



## Title Page

Function: **Experimental Toxicology** **Nonclinical Study Report**

GLP: No

Report ID: PH-42754

Test Item: **BAY 2469430**

Title: **Non-GLP report version 1**  
**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]	Concentration	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 Dosing: twice daily
Mortality	Twice daily
Body weight	Pre-random: once Pre-dosing: once Dosing: day 1, 3 and 7
Food intake	Daily
EKG / Blood Pressure	Pre-Dosing: once Dosing: week 2 (prior to and 1-2 h after administration)
Hematology / Hemostasis	Predosing: once Dosing week 2
Clinical chemistry	Predosing: once 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)**

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

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

AUC <sub>(0-24)</sub>	[mg·h/L]	–	44	120	699	–	40	171	751
AUC <sub>(0-24)norm</sub>	[kg·h/L]	–	8.8	6.0	8.7	–	7.9	8.6	9.4
C <sub>max</sub>	[mg/L]	–	4.2	17	62	–	5.2	18	63
C <sub>max,norm</sub>	[kg/L]	–	0.83	0.85	0.78	–	1.0	0.88	0.79
C <sub>(24)/C<sub>max</sub></sub>	[%]	–	15	3.7	15	–	4.5	10	21
t <sub>max</sub>	[h]	–	2.0	1.0	2.0	–	1.0	1.0	2.0
RA <sub>AUC</sub>	[%]	–	116	110	123	–	103	106	124
RA <sub>Cmax</sub>	[%]	–	111	110	117	–	100	105	116
<hr/>									
RA <sub>AUC</sub> =	Accumulation ratio (AUC <sub>(0-24)</sub> , SS / AUC <sub>(0-24)</sub> , Day 1)								
RA <sub>Cmax</sub> =	Accumulation ratio (C <sub>max</sub> , SS / C <sub>max</sub> , 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, t<sub>max</sub> between 1-2 h after administration and no relevant accumulation potential.

### 4. Signature

Valid without signature.

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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	

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PREPARED BY: Dr. Katrin Gutberlet  
Veterinary Pathologist

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EXPLANATION OF CODES AND SYMBOLS

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CODES AND SYMBOLS USED AT ANIMAL LEVEL:

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

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CODES AND SYMBOLS USED AT ORGAN LEVEL:

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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

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CODES AND SYMBOLS USED AT FINDING LEVEL:

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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

ORGAN/FINDING	DOSE GROUP:		01		02		03		04	
	SEX:		M	F	M	F	M	F	M	F
	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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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
EPIDIDYMITIS :			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, - uneven blood distribution  
approx 1 cm in diameter.

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INDIVIDUAL ANIMAL DATA

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

ANIMAL NUMBER :

0001 0005  
MK0 FK0

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

ANIMAL NUMBER :

0001 0005  
MK0 FK0

EPIDIDYMITIS +  
- Cell Debris 1.

.....



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

ANIMAL NUMBER :

0002 0006  
MK0 FK0

	0002	0006
	MK0	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.	
EPIDIDYIMIDES	-	

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

ANIMAL NUMBER :

0003 0007  
MK0 FK0

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

ANIMAL NUMBER :

0004 0008  
MK0 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.	.
.....		

PATHOLOGY REPORT (FINAL DRAFT)  
INDIVIDUAL ANIMAL DATA

PAGE : 12/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
PathData®System V6.2e2

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

ANIMAL NUMBER :

0004 0008  
MK0 FK0

TESTES +  
- Immaturity 1.  
- Tubular Atrophy 2.  
- Multinucl.Giant C. 1.

.....  
EPIDIDYIMIDES +  
- Cell Debris 1.  
.....

PATHOLOGY REPORT (FINAL DRAFT)  
INDIVIDUAL ANIMAL DATA

PAGE : 13/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
INDIVIDUAL ANIMAL DATA

PAGE : 14/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
PathData@System V6.2e2

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TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 01, vehicle

MALE

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\* 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.

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PATHOLOGY REPORT (FINAL DRAFT)  
INDIVIDUAL ANIMAL DATA

PAGE : 15/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
INDIVIDUAL ANIMAL DATA

PAGE : 16/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
INDIVIDUAL ANIMAL DATA

PAGE : 17/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
PathData®System V6.2e2

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TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 02, low dose (5 mg/kg) MALE

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\* 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.

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PATHOLOGY REPORT (FINAL DRAFT)  
INDIVIDUAL ANIMAL DATA

PAGE : 18/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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.

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PATHOLOGY REPORT (FINAL DRAFT)  
INDIVIDUAL ANIMAL DATA

PAGE : 19/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
INDIVIDUAL ANIMAL DATA

PAGE : 20/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
INDIVIDUAL ANIMAL DATA

PAGE : 21/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
INDIVIDUAL ANIMAL DATA

PAGE : 22/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
INDIVIDUAL ANIMAL DATA

PAGE : 23/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
INDIVIDUAL ANIMAL DATA

PAGE : 24/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 25/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
PathData®System V6.2e2

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TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS

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Explanation of Symbols:

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

PATHOLOGY REPORT (FINAL DRAFT)  
BODY/ORGAN WEIGHTS

PAGE : 26/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

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PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

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PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

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TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
 BODY/ORGAN WEIGHTS

PAGE : 30/ 49  
 PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
 TEST SYSTEM : DOG, 2 weeks, p.o.  
 SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
 DATE : 08-NOV-17  
 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

PATHOLOGY REPORT (FINAL DRAFT)  
BODY/ORGAN WEIGHTS

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PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
PathData®System V6.2e2

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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)  
BODY/ORGAN WEIGHTS

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PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
PathData®System V6.2e2

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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)  
BODY/ORGAN WEIGHTS

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TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

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PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
PathData®System V6.2e2

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

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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)  
BODY/ORGAN WEIGHTS

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PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

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PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
PathData®System V6.2e2

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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)  
BODY/ORGAN WEIGHTS

PAGE : 37/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 38/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 39/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 40/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 41/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 42/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 43/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 44/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 45/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 46/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 47/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 48/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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)  
BODY/ORGAN WEIGHTS

PAGE : 49/ 49  
PROJECT : T 103508-7

TEST ITEM : BAY 2469430  
TEST SYSTEM : DOG, 2 weeks, p.o.  
SPONSOR : Bayer AG

PATHOL. NO.: 13508 GUT  
DATE : 08-NOV-17  
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

Bayer AG

**Animal Death Status Report**

T103508-7

Page 1 of 2

July 9, 2018 09:06

**Males**

<b>Animal #</b>	<b>Group Name</b>	<b>Death Status:</b>	<b>Death Type</b>	<b>Phase and Day of Phase</b>	<b>Date of Death</b>
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**

<b>Animal #</b>	<b>Group Name</b>	<b>Death Status:</b>	<b>Death Type</b>	<b>Phase and Day of Phase</b>	<b>Date of Death</b>
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

BAY 2469430

Bayer AG

**Animal Death Status Report**

T103508-7

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July 9, 2018 09:06

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**

BAY 2469430

T103508-7

Bayer AG

Page 1 of 3

**Clinical Observations****Cumulative Incidences**

September 25, 2017 10:48

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

	0mg/kg	5mg/kg	20mg/kg	80mg/kg
		BAY	BAY	BAY
		2469430	2469430	2469430
<b>No. Animals Examined</b>	1	1	1	1
<b>No. Animals with Observation</b>	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

BAY 2469430

T103508-7

Bayer AG

Page 2 of 3

**Clinical Observations****Cumulative Incidences**

September 25, 2017 10:48

**DETAILED CLINICAL OBSERVATION**

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

	5mg/kg	80mg/kg
	BAY	BAY
	2469430	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



BAY 2469430

T103508-7

Bayer AG

**Clinical Observations**

Page 3 of 3

**Cumulative Incidences**

September 25, 2017 10:48

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**DETAILED CLINICAL OBSERVATION**

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Please Note:

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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**

<b>Animal#</b>	<b>Category, Observation, Modifier(s)</b>	<b>Session</b>	<b>Period of Appearance</b>
0001	Excretion, Changed feces consistency, thin	2	day 11

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

<b>Animal#</b>	<b>Category, Observation, Modifier(s)</b>	<b>Session</b>	<b>Period of Appearance</b>
0002	Excretion, Changed feces consistency, thin	2	day 11

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

<b>Animal#</b>	<b>Category, Observation, Modifier(s)</b>	<b>Session</b>	<b>Period of Appearance</b>
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**

<b>Animal#</b>	<b>Category, Observation, Modifier(s)</b>	<b>Session</b>	<b>Period of Appearance</b>
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

BAY 2469430

T103508-7

Bayer AG

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**Clinical Observations****Individual Values**

September 25, 2017 10:53

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

---

<b>Animal#</b>	<b>Category, Observation, Modifier(s)</b>	<b>Session</b>	<b>Period of Appearance</b>
0006	Excretion, Vomited immediately after administration	2	day 3

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

---

<b>Animal#</b>	<b>Category, Observation, Modifier(s)</b>	<b>Session</b>	<b>Period of Appearance</b>
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

BAY 2469430

Bayer AG

T103508-7

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**Clinical Observations****Individual Values**

September 25, 2017 10:53

**DETAILED CLINICAL OBSERVATION**

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Please Note:

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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 1
	Animal#	1	2	3	4	5	6	7	
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

BAY 2469430

Bayer AG

T103508-7

Page 3 of 7

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

September 25, 2017 10:46

**Males****Session 1****Dosing****Day of Phase**

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



BAY 2469430

T103508-7

Bayer AG

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

September 25, 2017 10:46

**Females**

Session 1		Pre Dosing Day of Phase							Dosing Day of Phase 1
	Animal#	1	2	3	4	5	6	7	
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

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Bayer AG

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

September 25, 2017 10:46

**Females****Session 1****Dosing****Day of Phase**

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

BAY 2469430

Bayer AG

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

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September 25, 2017 10:46

**Females****Session 1****Dosing****Day of Phase**

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

BAY 2469430

Bayer AG

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

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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

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Bayer AG

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**Body Weights Individual Values**  
(kg)

September 25, 2017 10:45

**Males**

Session 1		Pre Random Day of Phase 1	Pre Dosing Day of Phase 1	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

BAY 2469430

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**Body Weights Individual Values**  
(kg)

September 25, 2017 10:45

**Females**

Session 1		Pre	Pre	Dosing				
		Random	Dosing					
		Day of	Day of	Day of Phase				
		Phase	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

BAY 2469430

Bayer AG

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

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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 2469430Abbreviation(s):

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## **Body weight gain**

BAY 2469430

Bayer AG

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

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July 9, 2018 09:45

**Males****Session 1****Dosing****Day of Phase**

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

BAY 2469430

Bayer AG

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

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July 9, 2018 09:45

**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

BAY 2469430

Bayer AG

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

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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

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**Abbreviation(s) :**

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## **Blood pressure**

Note:

Session 1: am

Session 2: before administration

Session 3: 1-2h after administration

BAY 2469430

Bayer AG

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## Generalized Measurements

## Individual Values

September 28, 2017 13:19

## 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

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BAY 2469430

Bayer AG

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## Generalized Measurements

## Individual Values

September 28, 2017 13:19

## 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

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BAY 2469430

Bayer AG

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## Generalized Measurements

## Individual Values

September 28, 2017 13:19

## 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

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BAY 2469430

Bayer AG

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## Generalized Measurements

## Individual Values

September 28, 2017 13:19

## 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

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BAY 2469430

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**Generalized Measurements  
Individual Values**

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September 28, 2017 13:19

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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

Bayer AG

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## Generalized Measurements

## Individual Values

July 9, 2018 09:11

## 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

BAY 2469430

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Bayer AG

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## Generalized Measurements

## Individual Values

July 9, 2018 09:11

## 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

BAY 2469430

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## Generalized Measurements

## Individual Values

July 9, 2018 09:11

## 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

BAY 2469430

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## Generalized Measurements

## Individual Values

July 9, 2018 09:11

## 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

BAY 2469430

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**Generalized Measurements  
Individual Values**

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July 9, 2018 09:11

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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

<b>Group</b>	<b>1</b>	0mg/kg
<b>Group</b>	<b>2</b>	5mg/kg BAY 2469430
<b>Group</b>	<b>3</b>	20mg/kg BAY 2469430
<b>Group</b>	<b>4</b>	80mg/kg BAY 2469430



## **Clinical Pathology**

Hematology

Hemostasis

Blood Enzyme Activities

Blood Substrate Concentrations

Blood Electrolytes

Electrophoresis of Proteins

BAY 2469430

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Bayer AG

## Clinical Pathology Individual Values

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## 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.

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## Clinical Pathology Individual Values

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## Hematology

September 14, 2017 11:21

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.

BAY 2469430

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**Clinical Pathology Individual Values**

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**Hematology**

September 14, 2017 11:21

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

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	<b>Animal#</b>	<b>THRO G/L</b>
0mg/kg	0001	275.
5mg/kg BAY	0002	245.
20mg/kg BAY	0003	265.
80mg/kg BAY	0004	239.

BAY 2469430

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Bayer AG

**Clinical Pathology Individual Values**

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**Hematology**

September 14, 2017 11:21

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

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	<b>Animal#</b>	<b>THRO G/L</b>
0mg/kg	0001	248.
5mg/kg BAY	0002	228.
20mg/kg BAY	0003	284.
80mg/kg BAY	0004	164.

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**Clinical Pathology Individual Values**

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**Hemostasis**

September 14, 2017 11:21

**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

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**Clinical Pathology Individual Values**

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**Hemostasis**

September 14, 2017 11:21

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

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

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## Clinical Pathology Individual Values

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## Hematology

September 14, 2017 11:21

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



BAY 2469430

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## Clinical Pathology Individual Values

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## Hematology

September 14, 2017 11:21

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

BAY 2469430

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Bayer AG

## Clinical Pathology Individual Values

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## Hematology

September 14, 2017 11:21

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

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## Clinical Pathology Individual Values

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## Hematology

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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

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**Blood Enzyme Activities**

September 14, 2017 11:21

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

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

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**Blood Enzyme Activities**

September 14, 2017 11:21

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

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

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**Blood Enzyme Activities**

September 14, 2017 11:21

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

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

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## Clinical Pathology Individual Values

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## Blood Substrate Concentrations

September 14, 2017 11:21

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

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**Blood Substrate Concentrations**

September 14, 2017 11:21

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

		GLUCOSE	CHOL	TRIGL	CREA	UREA	Bili-t	Protein	Albumin
Animal#		mmoL/L	mmoL/L	mmoL/L	µmoL/L	mmoL/L	µmoL/L	g/L	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



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## Clinical Pathology Individual Values

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## Blood Electrolytes

September 14, 2017 11:21

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

		Na-ISE	K-ISE	CL-ISE	Ca	P	Mg
Animal#		mmoL/L	mmoL/L	mmoL/L	mmoL/L	mmoL/L	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

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## Clinical Pathology Individual Values

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## Blood Electrolytes

September 14, 2017 11:21

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

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**Clinical Pathology Individual Values**

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**Electrophoresis of Proteins**

September 14, 2017 11:21

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

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

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**Clinical Pathology Individual Values**

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**Electrophoresis of Proteins**

September 14, 2017 11:21

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

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

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## Clinical Pathology Individual Values

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## Hematology

September 14, 2017 11:21

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.

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## Clinical Pathology Individual Values

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## Hematology

September 14, 2017 11:21

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.

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**Clinical Pathology Individual Values**

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**Hematology**

September 14, 2017 11:21

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

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	<b>Animal#</b>	<b>THRO G/L</b>
0mg/kg	0005	309.
5mg/kg BAY	0006	313.
20mg/kg BAY	0007	272.
80mg/kg BAY	0008	229.

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**Clinical Pathology Individual Values**

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**Hematology**

September 14, 2017 11:21

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

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	<b>Animal#</b>	<b>THRO G/L</b>
0mg/kg	0005	302.
5mg/kg BAY	0006	286.
20mg/kg BAY	0007	223.
80mg/kg BAY	0008	165.



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**Hemostasis**

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**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

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**Hemostasis**

September 14, 2017 11:21

**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

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**Hematology**

September 14, 2017 11:21

**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

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**Clinical Pathology Individual Values**

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**Hematology**

September 14, 2017 11:21

**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

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## Clinical Pathology Individual Values

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## Hematology

September 14, 2017 11:21

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

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## Clinical Pathology Individual Values

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## Hematology

September 14, 2017 11:21

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

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**Clinical Pathology Individual Values**

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**Blood Enzyme Activities**

September 14, 2017 11:21

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

		<b>ALAT</b>	<b>ASAT</b>	<b>APh</b>	<b>GLDH</b>	<b>gamma-GT</b>
		<b>U/L</b>	<b>U/L</b>	<b>U/L</b>	<b>U/L</b>	<b>U/L</b>
<b>Animal#</b>						
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

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**Clinical Pathology Individual Values**

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**Blood Enzyme Activities**

September 14, 2017 11:21

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

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



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**Blood Enzyme Activities**

September 14, 2017 11:21

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

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

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**Blood Substrate Concentrations**

September 14, 2017 11:21

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

		<b>GLUCOSE</b>	<b>CHOL</b>	<b>TRIGL</b>	<b>CREA</b>	<b>UREA</b>	<b>Bili-t</b>	<b>Protein</b>	<b>Albumin</b>
		<b>mmoL/L</b>	<b>mmoL/L</b>	<b>mmoL/L</b>	<b>µmoL/L</b>	<b>mmoL/L</b>	<b>µmoL/L</b>	<b>g/L</b>	<b>g/L</b>
<b>0mg/kg</b>	0005	4.05	4.42	0.61	60.	4.32	UDL	49.6	29.5
<b>5mg/kg BAY</b>	0006	4.99	5.53	0.72	56.	3.88	UDL	55.3	36.5
<b>20mg/kg BAY</b>	0007	5.13	4.35	0.93	47.	4.62	UDL	49.9	30.9
<b>80mg/kg BAY</b>	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 |**

		GLUCOSE	CHOL	TRIGL	CREA	UREA	Bili-t	Protein	Albumin
Animal#		mmoL/L	mmoL/L	mmoL/L	µmoL/L	mmoL/L	µmoL/L	g/L	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

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## Clinical Pathology Individual Values

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## Blood Electrolytes

September 14, 2017 11:21

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

		Na-ISE	K-ISE	CL-ISE	Ca	P	Mg
		mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	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

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## Blood Electrolytes

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

		Na-ISE	K-ISE	CL-ISE	Ca	P	Mg
		mmol/L	mmol/L	mmol/L	mmol/L	mmol/L	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

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**Electrophoresis of Proteins**

September 14, 2017 11:21

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

		ALBUMIN	TA GLOB	TB GLOB	TG GLOB	A/G
Animal#		%	%	%	%	
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

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**Electrophoresis of Proteins**

September 14, 2017 11:21

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

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		ALBUMIN	TA GLOB	TB GLOB	TG GLOB	A/G
Animal#		%	%	%	%	
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

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**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: 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

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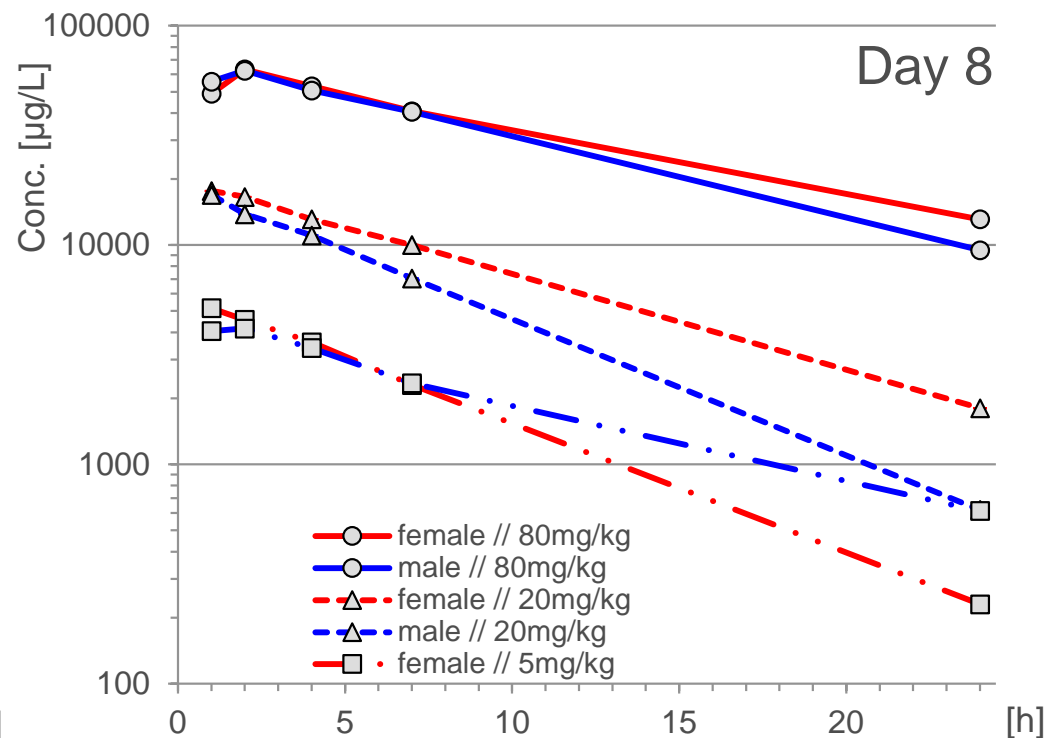
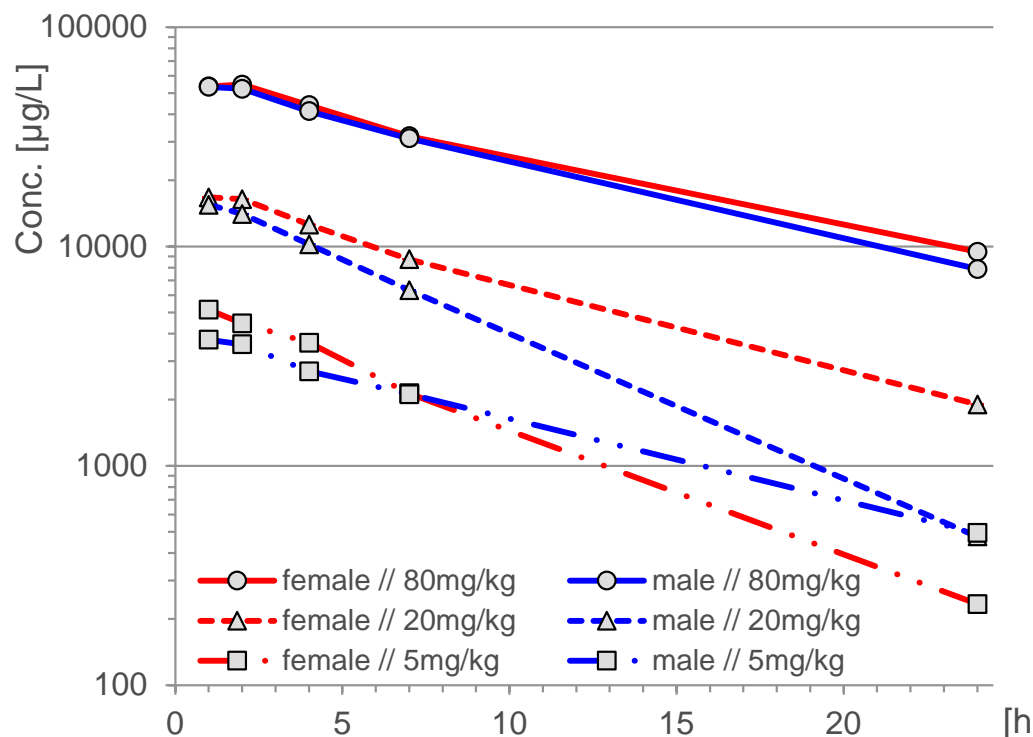
**Abbreviation(s) :**

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	Dose Admin	[mg/kg]	female								male							
			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(0-24) <sub>norm</sub>	[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**

<b>Animals</b>	«
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
<b>Study dates</b>	«
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 of [Appendix - 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**

<b>Abbreviation</b>	<b>Explanation</b>	<b>Method</b>	<b>Dimension</b>
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**

<b>Abbreviation</b>	<b>Explanation</b>	<b>Method</b>	<b>Dimension</b>
ECG	Electrocardiogram	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**

Abbreviation	Explanation	Method	Dimension
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	Thrombocytes	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**

Abbreviation	Explanation	Method	Dimension
FIBR	Fibrinogen	Mechanical measurement with reagent Triniclot Fibrinogen (claus method) by means of Destiny Max automatic analyzer, Stago	g/L
PTT	Activated partial thromboplastin 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**

<b>Abbreviation</b>	<b>Explanation</b>	<b>Method</b>	<b>Dimension</b>
LEUCO	Leucocytes	Cytochem. peroxidase reaction, Advia 2120i, Siemens AG	G/L
LYM	Lymphocytes		
NEUTRO	Neutrophils		
EOS	Eosinophils		
MONO	Monocytes		
LUC	Large unstained cells		
BASO-phils	Basophils	Cytochem. stripping reaction and flow cytometric light, scattering method, Advia 2120i, Siemens AG	G/L

**Table 1–7: Hematology**

<b>Abbreviation</b>	<b>Explanation</b>	<b>Method</b>	<b>Dimension</b>
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 unstained cells		
LI	Lubularity index	Calculated value: LI = polymorphnuclear cells/mononuclear cells	---

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

Abbreviation	Explanation	Method	Dimension		Transformation factor (F) [old * F = SI]
			actual	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
SI	Système international d'unités				

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

Abbreviation	Explanation	Method	Dimension		Transformation factor (F) [old * F = SI]
			actual	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
SI	Système international d'unités				

**Table 1–10: Blood Electrolytes**

Abbreviation	Explanation	Method	Dimension		Transformation factor (F) [old * F = SI]
			actual	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
SI	Système international d'unités				

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

Abbreviation	Explanation	Method	Dimension
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]
<b>1. Major nutrients and minerals</b>		<b>2. Vitamins</b>	
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
		Inositol	100 mg
<b>3. Essential amino acids</b>		<b>4. Trace elements</b>	
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		