GLANDS |
|---|---|---|---|
| 0008 | F | 2.72 | 1.44 |
| NO.EXAM. | | 1 | 1 |
| MEAN | | 2.719 | 1.435 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 34/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BRAIN WEIGHT RATIOS IN %

DOSE GROUP : 01, vehicle
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0001 | M | 0 | 0 | 0 | 0 | 0 |
| NO.EXAM. | | 0 | 0 | 0 | 0 | 0 |
| MEAN | | 0 | 0 | 0 | 0 | 0 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS | TESTES |
|---|---|---|---|
| 0001 | M | 0 | 0 |
| NO.EXAM. | | 0 | 0 |
| MEAN | | 0 | 0 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 35/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BRAIN WEIGHT RATIOS IN %

DOSE GROUP : 01, vehicle
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0005 | F | 0 | 0 | 0 | 0 | 0 |
| NO.EXAM. | | 0 | 0 | 0 | 0 | 0 |
| MEAN | | 0 | 0 | 0 | 0 | 0 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS |
|---|---|---|
| 0005 | F | 0 |
| NO.EXAM. | | 0 |
| MEAN | | 0 |
| STD.DEV. | | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 36/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BRAIN WEIGHT RATIOS IN %

DOSE GROUP : 02, low dose (5 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0002 | M | 0 | 0 | 0 | 0 | 0 |
| NO.EXAM. | | 0 | 0 | 0 | 0 | 0 |
| MEAN | | 0 | 0 | 0 | 0 | 0 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS | TESTES |
|---|---|---|---|
| 0002 | M | 0 | 0 |
| NO.EXAM. | | 0 | 0 |
| MEAN | | 0 | 0 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 37/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BRAIN WEIGHT RATIOS IN %

DOSE GROUP : 02, low dose (5 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0006 | F | 0 | 0 | 0 | 0 | 0 |
| NO.EXAM. | | 0 | 0 | 0 | 0 | 0 |
| MEAN | | 0 | 0 | 0 | 0 | 0 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS |
|---|---|---|
| 0006 | F | 0 |
| NO.EXAM. | | 0 |
| MEAN | | 0 |
| STD.DEV. | | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 38/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BRAIN WEIGHT RATIOS IN %

DOSE GROUP : 03, mid dose (20 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0003 | M | 0 | 0 | 0 | 0 | 0 |
| NO.EXAM. | | 0 | 0 | 0 | 0 | 0 |
| MEAN | | 0 | 0 | 0 | 0 | 0 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS | TESTES |
|---|---|---|---|
| 0003 | M | 0 | 0 |
| NO.EXAM. | | 0 | 0 |
| MEAN | | 0 | 0 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 39/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BRAIN WEIGHT RATIOS IN %

DOSE GROUP : 03, mid dose (20 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0007 | F | 0 | 0 | 0 | 0 | 0 |
| NO.EXAM. | | 0 | 0 | 0 | 0 | 0 |
| MEAN | | 0 | 0 | 0 | 0 | 0 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS |
|---|---|---|
| 0007 | F | 0 |
| NO.EXAM. | | 0 |
| MEAN | | 0 |
| STD.DEV. | | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 40/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BRAIN WEIGHT RATIOS IN %

DOSE GROUP : 04, high dose (80 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0004 | M | 0 | 0 | 0 | 0 | 0 |
| NO.EXAM. | | 0 | 0 | 0 | 0 | 0 |
| MEAN | | 0 | 0 | 0 | 0 | 0 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS | TESTES |
|---|---|---|---|
| 0004 | M | 0 | 0 |
| NO.EXAM. | | 0 | 0 |
| MEAN | | 0 | 0 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 41/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BRAIN WEIGHT RATIOS IN %

DOSE GROUP : 04, high dose (80 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0008 | F | 0 | 0 | 0 | 0 | 0 |
| NO.EXAM. | | 0 | 0 | 0 | 0 | 0 |
| MEAN | | 0 | 0 | 0 | 0 | 0 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS |
|---|---|---|
| 0008 | F | 0 |
| NO.EXAM. | | 0 |
| MEAN | | 0 |
| STD.DEV. | | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 42/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BODY WEIGHT RATIOS IN %

DOSE GROUP : 01, vehicle
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0001 | M | 3.9041 | 0.90766 | 0.48515 | 0.35841 | 0.02966 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 3.90405 | 0.90766 | 0.48515 | 0.35841 | 0.02966 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS | TESTES |
|---|---|---|---|
| 0001 | M | 0.02496 | 0.18074 |
| NO.EXAM. | | 1 | 1 |
| MEAN | | 0.02496 | 0.18074 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 43/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BODY WEIGHT RATIOS IN %

DOSE GROUP : 01, vehicle
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0005 | F | 3.9065 | 0.93381 | 0.40608 | 0.27508 | 0.03248 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 3.90652 | 0.93381 | 0.40608 | 0.27508 | 0.03248 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS |
|---|---|---|
| 0005 | F | 0.05190 |
| NO.EXAM. | | 1 |
| MEAN | | 0.05190 |
| STD.DEV. | | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 44/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BODY WEIGHT RATIOS IN %

DOSE GROUP : 02, low dose (5 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0002 | M | 3.8372 | 0.79420 | 0.45368 | 1.4806 | 0.05423 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 3.83721 | 0.79420 | 0.45368 | 1.48056 | 0.05423 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS | TESTES |
|---|---|---|---|
| 0002 | M | 0.01808 | 0.15461 |
| NO.EXAM. | | 1 | 1 |
| MEAN | | 0.01808 | 0.15461 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 45/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BODY WEIGHT RATIOS IN %

DOSE GROUP : 02, low dose (5 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0006 | F | 4.4704 | 0.99887 | 0.44715 | 0.30513 | 0.07617 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 4.47039 | 0.99887 | 0.44715 | 0.30513 | 0.07617 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS |
|---|---|---|
| 0006 | F | 0.01731 |
| NO.EXAM. | | 1 |
| MEAN | | 0.01731 |
| STD.DEV. | | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 46/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BODY WEIGHT RATIOS IN %

DOSE GROUP : 03, mid dose (20 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0003 | M | 3.6670 | 0.99388 | 0.53440 | 0.28271 | 0.08859 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 3.66704 | 0.99388 | 0.53440 | 0.28271 | 0.08859 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS | TESTES |
|---|---|---|---|
| 0003 | M | 0.01719 | 0.14972 |
| NO.EXAM. | | 1 | 1 |
| MEAN | | 0.01719 | 0.14972 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 47/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BODY WEIGHT RATIOS IN %

DOSE GROUP : 03, mid dose (20 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0007 | F | 4.2659 | 0.94789 | 0.43453 | 0.28317 | 0.05931 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 4.26589 | 0.94789 | 0.43453 | 0.28317 | 0.05931 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS |
|---|---|---|
| 0007 | F | 0.02141 |
| NO.EXAM. | | 1 |
| MEAN | | 0.02141 |
| STD.DEV. | | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 48/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BODY WEIGHT RATIOS IN %

DOSE GROUP : 04, high dose (80 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0004 | M | 3.4982 | 0.86518 | 0.57380 | 0.67033 | 0.05549 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 3.49816 | 0.86518 | 0.57380 | 0.67033 | 0.05549 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS | TESTES |
|---|---|---|---|
| 0004 | M | 0.01870 | 0.13659 |
| NO.EXAM. | | 1 | 1 |
| MEAN | | 0.01870 | 0.13659 |
| STD.DEV. | | 0 | 0 |

PATHOLOGY REPORT (FINAL DRAFT) PAGE : 49/ 49
BODY/ORGAN WEIGHTS PROJECT :T 103508-7

TEST ITEM : BAY 2469430 PATHOL. NO.: 13508 GUT
TEST SYSTEM : DOG, 2 weeks, p.o. DATE : 08-NOV-17
SPONSOR : Bayer AG PathData®System V6.2e2

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS: ORGAN/BODY WEIGHT RATIOS IN %

DOSE GROUP : 04, high dose (80 mg/kg)
DEFINED NECROPSY STATUS : K0

| ANIMAL NUMBER | SEX | LIVER | HEART | KIDNEYS | SPLEEN | THYMUS |
|---|---|---|---|---|---|---|
| 0008 | F | 4.0399 | 0.98357 | 0.46504 | 0.55991 | 0.03912 |
| NO.EXAM. | | 1 | 1 | 1 | 1 | 1 |
| MEAN | | 4.03988 | 0.98357 | 0.46504 | 0.55991 | 0.03912 |
| STD.DEV. | | 0 | 0 | 0 | 0 | 0 |

| ANIMAL NUMBER | SEX | ADRENAL GLANDS |
|---|---|---|
| 0008 | F | 0.02065 |
| NO.EXAM. | | 1 |
| MEAN | | 0.02065 |
| STD.DEV. | | 0 |

# Appendix

# Individual Data

# Animal status

BAY 2469430 T103508-7
Bayer AG **Animal Death Status Report** Page 1 of 2
July 9, 2018 09:06

**Males**

| Animal # | Group Name | Death Status: | Death Type | Phase and Day of Phase | Date of Death |
|---|---|---|---|---|---|
| 0001 | 0mg/kg | Final Sacrifice | Scheduled | Dosing,Day 15 | September 19, 2017 |
| 0002 | 5mg/kg BAY 2469430 | Final Sacrifice | Scheduled | Dosing,Day 15 | September 19, 2017 |
| 0003 | 20mg/kg BAY 2469430 | Final Sacrifice | Scheduled | Dosing,Day 15 | September 19, 2017 |
| 0004 | 80mg/kg BAY 2469430 | Final Sacrifice | Scheduled | Dosing,Day 15 | September 19, 2017 |

**Females**

| Animal # | Group Name | Death Status: | Death Type | Phase and Day of Phase | Date of Death |
|---|---|---|---|---|---|
| 0005 | 0mg/kg | Final Sacrifice | Scheduled | Dosing,Day 15 | September 19, 2017 |
| 0006 | 5mg/kg BAY 2469430 | Final Sacrifice | Scheduled | Dosing,Day 15 | September 19, 2017 |
| 0007 | 20mg/kg BAY 2469430 | Final Sacrifice | Scheduled | Dosing,Day 15 | September 19, 2017 |
| 0008 | 80mg/kg BAY 2469430 | Final Sacrifice | Scheduled | Dosing,Day 15 | September 19, 2017 |

Please Note:
Displayed date in the header is the creation date of the report

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System Version 6.4.0 Build 87.B05

Report Code and Name: DEATH Animal Death Status Report
Report Version: 5.2
Job:341832, ID:343367

**Report Selections**

| | |
|---|---|
| All records | True |

# Clinical observations

**Clinical Observations**
**Cumulative Incidences**
**DETAILED CLINICAL OBSERVATION**

**Males | Phase: Dosing | Session 2: am after admin | Scheduled**
**Day 1 until Day 15**

| | | 0mg/kg | 5mg/kg BAY 2469430 | 20mg/kg BAY 2469430 | 80mg/kg BAY 2469430 |
|---|---|---|---|---|---|
| **No. Animals Examined** | | 1 | 1 | 1 | 1 |
| **No. Animals with Observation** | | 1 | 1 | 1 | 1 |
| **Category, Observation, Modifier(s)** | | | | | |
| Excretion, Changed feces consistency | #A | 1 | 1 | 1 | 1 |
| | #D | 1 | 1 | 1 | 3 |
| Excretion, Increased salivation | #A | 0 | 0 | 0 | 1 |
| | #D | 0 | 0 | 0 | 1 |
| Excretion, Increased salivation after administration | #A | 0 | 0 | 0 | 1 |
| | #D | 0 | 0 | 0 | 1 |
| Excretion, Vomited immediately after administration | #A | 0 | 0 | 1 | 0 |
| | #D | 0 | 0 | 1 | 0 |

Note: #A = Number of animals with Observation
#D = Number of sessions Observation seen
in case of comments see individual values

**Clinical Observations**
**Cumulative Incidences**
**DETAILED CLINICAL OBSERVATION**

**Females | Phase: Dosing | Session 2: am after admin | Scheduled**
**Day 1 until Day 15**

| | | 5mg/kg BAY 2469430 | 80mg/kg BAY 2469430 |
|---|---|---|---|
| **No. Animals Examined** | | 1 | 1 |
| **No. Animals with Observation** | | 1 | 1 |
| **Category, Observation, Modifier(s)** | | | |
| Excretion, Changed feces consistency | #A | 0 | 1 |
| | #D | 0 | 2 |
| Excretion, Vomited | #A | 0 | 1 |
| | #D | 0 | 1 |
| Excretion, Vomited immediately after administration | #A | 1 | 1 |
| | #D | 1 | 1 |

Note: #A = Number of animals with Observation
#D = Number of sessions Observation seen
in case of comments see individual values

Please Note:
Displayed date in the header is the creation date of the report

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System Version 6.4.0 Build 87.B05

Report Code and Name: COCI Clinical Observations Cumulative Incidences
Report Version: 5.2
Job:325998, ID:327113

**Report Selections**

| | |
|---|---|
| Comparison group(s) | 2,3,4 |
| Control group(s) | 1 |

**Group 1** 0mg/kg
**Group 2** 5mg/kg BAY 2469430
**Group 3** 20mg/kg BAY 2469430
**Group 4** 80mg/kg BAY 2469430

BAY 2469430
Bayer AG

T103508-7
Page 1 of 3
September 25, 2017 10:53

**Clinical Observations**
**Individual Values**
**DETAILED CLINICAL OBSERVATION**

**Males | Phase: Dosing | Scheduled**
**Day 1 until Day 15**
**Group: 0mg/kg**

| Animal# | Category, Observation, Modifier(s) | Session | Period of Appearance |
|---|---|---|---|
| 0001 | Excretion, Changed feces consistency, thin | 2 | day 11 |

**Males | Phase: Dosing | Scheduled**
**Day 1 until Day 15**
**Group: 5mg/kg BAY 2469430**

| Animal# | Category, Observation, Modifier(s) | Session | Period of Appearance |
|---|---|---|---|
| 0002 | Excretion, Changed feces consistency, thin | 2 | day 11 |

**Males | Phase: Dosing | Scheduled**
**Day 1 until Day 15**
**Group: 20mg/kg BAY 2469430**

| Animal# | Category, Observation, Modifier(s) | Session | Period of Appearance |
|---|---|---|---|
| 0003 | Excretion, Changed feces consistency, thin | 2 | day 11 |
| | Excretion, Vomited immediately after administration | 2 | day 13 |

**Males | Phase: Dosing | Scheduled**
**Day 1 until Day 15**
**Group: 80mg/kg BAY 2469430**

| Animal# | Category, Observation, Modifier(s) | Session | Period of Appearance |
|---|---|---|---|
| 0004 | Excretion, Changed feces consistency, thin | 2 | day 11,13 |
| | Excretion, Changed feces consistency, watery | 2 | day 10 |
| | Excretion, Increased salivation | 2 | day 7 |
| | Excretion, Increased salivation after administration | 2 | day 8 |

**Clinical Observations**
**Individual Values**
**DETAILED CLINICAL OBSERVATION**

**Females | Phase: Dosing | Scheduled**
**Day 1 until Day 15**
**Group: 5mg/kg BAY 2469430**

| Animal# | Category, Observation, Modifier(s) | Session | Period of Appearance |
|---|---|---|---|
| 0006 | Excretion, Vomited immediately after administration | 2 | day 3 |

**Females | Phase: Dosing | Scheduled**
**Day 1 until Day 15**
**Group: 80mg/kg BAY 2469430**

| Animal# | Category, Observation, Modifier(s) | Session | Period of Appearance |
|---|---|---|---|
| 0008 | Excretion, Changed feces consistency, thin | 2 | day 8,11 |
| | Excretion, Vomited immediately after administration | 2 | day 11 |
| | Excretion, Vomited, whitish, foamy | 2 | day 1 |

Please Note:
Displayed date in the header is the creation date of the report

System Version 6.4.0 Build 87.B05

Report Code and Name: COIV Clinical Observations Individual Values
Report Version: 5.1
Job:326003, ID:327118

**Report Selections**

**Group 1** 0mg/kg
**Group 2** 5mg/kg BAY 2469430
**Group 3** 20mg/kg BAY 2469430
**Group 4** 80mg/kg BAY 2469430

**Scheduled session 1:** am
**Scheduled session 2:** am after admin
**Scheduled session 3:** pm after admin

# Food consumption

BAY 2469430 T103508-7
Bayer AG Page 1 of 7

**Food Intake Individual Values**
**(g/Animal/Day)**

September 25, 2017 10:46

**Males**

| **Session** 1 | | **Pre Dosing Day of Phase** | | | | | | | **Dosing Day of Phase** |
|---|---|---|---|---|---|---|---|---|---|
| | **Animal#** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **1** |
| **0mg/kg** | 0001 | 191.3 | 181.6 | 246.1 | 214.9 | 364.7 | 231.6 | 229.1 | 157.0 |
| **5mg/kg BAY** | 0002 | 151.5 | 201.5 | 215.2 | 256.4 | 102.4 | 181.3 | 201.9 | 169.2 |
| **20mg/kg BA** | 0003 | 136.2 | 212.6 | 157.3 | 193.3 | 126.5 | 203.3 | 200.6 | 211.7 |
| **80mg/kg BA** | 0004 | 168.6 | 202.7 | 242.2 | 227.2 | 158.2 | 148.3 | 239.0 | 157.8 |

BAY 2469430 T103508-7
Bayer AG Page 2 of 7

**Food Intake Individual Values**
**(g/Animal/Day)**

September 25, 2017 10:46

**Males**

**Session** 1 **Dosing**

**Day of Phase**

| | Animal# | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 180.0 | 244.6 | 189.6 | 213.8 | 203.3 | 251.4 | 239.6 | 226.4 |
| **5mg/kg BAY** | 0002 | 219.3 | 243.1 | 269.2 | 209.2 | 210.6 | 322.2 | 234.3 | 259.4 |
| **20mg/kg BA** | 0003 | 161.1 | 203.3 | 395.6 | 80.7 | 245.8 | 394.6 | 205.5 | 353.8 |
| **80mg/kg BA** | 0004 | 190.7 | 305.6 | 236.7 | 183.1 | 207.9 | 257.6 | 297.3 | 202.0 |

**Food Intake Individual Values**
**(g/Animal/Day)**



**Males**

**Session** 1 **Dosing**

**Day of Phase**

| | Animal# | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 261.4 | 240.0 | 231.8 | 227.2 | 241.2 |
| **5mg/kg BAY** | 0002 | 341.0 | 273.0 | 338.9 | 239.8 | 330.6 |
| **20mg/kg BA** | 0003 | 260.9 | 310.1 | 338.8 | 326.1 | 226.5 |
| **80mg/kg BA** | 0004 | 374.5 | 313.4 | 289.5 | 289.3 | 339.4 |

BAY 2469430 T103508-7
Bayer AG Page 4 of 7

**Food Intake Individual Values**
**(g/Animal/Day)**

September 25, 2017 10:46

**Females**

| **Session** 1 | | **Pre Dosing Day of Phase** | | | | | | | **Dosing Day of Phase** |
|---|---|---|---|---|---|---|---|---|---|
| | **Animal#** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **1** |
| **0mg/kg** | 0005 | 0.0 | 233.1 | 225.1 | 120.1 | 176.7 | 90.1 | 161.7 | 151.9 |
| **5mg/kg BAY** | 0006 | 74.0 | 112.0 | 160.9 | 104.8 | 224.1 | 219.6 | 183.4 | 124.5 |
| **20mg/kg BA** | 0007 | 134.5 | 49.2 | 146.0 | 144.8 | 155.2 | 304.0 | 163.4 | 99.9 |
| **80mg/kg BA** | 0008 | 336.0 | 238.1 | 277.6 | 389.6 | 106.9 | 115.0 | 409.5 | 209.5 |

BAY 2469430 T103508-7
Bayer AG **Food Intake Individual Values** Page 5 of 7
**(g/Animal/Day)** September 25, 2017 10:46

**Females**

**Session** 1 **Dosing**

**Day of Phase**

| | Animal# | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 165.0 | 204.9 | 183.3 | 190.9 | 182.4 | 225.1 | 149.0 | 212.3 |
| **5mg/kg BAY** | 0006 | 170.9 | 212.8 | 210.0 | 200.2 | 194.0 | 262.8 | 189.1 | 223.7 |
| **20mg/kg BA** | 0007 | 114.6 | 209.9 | 179.4 | 185.2 | 172.7 | 210.0 | 221.8 | 125.6 |
| **80mg/kg BA** | 0008 | 264.3 | 300.4 | 377.5 | 258.3 | 249.5 | 409.9 | 152.3 | 329.8 |

BAY 2469430 T103508-7
Bayer AG Page 6 of 7

**Food Intake Individual Values**
**(g/Animal/Day)**

September 25, 2017 10:46

**Females**

**Session** 1 **Dosing**

**Day of Phase**

| | Animal# | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 174.8 | 191.7 | 137.3 | 201.5 | 209.4 |
| **5mg/kg BAY** | 0006 | 245.3 | 192.2 | 246.5 | 233.3 | 240.4 |
| **20mg/kg BA** | 0007 | 190.2 | 159.5 | 154.0 | 195.7 | 195.4 |
| **80mg/kg BA** | 0008 | 336.6 | 223.0 | 245.7 | 288.9 | 243.6 |

Please Note:
Displayed date in the header is the creation date of the report

System Version 6.4.0 Build 87.B05

Report Code and Name: FIIV Food Intake Individual Values
Report Version: 5.1
Job:325997, ID:327112

**Report Selections**

| | |
|---|---|
| By_Animal | True |
| Comparison group(s) | 2,3,4 |
| Control group(s) | 1 |

**Group 1** 0mg/kg
**Group 2** 5mg/kg BAY 2469430
**Group 3** 20mg/kg BAY 2469430
**Group 4** 80mg/kg BAY 2469430

Abbreviation(s):

# Body weight

BAY 2469430 T103508-7
Bayer AG Page 1 of 3

**Body Weights Individual Values**
**(kg)**

September 25, 2017 10:45

**Males**

| Session | 1 | Pre Random Day of Phase | Pre Dosing Day of Phase | Dosing Day of Phase | | | | |
|---|---|---|---|---|---|---|---|---|
| | Animal# | 1 | 1 | 1 | 4 | 8 | 11 | 15 |
| 0mg/kg | 0001 | 6.4 | 6.4 | 6.6 | 6.5 | 6.8 | 6.8 | 7.0 |
| 5mg/kg BAY | 0002 | 7.6 | 7.7 | 7.8 | 7.8 | 8.2 | 8.1 | 8.3 |
| 20mg/kg BA | 0003 | 5.9 | 5.9 | 5.9 | 5.9 | 6.4 | 6.0 | 6.3 |
| 80mg/kg BA | 0004 | 7.8 | 8.1 | 8.2 | 8.2 | 8.3 | 8.2 | 8.5 |

**Body Weights Individual Values**
**(kg)**



**Females**

| Session | 1 | Pre Random Day of Phase | Pre Dosing Day of Phase | Dosing Day of Phase | | | | |
|---|---|---|---|---|---|---|---|---|
| | Animal# | 1 | 1 | 1 | 4 | 8 | 11 | 15 |
| 0mg/kg | 0005 | 6.4 | 6.4 | 6.5 | 6.4 | 6.7 | 6.5 | 6.6 |
| 5mg/kg BAY | 0006 | 6.5 | 6.5 | 6.4 | 6.6 | 6.8 | 6.6 | 6.8 |
| 20mg/kg BA | 0007 | 6.8 | 6.9 | 6.7 | 6.7 | 6.9 | 6.8 | 6.8 |
| 80mg/kg BA | 0008 | 7.2 | 7.1 | 7.6 | 7.5 | 7.9 | 7.5 | 7.7 |

Please Note:
Displayed date in the header is the creation date of the report

System Version 6.4.0 Build 87.B05

Report Code and Name: BWIV Body Weights Individual Values
Report Version: 5.1
Job:325996, ID:327111

**Report Selections**

| | |
|---|---|
| Comparison group(s) | 2,3,4 |
| Control group(s) | 1 |

**Group 1** 0mg/kg
**Group 2** 5mg/kg BAY 2469430
**Group 3** 20mg/kg BAY 2469430
**Group 4** 80mg/kg BAY 2469430

Abbreviation(s):

## Body weight gain

BAY 2469430 T103508-7
Bayer AG Page 1 of 3
July 9, 2018 09:45

**Cumulative Body Weight Gain**
**Individual Values(kg)**

**Males**

**Session 1** **Dosing**

**Day of Phase**

| | Animal# | 1 | 4 | 8 | 11 | 15 |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 0.0 | -0.1 | 0.2 | 0.2 | 0.4 |
| **5mg/kg BAY** | 0002 | 0.0 | 0.0 | 0.4 | 0.3 | 0.5 |
| **20mg/kg BA** | 0003 | 0.0 | 0.0 | 0.5 | 0.1 | 0.4 |
| **80mg/kg BA** | 0004 | 0.0 | 0.0 | 0.1 | 0.0 | 0.3 |

**Cumulative Body Weight Gain**
**Individual Values(kg)**

**Females**

**Session 1** **Dosing**

**Day of Phase**

| | Animal# | 4 | 8 | 11 | 15 |
|---|---|---|---|---|---|
| **0mg/kg** | 0005 | -0.1 | 0.2 | 0.0 | 0.1 |
| **5mg/kg BAY** | 0006 | 0.2 | 0.4 | 0.2 | 0.4 |
| **20mg/kg BA** | 0007 | 0.0 | 0.2 | 0.1 | 0.1 |
| **80mg/kg BA** | 0008 | -0.1 | 0.3 | -0.1 | 0.1 |

Please Note:
Displayed date in the header is the creation date of the report

System Version 6.4.0 Build 87.B05

Report Code and Name: BGIVC Cumulative Body Weight Gain Individual Values
Report Version: 5.1
Job:341840, ID:343375

**Report Selections**

| | |
|---|---|
| Phase : Day of Phase : Session : Sch | Dosing : Day 1 : S1 : S |
| Phase : Day of Phase : Session : Sch | Dosing : Day 4 : S1 : S |
| Phase : Day of Phase : Session : Sch | Dosing : Day 8 : S1 : S |
| Phase : Day of Phase : Session : Sch | Dosing : Day 11 : S1 : S |
| Phase : Day of Phase : Session : Sch | Dosing : Day 15 : S1 : S |
| Comparison group(s) | 2,3,4 |
| Control group(s) | 1 |

**Group 1** 0mg/kg
**Group 2** 5mg/kg BAY 2469430
**Group 3** 20mg/kg BAY 2469430
**Group 4** 80mg/kg BAY 2469430

Abbreviation(s):

## Blood pressure

Note:
Session 1: am
Session 2: before administration
Session 3: 1-2h after administration

**Generalized Measurements**
**Individual Values**

**Males, PreDosing, Scheduled**

**BLOOD PRESSURE NONRODENT**

**0mg/kg**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0001 | 2 | 1 | 86 | 142 |

**5mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0002 | 2 | 1 | 98 | 164 |

**20mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0003 | 2 | 1 | 76 | 118 |

**80mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0004 | 2 | 1 | 70 | 130 |

**Males, Dosing, Scheduled**

**BLOOD PRESSURE NONRODENT**

**0mg/kg**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0001 | 11 | 2 | 98 | 155 |
| | | 3 | 94 | 143 |

**5mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0002 | 11 | 2 | 51 | 145 |
| | | 3 | 86 | 132 |

**20mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0003 | 11 | 2 | 86 | 139 |
| | | 3 | 81 | 124 |

**80mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0004 | 11 | 2 | 65 | 124 |
| | | 3 | 71 | 112 |

**Females, PreDosing, Scheduled**

**BLOOD PRESSURE NONRODENT**

**0mg/kg**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0005 | 2 | 1 | 88 | 146 |

**5mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0006 | 2 | 1 | 74 | 121 |

**20mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0007 | 2 | 1 | 84 | 146 |

**80mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0008 | 2 | 1 | 95 | 153 |

**Females, Dosing, Scheduled**

**BLOOD PRESSURE NONRODENT**

**0mg/kg**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0005 | 11 | 2 | 97 | 143 |
| | | 3 | 123 | 156 |

**5mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0006 | 11 | 2 | 65 | 147 |
| | | 3 | 54 | 124 |

**20mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0007 | 11 | 2 | 66 | 133 |
| | | 3 | 69 | 136 |

**80mg/kg BAY 2469430**

| Animal No. | Day | Session | DIA mmHg | SYS mmHg |
|---|---|---|---|---|
| 0008 | 11 | 2 | 75 | 147 |
| | | 3 | 84 | 137 |

Please Note:
Displayed date in the header is the creation date of the report

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System Version 6.4.0 Build 87.B05

Report Code and Name: GMIV Generalized Measurements Individual Values
Report Version: 5.0
Job:326412, ID:327527

**Report Selections**

| | |
|---|---|
| Comparison group(s) | 2,3,4 |
| Control group(s) | 1 |

**Group 1** 0mg/kg
**Group 2** 5mg/kg BAY 2469430
**Group 3** 20mg/kg BAY 2469430
**Group 4** 80mg/kg BAY 2469430

## Heart rate and Electrocardiogram

Note:
Session 1: am
Session 2: before administration
Session 3: 1-2h after administration

BAY 2469430 T103508-7
Bayer AG Page 1 of 5
**Generalized Measurements** July 9, 2018 09:11
**Individual Values**

**Males, PreDosing, Scheduled**

**ECG (Lead2)**

**0mg/kg**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0001 | 2 | 1 | 114.1 | 209.4 | 259.3 | 250.6 | 38.7 | 526.1 | 79.8 |

**5mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0002 | 2 | 1 | 84.1 | 229.7 | 257.1 | 254.7 | 34.9 | 713.2 | 100.2 |

**20mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0003 | 2 | 1 | 71.3 | 229.6 | 243.1 | 243.3 | 38.6 | 841.6 | 110.2 |

**80mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0004 | 2 | 1 | 80.7 | 207.3 | 228.8 | 229.6 | 44.1 | 743.7 | 96.1 |

**Generalized Measurements**
**Individual Values**

**Males, Dosing, Scheduled**

**ECG (Lead2)**

**0mg/kg**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0001 | 11 | 2 | 136.0 | 199.0 | 261.4 | 247.6 | 39.0 | 441.3 | 80.3 |
| | | 3 | 126.0 | 204.8 | 262.3 | 250.4 | 39.0 | 476.1 | 85.2 |

**5mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0002 | 11 | 2 | 80.3 | 208.9 | 230.2 | 230.9 | 37.0 | 747.5 | 103.0 |
| | | 3 | 101.2 | 207.6 | 247.1 | 243.0 | 37.2 | 593.1 | 110.7 |

**20mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0003 | 11 | 2 | 70.8 | 218.7 | 231.1 | 232.0 | 36.8 | 847.3 | 102.3 |
| | | 3 | 78.1 | 207.1 | 226.2 | 227.4 | 40.0 | 767.8 | 109.0 |

**80mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0004 | 11 | 2 | 88.9 | 210.9 | 240.4 | 239.2 | 43.6 | 674.8 | 96.1 |
| | | 3 | 131.6 | 198.4 | 257.8 | 245.8 | 45.6 | 455.8 | 96.0 |

**Generalized Measurements**
**Individual Values**

**Females, PreDosing, Scheduled**

**ECG (Lead2)**

**0mg/kg**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0005 | 2 | 1 | 110.5 | 202.4 | 248.1 | 242.2 | 41.5 | 543.0 | 108.4 |

**5mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0006 | 2 | 1 | 69.1 | 212.7 | 222.9 | 224.1 | 40.7 | 868.3 | 94.6 |

**20mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0007 | 2 | 1 | 50.2 | 234.4 | 220.9 | 217.5 | 41.7 | 1195.2 | 99.7 |

**80mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0008 | 2 | 1 | 100.0 | 230.1 | 272.8 | 264.9 | 35.9 | 600.2 | 107.5 |

**Generalized Measurements**
**Individual Values**

**Females, Dosing, Scheduled**

**ECG (Lead2)**

**0mg/kg**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0005 | 11 | 2 | 100.6 | 189.1 | 224.7 | 224.3 | 42.3 | 596.2 | 99.1 |
| | | 3 | 108.7 | 194.4 | 237.0 | 233.4 | 42.2 | 552.2 | 107.1 |

**5mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0006 | 11 | 2 | 82.6 | 219.7 | 244.5 | 243.6 | 41.1 | 726.1 | 85.9 |
| | | 3 | 86.3 | 224.5 | 253.4 | 251.0 | 42.8 | 695.4 | 92.9 |

**20mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0007 | 11 | 2 | 77.3 | 213.6 | 232.4 | 233.1 | 43.2 | 775.8 | 97.3 |
| | | 3 | 97.4 | 226.4 | 266.0 | 259.8 | 44.6 | 616.3 | 97.9 |

**80mg/kg BAY 2469430**

| Animal No. | Day | Session | HR bts/min | QT-I ms | QTcf ms | QTcv ms | QRS ms | RR-I ms | PR-I ms |
|---|---|---|---|---|---|---|---|---|---|
| 0008 | 11 | 2 | 110.3 | 214.8 | 263.2 | 254.5 | 38.7 | 543.8 | 101.8 |
| | | 3 | 122.5 | 232.8 | 295.3 | 277.2 | 38.9 | 489.6 | 104.6 |

Please Note:
Displayed date in the header is the creation date of the report

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System Version 6.4.0 Build 87.B05

Report Code and Name: GMIV Generalized Measurements Individual Values
Report Version: 5.0
Job:341834, ID:343369

**Report Selections**

| | |
|---|---|
| Parameter(s) | ECG (Lead2) Dog:HR#26 |
| Parameter(s) | ECG (Lead2) Dog:PR-I#26 |
| Parameter(s) | ECG (Lead2) Dog:QRS#26 |
| Parameter(s) | ECG (Lead2) Dog:QT-I#26 |
| Parameter(s) | ECG (Lead2) Dog:QTcf#26 |
| Parameter(s) | ECG (Lead2) Dog:QTcv#26 |
| Parameter(s) | ECG (Lead2) Dog:RR-I#26 |
| Comparison group(s) | 2,3,4 |
| Control group(s) | 1 |

**Group 1** 0mg/kg
**Group 2** 5mg/kg BAY 2469430
**Group 3** 20mg/kg BAY 2469430
**Group 4** 80mg/kg BAY 2469430

## Clinical Pathology

Hematology

Hemostasis

Blood Enzyme Activities

Blood Substrate Concentrations

Blood Electrolytes

Electrophoresis of Proteins

BAY 2469430 T103508-7

Bayer AG **Clinical Pathology Individual Values** Page 1 of 39

**Hematology** September 14, 2017 11:21

**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | ERY T/L | HB g/L | HCT L/L | MCH pg | MCHC g/L | MCV fL | RETIC T/L | RETI % |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 5.63 | 125. | 0.388 | 22.3 | 323. | 68.9 | 0.025 | 0. |
| **5mg/kg BAY** | 0002 | 6.45 | 155. | 0.459 | 24.0 | 337. | 71.1 | 0.036 | 1. |
| **20mg/kg BAY** | 0003 | 7.62 | 168. | 0.512 | 22.1 | 329. | 67.2 | 0.023 | 0. |
| **80mg/kg BAY** | 0004 | 6.88 | 164. | 0.480 | 23.8 | 341. | 69.8 | 0.036 | 1. |

**Clinical Pathology Individual Values**

**Hematology**

**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | ERY T/L | HB g/L | HCT L/L | MCH pg | MCHC g/L | MCV fL | RETIC T/L | RETI % |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 5.63 | 127. | 0.386 | 22.6 | 330. | 68.6 | 0.051 | 1. |
| **5mg/kg BAY** | 0002 | 6.15 | 146. | 0.430 | 23.6 | 338. | 69.9 | 0.025 | 0. |
| **20mg/kg BAY** | 0003 | 6.48 | 148. | 0.437 | 22.8 | 338. | 67.4 | 0.027 | 0. |
| **80mg/kg BAY** | 0004 | 6.00 | 140. | 0.414 | 23.2 | 337. | 68.9 | 0.022 | 0. |

**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | THRO G/L |
|---|---|---|
| **0mg/kg** | 0001 | 275. |
| **5mg/kg BAY** | 0002 | 245. |
| **20mg/kg BAY** | 0003 | 265. |
| **80mg/kg BAY** | 0004 | 239. |

**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | THRO G/L |
|---|---|---|
| **0mg/kg** | 0001 | 248. |
| **5mg/kg BAY** | 0002 | 228. |
| **20mg/kg BAY** | 0003 | 284. |
| **80mg/kg BAY** | 0004 | 164. |

**Clinical Pathology Individual Values**

**Hemostasis**

**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | PT s | PTT s | FIBR g/L | TT s |
|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 6.9 | 10.4 | 2.70 | 14.3 |
| **5mg/kg BAY** | 0002 | 7.2 | 11.4 | 1.62 | 15.5 |
| **20mg/kg BAY** | 0003 | 6.5 | 11.0 | 2.02 | 13.6 |
| **80mg/kg BAY** | 0004 | 6.5 | 11.2 | 2.17 | 15.1 |

**Clinical Pathology Individual Values**

**Hemostasis**

**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | PT s | PTT s | FIBR g/L | TT s |
|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 7.3 | 11.8 | 2.85 | 14.8 |
| **5mg/kg BAY** | 0002 | 7.0 | 11.7 | 1.83 | 15.0 |
| **20mg/kg BAY** | 0003 | 6.3 | 11.8 | 2.08 | 13.7 |
| **80mg/kg BAY** | 0004 | 6.4 | 11.3 | 2.60 | 14.2 |

**Clinical Pathology Individual Values**

**Hematology**



**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | LEUCO G/L | LYM G/L | NEUTRO G/L | Baso-phils G/L | EOS G/L | MONO G/L | LUC G/L |
|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 12.77 | 3.44 | 7.34 | 0.06 | 1.11 | 0.78 | 0.04 |
| **5mg/kg BAY** | 0002 | 11.69 | 3.16 | 6.76 | 0.07 | 0.90 | 0.76 | 0.05 |
| **20mg/kg BAY** | 0003 | 7.49 | 2.62 | 3.92 | 0.07 | 0.44 | 0.41 | 0.04 |
| **80mg/kg BAY** | 0004 | 12.40 | 2.08 | 8.46 | 0.04 | 1.17 | 0.63 | 0.03 |

**Clinical Pathology Individual Values**

**Hematology**

**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | LEUCO G/L | LYM G/L | NEUTRO G/L | Baso-phils G/L | EOS G/L | MONO G/L | LUC G/L |
|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 13.02 | 3.33 | 8.33 | 0.06 | 0.62 | 0.65 | 0.04 |
| **5mg/kg BAY** | 0002 | 12.69 | 2.99 | 8.32 | 0.07 | 0.43 | 0.85 | 0.03 |
| **20mg/kg BAY** | 0003 | 7.88 | 2.20 | 4.57 | 0.04 | 0.42 | 0.62 | 0.03 |
| **80mg/kg BAY** | 0004 | 11.70 | 1.83 | 8.63 | 0.04 | 0.45 | 0.72 | 0.03 |

**Clinical Pathology Individual Values**

**Hematology**

**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | LYM rel. % | NEUTRO rel. % | BASO rel. % | EO rel. % | MONO rel. % | LUC rel. % | LI |
|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 26.9 | 57.4 | 0.4 | 8.7 | 6.1 | 0.4 | 3.30 |
| **5mg/kg BAY** | 0002 | 27.0 | 57.8 | 0.6 | 7.7 | 6.5 | 0.4 | 3.09 |
| **20mg/kg BAY** | 0003 | 35.0 | 52.3 | 0.9 | 5.8 | 5.4 | 0.6 | 3.00 |
| **80mg/kg BAY** | 0004 | 16.8 | 68.2 | 0.3 | 9.4 | 5.0 | 0.2 | 3.25 |

**Clinical Pathology Individual Values**

**Hematology**

**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | LYM rel. % | NEUTRO rel. % | BASO rel. % | EO rel. % | MONO rel. % | LUC rel. % | LI |
|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 25.6 | 64.0 | 0.4 | 4.8 | 5.0 | 0.3 | 3.25 |
| **5mg/kg BAY** | 0002 | 23.6 | 65.6 | 0.6 | 3.4 | 6.7 | 0.2 | 3.05 |
| **20mg/kg BAY** | 0003 | 27.9 | 58.0 | 0.5 | 5.3 | 7.9 | 0.3 | 2.80 |
| **80mg/kg BAY** | 0004 | 15.6 | 73.8 | 0.3 | 3.8 | 6.1 | 0.3 | 3.05 |

**Clinical Pathology Individual Values**

**Blood Enzyme Activities**

**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | ALAT U/L | ASAT U/L | APh U/L | GLDH U/L | gamma-GT U/L |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 28. | 25. | 62. | 4.1 | UDL |
| **5mg/kg BAY** | 0002 | 42. | 30. | 60. | 7.5 | UDL |
| **20mg/kg BAY** | 0003 | 40. | 24. | 53. | 6.5 | UDL |
| **80mg/kg BAY** | 0004 | 31. | 28. | 79. | 3.3 | 4. |

**Clinical Pathology Individual Values**

**Blood Enzyme Activities**

**Males | Phase: Dosing | Day: 3 | Session: am | Scheduled |**

| | Animal# | ALAT U/L | ASAT U/L | APh U/L | GLDH U/L | gamma-GT U/L |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 27. | 22. | 68. | 4.6 | UDL |
| **5mg/kg BAY** | 0002 | 34. | 33. | 71. | 3.0 | UDL |
| **20mg/kg BAY** | 0003 | 40. | 28. | 60. | 5.8 | UDL |
| **80mg/kg BAY** | 0004 | 29. | 23. | 75. | 2.8 | 4. |

**Clinical Pathology Individual Values**

**Blood Enzyme Activities**

**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | ALAT U/L | ASAT U/L | APh U/L | GLDH U/L | gamma-GT U/L |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 23. | 26. | 71. | 4.4 | UDL |
| **5mg/kg BAY** | 0002 | 36. | 39. | 75. | 3.1 | UDL |
| **20mg/kg BAY** | 0003 | 52. | 38. | 83. | 8.0 | UDL |
| **80mg/kg BAY** | 0004 | 28. | 29. | 83. | 2.8 | UDL |

**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | GLUCOSE mmoL/L | CHOL mmoL/L | TRIGL mmoL/L | CREA µmoL/L | UREA mmoL/L | Bili-t µmoL/L | Protein g/L | Albumin g/L |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 4.86 | 4.14 | 0.55 | 48. | 3.02 | UDL | 52.7 | 28.7 |
| **5mg/kg BAY** | 0002 | 4.49 | 2.55 | 0.51 | 57. | 4.00 | UDL | 52.3 | 34.5 |
| **20mg/kg BAY** | 0003 | 4.41 | 3.28 | 0.53 | 70. | 5.14 | UDL | 53.8 | 34.2 |
| **80mg/kg BAY** | 0004 | 4.21 | 3.34 | 0.73 | 56. | 2.79 | UDL | 56.0 | 32.8 |

**Clinical Pathology Individual Values**

**Blood Substrate Concentrations**



**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | GLUCOSE mmoL/L | CHOL mmoL/L | TRIGL mmoL/L | CREA µmoL/L | UREA mmoL/L | Bili-t µmoL/L | Protein g/L | Albumin g/L |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 5.03 | 4.03 | 0.52 | 47. | 2.73 | UDL | 53.6 | 28.3 |
| **5mg/kg BAY** | 0002 | 4.96 | 2.57 | 0.43 | 56. | 4.87 | UDL | 52.8 | 34.4 |
| **20mg/kg BAY** | 0003 | 4.01 | 3.70 | 0.91 | 68. | 6.18 | UDL | 52.1 | 32.4 |
| **80mg/kg BAY** | 0004 | 4.44 | 3.34 | 0.39 | 55. | 4.45 | UDL | 53.7 | 31.1 |

**Clinical Pathology Individual Values**

**Blood Electrolytes**

**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | Na-ISE mmoL/L | K-ISE mmoL/L | CL-ISE mmoL/L | Ca mmoL/L | P mmoL/L | Mg mmoL/L |
|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 143. | 4.5 | 109. | 2.48 | 1.51 | 0.73 |
| **5mg/kg BAY** | 0002 | 146. | 4.5 | 113. | 2.50 | 1.77 | 0.71 |
| **20mg/kg BAY** | 0003 | 143. | 4.4 | 110. | 2.44 | 1.50 | 0.78 |
| **80mg/kg BAY** | 0004 | 143. | 4.2 | 109. | 2.46 | 1.37 | 0.78 |

**Clinical Pathology Individual Values**

**Blood Electrolytes**

**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | Na-ISE mmoL/L | K-ISE mmoL/L | CL-ISE mmoL/L | Ca mmoL/L | P mmoL/L | Mg mmoL/L |
|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 142. | 4.5 | 111. | 2.43 | 1.53 | 0.63 |
| **5mg/kg BAY** | 0002 | 145. | 4.5 | 111. | 2.51 | 1.50 | 0.72 |
| **20mg/kg BAY** | 0003 | 148. | 4.5 | 114. | 2.47 | 1.77 | 0.82 |
| **80mg/kg BAY** | 0004 | 146. | 4.0 | 112. | 2.40 | 1.24 | 0.78 |

**Clinical Pathology Individual Values**

**Electrophoresis of Proteins**

**Males | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | ALBUMIN % | TA GLOB % | TB GLOB % | TG GLOB % | A/G |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 46.3 | 22.9 | 18.9 | 11.9 | 0.86 |
| **5mg/kg BAY** | 0002 | 59.3 | 17.9 | 16.1 | 6.7 | 1.46 |
| **20mg/kg BAY** | 0003 | 58.8 | 18.9 | 16.6 | 5.7 | 1.43 |
| **80mg/kg BAY** | 0004 | 53.2 | 19.8 | 19.3 | 7.7 | 1.14 |

**Clinical Pathology Individual Values**

**Electrophoresis of Proteins**

**Males | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | ALBUMIN % | TA GLOB % | TB GLOB % | TG GLOB % | A/G |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0001 | 46.7 | 24.3 | 18.6 | 10.4 | 0.88 |
| **5mg/kg BAY** | 0002 | 57.7 | 18.3 | 16.5 | 7.5 | 1.36 |
| **20mg/kg BAY** | 0003 | 57.6 | 20.5 | 16.4 | 5.5 | 1.36 |
| **80mg/kg BAY** | 0004 | 53.8 | 20.0 | 19.2 | 7.0 | 1.16 |

**Clinical Pathology Individual Values**

**Hematology**

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | ERY T/L | HB g/L | HCT L/L | MCH pg | MCHC g/L | MCV fL | RETIC T/L | RETI % |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 5.75 | 132. | 0.389 | 23.0 | 341. | 67.6 | 0.021 | 0. |
| **5mg/kg BAY** | 0006 | 6.52 | 150. | 0.440 | 23.1 | 341. | 67.6 | 0.028 | 0. |
| **20mg/kg BAY** | 0007 | 6.48 | 149. | 0.442 | 23.0 | 337. | 68.3 | 0.023 | 0. |
| **80mg/kg BAY** | 0008 | 6.97 | 160. | 0.475 | 23.0 | 338. | 68.2 | 0.058 | 1. |

**Clinical Pathology Individual Values**

**Hematology**

**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | ERY T/L | HB g/L | HCT L/L | MCH pg | MCHC g/L | MCV fL | RETIC T/L | RETI % |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 6.62 | 147. | 0.445 | 22.1 | 329. | 67.2 | 0.026 | 0. |
| **5mg/kg BAY** | 0006 | 6.05 | 137. | 0.405 | 22.7 | 340. | 66.8 | 0.057 | 1. |
| **20mg/kg BAY** | 0007 | 6.44 | 147. | 0.429 | 22.8 | 343. | 66.6 | 0.043 | 1. |
| **80mg/kg BAY** | 0008 | 5.92 | 136. | 0.401 | 22.9 | 338. | 67.8 | 0.028 | 0. |

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | THRO G/L |
|---|---|---|
| **0mg/kg** | 0005 | 309. |
| **5mg/kg BAY** | 0006 | 313. |
| **20mg/kg BAY** | 0007 | 272. |
| **80mg/kg BAY** | 0008 | 229. |

**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | THRO G/L |
|---|---|---|
| **0mg/kg** | 0005 | 302. |
| **5mg/kg BAY** | 0006 | 286. |
| **20mg/kg BAY** | 0007 | 223. |
| **80mg/kg BAY** | 0008 | 165. |

**Clinical Pathology Individual Values**

**Hemostasis**

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | PT s | PTT s | FIBR g/L | TT s |
|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 6.7 | 11.8 | 2.67 | 14.0 |
| **5mg/kg BAY** | 0006 | 7.0 | 11.3 | 1.77 | 14.7 |
| **20mg/kg BAY** | 0007 | 7.0 | 11.7 | 1.89 | 14.9 |
| **80mg/kg BAY** | 0008 | 6.7 | 10.7 | 1.64 | 14.7 |

**Clinical Pathology Individual Values**

**Hemostasis**

**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | PT s | PTT s | FIBR g/L | TT s |
|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 6.8 | 10.8 | 2.42 | 14.4 |
| **5mg/kg BAY** | 0006 | 7.2 | 11.8 | 1.84 | 13.7 |
| **20mg/kg BAY** | 0007 | 7.2 | 11.6 | 1.72 | 14.3 |
| **80mg/kg BAY** | 0008 | 6.7 | 11.2 | 2.37 | 13.5 |

**Clinical Pathology Individual Values**

**Hematology**

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | LEUCO G/L | LYM G/L | NEUTRO G/L | Baso-phils G/L | EOS G/L | MONO G/L | LUC G/L |
|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 9.30 | 2.90 | 5.02 | 0.06 | 0.57 | 0.70 | 0.05 |
| **5mg/kg BAY** | 0006 | 9.47 | 3.39 | 5.31 | 0.04 | 0.41 | 0.29 | 0.03 |
| **20mg/kg BAY** | 0007 | 12.37 | 4.76 | 6.14 | 0.06 | 0.67 | 0.70 | 0.05 |
| **80mg/kg BAY** | 0008 | 12.63 | 3.96 | 7.13 | 0.10 | 0.68 | 0.71 | 0.05 |

**Clinical Pathology Individual Values**

**Hematology**

**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | LEUCO G/L | LYM G/L | NEUTRO G/L | Baso-phils G/L | EOS G/L | MONO G/L | LUC G/L |
|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 8.93 | 2.15 | 5.69 | 0.04 | 0.22 | 0.79 | 0.03 |
| **5mg/kg BAY** | 0006 | 9.05 | 3.02 | 5.49 | 0.04 | 0.18 | 0.30 | 0.03 |
| **20mg/kg BAY** | 0007 | 8.30 | 3.13 | 4.62 | 0.05 | 0.09 | 0.38 | 0.03 |
| **80mg/kg BAY** | 0008 | 18.00 | 4.08 | 11.85 | 0.10 | 0.32 | 1.59 | 0.06 |

**Clinical Pathology Individual Values**

**Hematology**

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | LYM rel. % | NEUTRO rel. % | BASO rel. % | EO rel. % | MONO rel. % | LUC rel. % | LI |
|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 31.1 | 54.0 | 0.6 | 6.1 | 7.5 | 0.6 | 3.05 |
| **5mg/kg BAY** | 0006 | 35.8 | 56.0 | 0.5 | 4.3 | 3.1 | 0.3 | 2.88 |
| **20mg/kg BAY** | 0007 | 38.5 | 49.6 | 0.5 | 5.4 | 5.6 | 0.4 | 3.05 |
| **80mg/kg BAY** | 0008 | 31.3 | 56.5 | 0.8 | 5.4 | 5.6 | 0.4 | 3.05 |

**Clinical Pathology Individual Values**

**Hematology**

**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | LYM rel. % | NEUTRO rel. % | BASO rel. % | EO rel. % | MONO rel. % | LUC rel. % | LI |
|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 24.1 | 63.7 | 0.5 | 2.5 | 8.8 | 0.3 | 3.05 |
| **5mg/kg BAY** | 0006 | 33.3 | 60.6 | 0.4 | 2.0 | 3.3 | 0.3 | 2.88 |
| **20mg/kg BAY** | 0007 | 37.7 | 55.7 | 0.7 | 1.1 | 4.5 | 0.4 | 3.09 |
| **80mg/kg BAY** | 0008 | 22.7 | 65.8 | 0.5 | 1.8 | 8.9 | 0.3 | 3.05 |

**Clinical Pathology Individual Values**

**Blood Enzyme Activities**

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | ALAT U/L | ASAT U/L | APh U/L | GLDH U/L | gamma-GT U/L |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 24. | 22. | 67. | 3.0 | 4. |
| **5mg/kg BAY** | 0006 | 20. | 20. | 42. | 3.6 | UDL |
| **20mg/kg BAY** | 0007 | 24. | 26. | 43. | 7.7 | UDL |
| **80mg/kg BAY** | 0008 | 45. | 56. | 81. | 6.6 | UDL |

**Clinical Pathology Individual Values**

**Blood Enzyme Activities**

**Females | Phase: Dosing | Day: 3 | Session: am | Scheduled |**

| | Animal# | ALAT U/L | ASAT U/L | APh U/L | GLDH U/L | gamma-GT U/L |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 22. | 25. | 93. | 3.5 | UDL |
| **5mg/kg BAY** | 0006 | 22. | 22. | 61. | 3.3 | UDL |
| **20mg/kg BAY** | 0007 | 22. | 22. | 42. | 4.0 | UDL |
| **80mg/kg BAY** | 0008 | 28. | 34. | 112. | 4.3 | UDL |

**Clinical Pathology Individual Values**

**Blood Enzyme Activities**

**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | ALAT U/L | ASAT U/L | APh U/L | GLDH U/L | gamma-GT U/L |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 20. | 24. | 102. | 3.2 | 4. |
| **5mg/kg BAY** | 0006 | 25. | 26. | 81. | 3.4 | UDL |
| **20mg/kg BAY** | 0007 | 22. | 39. | 47. | 4.3 | UDL |
| **80mg/kg BAY** | 0008 | 21. | 33. | 117. | 3.4 | UDL |

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | GLUCOSE mmoL/L | CHOL mmoL/L | TRIGL mmoL/L | CREA µmoL/L | UREA mmoL/L | Bili-t µmoL/L | Protein g/L | Albumin g/L |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 4.05 | 4.42 | 0.61 | 60. | 4.32 | UDL | 49.6 | 29.5 |
| **5mg/kg BAY** | 0006 | 4.99 | 5.53 | 0.72 | 56. | 3.88 | UDL | 55.3 | 36.5 |
| **20mg/kg BAY** | 0007 | 5.13 | 4.35 | 0.93 | 47. | 4.62 | UDL | 49.9 | 30.9 |
| **80mg/kg BAY** | 0008 | 4.94 | 3.39 | 0.81 | 64. | 5.05 | UDL | 59.4 | 37.0 |

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**Blood Substrate Concentrations** September 14, 2017 11:21

**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | GLUCOSE mmoL/L | CHOL mmoL/L | TRIGL mmoL/L | CREA µmoL/L | UREA mmoL/L | Bili-t µmoL/L | Protein g/L | Albumin g/L |
|---|---|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 4.91 | 4.97 | 0.44 | 56. | 4.78 | UDL | 55.0 | 33.1 |
| **5mg/kg BAY** | 0006 | 5.13 | 6.03 | 0.67 | 56. | 4.20 | UDL | 55.1 | 37.4 |
| **20mg/kg BAY** | 0007 | 5.14 | 4.07 | 0.51 | 51. | 5.77 | UDL | 49.8 | 28.0 |
| **80mg/kg BAY** | 0008 | 5.09 | 3.21 | 0.44 | 51. | 4.37 | UDL | 55.3 | 31.4 |

**Clinical Pathology Individual Values**

**Blood Electrolytes**

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | Na-ISE mmoL/L | K-ISE mmoL/L | CL-ISE mmoL/L | Ca mmoL/L | P mmoL/L | Mg mmoL/L |
|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 145. | 4.3 | 112. | 2.48 | 1.34 | 0.78 |
| **5mg/kg BAY** | 0006 | 145. | 4.8 | 112. | 2.61 | 1.31 | 0.75 |
| **20mg/kg BAY** | 0007 | 142. | 4.8 | 109. | 2.57 | 1.91 | 0.76 |
| **80mg/kg BAY** | 0008 | 145. | 4.3 | 111. | 2.67 | 1.72 | 0.94 |

**Clinical Pathology Individual Values**

**Blood Electrolytes**



**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | Na-ISE mmoL/L | K-ISE mmoL/L | CL-ISE mmoL/L | Ca mmoL/L | P mmoL/L | Mg mmoL/L |
|---|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 146. | 4.0 | 111. | 2.54 | 1.42 | 0.78 |
| **5mg/kg BAY** | 0006 | 147. | 4.4 | 112. | 2.55 | 1.36 | 0.78 |
| **20mg/kg BAY** | 0007 | 144. | 4.7 | 110. | 2.40 | 1.35 | 0.71 |
| **80mg/kg BAY** | 0008 | 146. | 4.0 | 114. | 2.42 | 1.36 | 0.77 |

**Clinical Pathology Individual Values**

**Electrophoresis of Proteins**

**Females | Phase: PreDosing | Day: 1 | Session: am | Scheduled |**

| | Animal# | ALBUMIN % | TA GLOB % | TB GLOB % | TG GLOB % | A/G |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 49.0 | 24.3 | 19.8 | 6.9 | 0.96 |
| **5mg/kg BAY** | 0006 | 57.4 | 21.1 | 15.5 | 6.0 | 1.35 |
| **20mg/kg BAY** | 0007 | 52.8 | 22.9 | 18.4 | 5.9 | 1.12 |
| **80mg/kg BAY** | 0008 | 53.8 | 19.8 | 17.9 | 8.5 | 1.16 |

**Clinical Pathology Individual Values**

**Electrophoresis of Proteins**



**Females | Phase: Dosing | Day: 10 | Session: am | Scheduled |**

| | Animal# | ALBUMIN % | TA GLOB % | TB GLOB % | TG GLOB % | A/G |
|---|---|---|---|---|---|---|
| **0mg/kg** | 0005 | 52.7 | 23.5 | 17.1 | 6.7 | 1.11 |
| **5mg/kg BAY** | 0006 | 56.9 | 22.6 | 15.3 | 5.2 | 1.32 |
| **20mg/kg BAY** | 0007 | 51.8 | 22.9 | 18.2 | 7.1 | 1.07 |
| **80mg/kg BAY** | 0008 | 53.5 | 20.6 | 18.0 | 7.9 | 1.15 |

Please Note:
Displayed date in the header is the creation date of the report

System Version 6.4.0 Build 87.B05

Report Code and Name: CPMIV Clinical Pathology Individual Values
Report Version: 5.2
Job:325504, ID:326619

**Report Selections**

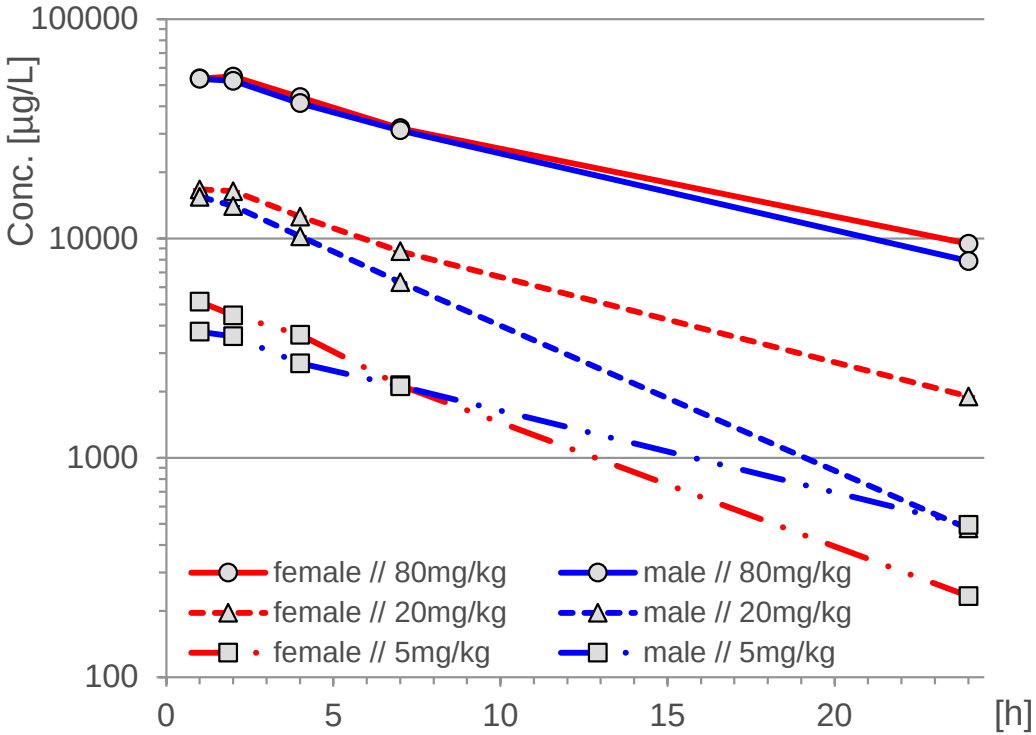
| | |
|---|---|
| Comparison group(s) | 2,3,4 |
| Control group(s) | 1 |

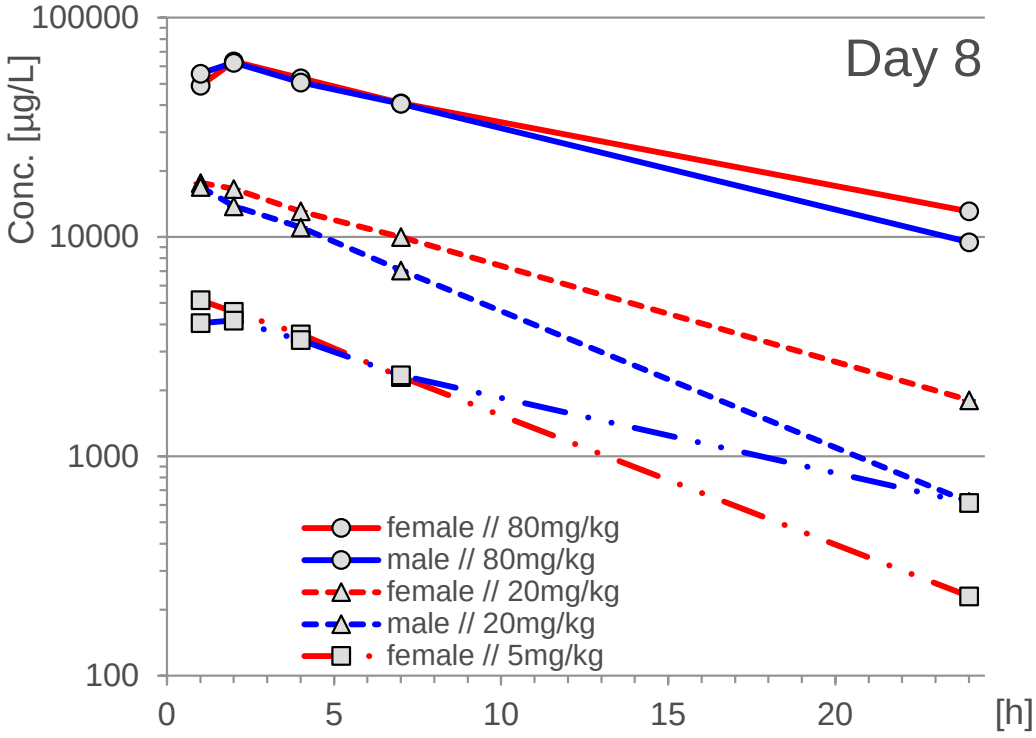
**Group 1** 0mg/kg
**Group 2** 5mg/kg BAY 2469430
**Group 3** 20mg/kg BAY 2469430
**Group 4** 80mg/kg BAY 2469430

**Abbreviation(s):**

UDL = under limit of detection

# T103508-7 – TK of BAY 2469430 after oral administration in Beagle dogs




- Exposures generally increased with dose in both genders
- No relevant accumulation of $C_{max}$ or AUC

| Sex | | female | | | | | | male | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dose Admin | [mg/kg] | 5.0 | | 20 | | 80 | | 5.0 | | 20 | | 80 | |
| Admin Day | | 1 | 8 | 1 | 8 | 1 | 8 | 1 | 8 | 1 | 8 | 1 | 8 |
| AUC(0-24) | [mg·h/L] | 39 | 40 | 162 | 171 | 605 | 751 | 38 | 44 | 109 | 120 | 568 | 699 |
| $AUC(0\text{-}24)_{norm}$ | [kg·h/L] | 7.7 | 7.9 | 8.1 | 8.6 | 7.6 | 9.4 | 7.6 | 8.8 | 5.5 | 6.0 | 7.1 | 8.7 |
| $C_{max}$ | [mg/L] | 5.1 | 5.2 | 17 | 18 | 55 | 63 | 3.8 | 4.2 | 15 | 17 | 53 | 62 |
| $C_{max,norm}$ | [kg/L] | 1.0 | 1.0 | 0.84 | 0.88 | 0.68 | 0.79 | 0.75 | 0.83 | 0.77 | 0.85 | 0.67 | 0.78 |
| $C(24)/C_{max}$ | [%] | 4.5 | 4.5 | 11 | 10 | 17 | 21 | 13 | 15 | 3.1 | 3.7 | 15 | 15 |
| $t_{max}$ | [h] | 1.0 | 1.0 | 1.0 | 1.0 | 2.0 | 2.0 | 1.0 | 2.0 | 1.0 | 1.0 | 1.0 | 2.0 |

# 1. In-Life, Materials and Methods

## 1.1 Study design

**Table 1-1: Test system and Study dates**

| **Animals** | **«** |
|---|---|
| Species: | Beagle, Purebred Marshall |
| Breeder: | Marshall BIO Resources, USA |
| Animals per cage: | 1 |
| Age of males at start of treatment: | 11 months |
| Age of females at start of treatment: | 11 months |
| **Study dates** | **«** |
| Start of treatment: | 05-Sep-2017 |
| Termination of treatment: | 18-Sep-2017 |
| Termination of study (in-life-phase): | 19-Sep-2017 |

## 1.2 Definition of Study Dates

The chronological information is generally given in absolute days (first day of treatment= day 1 of the study). In Report tables of in-life data the time for an activity is stated principally as the planned day of phase.

## 1.3 Collection, Processing and Evaluation of Data

During the study collection, storage and evaluation including statistics of in-life data as well as data of clinical pathology were done on- or offline by using the validated PRISTIMA SYSTEM Next Generation produced by Xybion Medical Systems Corporation, 240 Cedar Knolls Road, Cedar Knolls, New Jersey 07927, USA

In the tables ofAppendix - In-Life Data - Individual Data individual values of the clinical laboratory examination, body weights, body weight gain and food have been rounded. In the calculation of means and variances, etc. original, non-rounded values were taken as the basis in some cases.

For individual body weights or mean food intake data occasionally values may be missing. Such gaps in primary data occur when a measurement value was not recorded as a result of technical error in the on-line processing or was suppressed as an unrealistic value (e.g. negative food consumption). In addition, after-weight values were suppressed, if the corresponding before-weight values were missing.

An individual value, which was recorded on-line occasionally could have been identified as an outlier in tables of individual values and could have been then, therefore, excluded from further analysis (e.g. calculation of group mean, etc., and statistical comparison). This could have happened, if the value appeared implausible, i.e. in the event of an inexplicably large discrepancy compared with the expected or previously recorded value.

In tables with individual data on clinical laboratory examinations, isolated values may be missing, if no sample was available (animal dead, sample collection not possible etc.), or if the sample amount was not sufficient for determination of all parameters or if the reaction was disturbed and, therefore, could not be evaluated. Furthermore, additional comments

concerning the appearance of the samples that were recorded in the raw data in connection with certain measurements were not included in the report lists when they were considered to have no bearing on the result, i.e. when there was no detectable relationship with treatment and the results showed that measurement had not been affected.

The clinical symptoms (findings), if any, were presented by means of cumulative group incidence and individual animal findings with information on the time of occurrence in question. For reasons of a better overview for main findings, only information on localization was given, without any further details of the findings.

## 1.4 Methods

### 1.4.1.1 Clinical Observations

The findings are summarized, giving the incidence (number of animals affected) as well as the frequency of the findings (total number of observations). No information is given for groups without any clinical findings.

The alterations from baseline condition are recorded.

Predosing:

Each animal was checked once daily at the time sequence:

- Session 1 = in the morning

Dosing:

Each animal was checked twice daily at the time sequence:

- Session 1 = in the morning – including all observations prior to, during and immediately after administration
- Session 2 = in the afternoon

On the weekend the last check was performed just before the technician left the laboratory in the late morning.

### 1.4.2 Food Consumption

Principle: using an electronic scale

Food was offered to animals for a period of 1 hour per day.

### 1.4.3 Body weight

Principle: using an electronic scale

Body weight was recorded on given days of the study period.

### 1.4.4 Body weight gain

Body weight gain of each animal was determined as difference between the body weight at end and the body weight at start of the respective observation period.

### 1.4.5 Blood pressure

**Table 1–2: Blood pressure parameters**

| Abbre-viation | Explanation | Method | Dimen-sion |
|---|---|---|---|
| SYST | Systolic blood pressure | Direct oscillometric determination in the femoral artery | mmHg |
| DIAST | Diastolic blood pressure | Direct oscillometric determination in the femoral artery | mmHg |

### 1.4.6 Heart rate and Electrocardiogram

**Table 1–3: Heart rate and Electrocardiogram**

| Abbre-viation | Explanation | Method | Dimen-sion |
|---|---|---|---|
| ECG | Electrocardio-gram | Lead II using PoNeMah System | millisecond (ms) |
| HR | Heart rate | Counting from ECG (PoNeMah Software) | beats/min. (bts/min) |

For each animal, the different amplitudes and intervals were measured in lead II.

Based on these individual values, group mean values were calculated.

Leads I, III, aVR, aVL and aVF were checked visually.

## 1.4.7 Clinical Pathology

**Table 1–4: Hematology**

| Abbre-viation | Explanation | Method | Dimen-sion |
|---|---|---|---|
| ERY | Erythrocytes | Flow-cytometric light scattering method, Advia 2120i, Siemens AG | T/L |
| HB | Hemoglobin | Mod. cyanmethemoglobin reaction, Advia 2120i, Siemens AG | g/L |
| HCT | Hematocrit | Calculated from RBC count and MCV, Advia 2120i, Siemens AG | L/L |
| MCH | Mean cell hemoglobin | Calculated from RBC count and hemoglobin concentration, Advia 2120i, Siemens AG | pg |
| MCHC | Mean cell hemoglobin concentration | Calculated from hemoglobin and hematocrit concentration, Advia 2120i, Siemens AG | g/L |
| MCV | Mean cell volume | Flow-cytometric light scattering method, Advia 2120i, Siemens AG | fl |
| THRO | Thrombo-cytes | Flow-cytometric light scattering method, Advia 2120, Siemens AG | G/L |
| RETIC | Reticulocytes | Flow-cytometric light scattering method and specific RNA color reaction, Advia 2120i, Siemens AG | T/L |
| RETI | Reticulocytes (relative) | Flow-cytometric light scattering method and specific RNA color reaction, Advia 2120, Siemens AG | % |

**Table 1–5: Hemostasis**

| Abbre-viation | Explanation | Method | Dimen-sion |
|---|---|---|---|
| FIBR | Fibrinogen | Mechanical measurement with reagent Triniclot Fibrinogen (clauss method) by means of Destiny Max automatic analyzer, Stago | g/L |
| PTT | Activated partial throm-boplastin time | Mechanical measurement with reagent C.K. Prest by means of Destiny Max automatic analyzer, Stago | s |
| PT | Prothrombin time | Mechanical measurement with reagent Thromborel S, Siemens by means of Destiny Max automatic analyzer, Stago | s |
| TT | Thrombin time | Mechanical measurement with reagent Test-Thrombin, Siemens by means of Destiny Max automatic analyzer, Stago | s |

**Table 1–6: Hematology**

| Abbre-viation | Explanation | Method | Dimen-sion |
|---|---|---|---|
| LEUCO | Leucocytes | Cytochem. peroxidase reaction, Advia 2120i, Siemens AG | G/L |
| LYM | Lymphocytes | | |
| NEUTRO | Neutrophils | | |
| EOS | Eosinophils | | |
| MONO | Monocytes | | |
| LUC | Large un-stained cells | | |
| BASO-phils | Basophils | Cytochem. stripping reaction and flow cytometric light, scattering method, Advia 2120i, Siemens AG | G/L |

**Table 1–7: Hematology**

| Abbre-viation | Explanation | Method | Dimen-sion |
|---|---|---|---|
| LYM rel. | Lymphocytes relativ | Cytochem. peroxidase reaction and flow cytometric light, scattering method, Advia 2120i, Siemens AG | % |
| NEUTRO rel. | Neutrophils relativ | | |
| BASO rel. | Basophils relativ | | |
| EO rel. | Eosinophils relativ | | |
| MONO rel. | Monocytes relativ | | |
| LUC rel. | Large un-stained cells | | |
| LI | Lubularity index | Calculated value: LI = polymorphnuclear cells/mononuclear cells | --- |

**Table 1–8: Blood Enzyme Activities**

| Abbre-viation | Explanation | Method | Dimension | | Transformation factor (F) |
|---|---|---|---|---|---|
| | | | actual | SI | [old * F = SI] |
| ALAT | Alanine aminotrans-ferase (E.C. 2.6.1.2.) | IFCC method at 37 °C with pyridoxalphosphate by means of Cobas C501 automatic analyzer, Roche | U/L | µkat/L | 0.0167 |
| ASAT | Aspartate amino-transferase (E.C. 2.6.1.1.) | IFCC method at 37 °C with pyridoxalphosphate by means of Cobas C501 automatic analyzer, Roche | U/L | µkat/L | 0.0167 |
| APh | Alkaline phosphatase (E.C. 3.1.3.1.) | IFCC method at 37 °C by means of Cobas C501 automatic analyzer, Roche | U/L | µkat/L | 0.0167 |
| GLDH | Glutamat-dehydrogenase (E.C. 1.4.1.3.) | Optimized method at 37 °C with roche reagents by means of Cobas C501 automatic analyzer, Roche | U/L | µkat/L | 0.0167 |
| gamma-GT | Gamma-gluta-myl-transferase (E.C. 2.3.2.2.) | Enzymatic method at 37 °C by means of Cobas C501 automatic analyzer, Roche | U/L | µkat/L | 0.0167 |

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**Table 1–9: Blood Substrate Concentrations – standard set of parameters**

| Abbre-viation | Explanation | Method | Dimension | | Transformation factor (F) |
|---|---|---|---|---|---|
| | | | actual | SI | [old * F = SI] |
| GLUCOSE | Glucose | Hexokinase-method by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| CHOL | Total cholesterol | Enzymatic- colorimetric -method by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| TRIGL | Triglycerides | colorimetric -method by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| CREA | Creatinine | Jaffé-reaction by means of Cobas C501 automatic analyzer, Roche | µmol/L | µmol/L | 1.0 |
| UREA | Urea | Kinetic urease-method by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| Bili-t | Total bilirubin | Colorimetric Diazo method by means of Cobas C501 automatic analyzer, Roche | µmol/L | µmol/L | 1.0 |
| Protein | Total protein | Biuret reaction by means of Cobas C501 automatic analyzer, Roche | g/L | g/L | 1.0 |
| Albumin | Albumin | Bromcresol green-method by means of Cobas C501 automatic analyzer, Roche | g/L | g/L | 1.0 |

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**Table 1–10: Blood Electrolytes**

| Abbre-viation | Explanation | Method | Dimension | | Transformation factor (F) |
|---|---|---|---|---|---|
| | | | actual | SI | [old * F = SI] |
| Na-ISE | Sodium | Indirect ion selective electrode method by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| K-ISE | Potassium | Indirect ion selective electrode method by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| CL-ISE | Chloride | Indirect ion selective electrode method by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| Ca | Calcium | Photometric method with NM-BAPTA complexone by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| P | Inorganic phosphate | UV-method, molybdate reaction by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |
| Mg | Magnesium | Colorimetric chlorophosphonazo III reaction by means of Cobas C501 automatic analyzer, Roche | mmol/L | mmol/L | 1.0 |

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**Table 1–11: Electrophoresis of Proteins**

| Abbre-viation | Explanation | Method | Dimen-sion |
|---|---|---|---|
| Albumin | Albumin | Serum protein electrophoresis, Agarose gel electrophoresis staining with Amidoblack and evaluation by means of Densitometer Gelscan, Sebia | % |
| TA GLOB | Alpha globulin | | % |
| TB GLOB | Beta globulin | | % |
| TG GLOB | Gamma globulin | | % |
| A/G | Albumin globulin quotient | | --- |

## 1.5 Specification of Diet

Ssniff® Hd-H diet, manufacturer: ssniff Spezialdiäten GmbH

**Table 1–12: Chemical composition of the ssniff® Hd-H diet**

| Ingredients | Content [in 1 kg diet] | Ingredients | Content [in 1 kg diet] |
|---|---|---|---|
| **1. Major nutrients and minerals** | | **2. Vitamins** | |
| Crude protein | 220.0 g | Vitamin A | 17000 IE |
| Crude fat | 55.0 g | Vitamin B1 | 18 mg |
| Crude fibre | 23.0 g | Vitamin B2 | 23 mg |
| Crude ash | 55.0 g | Vitamin B6 | 21 mg |
| Calcium | 11.0 g | Vitamin B12 | 105 µg |
| Glucose | 33.0 g | Vitamin D3 | 1100 IE |
| Magnesium | 2.1 g | Vitamin E | 130 mg |
| N-free extractsubstance | 540.0 g | Vitamin K | 5 mg |
| Phosphorus | 9.0 g | Biotin | 480 µg |
| Potassium | 6.0 g | Folic acid | 6 mg |
| Sodium | 3.1 g | Pantothenic acid | 41 mg |
| Starch content | 416.0 g | Nicotinic acid | 125 mg |
| | | Choline | 3250 mg |
| | | Inositole | 100 mg |
| **3. Essential amino acids** | | **4. Trace elements** | |
| Alanine | 12.7 g | Cobalt | 2.1 mg |
| Arginine | 12.9 g | Copper | 15.0 mg |
| Aspartic acid | 15.7 g | Iodine | 2.3 mg |
| Glutamic acid | 36.8 g | Iron | 225.0 mg |
| Glycine | 16.9 g | Manganese | 63.0 mg |
| Histine | 5.2 g | Selen | 0.4 mg |
| Isoleucine | 8.0 g | Zinc | 101.0 mg |
| Lysine | 15.4 g | | |
| Leucine | 17.4 g | | |
| Methionine | 7.0 g | | |
| Met + cystine | 10.4 g | | |
| Phenylalanine | 9.3 g | | |
| Phe + tyr | 15.1 g | | |
| Proline | 15.9 g | | |
| Serine | 9.2 g | | |
| Tryptophane | 2.3 g | | |
| Threonine | 7.7 g | | |
| Valine | 10.5 g | | |