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BASF DocID: 2017/1078223

STUDY TITLE

Report

BAS 850 H

Repeated-dose 28-day oral toxicity study in C57BL/6 J Rj mice
Administration via the diet

TEST GUIDELINE(S)

OECD 407
Commission Regulation (EC) No 440/2008
US EPA OPPTS 870.3050

AUTHOR(S)

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E. Grauert
Prof. Dr. B. van Ravenzwaay

STUDY COMPLETED ON

03 Jan 2018

TEST FACILITY

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

TEST FACILITY PROJECT IDENTIFICATION

Project No. 31C0343/09S078

SPONSOR

BASF SE
67056 Ludwigshafen, Germany

SPONSOR IDENTIFICATION NUMBER

AP study ID 405222

PART I OF III (REPORT SECTION AND SUMMARY TABLES)

The following statement is for US EPA submissions only:

STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality, on any basis whatsoever, is made for any information contained in this document. I acknowledge that information not designated as within the scope of FIFRA sec.10(d)(1)(A), (B) or (C) and which pertains to a registered or previous registered pesticide is not entitled to confidential treatment and may be released to the public, subject to the provisions regarding disclosure to multinational entities under FIFRA 10(g).

Submitter: ..... Date: .....

Typed Name of Signer:

Typed Name of Company: BASF Corporation, Agricultural Products
P.O. Box 13528
Research Triangle Park, NC 27709-3528

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with the OECD Principles of Good Laboratory Practice and the GLP Principles of the German "Chemikaliengesetz" (Chemicals Act) which meet the United States Environmental Protection Agency Good Laboratory Practice Standards [40 CFR Part 160 (FIFRA) and Part 792 (TSCA)], with the exception that recognized differences exist between the GLP Principles/Standards of OECD and the Principles/Standards of FIFRA and TSCA.

Study Director: ..... Date: 03 Jan 2018

Typed name of Study Director: R. Buesen, Ph.D.

Typed name of Laboratory: BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen
Germany

To be filled for USA EPA submission only:

Sponsor: ..... Date: .....

Typed Name of Sponsor:

Typed Name of Company:

Submitter: ..... Date: .....

Typed Name of Submitter:

Typed Name of Company:

The following statement is for US EPA submissions only:

FLAGGING CRITERIA

I have applied the criteria of 40 CFR 158.34/40 CFR 161.34 for flagging studies for potential adverse effects to the results of the attached study. This study neither meets nor exceeds any of the applicable criteria.

Submitter: ..... Date: .....

Typed Name of Signer:

Typed Name of Company: BASF Corporation, Agricultural Products
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SIGNATURE PAGE

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R. Buesen, Ph.D.

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Pathology: ..... 02. Jan. 2018
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for: E. Grauert

Test Facility Management: ..... 03 Jan. 2018
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Central Food Mixing Laboratory:	K. Hummel

STATEMENT OF THE QUALITY ASSURANCE UNIT

The Quality Assurance Unit (QAU) inspected the study and reported any inspection results to the Study Director and to Test Facility Management.

The final report reflects the raw data.

Phase of study:	Date of inspection (mm-dd-yyyy)	Reported to Study Director and to Test Facility Management (mm-dd-yyyy)
Study Plan:	08-22-2011	08-22-2011
Conduct of study:	09-13-2011 09-21-2011	09-13-2011 09-21-2011
Report:	09-07-2017 12-04-2017	09-07-2017 12-04-2017

Ludwigshafen, 03 Jan. 2018

ABT

M.ABT

GLP CERTIFICATE (FROM THE COMPETENT AUTHORITY)

RheinlandPfalz
LANDESAMT FÜR UMWELT

GUTE LABORPRAXIS – GOOD LABORATORY PRACTICE

GLP-BESCHEINIGUNG
STATEMENT OF GLP COMPLIANCE

gemäß/according to § 19b Abs. 1 Chemikaliengesetz

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at:

Prüfeinrichtung / Test facility

BASF SE
Experimentelle Toxikologie und Ökologie
67056 Ludwigshafen

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

Prüfung nach Kategorien / Areas of Expertise
(gemäß / according ChemVwV-GLP Nr. 5.3/OECD guidance)
1,2,3,4,5,8,9
Kat. 9 – Biochemische und pathologische Untersuchungen zu Wirkmechanismen / Biochemical and pathological examinations concerning mode of action

Datum der Inspektion / Date of Inspection
(Tag.Monat.Jahr / day.month.year)
12. bis 14.09.2016

Die genannte Prüfeinrichtung befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können.

Eine erneute behördliche Überprüfung der Einhaltung der GLP-Grundsätze durch die Prüfeinrichtung ist spätestens drei Jahre nach der letzten Inspektion zu beantragen. Ohne diesen Antrag wird die Prüfeinrichtung nach Ablauf der Frist aus dem deutschen GLP-Überwachungsprogramm genommen und diese GLP-Bescheinigung verliert ihre Gültigkeit.

The above mentioned test facility is included in the national GLP Compliance Programme and is inspected on a regular basis.

Based on the inspection report it can be con- firmed, that the test facility is able to conduct the aforementioned studies in compliance with the Principles of GLP.

Verification of the compliance of the test facility with the Principles of the GLP has to be applied for not later than three years after the last inspection. Elapsing this term, the test facility will be taken out of the German GLP-Monitoring Programme and this GLP Certificate becomes invalid.

Unterschrift, Datum / Signature, Date

21.03.17

Dr.-Ing. Stefan Hill - Präsident -
(Name und Funktion der verantwortlichen Person / name and function of responsible person)

Landesamt für Umwelt, Wasserwirtschaft und Gewerbeaufsicht
Kaiser-Friedrich-Straße 7, 55116 Mainz
(Name und Adresse der GLP-Überwachungsbehörde / Name and adress of the GLP Monitoring Authority)

MESSEN
BEWERTEN
BERATEN

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CONTENTS OF PART I (REPORT SECTION AND SUMMARY TABLES)

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THIS REPORT CONSISTS OF PART I, II AND III.

1. SUMMARY

1.1. METHODS

BAS 850 H was administered via the diet to groups consisting of 5 male and 5 female C57BL/6 J Rj mice at concentrations of 0 (test group 0), 100 (test group 1), 500 (test group 2), 1000 (test group 3) and 1500 ppm (test group 4) over a period of 28 days.

1.2. OBSERVATIONS

Food consumption, water consumption and body weight were determined weekly. The animals were examined for signs of toxicity or mortality at least once a day. Moreover, detailed clinical examinations in an open field were conducted prior to the start of the administration period and weekly thereafter.
Clinicochemical and hematological examinations were performed towards the end of the administration period. After the administration period, all animals were sacrificed and assessed by gross pathology. Organ weights were determined followed by histopathological examinations.

1.3. RESULTS

1.3.1. Analytics

The various analyses confirmed

- the stability of the test-substance preparations for a period of 34 days at room temperature,
- the homogeneous distribution of the test substance in the vehicle,
- the correctness of the prepared concentrations.

1.3.2. Findings

The following test substance-related, adverse findings were noted:

Test group 4: 1500 ppm
(224 mg/kg bw/d in males and 261 mg/kg bw/d in females)

Clinical Examinations
- Apathy was observed in 2 female animals between study days 6 to 12.
- High stepping gait in 1 male animal (study days 21 to 29) and in 3 female animals (starting on study day 7 until sacrifice)
- In one female animal, hunched posture (study days 6 to 13) and semi-closed eyelids (study days 10 to 13) were observed.
- Poor general condition was observed in 3 female animals (starting on study day 6 until study day 20 in two animals and from study day 7 until study day 13 in one animal).
- Food and water consumption were reduced in male and female animals over the entire administration period.
- Body weight loss was observed in male animals on study days 14 and 28 as well as in female animals on study day 7. Significantly lower mean body weights were observed for male animals from study day 14 onwards (about -13% at the end of the administration period) and for female animals between study day 7 and 21 (with a maximum deviation of about -10% to the control on study day 7). Significantly lower body weight change values were observed for male animals from study day 14 onwards and for female animals during the entire study period.

Clinical Pathology
- Decreased red blood cell counts, hematocrit and hemoglobin values in male animals
- Increased alanine aminotransferase activities in male animals
- Decreased total protein and albumin levels in both sexes
- Increased triglyceride levels in both sexes
- Increased inorganic phosphate levels in male animals
- Increased globulin levels in females

Pathology
- Lower terminal body weight in male (significantly, -10%) and female animals (not significantly, -7%)
- Increased absolute and relative liver weights in male and female animals
- Randomly distributed coagulative necrosis of hepatocytes and multinucleated hepatocytes in male animals
- Diffuse hepatocellular hypertrophy in male and female animals
- Centrilobular fatty change in male and female animals
- Reduced amount of secretory product in seminal vesicles accompanied by decreased organ weights
- Advanced involution of X-zone in adrenal glands of female animals
- Interstitial gland hyperplasia/hypertrophy in ovaries
- Diffuse atrophy of the uterus

- Epithelial hypertrophy with mucification of the vagina

Test group 3: 1000 ppm
(149 mg/kg bw/d in males and 194 mg/kg bw/d in females)

Clinical Examinations and Clinical Pathology
- No treatment-related, adverse effects were observed.

Pathology
- Increased liver weights in male and female animals
- Centrilobular hepatocellular hypertrophy accompanied by centrilobular fatty change in female animals
- Advanced involution of X-zone in adrenal glands of female animals

Test group 2: 500 ppm
(79 mg/kg bw/d in males and 96 mg/kg bw/d in females)

Clinical Examinations and Clinical Pathology
- No treatment-related, adverse effects were observed.

Pathology
- Advanced involution of X-zone in adrenal glands of female animals

Test group 1: 100 ppm
(15 mg/kg bw/d in males and 22 mg/kg bw/d in females)

Clinical Examinations, Clinical Pathology and Pathology
- No treatment-related, adverse effects were observed.

1.4. CONCLUSION

The oral administration of BAS 850 H via the diet to male and female C57BL/6 J Ri mice over a period of 4 weeks caused test substance-related adverse signs of systemic toxicity at a concentration of 1000 ppm in male (about 149 mg/kg bw/d) and of 500 ppm and above in female (about 96 mg/kg bw/d) C57BL/6 J Ri mice.
Therefore, under the conditions of the present study, the no observed adverse effect level (NOAEL) was 500 ppm in male (about 79 mg/kg bw/d) and 100 ppm (about 22 mg/kg bw/d) in female C57BL/6 J Ri mice.

2. INTRODUCTION

2.1. OBJECTIVES

The aim of the study was to assess the toxicological profile of BAS 850 H including the target organs and the “no observed adverse effect level” (NOAEL) after 4-week administration via the diet to male and female C57BL/6 J Ri mice.

2.2. SELECTION OF DOSES/ CONCENTRATIONS

At the request of the sponsor, the following concentrations in the diet were selected for the present study:

1500 ppm	as high concentration
1000 ppm	as mid concentrations
500 ppm	
100 ppm	as low concentration

The oral route was selected since this was proven to be suitable for the detection of a toxicological hazard.

2.3. TEST GUIDELINES

The study was conducted according to the following test guidelines:

- Commission Regulation (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), Part B.7.: Repeated Dose (28 Days) Toxicity (Oral); Official Journal of the European Union, No. L 142.
- OECD Guidelines for Testing of Chemicals; Method No. 407: Repeated Dose 28-day Oral Toxicity Study in Rodents; adopted 03 Oct 2008
- U.S. EPA Health Effects Test Guidelines. OPPTS 870.3050; Jul 2000

2.4. STUDY DATES

In the following table, the relevant intervals for certain study phases are given:

Dates	Phase of study/ Examination	Study day
23 Jul 2011	Study initiation date: signature of study director	
17 Aug 2011	Experimental starting date: arrival of the animals and start of the acclimatization period	-6
22 Aug 2011	Randomization of the animals	-1
23 Aug 2011	Start of the administration period	0
20 Sep 2011	Last weighing	28
21 Sep 2011	Blood sampling and necropsy [a)]	29
14 Aug 2017	Experimental completion date; draft report to QAU	

a) = Fasting period (withdrawal of food) of about 16 to 20 hours before blood sampling and necropsy

2.5. RETENTION OF RECORDS

GLP-relevant records and materials are archived at BASF SE for at least the period of time specified in the GLP principles. Details concerning responsibilities or locations of archiving can be seen from the respective SOPs as well as from the raw data.

2.6. ANIMAL WELFARE

This study was performed in an AAALAC-approved laboratory in accordance with the German Animal Welfare Act and the effective European Council Directive.

3. MATERIAL AND METHODS

3.1. TEST ITEM

The analyses of the test item (= test substance) was carried out at the Crop Protection - Ecology and Environmental Analytics of BASF SE, Speyerer Straße 2, 67117 Limburgerhof, Germany.

Name of test substance:	BAS 850 H
CAS No.	1258836-72-4
Test substance No.:	09/0343-9
Batch No.:	COD-001484
Purity:	99.3% (tolerance ± 1.0%; study code 386120_4)
Homogeneity:	Given (study code 386120_4)
Stability:	Stable until 01 Jul 2013 (study code 415835_2) The stability of the test substance under storage conditions over the test period was guaranteed by the sponsor, and the sponsor holds this responsibility. The test facility is organizationally independent from the BASF SE sponsor division.

ADDITIONAL TEST SUBSTANCE INFORMATION

Synonym:	Reg.No. 5654329
Physical state/ color:	Solid/ beige
Storage conditions:	Ambient (room temperature)

3.2. TEST SYSTEM

Species:	Mouse
Strain:	C57BL/6 J Rj
Supplier:	Raison sociale: JANVIER LABS Route des Chenês Secs – C.S. 4105 Le Genest-St-Isle F-53941 ST Berthevin Cedex
Sex:	Males and females
Age when supplied:	42 ± 1 days
Age at the start of administration period:	48 ± 1 days
Reason for the selection:	The mouse is a frequently used laboratory animal, and there is comprehensive experience with this animal species. Moreover, the mouse has been proposed as a suitable animal species by the OECD and the EPA.
Animal identification:	Ear tattoo (animal number)

3.3. HOUSING AND DIET

The animals were housed together (5 animals per cage) in polycarbonate cages type M III (floor area about 800 cm^2). Both with mesh wire tops, supplied by BECKER & Co., Castrop–Rauxel, Germany. Dust-free wooden bedding was used in this study (the present supplier is documented in the raw data). Nest building material Nestlets NES 3600 (PLEXX b.v.; Elst, The Netherlands) were added for enrichment. The mice were accommodated in fully air-conditioned rooms in which central air conditioning guaranteed a range of temperature of 20-24 °C, a range of relative humidity of 30-70% and 15 air changes per hour. The day/night cycle was 12 hours (12 hours light from 06.00 h-18.00 h, 12 hours dark from 18.00 h-06.00 h). There were no or only minimal deviations from these limits.
The animal room was completely disinfected prior to the study using a disinfector ("AUTEX", fully automatic, formalin-ammonia-based terminal disinfector). The floor and the walls were cleaned once a week with water containing an appropriate disinfectant.
The food used was ground Kliba maintenance diet mouse/rat “GLP” meal, supplied by Provimi Kliba SA, Kaiseraugst, Switzerland. Food and drinking water (from water bottles) were available ad libitum.

3.4. TEST GROUPS AND DOSES/ CONCENTRATIONS

Males

Test group	Concentration (ppm)	No. of animals	Animal No.	Cage No.
0	0	5	1 – 5	1
1	100	5	6 – 10	2
2	500	5	11 – 15	3
3	1000	5	16 – 20	4
4	1500	5	21 – 25	5

Females

Test group	Concentration (ppm)	No. of animals	Animal No.	Cage No.
0	0	5	26 – 30	6
1	100	5	31 – 35	7
2	500	5	36 – 40	8
3	1000	5	41 – 45	9
4	1500	5	46 – 50	10

3.5. TEST SUBSTANCE PREPARATIONS AND PREPARATION FREQUENCY

For each concentration, the test substance was weighted out and mixed with a small amount of food. In order to obtain the desired concentrations, these premixes were added to the corresponding amounts of food, depending on test group. Mixing was carried out for about 10 minutes in a laboratory mixer. Details to the used mixers and to the mixing procedure are retained with the raw data.

3.6. ANALYSES

3.6.1. Analyses of the test-substance preparations

The analyses of the test-substance preparations were carried out at the Analytical Chemistry Laboratory of Experimental Toxicology and Ecology of BASF SE as a part of this study. The study was carried out in compliance with the Principles of Good Laboratory Practice.

Homogeneity was verified in 3 samples in the highest and lowest concentration (was used as concentration control at the same time) at the beginning of the study; additional concentration control analyses were done in the mid concentration. The samples were taken from the specific food containers by staff of the Central Food Mixing unit (see PART III, Supplement).

The stability of the test substance in the diet at room temperature for a period up to 34 days was demonstrated before the start of the administration period (see PART III, Supplement, project No. 01Y0343/09Y049).

3.6.2. Analytical methods

The methods used for analytical investigations of the test-substance preparations and plasma kinetics can be found in PART III (Supplement).

3.6.3. Food analyses

The supplier assayed the food used in the study for chemical and microbiological contaminants.

3.6.4. Drinking water analyses

The drinking water is regularly assayed for chemical contaminants by the municipal authorities of Frankenthal and by the Environmental Analytics Water/Steam Monitoring Department of BASF SE as well as for the presence of microorganisms by a contract laboratory.

3.6.5. Bedding and enrichment analyses

The bedding and the enrichment are regularly assayed for contaminants (chlorinated hydrocarbons and heavy metals).

3.7. EXPERIMENTAL PROCEDURE

Starting on day of arrival the animals were accustomed to the environmental conditions of the study for an adaptation period during which they received ground diet and drinking water ad libitum. Prior to the first detailed clinical observation, the animals were distributed according to weight among the individual test groups, separated by sex. The weight variation of the animals used did not exceed 20 percent of the mean weight of each sex. The list of randomization instructions was compiled with a computer.
The test substance was administered daily for 28 days. Control animals received only the vehicle. All remaining animals were sacrificed after a fasting period (withdrawal of food) of at least 16 hours.

3.8. CLINICAL EXAMINATIONS

3.8.1. Mortality

A check for moribund and dead animals was made twice daily on working days and once daily on Saturdays, Sundays and public holidays. If animals were in a moribund state, they were sacrificed and necropsied.

3.8.2. Clinical observations

All animals were checked daily for any clinically abnormal signs. Abnormalities and changes were documented for each animal.

3.8.3. Detailed clinical observations

Detailed clinical observations (DCO) were performed in all animals prior to the administration period and thereafter at weekly intervals. The findings were ranked according to the degree of severity, if applicable. The animals were transferred to a standard arena (50 × 37.5 cm with sides of 25 cm high). The following parameters were examined:

1. Abnormal behavior during “handling”
2. Fur
3. Skin
4. Posture
5. Salivation
6. Respiration
7. Activity/ arousal level
8. Tremors
9. Convulsions
10. Abnormal movements

11. Impairment of gait
12. Lacrimation
13. Palpebral closure
14. Exophthalmus
15. Assessment of the feces discharged during the examination (appearance/ consistency)
16. Assessment of the urine discharged during the examination
17. Pupil size

3.8.4. Food consumption

Food consumption was determined weekly and calculated as mean food consumption in grams per animal and day.

3.8.5. Water consumption

Drinking water consumption was determined on study days 7, 14, 21 and 28 and calculated as mean water consumption in grams per mouse and day.

3.8.6. Body weight data

Body weights were determined before the start of the administration period to randomize the animals. During the administration period, the body weights were determined on study day 0 (start of administration period) and thereafter at weekly intervals.
The difference between the body weight on the respective day of weighing and the body weight on study day 0 was calculated as body weight change.

3.8.7. Intake of test substance

The mean daily intake of test substance (group means) was calculated based upon individual values for body weight and mean food consumption per cage.

$$\frac{FC_x \times C}{BW_x} = \text{test substance intake for study day x}$$

BW_x = body weight on study day x [g]
FC_x = mean daily food consumption on study day x [g]
C = concentration in the diet on study day x [mg/kg]

3.8.8. Statistics of clinical examinations

Means and standard deviations of each test group were calculated for several parameters (see tables). Further statistical analyses were performed according to following table:

Parameters	Statistical test	Markers in the tables	References
Body weight, body weight change	A comparison of each group with the control group was performed using DUNNETT's test (two-sided) for the hypothesis of equal means.	* for $p \leq 0.05$ ** for $p \leq 0.01$	DUNNETT, C.W. (1955): A multiple comparison procedure for comparing several treatments with a control. JASA, Vol. 50, 1096-1121 DUNNETT, C.W. (1964). New tables for multiple comparisons with a control. Biometrics, Vol. 20, 482-491

3.9. CLINICAL PATHOLOGY

In the morning blood was taken from the retro-bulbar venous plexus (for hematology) or after decapitation (for clinical chemistry) from fasted animals. The animals were anaesthetized using isoflurane (Isoba®, Essex GmbH, Munich, Germany). The blood sampling procedure and subsequent analysis of blood and serum samples were carried out in a randomized sequence. The assays of blood and serum parameters were performed under internal laboratory quality control conditions with reference controls to assure reliable test results.
The results of clinical pathology examinations were expressed in International System (SI) units.
The following examinations were carried out in 5 animals per test group and sex.

3.9.1. Hematology

The following parameters were determined in blood with EDTA-K_3 as anticoagulant using a particle counter (Advia 120 model; Bayer, Fernwald, Germany):

Parameters and methods:

Parameter	Unit	Method	References
Leukocyte count (WBC)	giga/L	cytochemistry coupled with flow cytometry	Operator's Guide for Advia 120 System
Erythrocyte count (RBC)	tera/L	flow cytometric laserlight scattering	
Hemoglobin (HGB)	mmol/L	cyanmethemoglobin method; according to ICSH	
Hematocrit (HCT)	L/L	calculation: MCV x erythrocytes	
Mean corpuscular volume (MCV)	fL	RBC/PLT method; mean of RBC volume distribution curve (histogram)	
Mean corpuscular hemoglobin (MCH)	fmol	calculation: $\frac{\text{hemoglobin}}{\text{erythrocytes}}$	
Mean corpuscular hemoglobin concentration (MCHC)	mmol/L	calculation: $\frac{\text{hemoglobin}}{\text{hematocrit}}$	
Platelet count (PLT)	giga/L	flow cytometric laserlight scattering	
Differential blood count	% and giga/L	cytochemistry coupled with flow cytometry	
Reticulocytes	%	cytochemistry coupled with flow cytometry	

Furthermore, blood smears were prepared and stained according to WRIGHT without being evaluated, because of non-ambiguous results of the differential blood cell counts measured by the automated instrument. (reference: Hematology: Principles and Procedures, 6th Edition, Brown AB, Lea & Febiger, Philadelphia, 1993, page 101). Only evaluated blood smears were archived.

3.9.2. Clinical chemistry

An automatic analyzer (Hitachi 917; Roche, Mannheim, Germany) was used to examine the clinicochemical parameters.

Parameters and methods:

Enzyme (systematic name and system number)	**Unit**	**Method, wave-length and measuring temperature**	**References**
Alanine aminotransferase (ALT) (L-alanine: 2-oxoglutarate aminotransferase; EC 2.6.1.2.)	µkat/L	kinetic UV test, 340 nm; 37°C	Recommendations of the German Society for Clinical Chemistry: "Standardization of methods for determining enzyme activities in biological liquids". J. Clin. Chem. Clin. Biochem. 8, 658-660 (1970); J. Clin. Chem. Clin. Biochem. 9, 464-465 (1971); J. Clin. Chem. Clin. Biochem. 10, 182-192 (1972) Roche working instructions
Aspartate aminotransferase (AST) (L-aspartate: 2-oxoglutarate aminotransferase; EC 2.6.1.1.)	µkat/L	kinetic UV test, 340 nm; 37°C	
Alkaline phosphatase (ALP) (orthophosphoric acid monoester phosphohydrolase; EC 3.1.3.1.)	µkat/L	kinetic color test, 415 nm, 37°C	
γ-Glutamyltransferase (GGT) (γ -glutamyl) peptide: aminoacid-γ-glutamyl-transferase; EC 2.3.2.2.)	nkat/L	kinetic color test, 415 nm, 37°C	Szasz, G. et al., J. Clin. Chem. Clin. Biochem. 12, 228 (1974) Roche working instructions

Blood Chemistry Parameter	Unit	Method	References
Sodium (NA)	mmol/L	ion selective electrodes (ISE)	Hitachi 917 - working instructions
Potassium (K)	mmol/L		
Chloride (CL)	mmol/L		
Inorganic phosphate (INP)	mmol/L	molybdate reaction	Henry, R.J. in: "Clinical Chemistry", Harper and Row Publishers, New York (1974); Roche working instructions
Calcium (CA)	mmol/L	o-cresolphthalein complex without deproteinization	Ray Sarkar, B.C. and Chauhan, U.P.S., Anal. Biochem. 20, 155 (1967); Roche working instructions
Urea (UREA)	mmol/L	enzymatic determination with the urease/ glutamate dehydro-genase method	Neumann, U. and Ziegenhorn, J.: XVI, Nordiska kongressen for klinisk kemi och klinisk fysiologi 1977, Oulu, Finland; Roche working instructions
Creatinine (CREA)	µmol/L	kinetic Jaffé method without deproteinization	Bartels, H. et al., Clin. Chim. Acta 37, 193 (1972); Roche working instructions
Glucose (GLUC)	mmol/L	hexokinase/glucose-6-phosphate dehydrogenase method	Schmidt, F.H., Klin. Wschr. 39, 1244-1247 (1961); Roche working instructions
Total bilirubin (TBIL)	µmol/L	DPD method	Wahlefeld, A.W. et al., Scand. J. Clin. Lab. Invest. 29, Suppl. 126 (1972) Abstract 11.12; Roche working instructions
Total protein (TPROT)	g/L	biuret method	Weichselbaum, T.E., Amer. J. Clin. Path. 10, 40 (1946); Roche working instructions
Albumin (ALB)	g/L	bromocresol green method	Doumas et al., Clin. Chim. Acta 31, 87 (1971); Roche working instructions
Globulins (GLOB)	g/L	difference between total protein and albumin	
Triglycerides (TRIG)	mmol/L	enzymatic color test with lipase esterase/ glycerokinase/ glycerol-3-phosphate oxidase/4-amino-phenazone	mod. method by Wahlefeld, A.W., in "Methoden der enzymatischen Analyse" [Methods of enzymatic analysis] (Bergmeyer, H.U., ed.) Vol. II, 3rd ed., Verlag Chemie Weinheim, GERMANY, pp. 1878-1882 (1974); Roche working instructions
Cholesterol (CHOL)	mmol/L	enzymatic determination with cholesterol esterase/ cholesterol oxidase/4-amino-phenazone (CHOD-PAP method)	Siedel, J. et al., J. Clin. Chem. Clin. Biochem. 19, 838 (1981); Roche working instructions
Magnesium (MG)	mmol/L	xylidylblue method	Mann, C.K. and Yoe, J.H., Anal. Chem. 28, 202-205 (1956) Bohnon, C., Clin. Chim. Acta 7, 811-817 (1962)
Bile acids (TBA)	µmol/L	enzymatic colorimetric determination with 3α-hydroxy-steroid dehydrogenase and NAD	Agape, V. et al., Minerva Dietol Gastroenterol, 35, 159 – 164 (1989); Randox working instruction

3.9.3. Statistics of clinical pathology

Means, medians and standard deviations of each test group were calculated for several parameters (see tables).

Further statistical analyses were performed according to following tables:

Parameter	Statistical test	Markers in the tables	References
Clinical pathology parameters	Non-parametric one-way analysis using KRUSKAL-WALLIS test (two-sided). If the resulting p-value was equal or less than 0.05, a pairwise comparison of each dose group with the control group was performed using Wilcoxon-test (two-sided) for the equal medians.	* for $p \leq 0.05$ ** for $p \leq 0.01$	SIEGEL, S. (1956): Non-parametric statistics for the behavioural sciences. McGraw-Hill New York

3.10. PATHOLOGY

3.10.1. Necropsy

The animals were sacrificed by decapitation under isoflurane anesthesia. The exsanguinated animals were necropsied and assessed by gross pathology.

3.10.2. Organ weights

The following weights were determined in all animals sacrificed on schedule:

1. Anesthetized animals
2. Adrenal glands
3. Brain
4. Epididymides
5. Heart
6. Kidneys
7. Liver
8. Ovaries
9. Prostate
10. Seminal vesicles with coagulating glands
11. Spleen
12. Testes
13. Thymus
14. Uterus with cervix

3.10.3. Organ/tissue fixation

The following organs or tissues were fixed in 4% formaldehyde solution or in modified Davidson's solution:

1. All gross lesions
2. Adrenal glands
3. Aorta
4. Bone marrow (femur)
5. Brain
6. Cecum
7. Cervix
8. Coagulating glands
9. Colon
10. Duodenum
11. Epididymides (modified Davidson's solution)
12. Esophagus
13. Extraorbital lacrimal glands

14. Eyes with optic nerve (modified Davidson’s solution)
15. Femur with knee joint
16. Gall bladder
17. Harderian glands
18. Heart
19. Ileum
20. Jejunum (with Peyer’s patches)
21. Kidneys
22. Larynx
23. Liver
24. Lung
25. Lymph nodes (mesenteric and axillary lymph nodes)
26. Mammary gland (male and female)
27. Nose (nasal cavity)
28. Ovaries
29. Oviducts
30. Pancreas
31. Parathyroid glands
32. Pharynx
33. Pituitary gland
34. Prostate
35. Rectum
36. Salivary glands (mandibular and sublingual glands)
37. Sciatic nerve
38. Seminal vesicles
39. Skeletal muscle
40. Skin
41. Spinal cord (cervical, thoracic and lumbar cord)
42. Spleen
43. Sternum with marrow
44. Stomach (forestomach and glandular stomach)
45. Testes (modified Davidson’s solution)
46. Thymus
47. Thyroid glands
48. Trachea
49. Urinary bladder
50. Uterus
51. Vagina

From the liver, each one slice of the Lobus dexter medialis and of the Lobus sinister lateralis was fixed in Carnoy’s solution and embedded in paraplast.

3.10.4. Histopathology

Fixation was followed by histotechnical processing, examination by light microscopy and assessment of findings according to the table below:

Organs	Test group				
	0	1	2	3	4
1. All gross lesions	A2	A2	A2	A2	A2
2. Adrenal glands	A1	A3	A3	A3	A1
3. Bone marrow (femur)	A1				A1
4. Brain	A1				A1
5. Cecum	A1				A1
6. Cervix	A1	A3	A3	A3	A1
7. Coagulating glands	A1				A1
8. Colon	A1				A1
9. Duodenum	A1				A1
10. Epididymides	A1				A1
11. Eyes with optic nerve	A1				A1
12. Heart	A1				A1
13. Ileum	A1				A1
14. Jejunum	A1				A1
15. Kidneys	A1	A1	A1	A1	A1
16. Liver	A1	A1	A1	A1	A1
17. Lung	A1				A1
18. Lymph nodes (mesenteric and axillary lymph nodes)	A1				A1
19. Ovaries	A1	A3	A3	A3	A1
20. Peyer's patches	A1				A1
21. Pituitary gland	A1				A1
22. Prostate	A1				A1
23. Rectum	A1				A1
24. Sciatic nerve	A1				A1
25. Seminal vesicles	A1	A4	A4	A4	A1
26. Skeletal muscle	A1				A1
27. Spinal cord (cervical, thoracic and lumbar cord)	A1				A1
28. Spleen	A1	A3	A3	A3	A1
29. Sternum with marrow	A1				A1

Organs	Test group				
	0	1	2	3	4
30. Stomach (forestomach and glandular stomach)	A1				A1
31. Testes	A1				A1
32. Thymus	A1	A4	A4	A4	A1
33. Thyroid glands	A1				A1
34. Trachea	A1				A1
35. Urinary bladder	A1				A1
36. Uterus	A1	A3	A3	A3	A1
37. Vagina	A1	A3	A3	A3	A1

A = Hematoxylin-eosin stain
1 = All animals/test group
2 = All animals affected/test group
3 = All female animals/test group
4 = All male animals/test group

The immunorelevant organs and tissues were evaluated according to the following parameters:

Thymus:
- Increased/decreased grade of cortico-medullar ratio (related only to area)
- Increase of starry sky cells
- Changes of cellular density in the cortex
- Changes of cellular density in the medulla

Spleen:
- Changes of the cellularity of PALS (periarteriolar lymphoid sheath), lymphoid follicles, marginal zone, red pulp
- Altered cellular composition of follicles
- Altered number of germinal centers

Lymph nodes (mesenteric and axillary lymph nodes):
- Changes in the cellularity of follicles, interfollicular area, paracortical area, medulla
- Altered cellular composition of paracortex
- Altered number of germinal centers
- Hyperplasia of high endothelial venules

Peyer's patches (of the jejunum):
- Changes of the cellularity of follicles (including mantle zone and germinal centers)
- Changes of the cellularity of interfollicular area

Bone marrow:
- Changes of the cellularity
- Changes of the myeloid/erythroid ratio

Whenever the histopathologic evaluation of the immunorelevant organs and tissues did not reveal a morphologic alteration of these items and/or whenever no other pathologic finding was noted, these organs were diagnosed as "no abnormalities detected".

Special attention was given for the synchrony of the morphology of the estrous cycle in ovaries, uterus, cervix, and vagina.

A correlation between gross lesions and histopathological findings was attempted.

3.10.5. Statistics of pathology

Means and standard deviations were calculated. In addition, the following statistical analyses were carried out:

Parameter	Statistical test	Markers in the tables	References
Weight parameters	Non-parametric one-way analysis using KRUSKAL-WALLIS test (two-sided). If the resulting p-value was equal or less than 0.05, a pairwise comparison of each dose group with the control group was performed using WILCOXON-test (two-sided) for the equal medians.	* for $p \leq 0.05$ ** for $p \leq 0.01$	HETTMANNSPERGER, T.P. (1984): Statistical Inference based on Ranks, John Wiley & Sons New York, 132-140. International Mathematical and Statistical Libraries, Inc., 2500 Park West Tower One, Houston, Texas 77042-3020, USA, nakl-1 - nakl-3 MILLER, R.G. (1981): Simultaneous Statistical Inference, Springer-Verlag New York Inc., 165-167 NIJENHUIS, A. and S.W. WILF (1978): Combinatorial Algorithms, Academic Press, New York, 32-33

4. RESULTS

Throughout the chapter "results", the term "significant" implies that the inter-group differences have attained *statistical* significance ($p \leq 0.05$) when compared with the control group.

4.1. ANALYSES

4.1.1. Stability analyses

The stability of the test substance in the diet at room temperature over a period of up to 34 days was proven before the start of the administration period (BASF project No.: 01Y0343/09Y049; PART III, Supplement).

4.1.2. Homogeneity control analyses

Considering the low relative standard deviation in the homogeneity analysis, it can be concluded that BAS 850 H was distributed homogeneously in ground Kliba maintenance diet mouse/rat “GLP” meal.

4.1.3. Concentration control analyses

The determined mean values and single values of BAS 850 H in ground Kliba maintenance diet mouse/rat “GLP” meal were found to be in the range of 93.7-104.0% of the nominal concentrations. These results demonstrated the correctness of the concentrations of BAS 850 H in ground Kliba maintenance diet mouse/rat “GLP” meal (see PART III, Supplement).

4.1.4. Food analyses

On the basis of duration of use and the analytical findings with respect to chemical and microbiological contaminants the diet was found to be suitable. Fed. Reg. Vol. 44, No. 91 of 09 May 1979, p. 27354 (EPA), served as a guideline for maximum tolerable chemical contaminants. The number of microorganisms did not exceed 1×10^5/g food. Individual results can be found in the archives of the Experimental Toxicology and Ecology of BASF SE.

4.1.5. Drinking water analyses

On the basis of the analytical findings the drinking water was found to be suitable. German “Trinkwasserverordnung” (Drinking Water Regulation) served as a guideline for maximum tolerable contaminants. Individual results can be found in the archives of the Experimental Toxicology and Ecology of BASF SE.

4.1.6. Bedding and enrichment analyses

On the basis of the analytical findings the bedding and the enrichment were found to be suitable. Levels given in Lab. Animal, Nov-Dec 1979, pp. 24-34, served as a guideline for maximum tolerable contaminants. Individual results are to be found in the archives of the Experimental Toxicology and Ecology of BASF SE.

4.2. CLINICAL EXAMINATIONS

Summary tables of the results are given in the Appendix of PART I; individual values are given in Part A of PART II.

4.2.1. Mortality

(Tables IA 1 – IA 2)

No animal died prematurely in the present study.

4.2.2. Clinical observations

(Tables IA 1 – IA 2)

No treatment-related findings were observed in male and female animals of test groups 1 to 3 (100, 500 and 1000 ppm).

In test group 4 (1500 ppm), male animal No. 24 showed high-stepping gait from study day 21 until sacrifice. No other treatment-related findings were observed in male animals of this test group.
Female animal Nos. 46 and 47 showed apathy from study day 6 until study day 12. Poor general condition was observed in animal Nos. 46 and 47 from study day 6 until study day 20 as well as in female animal No. 48 from study day 7 until study day 13. High stepping gait was observed in animal Nos. 46 and 48 from study day 7 onwards as well as in female animal No. 47 from study day 10 onwards. In addition, female animal No. 46 showed hunched posture from study day 6 until study day 13 and semi-closed eyelids from study day 10 until study day 13. No other treatment-related findings were observed in female animals of this test group.

4.2.3. Food consumption

(Tables IA 3 – IA 4)

No treatment-related findings were observed in male and female animals of test groups 1 to 3 (100, 500 and 1000 ppm).

Food consumption was reduced in male and in female animals of test group 4 (1500 ppm) over the entire study period with a maximum of -16% in male animals on study day 28 and of -25 % in female animals on study day 7. In male animals of test group 3 (1000 ppm) food consumption was reduced between study days 0 and 7 by -14%. However, no deviations to the control values occurred during the rest of the treatment period. Thus, this deviation was regarded to be incidental.

4.2.4. Water consumption

(Tables IA 5 – IA 6)

No treatment-related findings were observed in male and female animals of test groups 1 to 3 (100, 500 and 1000 ppm).

Water consumption was reduced in male and in female animals of test group 4 (1500 ppm) over the entire study period with a maximum by -33% in male animals on study day 28 and of -47% in female animals on study day 7.

4.2.5. Body weight data

(Tables IA 7 – IA 10; figures 4.2.5.1. and 4.2.5.2.)

No relevant changes in mean body weight or in body weight change values were observed in male and female animals of test groups 1 to 3 (100 ppm, 500 ppm and 1000 ppm) over the entire administration period.

In test group 4 (1500 ppm), body weight loss was observed in male animals on study days 14 and 28 and in female animals on study day 7. Mean body weights were significantly decreased in male animals from study day 14 onwards with a maximum of -13% on study day 28. In female animals mean body weights were significantly decreased from study day 7 until study day 21 with a maximum of -10% on study day 7.
Body weight change values were significantly lower in male animals from study day 14 onwards with a maximum of -123% on study day 14. In female animals, body weight change values were significantly decreased during the entire study period with a maximum of -153% on study day 7.

Figure 4.2.5.1.: Mean body weights of male animals

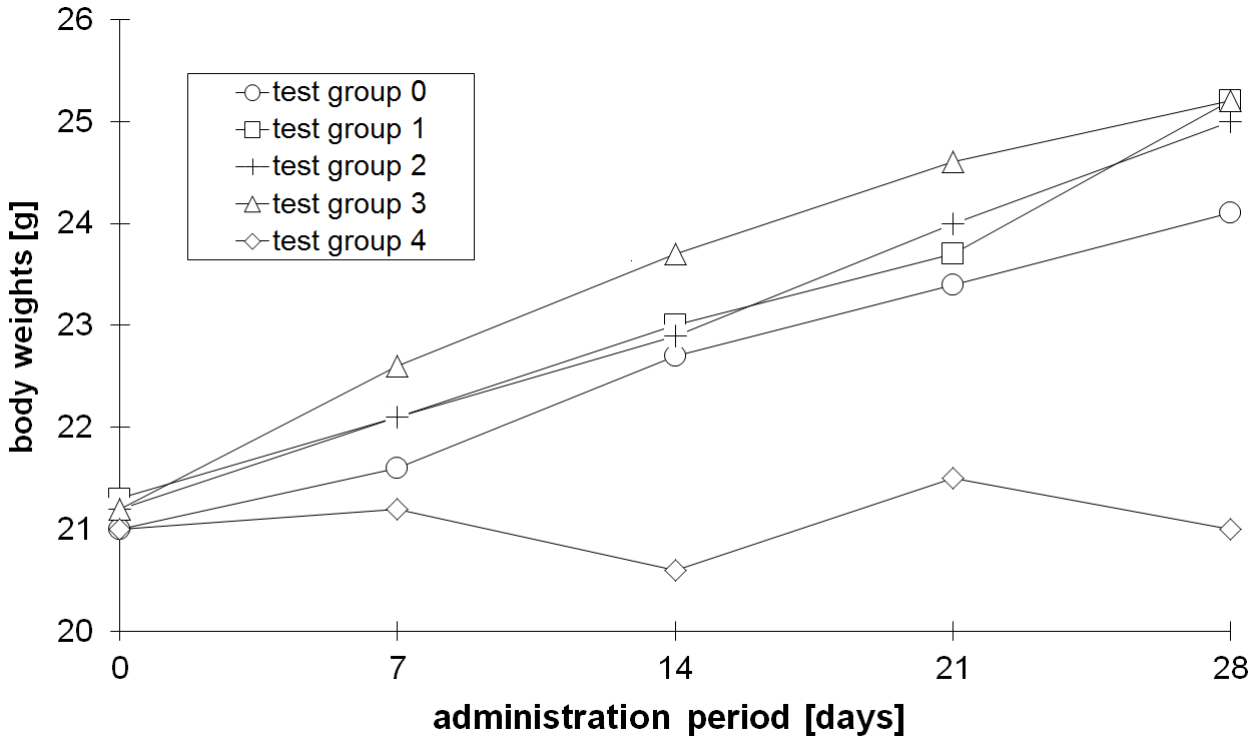
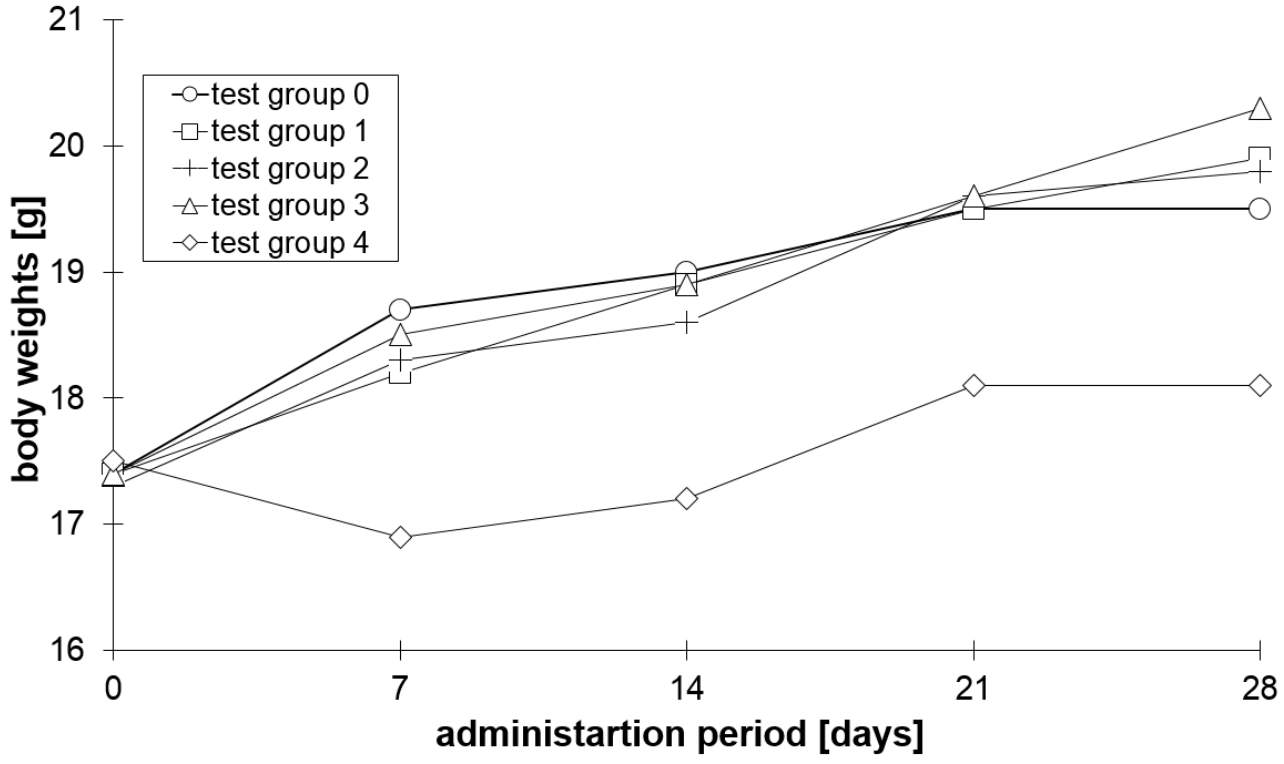


Figure 4.2.5.2.: Mean body weights of female animals



4.2.6. Intake of test substance

(Tables IA 11 - IA 12)

The mean daily test substance intake in mg/kg body weight/day (mg/kg bw/d) over the entire study period was calculated and is shown in the following table:

Test group	Concentration in the diet (ppm)	Mean daily test-substance intake (mg/kg bw/d)	
		Males	Females
1	100	15	22
2	500	79	96
3	1000	149	194
4	1500	224	261

4.3. CLINICAL PATHOLOGY

Summary tables of the results are given in the Appendix of PART I; individual values are given in Part B of PART II.

4.3.1. Hematology

(Tables IB 1 – IB 2 Red blood cell parameters)
(Tables IB 3 – IB 4 White blood cell parameters)

At the end of the study, in males of test group 4 (1500 ppm) red blood cell (RBC) counts, hemoglobin as well as hematocrit values were decreased, the two latter parameters not statistically significant.
In females of test group 4 (1500 ppm) the calculated red blood cell parameter mean corpuscular volume (MCV) was lower compared to controls. In these animals, no measured red blood cell parameter (RBC, hematocrit, hemoglobin) was changed. Therefore, the decrease of MCV was regarded as incidental and not treatment-related.

In males of test group 2 (500 ppm) relative lymphocyte counts were increased and in females of test group 1 (100 ppm) relative lymphocyte counts were higher and relative neutrophil counts were lower compared to controls. All these parameters were not changed dose-dependently and, therefore, the changes were regarded as incidental and not treatment-related.

4.3.2. Clinical chemistry

(Tables IB 5 – IB 6 Enzymes)
(Tables IB 7 – IB 8 Substrates)
(Tables IB 9 – IB 10 Electrolytes + minerals)

After 4 weeks of administration, in males of test groups 1 and 3 (100 and 1000 ppm) alanine aminotransferase (ALT) activities were decreased, but in males of test group 4 (1500 ppm) the values were increased. The ALT decrease was not dose-dependent and, therefore, it was regarded as incidental and not treatment-related. In contrast, the ALT increase in males of test group 4 was regarded as adverse.

In males of test group 4 (1500 ppm) total protein and albumin levels were decreased and triglyceride and inorganic phosphate levels were increased. In females of the same test group total protein (not statistically significant) and albumin levels were lower, but globulin and triglyceride (not statistically significant) levels were higher compared to controls.

In males of test group 1 (100 ppm) chloride levels were lower and calcium levels were higher compared to control. These values were not changed dose-dependently and, therefore, these alterations were regarded as incidental and not treatment-related.

4.4. PATHOLOGY

Summary tables of the results can be found in the Part C of PART I; individual tables can be found in Part C of PART II. Abbreviations and histopathological grading used in pathology report and tables can be found in the appendix.

4.4.1. Weight parameters

(Tables IC-1 – IC-8)

Absolute weights

When compared to control group 0 (set to 100%), the mean absolute weights of following organs were significantly increased or decreased (printed in bold):

	Male animals				Female animals			
Test group (ppm)	1 (100)	2 (500)	3 (1000)	4 (1500)	1 (100)	2 (500)	3 (1000)	4 (1500)
Terminal body weight	105%	103%	**106%***	**90%***	100%	100%	102%	93%
Liver	98%	**111%****	**129%****	115%	94%	103%	**122%****	**126%****
Seminal vesicles	102%	110%	108%	**60%***				
Spleen					103%	98%	103%	**69%***
Thymus	**125%***	**118%***	121%	68%				

*: p ≤ 0.05; **: p ≤ 0.01

All other mean absolute weight parameters did not show significant differences when compared to the control group 0.

Relative organ weights

When compared to control group 0 (set to 100%), the mean relative weights of following organs were significantly increased or decreased (printed in bold):

	Male animals				Female animals			
Test group (ppm)	1 (100)	2 (500)	3 (1000)	4 (1500)	1 (100)	2 (500)	3 (1000)	4 (1500)
Liver	**93%***	**107%****	**122%****	**127%****	93%	103%	**120%****	**135%****
Brain	95%	98%	**94%***	107%				
Kidneys	**93%***	99%	97%	109%				
Seminal vesicles	97%	107%	102%	**65%***				
Spleen					102%	98%	101%	**75%***
Thymus	**119%***	115%	115%	74%				

*: p ≤ 0.05; **: p ≤ 0.01

All other mean relative weight parameters did not show significant differences when compared to the control group 0.

The decreased terminal body weights of male (significantly, -10%) and female animals (not significantly, -7%) of test group 4 (1500 ppm) were considered to be related to treatment.

Increased absolute liver weights in male animals of test groups 2 and 3 (significant) as well as test group 4 (not significant) and in female animals of test groups 3 and 4, and significantly

increased relative liver weights in male animals of test groups 2 to 4 and in female animals of test groups 3 and 4 were regarded as treatment-related.
The significantly decreased relative liver weight in group 1 (100 ppm) males was considered not to be treatment-related and was regarded as an incidental finding.

The significantly decreased absolute and relative weights of seminal vesicles in test group 4 (1500 ppm) males were considered to be treatment-related.

The significantly decreased absolute and relative weights of spleens in female animals of test group 4 (1500 ppm) were regarded as a secondary effect due to the decreased terminal body weight. There were no histopathological findings which would explain the decreased organ weights.

The significantly increased absolute (test groups 1 and 2; 100, 500 ppm) and relative (test group 1; 100 ppm) thymus weights in male animals were also interpreted to be incidental in origin, since there were no correlating histopathological findings, there was no dose-response relationship. In addition, the weight changes in test groups 1 and 2 (100 and 500 ppm) were within the range of historical control data (see PART III, Supplement).

The significantly decreased relative brain weight in test group 3 males (1000 ppm) was related to the slightly, but significantly increased terminal body weight in these animals.

The significantly decreased relative weight of kidneys in test group 1 (100 ppm) males was considered to be incidental, since there was neither a dose-response relationship nor a correlating histopathological finding.

4.4.2. Gross lesions
(Table IC-9)

Macroscopically observed findings occurred only singly. They were considered to be incidental.

4.4.3. Histopathology
(Tables IC-10 – IC-14)

Liver
The liver of male animals in test group 4 (1500 ppm) showed a randomly distributed coagulative necrosis of hepatocytes and increased numbers of multinucleated hepatocytes. Additionally, either a minimal (grade 1) to mild (grade 2) centrilobular hypertrophy was observed in males test groups 1-3 (100, 500, 1000 ppm) and in females of test group 3 or a minimal to mild diffuse hypertrophy was observed in males and females of test group 4.

The livers of male animals in test groups 1 to 4 (100, 500, 1000 and 1500 ppm) and of female animals in test groups 2 to 4 (500, 1000, 1500 ppm) showed a reduction of small, clear, sharply

demarcated cytoplasmic vacuoles, which probably represented lipid droplets. In contrast, male animals of test group 4 and female animals of test groups 3 and 4 showed a minimal (grade 1) to moderate (grade 3) cytoplasmic macrovesicular vacuolar changes of zone 3 hepatocytes. These vacuoles were as well sharply demarcated and of clear appearance and were, therefore, interpreted to be a fatty change. Detailed data are shown in the table below:

Liver	**Male animals**				**Female animals**			
Test group (ppm)	1 (100)	2 (500)	3 (1000)	4 (1500)	1 (100)	2 (500)	3 (1000)	4 (1500)
No. of animals	5	5	5	5	5	5	5	5
Necrosis, coag., randomly				2				
• Grade 1				1				
• Grade 3				1				
Multinucl. Hepatocytes, increased				3				
• Grade 1				2				
• Grade 2				1				
Hypertrophy, centrilobular	2	1	5				5	
• Grade 1	2	1	1				4	
• Grade 2			4				1	
Hypertrophy, diffuse				5				5
• Grade 1								3
• Grade 2				5				2
Vacuolar change reduced	2	1	4	4		3	3	5
• Grade 1	2	1	1	2		3	1	4
• Grade 2			3	2			2	1
Vacuolar change, macrovesicular, centrilobular				2			4	5
• Grade 1				2			4	
• Grade 2								3
• Grade 3								2

The increased numbers of multinucleated hepatocytes in male animals of test group 4 (1500 ppm), the centrilobular and diffuse hypertrophy of hepatocytes in male animals of groups 1 to 4 (100, 500, 1000 and 1500 ppm) and female animals of test groups 3 and 4, the reduced vacuolar change in male animals of test groups 1 to 4 and female animals of test groups 2 to 4, and the macrovesicular vacuolar change of centrilobular hepatocytes in test group 4 males and test groups 3 and 4 females were regarded to be treatment-related.
The randomly distributed coagulative necrosis of hepatocytes in 2 of 5 males in test group 4 was as well considered to be treatment-related, although a clear association to a specific hepatic zone was not observed.

Kidneys
Kidneys of male animals of test groups 2 to 4 (500, 1000 and 1500 ppm) and of female animals of test groups 1 to 4 (100, 500, 1000 and 1500 ppm) showed a minimally (grade 1) to mildly (grade 2) increased cytoplasmic vacuolation of proximal tubular epithelial cells. Detailed data are shown in the table below:

Kidneys	Male animals					Female animals				
Test group (ppm)	0 (0)	1 (100)	2 (500)	3 (1000)	4 (1500)	0 (0)	1 (100)	2 (500)	3 (1000)	4 (1500)
No. of animals	5	5	5	5	5	5	5	5	5	5
Vacuolation increased	1	0	2	1	5	1	1	1	2	5
• Grade 1	1		2	1	1	1	1	1	2	2
• Grade 2					4					3

The occurrence of more cytoplasmic vacuoles in proximal tubular epithelial cells in male and female animals of test group 4 was considered to be treatment-related.
Since the increase in cytoplasmic vacuoles in males of test groups 2 and 3 and in females of test groups 1 to 3 was only minimal, there were only 1 or 2 animals affected and one male and one female animal of the control group (0 ppm) also showed an increased vacuolation of proximal tubular epithelial cells, the findings in animals of test groups 1 to 3 were regarded as spontaneous and not treatment-related.

Seminal vesicles
Seminal vesicles in 2 of 5 male animals of test group 4 (1500 ppm) showed a minimally (grade 1) to moderately (grade 3) reduced amount of secretory product (see table below).

Seminal vesicles	Male animals			
Test group (ppm)	1 (100)	2 (500)	3 (1000)	4 (1500)
No. of animals	5	5	5	5
Reduced content				2
• Grade 1				1
• Grade 3				1

The reduced amount of secretory product in seminal vesicles was considered to be treatment-related.

Adrenal glands
Adrenal glands of female animals of test groups 2 to 4 (500, 1000 and 1500 ppm) showed an advanced involution of the X-zone in comparison to control animals. The X-zone is located at the junction of the cortex and medulla, is unique to the mouse and appears a few days after birth. In female animals, it reaches a maximum at about 9 weeks and regresses gradually in virgins.
The advanced involution was characterized by an extensive reduction in width or a complete loss of the X-zone, whereas all control animals still showed a marked X-zone. Detailed data are shown in the table below:

Adrenal glands	Female animals			
Test group (ppm)	1 (100)	2 (500)	3 (1000)	4 (1500)
No. of animals	5	5	5	5
Advanced involution X-zone		1	3	4
• Grade 1		1	2	2
• Grade 2			1	2

The advanced involution of the X-zone in adrenal glands was considered to be treatment-related.

Female reproductive organs (ovaries, uterus, vagina)

The ovaries of group 4 (1500 ppm) females showed a minimal (grade 1) to moderate (grade 3) hyperplasia and hypertrophy of interstitial cells that was characterized by an increased size and amount of interstitial stromal cells with large amounts of a finely vacuolated cytoplasm.
The uterus of 2 females in test group 4 (1500 ppm) was minimally to moderately atrophic which was characterized by a reduced overall size and a densely-packed stroma with thinned smooth muscle layers.
The vagina of 2 females in test group 4 (1500 ppm) showed a moderate epithelial hypertrophy with mucification. In both animals affected, it was not possible to determine the exact stage. The vaginal epithelium showed 4 to 6 layers. Epithelial cells of the upper layers were of increased size and showed large, intracytoplasmic, mucus-filled vacuoles. The epithelial surface was covered by a secretory product composed of mucus admixed with neutrophils and sloughed cornified keratinocytes.
Details of incidence and severity of all lesions are shown in the tables below.

	Female animals			
Test group (ppm)	1 (100)	2 (500)	3 (1000)	4 (1500)
No. of animals	5	5	5	5
Ovaries: Hyperplasia/hypertrophy interstitial cells				4
• Grade 1				1
• Grade 2				2
• Grade 3				1
Uterus: Atrophy, diffuse				2
• Grade 1				1
• Grade 3				1
Vagina: Epithelial hypertrophy with mucification				2
• Grade 3				2

The interstitial cell hyperplasia and hypertrophy in ovaries, the diffuse atrophy in the uterus and the epithelial hypertrophy with mucification in the vagina were considered to be treatment-related.

Spleen
Female animals of all treatment groups showed an extramedullary hematopoiesis in the spleen, which was mainly characterized by the presence of erythropoietic precursor cells. The incidence and severity of extramedullary erythropoiesis was minimally decreased in group 4 (1500 ppm) animals, but since there was no dose-response-relationship, this finding was regarded not to be treatment-related.

Spleen	**Female animals**				
Test group (ppm)	0 (0)	1 (100)	2 (500)	3 (1000)	4 (1500)
No. of animals	5	5	5	5	5
Hematopoiesis extramedullar	4	4	5	5	3
• Grade 1	1	2	1		3
• Grade 2	2	1	3	4	
• Grade 3	1	1	1	1	

Thymus
The thymus of 2 of 5 male animals and 1 of 5 female animals of test group 4 (1500 ppm) showed a diffuse atrophy. Thymic atrophy in male animals was considered to be related to the significantly decreased body weight in these animals and not directly related to the test substance administration. Also, there were no corresponding significant weight changes. The thymic atrophy in one female animal of test group 4 was considered to be incidental.

All other findings occurred either individually or were biologically equally distributed over the control group and the treatment groups. They were considered to be incidental or spontaneous in origin and without any relation to treatment.
In the **nervous system**, there were no histopathological findings which could explain the observed neurotoxicity in high-dose animals.

5. DISCUSSION

BAS 850 H was administered via the diet to groups consisting of 5 male and 5 female C57BL/6 J Rj mice at concentrations of 0 (test group 0), 100 (test group 1), 500 (test group 2), 1000 (test group 3) and 1500 ppm (test group 4) over a period of 4 weeks.

Regarding clinical examinations, the oral administration of BAS 850 H via the diet caused signs of general systemic toxicity in male and female C57BL/6 J Rj mice of test groups 04 (1500 ppm). Clinical observations, decreased food and water consumptions the temporarily observed body weight loss were indication for the toxic potential of the test substance.
No clinical changes were observed for male and female animals of test groups 1-3 (100, 500 and 1000 ppm).

Regarding clinical pathology, in males of test group 4 (1500 ppm) decreased red blood cell parameters, i.e. RBC, hematocrit and hemoglobin, indicated an anemia. Higher ALT activities in these animals were due to a slight liver cell membrane degradation, and decreased total protein and albumin values were most probably the consequence of a dysregulation of the liver cell metabolism. Females of the same test group seemed to be less sensitive. In these mice, total protein and albumin levels were decreased, but globulin and triglyceride concentrations were increased.

Regarding pathology, target organs were liver and kidneys in male and female animals. Additional target organs in males included the seminal vesicles, and in female animals, the ovaries, uterus, vagina and adrenal glands.

Livers of test group 4 males (1500 ppm) showed increased amounts of multinucleated hepatocytes. The increased numbers of multinucleated hepatocytes were indicative of hepatocellular hyperplasia and therefore, regarded to be treatment-related and adverse.
Additionally, the livers in male animals of groups 1 to 4 (100, 500, 1000 and 1500 ppm) and female animals of test groups 3 and 4 showed a minimal centrilobular or diffuse hypertrophy. Histopathological findings correlated with increased liver weights in males of test groups 2 to 4 and in females of test groups 3 and 4.
According to Maronpot et al. (2010), hepatic effects which are considered adverse include histological evidence of fatty change and hepatocellular degeneration and necrosis, as well as abnormal clinical chemistry parameters.
Hepatocellular hypertrophy accompanied by abnormal clinical chemistry parameters and a fatty change of zone 3 hepatocytes in males of test group 4 (1500 ppm) and hepatocellular hypertrophy accompanied by fatty change of zone 3 hepatocytes in females of test groups 3 and 4 (1000 and 1500 ppm) were considered to be adverse. The increased liver weights in males of test group 3, which were accompanied by a minimal to slight centrilobular hypertrophy were regarded as treatment-related and adverse, due to the considerable weight increase (+29% absolute, +22% relative). Findings in male animals of test groups 1 and 2 (100, 500 ppm) were considered to be adaptive.
Furthermore, in livers of 2 of 5 males in test group 4 (1500 ppm), a randomly distributed coagulative necrosis of hepatocytes was observed. Although a clear association to a specific hepatic zone was not observed, this finding was assumed to be treatment-related and adverse.

The minimally to mildly reduced vacuolar change in males of test groups 1 to 4 (100, 500, 1000 and 1500 ppm) and in females of test groups 2 to 4 (500, 1000 and 1500 ppm) was regarded to be treatment-related but non-adverse.

Kidneys of male and female animals of test group 4 (1500 ppm) showed a minimal to mild increase in cytoplasmic vacuolation of proximal tubular epithelial cells in comparison to control animals. This finding was considered to be treatment-related but non-adverse.

Seminal vesicles of test group 4 (1500 ppm) males showed a reduced amount of secretory product that correlated to decreased absolute and relative weights. The decreased filling of seminal vesicles was considered to be treatment-related and adverse.

For the **adrenal glands**, the finding of advanced involution of the X-zone in female mice of test groups 2 to 4 (500, 1000 and 1500 ppm) was regarded to be a treatment-related and adverse effect.

Female animals of test group 4 (1500 ppm) showed a hyperplasia/hypertrophy of interstitial stromal cells in **ovaries**, a diffuse atrophy of the **uterus** and an epithelial hypertrophy with mucification in the **vagina**. Hyperplasia/hypertrophy of interstitial cells in ovaries might be a first sign of ovarian atrophy (OECD, 2009).
Findings in ovaries, uteri and vagina were indicative of a dysregulation of the estrus cycle. Therefore, they were interpreted as treatment-related, adverse effects.

6. CONCLUSION

The oral administration of BAS 850 H via the diet to male and female C57BL/6 J Ri mice over a period of 4 weeks caused test substance-related adverse signs of systemic toxicity at a concentration of 1000 ppm in male (about 149 mg/kg bw/d) and of 500 ppm and above in female (about 96 mg/kg bw/d) C57BL/6 J Ri mice.
Therefore, under the conditions of the present study, the no observed adverse effect level (NOAEL) was 500 ppm in male (about 79 mg/kg bw/d) and 100 ppm (about 22 mg/kg bw/d) in female C57BL/6 J Ri mice.

7. REFERENCES

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8. APPENDIX

The following list contains abbreviations and definitions generally used in reports for this study type. This report will not necessarily use all expressions listed below.

8.1. LIST OF ABBREVIATIONS USED IN TABLES CLINICAL EXAMINATIONS

%	=	percent
%dev	=	deviation in percent
Animal No.	=	animal number
anm	=	animal
AT	=	after treatment
BT	=	before treatment
Bw or bw	=	body weight
cm	=	centimeter
Control	=	control animals
d	=	day
DCO	=	detailed clinical observation
Deviation Vs Control	=	deviation versus control in percent
F	=	female animals
FST	=	landing foot-splay test
g	=	weight in gram
GS F	=	grip strength forelimbs
GS H	=	grip strength hindlimbs
h	=	hour
Interr.	=	beam Interrupts
Interv.	=	Interval
kg or KG	=	kilogram
M	=	male animals or mean value
mg/kg bw/d	=	milligrams per kilogram bodyweight per day
mg or MG	=	milligram
min.	=	minute
N	=	number of animals for determining M and SD
NaCl	=	sodium chloride
NAD	=	nothing abnormal detected
NM	=	not measured
ppm	=	parts per million
Rear	=	rearing
S.d. or SD	=	standard deviation
Vs	=	versus

8.2. LIST OF ABBREVIATIONS USED IN TABLES CLINICAL PATHOLOGY

CLINICAL PATHOLOGY:

S.d.	=	standard deviation
N	=	number of values

HEMATOLOGY:

RBC	=	red blood cells (erythrocytes)
HGB	=	hemoglobin
HCT	=	hematocrit
MCV	=	mean corpuscular volume
MCH	=	mean corpuscular hemoglobin
MCHC	=	mean corpuscular hemoglobin concentration
RET	=	reticulocytes
PLT	=	platelets
HQT	=	prothrombin time (Hepato Quick's test)
PTT	=	activated partial thromboplastin time
QT	=	prothrombin time (Quick's test)
WBC	=	white blood cells (leukocytes)
NEUTA	=	polymorphonuclear neutrophils (absolute)
LYMPHA	=	lymphocytes (absolute)
MONOA	=	monocytes (absolute)
EOSA	=	eosinophils (absolute)
BASOA	=	basophils (absolute)
LUCA	=	large unstained cells (absolute)
NEUT	=	polymorphonuclear neutrophils
LYMPH	=	lymphocytes
MONO	=	monocytes
EOS	=	eosinophils
BASO	=	basophils
LUC	=	large unstained cells

CLINICAL CHEMISTRY:

ALT	=	alanine aminotransferase
AST	=	aspartate aminotransferase
ALP	=	alkaline phosphatase
GGT_C	=	serum-γ-glutamyltransferase
UREA	=	urea
CREA	=	creatinine
GLUC	=	glucose
TBIL	=	total bilirubin

TBA	=	bile acids
TPROT	=	total protein
ALB	=	albumin
GLOB	=	globulins
TRIG	=	triglycerides
CHOL	=	cholesterol
NA	=	sodium
K	=	potassium
CL	=	chloride
INP	=	inorganic phosphate
CA	=	calcium

UNITS:

mmol/L	=	millimole/liter
µmol/L	=	micromole/liter
nmol/L	=	nanomole/liter
g/L	=	gram/liter
L/L	=	liter/liter
%	=	per cent
fmol	=	femtomole = 10^{-15} mole
fL	=	femtoliter = 10^{-15} liter
tera/L	=	tera/liter = 10^{12}/liter
giga/L	=	giga/liter = 10^{9} /liter
µkat/L	=	microkatal/liter
nkat/L	=	nanokatal/liter
PPM	=	parts per million
mg/kg	=	mg/kilogram
mL	=	milliliter
Mio/g	=	millions/gram

8.3. LIST OF ABBREVIATIONS USED IN TABLES PATHOLOGY

AI	=	Apoptotic index
A.-no.	=	animal number
BrdU	=	2'bromo-5-deoxyuridine
dev	=	deviation
exam	=	examined
F	=	female animals
F1	=	final sacrifice group
g	=	weight determination in grams
I1, I2 …	=	satellite groups; animals selected for perfusion fixation in neurotoxicology studies
l	=	left
LI	=	Labeling index
M	=	male animals (under sex); mean value (on weight level)
mg	=	weight determination in milligrams
mg/m³	=	milligram per cubic meter
mg/kg bw/day	=	milligram per kilogram body weight and day
ml	=	milliliter
n	=	number of values measured for the determination of mean value and standard deviation
ppm	=	parts per million
r	=	right
R1, R2 …	=	recovery groups
s	=	suspect weight (not included in the mean values)
SD	=	standard deviation
TUNEL	=	Terminal deoxynucleotidyl transferase-mediated dUTP nick end-labelling
u	=	unilaterally weighed
u/a	=	not measureable

%	=	percentage related to the reference weight in relative organ weight calculations
.	=	for incidences of gross lesions: no gross finding in that organ for incidences of microscopic findings: • on organ level: not examined • on finding level: no such finding observed

Codes for the status at necropsy:

1 (P)	=	planned sacrifice
2 (K)	=	killed moribund
3 (S)	=	spontaneous death

Codes used at finding level:

The codes are used for a grading system that takes into consideration either the severity or the number or the size of a microscopic finding.

	Severity	**Number**	**Size**
Grade 1	Minimal	Very few	Very small
Grade 2	Slight, mild	Few	Small
Grade 3	Moderate	Moderate number	Moderate size
Grade 4	Marked; severe	Many	Large
Grade 5	Massive; extreme	Extensive number	Extensive size

Whenever a grading was not used, the microscopic finding was indicated to be present (P).

IA 1
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Study 31C0343/09S078

Summary - Clinical Observation

Sex: **Male** - Phase: **In-life**

			0/M	1/M	2/M	3/M	4/M
day 0 [DCO] -> day 29 [00:00 - 24:00]	Animals examined	N	5	5	5	5	5
	Animals with signs	N	0	0	0	0	1
		%	0.0	0.0	0.0	0.0	20.0
	dead	N	5	5	5	5	5
	sacrificed scheduled	%	100.0	100.0	100.0	100.0	100.0
	normal	N	5	5	5	5	5
	NAD	%	100.0	100.0	100.0	100.0	100.0
	gait	N	0	0	0	0	1
	high-stepping gait	%	0.0	0.0	0.0	0.0	20.0

IA 2
08-Aug-2017 11:17
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Study 31C0343/09S078

Summary - Clinical Observation

Sex: **Female** - Phase: **In-life**

			0/F	1/F	2/F	3/F	4/F
day 0 [DCO] -> day 29 [00:00 - 24:00]	Animals examined	N	5	5	5	5	5
	Animals with signs	N	0	0	0	0	3
		%	0.0	0.0	0.0	0.0	60.0
	dead	N	5	5	5	5	5
	sacrificed scheduled	%	100.0	100.0	100.0	100.0	100.0
	activity/ behavior	N	0	0	0	0	2
	apathy	%	0.0	0.0	0.0	0.0	40.0
	posture	N	0	0	0	0	1
	hunched posture	%	0.0	0.0	0.0	0.0	20.0
	general condition	N	0	0	0	0	3
	poor	%	0.0	0.0	0.0	0.0	60.0
	normal	N	5	5	5	5	5
	NAD	%	100.0	100.0	100.0	100.0	100.0
	gait	N	0	0	0	0	3
	high-stepping gait	%	0.0	0.0	0.0	0.0	60.0
	eye	N	0	0	0	0	1
	semiclosed eyelid	%	0.0	0.0	0.0	0.0	20.0

IA 3
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Study 31C0343/09S078

Summary Food Consumption Per Animal And Day

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
d 0 -> 7	Mean [g]	3.5	3.4	3.5	3.0	3.2
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		-2.9	0.0	-14.3	-8.6
d 7 -> 14	Mean [g]	3.5	3.4	3.6	3.7	3.0
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		-2.9	2.9	5.7	-14.3
d 14 -> 21	Mean [g]	3.6	3.4	3.5	3.6	3.3
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		-5.6	-2.8	0.0	-8.3
d 21 -> 28	Mean [g]	3.7	3.5	3.9	3.7	3.1
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		-5.4	5.4	0.0	-16.2

d = day

IA 4
08-Aug-2017 13:45
ToxData© System 3.0

Study 31C0343/09S078

Summary Food Consumption Per Animal And Day

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
d 0 -> 7	Mean [g]	3.6	3.9	3.3	3.4	2.7
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		8.3	-8.3	-5.6	-25.0
d 7 -> 14	Mean [g]	3.8	4.1	3.6	3.6	3.2
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		7.9	-5.3	-5.3	-15.8
d 14 -> 21	Mean [g]	3.8		3.6	3.8	3.0
	S.d.					
	N	1	0	1	1	1
	Deviation Vs Control			-5.3	0.0	-21.1
d 21 -> 28	Mean [g]	4.1	4.5	3.9	4.0	3.3
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		9.8	-4.9	-2.4	-19.5

d = day

IA 5
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Study 31C0343/09S078

Summary Water Consumption Per Animal And Day

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
d 3 -> 7	Mean [g]	3.1	2.9	3.1	3.2	2.3
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		-6.5	0.0	3.2	-25.8
d 10 -> 14	Mean [g]	3.1	3.2	3.2	3.1	2.2
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		3.2	3.2	0.0	-29.0
d 17 -> 21	Mean [g]	3.3	3.2	3.1	2.9	2.3
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		-3.0	-6.1	-12.1	-30.3
d 24 -> 28	Mean [g]	3.3	3.3	3.4	3.0	2.2
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		0.0	3.0	-9.1	-33.3

d = day

IA 6
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Study 31C0343/09S078

Summary Water Consumption Per Animal And Day

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
d 3 -> 7	Mean [g]	3.4	3.2	3.4	3.3	1.8
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		-5.9	0.0	-2.9	-47.1
d 10 -> 14	Mean [g]	3.5	3.3	3.5	3.3	2.0
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		-5.7	0.0	-5.7	-42.9
d 17 -> 21	Mean [g]	3.4	3.7	3.7	3.4	2.2
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		8.8	8.8	0.0	-35.3
d 24 -> 28	Mean [g]	3.5	3.9	3.6	3.4	2.4
	S.d.					
	N	1	1	1	1	1
	Deviation Vs Control		11.4	2.9	-2.9	-31.4

d = day

IA 7
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Study 31C0343/09S078

Summary Body Weights - BW / Body Weights [g]

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
day 0	Mean	21.0 n	21.3	21.2	21.2	21.0
	S.d.	0.7	0.9	0.9	0.4	0.6
	N	5	5	5	5	5
	Deviation Vs Control		1.7	1.3	1.0	0.2
day 7	Mean	21.6 n	22.1	22.1	22.6	21.2
	S.d.	0.7	1.0	0.9	0.6	1.0
	N	5	5	5	5	5
	Deviation Vs Control		2.2	2.4	4.5	-1.9
day 14	Mean	22.7 n	23.0	22.9	23.7	20.6 **
	S.d.	0.9	1.1	1.1	0.7	0.8
	N	5	5	5	5	5
	Deviation Vs Control		1.5	1.1	4.6	-9.2
day 21	Mean	23.4 n	23.7	24.0	24.6	21.5 *
	S.d.	1.2	1.5	1.0	0.7	1.0
	N	5	5	5	5	5
	Deviation Vs Control		1.2	2.3	5.1	-8.4
day 28	Mean	24.1 n	25.2	25.0	25.2	21.0 **
	S.d.	1.0	1.5	1.3	1.1	1.5
	N	5	5	5	5	5
	Deviation Vs Control		4.5	3.6	4.6	-12.8

Statistic Profile = Dunnett test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
n=DUNNETT

Study 31C0343/09S078

Summary Body Weights - BW / Body Weights [g]

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
day 0	Mean	17.4 n	17.4	17.3	17.4	17.5
	S.d.	0.4	0.8	0.6	0.6	0.5
	N	5	5	5	5	5
	Deviation Vs Control		0.1	-0.8	-0.2	0.7
day 7	Mean	18.7 n	18.2	18.3	18.5	16.9 *
	S.d.	0.5	0.5	0.7	0.7	1.8
	N	5	5	5	5	5
	Deviation Vs Control		-2.3	-1.9	-1.0	-9.5
day 14	Mean	19.0 n	18.9	18.6	18.9	17.2 **
	S.d.	0.5	0.3	1.2	0.5	1.0
	N	5	5	5	5	5
	Deviation Vs Control		-0.5	-1.8	-0.2	-9.4
day 21	Mean	19.5 n	19.5	19.6	19.6	18.1 *
	S.d.	0.8	0.5	0.7	0.5	1.3
	N	5	5	5	5	5
	Deviation Vs Control		-0.1	0.3	0.5	-7.4
day 28	Mean	19.5 n	19.9	19.8	20.3	18.1
	S.d.	0.9	0.2	0.7	0.8	1.4
	N	5	5	5	5	5
	Deviation Vs Control		1.7	1.1	4.0	-7.3

Statistic Profile = Dunnett test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
n=DUNNETT

IA 9
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Study 31C0343/09S078

Summary Changes Body Weights - BW / Body Weights [g]

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
d 0 -> 7	Mean	0.7 n	0.8	0.9	1.4	0.2
	S.d.	1.1	0.2	0.6	0.6	0.5
	N	5	5	5	5	5
	Deviation Vs Control		18.2	36.4	118.2	-69.7
d 0 -> 14	Mean	1.7 n	1.7	1.7	2.6	-0.4 **
	S.d.	0.9	0.4	0.8	0.9	0.4
	N	5	5	5	5	5
	Deviation Vs Control		-1.2	-1.2	48.8	-123.3
d 0 -> 21	Mean	2.5 n	2.4	2.7	3.5	0.5 **
	S.d.	1.2	0.9	1.0	0.8	0.6
	N	5	5	5	5	5
	Deviation Vs Control		-3.2	10.5	40.3	-80.6
d 0 -> 28	Mean	3.1 n	3.9	3.7	4.1	0.0 **
	S.d.	1.2	1.0	1.3	1.3	1.3
	N	5	5	5	5	5
	Deviation Vs Control		22.9	18.5	29.3	-99.4

Statistic Profile = Dunnett test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
d = day; n=DUNNETT

IA 10
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Study 31C0343/09S078

Summary Changes Body Weights - BW / Body Weights [g]

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
d 0 -> 7	Mean	1.2 n	0.8	1.0	1.1	-0.7 **
	S.d.	0.3	0.5	0.4	0.4	1.3
	N	5	5	5	5	5
	Deviation Vs Control		-35.5	-17.7	-11.3	-153.2
d 0 -> 14	Mean	1.5 n	1.4	1.3	1.5	-0.4 **
	S.d.	0.5	0.6	0.7	0.3	0.6
	N	5	5	5	5	5
	Deviation Vs Control		-7.8	-13.0	0.0	-123.4
d 0 -> 21	Mean	2.1 n	2.0	2.3	2.2	0.5 **
	S.d.	0.6	0.9	0.2	0.5	1.0
	N	5	5	5	5	5
	Deviation Vs Control		-1.9	9.6	6.7	-75.0
d 0 -> 28	Mean	2.1 n	2.4	2.5	2.9	0.6 **
	S.d.	0.6	0.7	0.3	0.6	1.1
	N	5	5	5	5	5
	Deviation Vs Control		15.1	17.0	38.7	-72.6

Statistic Profile = Dunnett test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
d = day; n=DUNNETT

IA 11
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Study 31C0343/09S078

Summary Substance Intake (mg/kg/Day)

Sex: **Male** - Phase: **In-life**

		1/M	2/M	3/M	4/M
d 0 -> 7	Mean	15.5	81.6	135.4	228.1
	S.d.				
	N	1	1	1	1
d 7 -> 14	Mean	15.0	79.7	161.5	213.3
	S.d.				
	N	1	1	1	1
d 14 -> 21	Mean	14.7	74.2	148.3	233.8
	S.d.				
	N	1	1	1	1
d 21 -> 28	Mean	14.5	79.0	149.6	221.8
	S.d.				
	N	1	1	1	1
Mean [mg/kg/Day]	Mean	14.9	78.6	148.7	224.2

d = day

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Study 31C0343/09S078

Summary Substance Intake (mg/kg/Day)

Sex: **Female** - Phase: **In-life**

		1/F	2/F	3/F	4/F
d 0 -> 7	Mean	21.8	93.8	187.7	238.6
	S.d.				
	N	1	1	1	1
d 7 -> 14	Mean	21.9	96.3	192.8	278.6
	S.d.				
	N	1	1	1	1
d 14 -> 21	Mean		95.1	197.7	256.9
	S.d.				
	N	0	1	1	1
d 21 -> 28	Mean	23.1	98.5	198.1	271.7
	S.d.				
	N	1	1	1	1
Mean [mg/kg/Day]	Mean	22.3	95.9	194.1	261.4

d = day

IB 1

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Red blood cell parameters

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
RBC	Mean	10.06 v	9.29	9.88	10.30	8.36 *
[tera/L]	S.d.	0.68	1.47	0.75	0.22	1.14
day 29	N	5	5	5	5	5
	Median	10.20	9.64	9.98	10.26	8.50
HGB	Mean	8.6 k	8.4	8.4	8.7	7.0
[mmol/L]	S.d.	0.7	0.6	0.8	0.2	1.0
day 29	N	5	5	5	5	5
	Median	8.6	8.4	8.4	8.6	7.2
HCT	Mean	0.446 k	0.418	0.441	0.454	0.371
[L/L]	S.d.	0.031	0.070	0.035	0.008	0.044
day 29	N	5	5	5	5	5
	Median	0.456	0.430	0.448	0.456	0.384
MCV	Mean	44.3 k	44.9	44.7	44.1	44.4
[fL]	S.d.	0.7	1.0	0.5	0.5	1.0
day 29	N	5	5	5	5	5
	Median	44.5	44.6	44.9	43.9	44.2
MCH	Mean	0.85 k	0.92	0.85	0.84	0.83
[fmol]	S.d.	0.01	0.16	0.01	0.02	0.02
day 29	N	5	5	5	5	5
	Median	0.84	0.86	0.85	0.84	0.83
MCHC	Mean	19.16 k	20.58	19.07	19.13	18.72
[mmol/L]	S.d.	0.27	3.72	0.47	0.38	0.52
day 29	N	5	5	5	5	5
	Median	19.20	19.05	19.01	18.96	18.88
RET	Mean	2.6 k	2.6	2.6	2.4	2.9
[%]	S.d.	0.1	0.3	0.2	0.2	1.1
day 29	N	5	5	5	5	5
	Median	2.5	2.7	2.6	2.4	2.6
PLT	Mean	1,500 k	1,611	1,636	1,808	1,377
[giga/L]	S.d.	94	202	108	119	551
day 29	N	5	5	5	5	5
	Median	1,486	1,576	1,582	1,846	1,742

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
v=KRUSKAL-WALLIS-WILCOX; k=KRUSKAL-WALLIS

Red blood cell parameters

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
RBC	Mean	9.33 k	9.74	10.05	9.45	8.98
[tera/L]	S.d.	1.11	0.58	0.93	0.70	1.21
day 29	N	5	5	5	5	5
	Median	9.60	9.74	9.86	9.18	9.34
HGB	Mean	8.0 k	8.6	8.6	8.1	7.6
[mmol/L]	S.d.	1.0	0.7	0.7	0.6	0.9
day 29	N	5	5	5	5	5
	Median	8.4	8.6	8.8	8.0	7.8
HCT	Mean	0.416 k	0.443	0.451	0.423	0.393
[L/L]	S.d.	0.046	0.022	0.046	0.029	0.053
day 29	N	5	5	5	5	5
	Median	0.430	0.442	0.446	0.418	0.408
MCV	Mean	44.7 v	45.5	44.9	44.7	43.8 *
[fL]	S.d.	0.4	0.8	0.5	0.7	0.3
day 29	N	5	5	5	5	5
	Median	44.7	45.4	44.7	44.7	43.8
MCH	Mean	0.86 k	0.88	0.86	0.86	0.85
[fmol]	S.d.	0.01	0.02	0.02	0.02	0.02
day 29	N	5	5	5	5	5
	Median	0.86	0.88	0.86	0.86	0.85
MCHC	Mean	19.21 k	19.34	19.18	19.28	19.49
[mmol/L]	S.d.	0.41	0.60	0.54	0.33	0.51
day 29	N	5	5	5	5	5
	Median	19.30	19.14	19.33	19.20	19.30
RET	Mean	2.6 k	2.4	2.6	2.6	2.7
[%]	S.d.	0.3	0.5	0.3	0.5	0.8
day 29	N	5	5	5	5	5
	Median	2.5	2.3	2.5	2.6	2.6
PLT	Mean	1,149 k	1,283	1,260	1,520	1,452
[giga/L]	S.d.	488	255	129	163	288
day 29	N	5	5	5	5	5
	Median	1,322	1,384	1,294	1,476	1,524

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
k=KRUSKAL-WALLIS; v=KRUSKAL-WALLIS-WILCOX

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White blood cell parameters

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
WBC	Mean	4.12 k	4.67	4.28	4.95	3.58
[giga/L]	S.d.	1.25	1.52	1.22	1.51	1.76
day 29	N	5	5	5	5	5
	Median	4.42	4.22	4.56	5.78	3.00
NEUTA	Mean	0.38 k	0.34	0.30	0.39	0.57
[giga/L]	S.d.	0.08	0.14	0.09	0.23	0.44
day 29	N	5	5	5	5	5
	Median	0.36	0.28	0.30	0.36	0.38
LYMPHA	Mean	3.69 k	4.28	3.94	4.48	2.90
[giga/L]	S.d.	1.18	1.44	1.13	1.32	1.62
day 29	N	5	5	5	5	5
	Median	4.04	3.92	4.20	5.04	2.58
MONOA	Mean	0.02 k	0.02	0.02	0.02	0.02
[giga/L]	S.d.	0.01	0.01	0.02	0.01	0.02
day 29	N	5	5	5	5	5
	Median	0.02	0.02	0.02	0.02	0.02
EOSA	Mean	0.02 k	0.02	0.03	0.03	0.04
[giga/L]	S.d.	0.01	0.01	0.02	0.01	0.02
day 29	N	5	5	5	5	5
	Median	0.02	0.02	0.04	0.02	0.04
BASOA	Mean	0.00 k	0.00	0.00	0.00	0.00
[giga/L]	S.d.	0.00	0.00	0.00	0.00	0.00
day 29	N	5	5	5	5	5
	Median	0.00	0.00	0.00	0.00	0.00
LUCA	Mean	0.02 k	0.02	0.02	0.02	0.03
[giga/L]	S.d.	0.01	0.02	0.01	0.01	0.03
day 29	N	5	5	5	5	5
	Median	0.02	0.02	0.02	0.02	0.02
NEUT	Mean	9.7 k	7.4	6.9	7.4	17.0
[%]	S.d.	2.7	2.5	1.1	2.8	9.1
day 29	N	5	5	5	5	5
	Median	9.3	7.0	7.3	5.7	12.9
LYMPH	Mean	88.9 v	91.4	91.7 *	91.1	79.7
[%]	S.d.	3.0	2.6	1.1	2.9	10.5
day 29	N	5	5	5	5	5
	Median	89.6	92.2	91.7	92.8	83.8
MONO	Mean	0.4 k	0.4	0.4	0.5	0.8
[%]	S.d.	0.2	0.1	0.2	0.1	0.4
day 29	N	5	5	5	5	5
	Median	0.5	0.4	0.3	0.4	0.9
EOS	Mean	0.6 k	0.3	0.5	0.5	1.3
[%]	S.d.	0.3	0.1	0.2	0.2	1.4
day 29	N	5	5	5	5	5
	Median	0.6	0.4	0.6	0.6	0.6
BASO	Mean	0.1 k	0.1	0.1	0.1	0.2
[%]	S.d.	0.1	0.1	0.0	0.1	0.1
day 29	N	5	5	5	5	5
	Median	0.1	0.1	0.1	0.1	0.2
LUC	Mean	0.3 k	0.4	0.4	0.4	1.1
[%]	S.d.	0.2	0.2	0.1	0.1	0.6
day 29	N	5	5	5	5	5
	Median	0.4	0.4	0.3	0.4	0.9

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
k=KRUSKAL-WALLIS; v=KRUSKAL-WALLIS-WILCOX

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White blood cell parameters

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
WBC	Mean	3.31 k	4.55	2.76	3.99	3.36
[giga/L]	S.d.	1.33	0.49	0.81	2.17	1.41
day 29	N	5	5	5	5	5
	Median	2.70	4.70	3.04	3.78	3.94
NEUTA	Mean	0.46 k	0.36	0.36	0.36	0.30
[giga/L]	S.d.	0.18	0.08	0.09	0.20	0.14
day 29	N	5	5	5	5	5
	Median	0.54	0.36	0.40	0.34	0.26
LYMPHA	Mean	2.80 k	4.08	2.34	3.56	3.00
[giga/L]	S.d.	1.17	0.43	0.69	1.96	1.28
day 29	N	5	5	5	5	5
	Median	2.10	4.16	2.58	3.38	3.58
MONOA	Mean	0.02 k	0.02	0.02	0.01	0.01
[giga/L]	S.d.	0.01	0.02	0.02	0.01	0.01
day 29	N	5	5	5	5	5
	Median	0.02	0.02	0.02	0.02	0.02
EOSA	Mean	0.02 k	0.05	0.02	0.03	0.02
[giga/L]	S.d.	0.01	0.02	0.03	0.02	0.01
day 29	N	5	5	5	5	5
	Median	0.02	0.06	0.02	0.02	0.02
BASOA	Mean	0.00 k	0.01	0.00	0.00	0.00
[giga/L]	S.d.	0.01	0.01	0.00	0.00	0.00
day 29	N	5	5	5	5	5
	Median	0.00	0.00	0.00	0.00	0.00
LUCA	Mean	0.01 k	0.02	0.01	0.02	0.01
[giga/L]	S.d.	0.01	0.01	0.01	0.01	0.01
day 29	N	5	5	5	5	5
	Median	0.02	0.02	0.02	0.02	0.00
NEUT	Mean	14.1 v	8.0 **	13.2	9.4	9.4
[%]	S.d.	3.8	1.6	1.3	2.5	2.6
day 29	N	5	5	5	5	5
	Median	13.5	8.0	12.5	8.7	8.8
LYMPH	Mean	84.2 v	89.8 **	84.5	88.7	88.9
[%]	S.d.	4.0	1.7	1.2	3.2	3.0
day 29	N	5	5	5	5	5
	Median	84.9	89.2	84.9	89.4	88.8
MONO	Mean	0.7 k	0.5	0.8	0.4	0.4
[%]	S.d.	0.3	0.2	0.6	0.3	0.3
day 29	N	5	5	5	5	5
	Median	0.8	0.5	0.6	0.4	0.3
EOS	Mean	0.5 k	1.1	0.9	1.0	0.7
[%]	S.d.	0.3	0.4	0.5	0.5	0.3
day 29	N	5	5	5	5	5
	Median	0.6	1.1	0.6	0.8	0.8
BASO	Mean	0.2 k	0.1	0.2	0.3	0.2
[%]	S.d.	0.1	0.1	0.2	0.3	0.2
day 29	N	5	5	5	5	5
	Median	0.2	0.1	0.1	0.1	0.1
LUC	Mean	0.3 k	0.5	0.4	0.3	0.4
[%]	S.d.	0.2	0.1	0.3	0.2	0.1
day 29	N	5	5	5	5	5
	Median	0.3	0.4	0.4	0.3	0.4

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
k=KRUSKAL-WALLIS; v=KRUSKAL-WALLIS-WILCOX

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Enzymes

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
ALT	Mean	0.71 v	0.50 *	0.57	0.53 *	1.20 *
[µkat/L]	S.d.	0.15	0.10	0.04	0.03	0.43
day 29	N	5	5	5	5	5
	Median	0.73	0.47	0.58	0.53	1.00
AST	Mean	5.00 k	3.46	4.41	3.83	6.47
[µkat/L]	S.d.	1.24	0.91	0.53	0.50	2.53
day 29	N	5	5	5	5	5
	Median	5.43	3.30	4.41	3.64	6.86
ALP	Mean	1.95 v	1.81	2.04	2.07	1.31
[µkat/L]	S.d.	0.40	0.13	0.11	0.63	0.45
day 29	N	5	5	5	5	5
	Median	1.72	1.76	2.06	1.88	1.58
GGT_C	Mean	0 k	0	0	0	0
[nkat/L]	S.d.	0	0	0	0	0
day 29	N	5	5	5	5	5
	Median	0	0	0	0	0

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
v=KRUSKAL-WALLIS-WILCOX; k=KRUSKAL-WALLIS

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Enzymes

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
ALT	Mean	0.97 v	0.90	0.81	0.97	1.33
[µkat/L]	S.d.	0.51	0.21	0.11	0.12	0.26
day 29	N	5	5	5	5	5
	Median	0.80	0.84	0.76	1.02	1.33
AST	Mean	6.29 k	6.86	5.53	6.34	5.70
[µkat/L]	S.d.	2.41	3.18	1.18	2.19	1.34
day 29	N	5	5	5	5	5
	Median	6.22	5.89	5.57	5.89	5.09
ALP	Mean	2.53 k	2.47	2.33	2.11	1.77
[µkat/L]	S.d.	0.37	0.26	0.16	0.32	0.71
day 29	N	5	5	5	5	5
	Median	2.45	2.46	2.31	2.25	1.94
GGT_C	Mean	0 k	0	0	0	0
[nkat/L]	S.d.	0	0	0	0	0
day 29	N	5	5	5	5	5
	Median	0	0	0	0	0

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
v=KRUSKAL-WALLIS-WILCOX; k=KRUSKAL-WALLIS

IB 7

Study 31C0343/09S078 15-Sep-2017 12:12

Ascentos™ 1.3

Substrates

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
UREA	Mean	10.83 k	11.71	10.60	11.86	11.65
[mmol/L]	S.d.	0.96	0.78	0.86	1.97	1.15
day 29	N	5	5	5	5	5
	Median	10.72	11.54	10.65	11.19	11.90
CREA	Mean	36.7 k	37.0	36.4	36.9	34.7
[µmol/L]	S.d.	3.4	3.4	1.7	2.1	6.1
day 29	N	5	5	5	5	5
	Median	38.1	36.2	36.8	37.0	35.8
GLUC	Mean	6.01 k	7.60	7.10	8.01	6.10
[mmol/L]	S.d.	0.84	1.35	1.29	1.64	1.73
day 29	N	5	5	5	5	5
	Median	6.52	7.15	7.92	7.08	6.45
TBIL	Mean	2.24 k	2.40	2.65	3.22	3.40
[µmol/L]	S.d.	0.53	0.37	0.34	0.89	0.99
day 29	N	5	5	5	5	5
	Median	2.05	2.35	2.65	3.52	3.72
TBA	Mean	4.2 k	6.3	4.5	4.2	27.9
[µmol/L]	S.d.	1.8	2.2	1.7	2.3	36.5
day 29	N	5	5	5	5	5
	Median	3.8	6.0	4.7	3.1	8.7
TPROT	Mean	50.97 v	52.12	50.77	49.92	45.84 *
[g/L]	S.d.	1.21	1.63	1.18	1.84	4.81
day 29	N	5	5	5	5	5
	Median	51.16	52.74	51.15	49.59	47.72
ALB	Mean	35.95 v	36.28	35.65	35.31	31.84 **
[g/L]	S.d.	0.55	1.26	0.72	1.65	3.31
day 29	N	5	5	5	5	5
	Median	36.00	36.97	35.67	35.29	33.35
GLOB	Mean	15.02 k	15.84	15.11	14.61	14.00
[g/L]	S.d.	0.87	0.63	0.50	0.36	1.60
day 29	N	5	5	5	5	5
	Median	15.27	15.98	15.42	14.56	14.37
CHOL	Mean	2.31 k	2.61	2.26	2.43	2.77
[mmol/L]	S.d.	0.29	0.25	0.15	0.26	0.44
day 29	N	5	5	5	5	5
	Median	2.44	2.63	2.30	2.52	2.84
TRIG	Mean	0.78 v	0.83	0.81	0.99	1.61 **
[mmol/L]	S.d.	0.11	0.21	0.17	0.32	0.22
day 29	N	5	5	5	5	5
	Median	0.77	0.86	0.81	1.02	1.68

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; v=KRUSKALL-WALLIS-WILCOX

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Ascentos™ 1.3

Substrates

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
UREA	Mean	10.90 k	9.33	10.00	11.58	9.27
[mmol/L]	S.d.	1.61	1.37	1.30	3.87	1.03
day 29	N	5	5	5	5	5
	Median	11.64	8.95	9.55	10.16	8.76
CREA	Mean	36.9 k	34.0	35.2	36.5	29.9
[µmol/L]	S.d.	3.0	8.5	4.7	5.0	5.5
day 29	N	5	5	5	5	5
	Median	36.4	37.4	33.3	34.7	29.9
GLUC	Mean	8.68 k	6.38	8.16	7.53	5.88
[mmol/L]	S.d.	1.32	3.29	0.85	0.70	1.65
day 29	N	5	5	5	4	5
	Median	8.40	5.32	8.12	7.46	5.06
TBIL	Mean	2.34 v	2.10	1.90	2.08	3.15
[µmol/L]	S.d.	0.45	0.47	0.33	0.41	0.78
day 29	N	5	5	5	5	5
	Median	2.31	2.03	2.10	1.92	2.82
TBA	Mean	7.4 k	23.4	9.6	9.8	6.4
[µmol/L]	S.d.	3.0	26.9	3.5	3.5	0.8
day 29	N	5	4	5	4	5
	Median	6.8	11.2	9.8	8.8	6.6
TPROT	Mean	49.22 k	50.24	48.63	49.38	43.83
[g/L]	S.d.	2.03	3.18	1.29	1.10	7.90
day 29	N	5	4	5	5	5
	Median	50.25	51.09	48.75	49.12	46.32
ALB	Mean	36.46 v	36.62	36.16	35.48	28.11 **
[g/L]	S.d.	1.24	2.93	0.73	0.94	11.66
day 29	N	5	4	5	4	5
	Median	36.53	37.52	36.20	35.38	33.27
GLOB	Mean	12.75 v	13.62	12.48	13.96	15.72 *
[g/L]	S.d.	1.04	0.50	0.67	0.56	3.91
day 29	N	5	4	5	4	5
	Median	12.94	13.64	12.28	14.06	14.53
CHOL	Mean	1.88 k	1.86	2.01	2.27	2.62
[mmol/L]	S.d.	0.27	0.30	0.16	0.17	1.19
day 29	N	5	4	5	4	5
	Median	1.95	1.92	2.07	2.22	2.90
TRIG	Mean	0.69 k	0.63	0.65	0.70	1.54
[mmol/L]	S.d.	0.14	0.10	0.27	0.23	0.89
day 29	N	5	4	5	4	5
	Median	0.76	0.64	0.65	0.71	1.56

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
k=KRUSKALL-WALLIS; v=KRUSKALL-WALLIS-WILCOX

IB 9

Study 31C0343/09S078 06-Dec-2011 16:18

ToxData© System 3.0

Electrolytes + minerals

Sex: **Male** - Phase: **In-life**

		0/M	1/M	2/M	3/M	4/M
NA	Mean	150.4 k	150.2	150.5	150.5	151.9
[mmol/L]	S.d.	1.4	0.6	0.8	1.1	2.1
day 29	N	5	5	5	5	5
	Median	149.7	150.3	150.4	150.4	151.8
K	Mean	6.29 k	5.95	6.18	5.98	6.01
[mmol/L]	S.d.	0.56	0.54	0.68	0.47	0.38
day 29	N	5	5	5	5	5
	Median	6.47	5.73	6.00	6.00	6.02
CL	Mean	115.9 v	113.7 **	115.9	114.8	117.3
[mmol/L]	S.d.	1.2	0.5	2.3	1.2	2.3
day 29	N	5	5	5	5	5
	Median	115.9	113.6	115.5	115.2	116.9
INP	Mean	2.39 v	2.55	2.69	2.61	3.08 **
[mmol/L]	S.d.	0.20	0.07	0.14	0.32	0.39
day 29	N	5	5	5	5	5
	Median	2.32	2.56	2.65	2.65	2.98
CA	Mean	2.36 v	2.47 *	2.45	2.44	2.34
[mmol/L]	S.d.	0.05	0.06	0.08	0.06	0.09
day 29	N	5	5	5	5	5
	Median	2.35	2.48	2.45	2.45	2.37
MG	Mean	1.19 k	1.28	1.25	1.27	1.26
[mmol/L]	S.d.	0.06	0.10	0.08	0.08	0.07
day 29	N	5	5	5	5	5
	Median	1.21	1.26	1.28	1.30	1.26

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
k=KRUSKAL-WALLIS; v=KRUSKAL-WALLIS-WILCOX

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Electrolytes + minerals

Sex: **Female** - Phase: **In-life**

		0/F	1/F	2/F	3/F	4/F
NA	Mean	150.5 k	149.9	150.7	151.6	151.1
[mmol/L]	S.d.	1.3	3.0	1.5	1.8	1.1
day 29	N	5	5	5	5	5
	Median	151.0	149.9	150.9	150.6	150.8
K	Mean	5.91 k	6.32	5.97	5.89	5.62
[mmol/L]	S.d.	0.70	1.30	0.68	0.62	0.39
day 29	N	5	5	5	5	5
	Median	5.59	6.31	5.75	5.64	5.57
CL	Mean	116.4 k	115.3	115.7	117.0	117.3
[mmol/L]	S.d.	1.3	1.6	1.0	1.8	1.5
day 29	N	5	5	5	5	5
	Median	116.2	115.1	115.9	117.3	117.1
INP	Mean	2.80 k	2.80	2.54	2.77	2.68
[mmol/L]	S.d.	0.62	0.31	0.17	0.36	0.13
day 29	N	5	5	5	5	5
	Median	2.84	2.69	2.58	2.65	2.72
CA	Mean	2.36 k	2.30	2.34	2.38	2.40
[mmol/L]	S.d.	0.04	0.12	0.06	0.05	0.09
day 29	N	5	5	5	5	5
	Median	2.38	2.34	2.32	2.37	2.40
MG	Mean	1.26 k	1.29	1.23	1.28	0.99
[mmol/L]	S.d.	0.12	0.09	0.03	0.09	0.53
day 29	N	5	4	5	4	5
	Median	1.20	1.32	1.23	1.31	1.23

Statistic Profile = Kruskal-Wallis + Wilcoxon test (two-sided), * p<=0.05, ** p <=0.01, X = Group excluded from statistics
k=KRUSKAL-WALLIS

ABSOLUTE WEIGHTS - MEAN VALUES (MALE)

Sacrifice			F1				
Sex			M				
Group			0	1	2	3	4
Terminal body weight	g	M	20.64	21.62	21.28	21.8 *	18.66 *
		% dev	100	105	103	106	90
		SD	0.68	1.052	0.786	0.648	1.303
		n	5	5	5	5	5
Adrenal glands	mg	M	4.0	5.8	5.2	4.6	5.6
		% dev	100	145	130	115	140
		SD	1.414	1.095	1.095	0.894	1.517
		n	5	5	5	5	5
Brain	mg	M	450.6	449.6	457.0	448.6	433.2
		% dev	100	100	101	100	96
		SD	9.788	15.837	23.033	15.06	13.535
		n	5	5	5	5	5
Epididymides	mg	M	55.2	55.4	57.8	58.2	51.0
		% dev	100	100	105	105	92
		SD	3.033	8.081	3.768	8.167	9.22
		n	5	5	5	5	5
Heart	mg	M	117.6	123.6	128.0	126.4	116.4
		% dev	100	105	109	107	99
		SD	10.237	19.731	4.637	13.297	16.041
		n	5	5	5	5	5
Kidneys	mg	M	291.4	284.8	297.2	298.4	287.0
		% dev	100	98	102	102	98
		SD	11.567	15.897	18.807	18.622	24.99
		n	5	5	5	5	5
Liver	mg	M	866.8	846.6	959.4 **	1122.2 **	995.6
		% dev	100	98	111	129	115
		SD	33.237	60.533	41.343	72.799	154.281
		n	5	5	5	5	5
Prostate	mg	M	46.4	46.6	44.6	52.4	40.2
		% dev	100	100	96	113	87
		SD	4.722	8.792	9.813	7.797	10.826
		n	5	5	5	5	5
Seminal vesicle	mg	M	152.6	155.4	168.4	165.0	91.6 *
		% dev	100	102	110	108	60
		SD	19.269	14.741	18.461	25.288	41.495
		n	5	5	5	5	5

*: P <= 0.05, **: P <= 0.01
Kruskal-Wallis H and Wilcoxon test, two sided

ABSOLUTE WEIGHTS - MEAN VALUES (MALE)

Sacrifice			F1				
Sex			M				
Group			0	1	2	3	4
Spleen	mg	M	38.2	44.0	44.8	42.6	33.8
		% dev	100	115	117	112	88
		SD	1.304	6.782	7.396	4.278	5.975
		n	5	5	5	5	5
Testes	mg	M	176.8	180.0	189.0	186.2	188.4
		% dev	100	102	107	105	107
		SD	11.189	13.172	7.211	7.396	56.221
		n	5	5	5	5	5
Thymus	mg	M	31.0	38.8 *	36.6 *	37.6	21.2
		% dev	100	125	118	121	68
		SD	2.915	4.604	3.435	6.878	10.78
		n	5	5	5	5	5

*: P <= 0.05, **: P <= 0.01
Kruskal-Wallis H and Wilcoxon test, two sided

ABSOLUTE WEIGHTS - MEAN VALUES (FEMALE)

Sacrifice			F1				
Sex			F				
Group			0	1	2	3	4
Terminal body weight	g	M	16.76	16.84	16.72	17.1	15.6
		% dev	100	100	100	102	93
		SD	0.74	0.365	0.814	0.43	0.957
		n	5	5	5	5	5
Adrenal glands	mg	M	7.2	7.2	8.2	8.0	8.8
		% dev	100	100	114	111	122
		SD	0.837	1.304	1.304	0.707	1.924
		n	5	5	5	5	5
Brain	mg	M	444.2	450.2	437.8	436.6	415.75
		% dev	100	101	99	98	94
		SD	23.232	14.704	20.241	11.126	27.439
		n	5	5	5	5	4
Heart	mg	M	108.2	111.2	106.4	110.0	97.4
		% dev	100	103	98	102	90
		SD	13.142	11.777	6.107	8.515	9.29
		n	5	5	5	5	5
Kidneys	mg	M	249.4	254.0	240.2	253.0	245.6
		% dev	100	102	96	101	98
		SD	18.716	13.172	13.882	17.819	22.579
		n	5	5	5	5	5
Liver	mg	M	781.0	733.2	807.2	956.4 **	981.8 **
		% dev	100	94	103	122	126
		SD	33.705	69.283	37.252	50.152	70.704
		n	5	5	5	5	5
Ovaries	mg	M	15.8	13.6	13.6	14.2	11.4
		% dev	100	86	86	90	72
		SD	1.924	1.673	1.949	2.683	3.847
		n	5	5	5	5	5
Spleen	mg	M	47.2	48.4	46.2	48.6	32.8 *
		% dev	100	103	98	103	69
		SD	6.907	5.03	7.662	7.956	6.834
		n	5	5	5	5	5
Thymus	mg	M	39.2	46.8	44.0	44.4	35.6
		% dev	100	119	112	113	91
		SD	1.924	4.207	2.915	6.066	14.153
		n	5	5	5	5	5

*: P <= 0.05, **: P <= 0.01
Kruskal-Wallis H and Wilcoxon test, two sided

ABSOLUTE WEIGHTS - MEAN VALUES (FEMALE)

Sacrifice			F1				
Sex			F				
Group			0	1	2	3	4
Uterus	mg	M	70.2	76.4	84.4	81.6	74.0
		% dev	100	109	120	116	105
		SD	25.821	21.267	42.618	23.137	40.639
		n	5	5	5	5	5

*: P <= 0.05, **: P <= 0.01
Kruskal-Wallis H and Wilcoxon test, two sided

RELATIVE WEIGHTS - MEAN VALUES (MALE)

Sacrifice			F1				
Sex			M				
Group			0	1	2	3	4
Terminal body weight	%	M	100.0	100.0	100.0	100.0	100.0
		% dev	100	100	100	100	100
		n	5	5	5	5	5
Adrenal glands	%	M	0.019	0.027	0.024	0.021	0.031
		% dev	100	138	127	109	159
		SD	0.006	0.004	0.005	0.004	0.011
		n	5	5	5	5	5
Brain	%	M	2.184	2.083	2.149	2.058*	2.329
		% dev	100	95	98	94	107
		SD	0.055	0.124	0.102	0.058	0.146
		n	5	5	5	5	5
Epididymides	%	M	0.268	0.256	0.272	0.267	0.272
		% dev	100	95	102	100	102
		SD	0.022	0.03	0.024	0.039	0.036
		n	5	5	5	5	5
Heart	%	M	0.569	0.57	0.602	0.579	0.625
		% dev	100	100	106	102	110
		SD	0.035	0.067	0.028	0.047	0.084
		n	5	5	5	5	5
Kidneys	%	M	1.412	1.318*	1.397	1.369	1.543
		% dev	100	93	99	97	109
		SD	0.05	0.055	0.08	0.074	0.156
		n	5	5	5	5	5
Liver	%	M	4.202	3.914*	4.508**	5.144**	5.316**
		% dev	100	93	107	122	127
		SD	0.167	0.155	0.071	0.218	0.556
		n	5	5	5	5	5
Prostate	%	M	0.225	0.216	0.209	0.241	0.213
		% dev	100	96	93	107	95
		SD	0.025	0.04	0.039	0.042	0.049
		n	5	5	5	5	5
Seminal vesicle	%	M	0.742	0.72	0.794	0.758	0.482*
		% dev	100	97	107	102	65
		SD	0.118	0.076	0.106	0.117	0.206
		n	5	5	5	5	5

*: P <= 0.05, **: P <= 0.01
Kruskal-Wallis H and Wilcoxon test, two sided

RELATIVE WEIGHTS - MEAN VALUES (MALE)

Sacrifice			F1				
Sex			M				
Group			0	1	2	3	4
Spleen	%	M	0.185	0.203	0.21	0.195	0.181
		% dev	100	110	113	105	97
		SD	0.012	0.024	0.031	0.017	0.025
		n	5	5	5	5	5
Testes	%	M	0.857	0.834	0.889	0.854	1.006
		% dev	100	97	104	100	117
		SD	0.054	0.074	0.039	0.035	0.264
		n	5	5	5	5	5
Thymus	%	M	0.15	0.179*	0.173	0.172	0.112
		% dev	100	119	115	115	74
		SD	0.01	0.017	0.022	0.028	0.053
		n	5	5	5	5	5

*: P <= 0.05, **: P <= 0.01
Kruskal-Wallis H and Wilcoxon test, two sided

RELATIVE WEIGHTS - MEAN VALUES (FEMALE)

Sacrifice			F1				
Sex			F				
Group			0	1	2	3	4
Terminal body weight	%	M	100.0	100.0	100.0	100.0	100.0
		% dev	100	100	100	100	100
		n	5	5	5	5	5
Adrenal glands	%	M	0.043	0.043	0.049	0.047	0.057
		% dev	100	99	114	109	131
		SD	0.005	0.008	0.007	0.004	0.012
		n	5	5	5	5	5
Brain	%	M	2.654	2.675	2.62	2.554	2.692
		% dev	100	101	99	96	101
		SD	0.176	0.125	0.077	0.049	0.07
		n	5	5	5	5	4
Heart	%	M	0.644	0.66	0.637	0.643	0.625
		% dev	100	102	99	100	97
		SD	0.057	0.062	0.026	0.05	0.059
		n	5	5	5	5	5
Kidneys	%	M	1.487	1.509	1.437	1.48	1.574
		% dev	100	101	97	99	106
		SD	0.075	0.096	0.054	0.098	0.104
		n	5	5	5	5	5
Liver	%	M	4.667	4.355	4.83	5.592**	6.295**
		% dev	100	93	103	120	135
		SD	0.285	0.422	0.147	0.245	0.271
		n	5	5	5	5	5
Ovaries	%	M	0.094	0.081	0.081	0.083	0.073
		% dev	100	86	86	88	77
		SD	0.01	0.01	0.01	0.015	0.023
		n	5	5	5	5	5
Spleen	%	M	0.281	0.288	0.275	0.284	0.21 *
		% dev	100	102	98	101	75
		SD	0.033	0.034	0.036	0.042	0.038
		n	5	5	5	5	5
Thymus	%	M	0.234	0.278	0.264	0.26	0.228
		% dev	100	119	113	111	97
		SD	0.009	0.027	0.027	0.036	0.089
		n	5	5	5	5	5

*: P <= 0.05, **: P <= 0.01
Kruskal-Wallis H and Wilcoxon test, two sided

RELATIVE WEIGHTS - MEAN VALUES (FEMALE)

Sacrifice			F1				
Sex			F				
Group			0	1	2	3	4
Uterus	%	M	0.418	0.453	0.501	0.479	0.467
		% dev	100	108	120	115	112
		SD	0.149	0.121	0.241	0.145	0.245
		n	5	5	5	5	5

*: P <= 0.05, **: P <= 0.01
Kruskal-Wallis H and Wilcoxon test, two sided

INCIDENCE OF GROSS LESIONS

Sacrifice	F1									
Sex	M					F				
Group	0	1	2	3	4	0	1	2	3	4
Animals in selected group	5	5	5	5	5	5	5	5	5	5
No abnormalities	5	4	5	5	3	5	5	4	5	4
Adrenal cortex	.	.	.	.	.	.	.	.	.	.
Organ size reduced	.	.	.	.	.	.	.	.	.	1
Liver	.	.	.	.	.	.	.	.	.	.
Deformation	.	1	.	.	.	.	.	.	.	.
Focus	.	.	.	.	.	.	.	1	.	.
Testes	.	.	.	.	.	.	.	.	.	.
Enlarged	.	.	.	.	1	.	.	.	.	.
Thymus	.	.	.	.	.	.	.	.	.	.
Organ size reduced	.	.	.	.	1	.	.	.	.	.

INCIDENCE OF ALL MICROSCOPIC FINDINGS

Sacrifice		F1									
Sex		M					F				
Group		0	1	2	3	4	0	1	2	3	4
Animals in selected group		5	5	5	5	5	5	5	5	5	5
Adrenal cortex	exam.	5	.	.	.	5	5	5	5	5	5
Adv. involution. X-zone		.	.	.	.	.	.	.	1	3	4
Accessory cortical tissue		.	.	.	.	.	.	1	.	.	.
Adrenal medulla	exam.	5	.	.	.	5	5	5	5	5	5
Axillary lymph nodes	exam.	5	.	.	.	5	5	.	.	.	5
Bone marrow (femur)	exam.	5	.	.	.	5	5	.	.	.	5
Brain	exam.	5	.	.	.	5	5	.	.	.	5
Cecum	exam.	5	.	.	.	5	5	.	.	.	5
Cervical cord	exam.	5	.	.	.	5	5	.	.	.	5
Cervix	exam.	.	.	.	.	.	5	5	5	5	5
Coagulating glands	exam.	5	.	.	.	4	.	.	.	.	.
Colon	exam.	5	.	.	.	5	5	.	.	.	5
Duodenum	exam.	5	.	.	.	5	5	.	.	.	5
Epididymides	exam.	5	.	.	.	5	.	.	.	.	.
Eyes with opt. nerve	exam.	5	.	.	.	5	5	.	.	.	5
Forestomach	exam.	5	.	.	.	5	5	.	.	.	5
Hyperplasia, squamous, focal		1	.	.	.	.	.	.	.	.	.
Glandular stomach	exam.	5	.	.	.	5	5	.	.	.	5
Dilation, fundic gland, (m)f		.	.	.	.	.	1	.	.	.	.
Heart	exam.	5	.	.	.	5	5	.	.	.	5
Mineralization, (multi)focal		.	.	.	.	.	1	.	.	.	.
Ileum	exam.	5	.	.	.	5	5	.	.	.	5
Jejunum	exam.	5	.	.	.	5	5	.	.	.	5
Kidneys	exam.	5	5	5	5	5	5	5	5	5	5
Vacuolation increased		1	.	2	1	5	1	1	1	2	5
Mineralization, papilla, (m)		2	.	1	.	4	1	1	.	.	2

INCIDENCE OF ALL MICROSCOPIC FINDINGS

Sacrifice		F1									
Sex		M					F				
Group		0	1	2	3	4	0	1	2	3	4
Animals in selected group		5	5	5	5	5	5	5	5	5	5
Kidneys	cont.										
Mineralization, tubular, (m)		.	.	.	.	.	1	.	.	.	.
Cast, tubular		1	1	4	2	2	1	.	1	1	2
Tubules, basophilic, (m)f		1	1	.	1	1	3	2	.	1	.
Infiltr., interst., lymphoid		1	.	.	1	.	.	.	.	.	.
Fibrosis, (multi)focal		.	1	.	.	.	1	.	.	.	.
Fibrosis, capsule		.	.	.	.	.	.	.	.	1	.
Infiltr. lymphoid, ren. pelv		.	1	1	.	.	.	1	.	.	.
Granuloma, focal		.	.	1	.	1	.	.	.	.	.
Liver	exam.	5	5	5	5	5	5	5	5	5	5
Necrosis, coag., rand.		.	.	.	.	2	.	.	.	.	.
Multinucl. hepatoc. incr.		.	.	.	.	3	.	.	.	.	.
Hypertrophy, centrilobular		.	2	1	5	.	.	.	.	5	.
Hypertrophy, diffuse		.	.	.	.	5	.	.	.	.	5
Vacuolar change reduced		.	2	1	4	4	.	.	3	3	5
Vac. change, macrov., centr.		.	.	.	.	2	.	.	.	4	5
Infiltration, lymphoid, (m)f		3	1	4	4	5	3	4	5	4	3
Infiltration, mixed, (m)f		.	.	.	2	.	.	.	.	.	.
Cyst(s), biliary		.	.	.	.	.	.	.	1	.	.
Lumbar cord	exam.	5	.	.	.	5	5	.	.	.	5
Lungs	exam.	5	.	.	.	5	5	.	.	.	5
Infiltr., interst., diffuse		.	.	.	.	1	.	.	.	.	1
Histiocytosis, alveolar, (m)		.	.	.	.	.	2	.	.	.	.
Mesenteric lymph n.	exam.	5	.	.	.	5	5	.	.	.	5
Ovaries	exam.	.	.	.	.	.	5	5	5	5	5
Hyperpl./hypertr. int. cell		.	.	.	.	.	.	.	.	.	4
Peyers patch	exam.	5	.	.	.	5	5	.	.	.	5
Pituitary gland	exam.	5	.	.	.	5	5	.	.	.	3
Cyst(s), pars distalis		1	.	.	.	1	.	.	.	.	.
Prostate	exam.	5	.	.	.	5	.	.	.	.	.
Rectum	exam.	5	.	.	.	5	5	.	.	.	5
Sciatic nerve	exam.	5	.	.	.	5	5	.	.	.	4
Seminal vesicle	exam.	5	5	5	5	5	.	.	.	.	.
Reduced content		.	.	.	.	2	.	.	.	.	.

INCIDENCE OF ALL MICROSCOPIC FINDINGS

Sacrifice		F1									
Sex		M					F				
Group		0	1	2	3	4	0	1	2	3	4
Animals in selected group		5	5	5	5	5	5	5	5	5	5
Skeletal muscle	exam.	5	.	.	.	5	5	.	.	.	5
Spleen	exam.	5	.	.	.	5	5	5	5	5	5
Pigment storage		2	.	.	.	2	5	3	5	5	5
Hematopoiesis, extramedullar		2	.	.	.	2	4	4	5	5	3
Sternum, with marrow	exam.	5	.	.	.	5	5	.	.	.	5
Testes	exam.	5	.	.	.	5	.	.	.	.	.
Dilation, tubular, diffuse		.	.	.	.	1	.	.	.	.	.
Degeneration, tubular, (m)f		2	.	.	.	2	.	.	.	.	.
Thoracic cord	exam.	5	.	.	.	5	5	.	.	.	5
Thymus	exam.	5	5	5	5	5	5	.	.	.	5
Atrophy, diffuse		.	.	.	.	2	.	.	.	.	1
Cyst(s)		1	1	.	.	1	1	.	.	.	.
Thyroid glands	exam.	5	.	.	.	5	5	.	.	.	5
Trachea	exam.	5	.	.	.	5	5	.	.	.	5
Urinary bladder	exam.	5	.	.	.	5	5	.	.	.	5
Uterus	exam.	.	.	.	.	.	5	5	5	5	5
Atrophy, diffuse		.	.	.	.	.	.	.	.	.	2
Vagina	exam.	.	.	.	.	.	5	5	5	5	5
Epith. hypertr. w. mucific.		.	.	.	.	.	.	.	.	.	2

MICROSCOPIC FINDINGS TARGET ORGANS

Sacrifice		F1									
Sex		M					F				
Group		0	1	2	3	4	0	1	2	3	4
Animals in selected group		5	5	5	5	5	5	5	5	5	5
Adrenal cortex	exam.	5	.	.	.	5	5	5	5	5	5
Adv. involution. X-zone		.	.	.	.	.	.	.	1	3	4
	. 1.	.	.	.	.	.	.	.	1	2	2
	. 2.	.	.	.	.	.	.	.	.	1	2
Kidneys	exam.	5	5	5	5	5	5	5	5	5	5
Vacuolation increased		1	.	2	1	5	1	1	1	2	5
	. 1.	1	.	2	1	1	1	1	1	2	2
	. 2.	.	.	.	.	4	.	.	.	.	3
Liver	exam.	5	5	5	5	5	5	5	5	5	5
Necrosis, coag., rand.		.	.	.	.	2	.	.	.	.	.
	. 1.	.	.	.	.	1	.	.	.	.	.
	. 3.	.	.	.	.	1	.	.	.	.	.
Multinucl. hepatoc. incr.		.	.	.	.	3	.	.	.	.	.
	. 1.	.	.	.	.	2	.	.	.	.	.
	. 2.	.	.	.	.	1	.	.	.	.	.
Hypertrophy, centrilobular		.	2	1	5	.	.	.	.	5	.
	. 1.	.	2	1	1	.	.	.	.	4	.
	. 2.	.	.	.	4	.	.	.	.	1	.
Hypertrophy, diffuse		.	.	.	.	5	.	.	.	.	5
	. 1.	.	.	.	.	.	.	.	.	.	3
	. 2.	.	.	.	.	5	.	.	.	.	2
Vacuolar change reduced		.	2	1	4	4	.	.	3	3	5
	. 1.	.	2	1	1	2	.	.	3	1	4
	. 2.	.	.	.	3	2	.	.	.	2	1
Vac. change, macrov., centr.		.	.	.	.	2	.	.	.	4	5
	. 1.	.	.	.	.	2	.	.	.	4	.
	. 2.	.	.	.	.	.	.	.	.	.	3
	. 3.	.	.	.	.	.	.	.	.	.	2
Ovaries	exam.	.	.	.	.	.	5	5	5	5	5
Hyperpl./hypertr. int. cell		.	.	.	.	.	.	.	.	.	4
	. 1.	.	.	.	.	.	.	.	.	.	1
	. 2.	.	.	.	.	.	.	.	.	.	2
	. 3.	.	.	.	.	.	.	.	.	.	1
Seminal vesicle	exam.	5	5	5	5	5	.	.	.	.	.
Reduced content		.	.	.	.	2	.	.	.	.	.
	. 1.	.	.	.	.	1	.	.	.	.	.
	. 3.	.	.	.	.	1	.	.	.	.	.

MICROSCOPIC FINDINGS TARGET ORGANS

Sacrifice		F1									
Sex		M					F				
Group		0	1	2	3	4	0	1	2	3	4
Animals in selected group		5	5	5	5	5	5	5	5	5	5
Uterus	exam.	.	.	.	.	.	5	5	5	5	5
Atrophy, diffuse		.	.	.	.	.	.	.	.	.	2
	. 1.	.	.	.	.	.	.	.	.	.	1
	. 3.	.	.	.	.	.	.	.	.	.	1
Vagina	exam.	.	.	.	.	.	5	5	5	5	5
Epith. hypertr. w. mucific.		.	.	.	.	.	.	.	.	.	2
	. 3.	.	.	.	.	.	.	.	.	.	2

STUDY TITLE

Report

BAS 850 H

Repeated dose 28-day oral toxicity study in C57BL/6 J Rj mice
Administration via the diet

TEST FACILITY

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

TEST FACILITY PROJECT IDENTIFICATION

Project No. 31C0343/09S078

PART II OF III
(TABLES SECTION, INDIVIDUAL VALUES)

CONTENTS OF PART II (TABLES SECTION; INDIVIDUAL VALUES)

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day														
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
0/M	001	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	002	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	003	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	004	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	005	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day													
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
1/M	006	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	007	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	008	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	009	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	010	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day														
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
2/M	011	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	012	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	013	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	014	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	015	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day													
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
3/M	016	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	017	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	018	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	019	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	020	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day														
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
4/M	021	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	022	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	023	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	024	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		gait	high-stepping gait																	
		dead	sacrificed scheduled																	
	025	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day																					
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
0/M	001	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	002	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	003	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	004	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	005	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day																					
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
1/M	006	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	007	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	008	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	009	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	010	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day																					
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
2/M	011	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	012	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	013	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	014	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	015	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day																					
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
3/M	016	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	017	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	018	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	019	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	020	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day																					
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
4/M	021	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	022	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	023	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	024	normal	NAD			1	1	1	1	1	1									
		gait	high-stepping gait									1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	025	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day													
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
0/F	026	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	027	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	028	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	029	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	030	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day													
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
1/F	031	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	032	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	033	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	034	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	035	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day													
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
2/F	036	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	037	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	038	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	039	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	040	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day													
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
3/F	041	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	042	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	043	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	044	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	045	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

IIA 15
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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day													
						0 [DCO]	1 [00:00 - 24:00]	2 [00:00 - 24:00]	3 [00:00 - 24:00]	4 [00:00 - 24:00]	5 [00:00 - 24:00]	6 [00:00 - 24:00]	7 [DCO]	8 [00:00 - 24:00]	9 [00:00 - 24:00]	10 [00:00 - 24:00]	11 [00:00 - 24:00]	12 [00:00 - 24:00]	13 [00:00 - 24:00]	14 [DCO]
4/F	046	normal	NAD			1	1	1	1	1	1									
		activity/ behavior	apathy									1	1	1	1	1	1	1		
		general condition	poor	Grade: moderate								1	1	1	1	1	1	1	1	1
		posture	hunched posture									1	1	1	1	1	1	1	1	
		gait	high-stepping gait										1	1	1	1	1	1	1	1
		eye	semiclosed eyelid	Directional terms: both												1	1	1	1	
		dead	sacrificed scheduled																	
	047	normal	NAD			1	1	1	1	1	1									
		general condition	poor	Grade: slight								1	1	1	1	1	1	1	1	1
		activity/ behavior	apathy									1	1	1	1	1	1	1		
		gait	high-stepping gait													1	1	1	1	1
		dead	sacrificed scheduled																	
	048	normal	NAD			1	1	1	1	1	1	1								
		general condition	poor	Grade: slight									1	1	1	1	1	1	1	
		gait	high-stepping gait										1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	049	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	
	050	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day														
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
0/F	026	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	027	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	028	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	029	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	030	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day																					
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
1/F	031	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	032	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	033	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	034	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	035	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day																					
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
2/F	036	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	037	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	038	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	039	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	040	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day														
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
3/F	041	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	042	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	043	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	044	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	045	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

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Study 31C0343/09S078

Individual Signs By Interval - Clinical Observation

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	Sign Type	Sign	Modifier	Remark	Day														
						15 [00:00 - 24:00]	16 [00:00 - 24:00]	17 [00:00 - 24:00]	18 [00:00 - 24:00]	19 [00:00 - 24:00]	20 [00:00 - 24:00]	21 [DCO]	22 [00:00 - 24:00]	23 [00:00 - 24:00]	24 [00:00 - 24:00]	25 [00:00 - 24:00]	26 [00:00 - 24:00]	27 [00:00 - 24:00]	28 [DCO]	29 [00:00 - 24:00]
4/F	046	normal	NAD																	
		activity/ behavior	apathy																	
		general condition	poor	Grade: moderate		1	1	1	1	1	1									
		posture	hunched posture																	
		gait	high-stepping gait			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		eye	semiclosed eyelid	Directional terms: both																
		dead	sacrificed scheduled																	1
	047	normal	NAD																	
		general condition	poor	Grade: slight		1	1	1	1	1	1									
		activity/ behavior	apathy																	
		gait	high-stepping gait			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	048	normal	NAD																	
		general condition	poor	Grade: slight																
		gait	high-stepping gait			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	049	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1
	050	normal	NAD			1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
		dead	sacrificed scheduled																	1

IIA 21
07-Aug-2017 12:13
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Study 31C0343/09S078

Individual Food Consumption Per Animal And Day [g/Day]

Sex: **Male** - Phase: **In-life**

Group	Cage	Animals	d 0 -> 7	d 7 -> 14	d 14 -> 21	d 21 -> 28
0/M	01	005, 004, 002, 001, 003	3.5	3.5	3.6	3.7
1/M	02	008, 010, 006, 009, 007	3.4	3.4	3.4	3.5
2/M	03	015, 012, 013, 011, 014	3.5	3.6	3.5	3.9
3/M	04	019, 016, 020, 017, 018	3.0	3.7	3.6	3.7
4/M	05	025, 024, 022, 023, 021	3.2	3.0	3.3	3.1

d = day

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Study 31C0343/09S078

Individual Food Consumption Per Animal And Day [g/Day]

Sex: **Female** - Phase: **In-life**

Group	Cage	Animals	d 0 -> 7	d 7 -> 14	d 14 -> 21	d 21 -> 28
0/F	06	029, 028, 030, 026, 027	3.6	3.8	3.8	4.1
1/F	07	034, 032, 033, 031, 035	3.9	4.1	0.5OL	4.5
2/F	08	038, 036, 039, 040, 037	3.3	3.6	3.6	3.9
3/F	09	042, 044, 045, 041, 043	3.4	3.6	3.8	4.0
4/F	10	049, 050, 048, 046, 047	2.7	3.2	3.0	3.3

d = day; OL = Outlier

IIA 23
08-Aug-2017 11:14
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Study 31C0343/09S078

Individual Water Consumption Per Animal And Day [g/Day]

Sex: **Male** - Phase: **In-life**

Group	Cage	Animals	d 3 -> 7	d 10 -> 14	d 17 -> 21	d 24 -> 28
0/M	01	005, 004, 002, 001, 003	3.1	3.1	3.3	3.3
1/M	02	008, 010, 006, 009, 007	2.9	3.2	3.2	3.3
2/M	03	015, 012, 013, 011, 014	3.1	3.2	3.1	3.4
3/M	04	019, 016, 020, 017, 018	3.2	3.1	2.9	3.0
4/M	05	025, 024, 022, 023, 021	2.3	2.2	2.3	2.2

d = day

IIA 24
08-Aug-2017 11:14
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Study 31C0343/09S078

Individual Water Consumption Per Animal And Day [g/Day]

Sex: **Female** - Phase: **In-life**

Group	Cage	Animals	d 3 -> 7	d 10 -> 14	d 17 -> 21	d 24 -> 28
0/F	06	029, 028, 030, 026, 027	3.4	3.5	3.4	3.5
1/F	07	034, 032, 033, 031, 035	3.2	3.3	3.7	3.9
2/F	08	038, 036, 039, 040, 037	3.4	3.5	3.7	3.6
3/F	09	042, 044, 045, 041, 043	3.3	3.3	3.4	3.4
4/F	10	049, 050, 048, 046, 047	1.8	2.0	2.2	2.4

d = day

Individual Body Weights - BW / Body Weights [g]

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	day 0	day 7	day 14	day 21	day 28
0/M	001	21.4	21.5	22.9	23.7	23.6
	002	21.8	21.7	22.4	23.0	23.9
	003	20.9	20.6	22.9	23.5	24.0
	004	20.0	21.6	21.4	21.9	23.2
	005	20.7	22.7	23.8	25.1	25.8
1/M	006	19.9	20.4	21.2	21.6	23.0
	007	21.6	22.4	23.6	24.0	25.5
	008	21.9	22.5	23.1	23.3	24.5
	009	22.1	23.1	24.1	25.6	26.7
	010	21.1	22.1	23.1	24.1	26.2
2/M	011	21.6	23.0	24.0	24.9	25.9
	012	20.6	21.0	21.5	22.5	23.3
	013	21.7	22.0	22.6	23.6	23.8
	014	22.2	23.1	24.0	24.6	26.2
	015	20.1	21.6	22.6	24.3	25.6
3/M	016	21.5	23.4	24.5	25.0	25.7
	017	21.5	22.9	23.8	25.0	25.4
	018	21.2	22.0	22.7	23.5	23.2
	019	21.1	22.1	23.3	24.6	25.8
	020	20.5	22.6	24.3	25.1	26.0
4/M	021	20.4	20.7	20.3	21.2	20.7
	022	21.9	22.9	21.9	22.7	21.6
	023	20.8	20.7	20.4	21.3	22.0
	024	20.6	20.3	19.6	20.0	18.6
	025	21.3	21.4	20.8	22.2	22.2

IIA 26
08-Aug-2017 11:15
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Study 31C0343/09S078

Individual Body Weights - BW / Body Weights [g]

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	day 0	day 7	day 14	day 21	day 28
0/F	026	17.1	18.3	18.5	18.7	18.6
	027	17.7	18.9	19.4	20.5	20.7
	028	17.1	18.7	19.4	19.6	19.6
	029	17.2	18.1	18.3	18.7	18.8
	030	18.0	19.3	19.2	20.0	20.0
1/F	031	18.3	18.8	19.3	20.2	20.2
	032	16.9	17.6	18.7	19.7	19.8
	033	18.3	18.4	18.8	18.9	19.9
	034	17.1	18.5	18.9	19.6	19.6
	035	16.6	17.9	18.6	19.0	19.9
2/F	036	17.1	18.3	18.5	19.2	19.8
	037	17.2	18.8	18.8	19.6	20.0
	038	18.2	19.1	20.3	20.7	20.6
	039	16.6	17.3	16.9	18.8	18.6
	040	17.3	18.0	18.6	19.5	19.8
3/F	041	17.7	18.5	19.0	19.5	19.8
	042	16.5	17.3	18.5	19.4	19.7
	043	17.2	18.5	18.4	18.9	19.8
	044	17.5	19.3	19.3	20.2	20.9
	045	18.0	18.8	19.4	20.0	21.4
4/F	046	17.3	15.1	16.0	16.2	16.1
	047	16.9	15.1	16.3	17.3	17.2
	048	17.5	17.0	17.2	19.0	18.5
	049	18.2	18.6	18.3	18.7	19.5
	050	17.8	18.6	18.1	19.1	19.3

IIB 1

06-Dec-2011 16:03

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Study 31C0343/09S078

Red blood cell parameters

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	RBC [tera/L] day 29	HGB [mmol/L] day 29	HCT [L/L] day 29	MCV [fL] day 29	MCH [fmol] day 29	MCHC [mmol/L] day 29	RET [%] day 29	PLT [giga/L] day 29
0/M	001	10.20	9.0	0.460	45.2	0.87	19.32	2.6	1,486
	002	10.22	8.6	0.456	44.6	0.84	18.93	2.5	1,460
	003	9.16	7.6	0.400	43.6	0.84	19.20	2.7	1,644
	004	9.72	8.2	0.432	44.5	0.84	18.84	2.7	1,520
	005	11.00	9.4	0.480	43.6	0.85	19.50	2.6	1,390
1/M	006	10.12	8.8	0.472	46.7	0.86	18.44	2.7	1,740
	007	6.92	8.4	0.308	44.6	1.21	27.22	2.3	1,888
	008	9.04	7.6	0.398	44.1	0.84	19.05	2.4	1,426
	009	10.74	9.2	0.480	44.6	0.86	19.26	2.7	1,576
	010	9.64	8.2	0.430	44.5	0.84	18.93	3.1	1,424
2/M	011	8.72	7.2	0.390	44.9	0.83	18.52	2.6	1,810
	012	10.72	9.2	0.486	45.3	0.86	19.01	2.8	1,578
	013	10.26	9.0	0.452	44.1	0.87	19.82	2.6	1,540
	014	9.72	8.2	0.430	44.3	0.85	19.11	2.4	1,582
	015	9.98	8.4	0.448	44.9	0.85	18.91	2.4	1,670
3/M	016	10.22	8.6	0.458	44.7	0.84	18.83	2.7	1,860
	017	10.00	8.6	0.444	44.5	0.86	19.25	2.6	1,922
	018	10.26	8.6	0.450	43.9	0.83	18.89	2.3	1,610
	019	10.56	8.8	0.464	43.9	0.83	18.96	2.2	1,846
	020	10.46	9.0	0.456	43.5	0.86	19.74	2.4	1,804
4/M	021	7.48	6.0	0.330	44.2	0.79	17.87	2.6	1,742
	022	8.50	7.2	0.384	45.1	0.85	18.88	3.4	812
	023	9.36	7.8	0.408	43.7	0.83	19.08	2.1	1,816
	024	6.94	6.0	0.318	45.8	0.85	18.62	4.6	738
	025	9.54	8.0	0.414	43.4	0.83	19.17	1.8	1,778

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Study 31C0343/09S078

Red blood cell parameters

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	RBC [tera/L] day 29	HGB [mmol/L] day 29	HCT [L/L] day 29	MCV [fL] day 29	MCH [fmol] day 29	MCHC [mmol/L] day 29	RET [%] day 29	PLT [giga/L] day 29
0/F	026	7.64	6.4	0.346	45.2	0.84	18.59	2.3	1,472
	027	9.60	8.4	0.430	44.9	0.88	19.66	2.9	1,404
	028	8.86	7.6	0.396	44.7	0.85	19.04	2.4	288
	029	10.32	8.8	0.456	44.2	0.86	19.45	2.7	1,322
	030	10.24	8.8	0.454	44.4	0.86	19.30	2.5	1,260
1/F	031	9.60	8.4	0.442	46.1	0.88	19.02	2.2	1,390
	032	9.74	8.8	0.436	44.8	0.89	19.95	1.8	1,544
	033	10.02	8.6	0.448	44.8	0.86	19.14	2.7	1,384
	034	8.88	7.6	0.414	46.6	0.87	18.62	3.2	874
	035	10.46	9.4	0.474	45.4	0.91	19.99	2.3	1,224
2/F	036	11.56	9.6	0.526	45.5	0.83	18.24	3.0	1,036
	037	10.20	8.8	0.456	44.6	0.86	19.33	2.5	1,330
	038	9.86	8.8	0.446	45.4	0.89	19.59	2.8	1,294
	039	9.20	7.8	0.408	44.4	0.85	19.25	2.5	1,280
	040	9.42	8.2	0.420	44.7	0.87	19.49	2.2	1,362
3/F	041	8.70	7.4	0.394	45.1	0.86	18.98	2.6	1,476
	042	10.54	9.0	0.470	44.7	0.86	19.17	2.2	1,560
	043	9.14	8.0	0.418	45.6	0.88	19.20	2.6	1,368
	044	9.18	8.0	0.406	44.2	0.88	19.85	3.5	1,782
	045	9.70	8.2	0.426	43.9	0.84	19.21	2.2	1,416
4/F	046	8.38	7.2	0.370	44.2	0.86	19.57	1.9	1,524
	047	9.64	8.2	0.424	44.1	0.85	19.30	2.6	1,704
	048	10.32	8.6	0.450	43.6	0.84	19.26	2.3	1,638
	049	9.34	7.8	0.408	43.8	0.83	18.98	2.6	1,422
	050	7.20	6.4	0.314	43.5	0.88	20.32	3.9	974

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06-Dec-2011 16:06

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Study 31C0343/09S078

White blood cell parameters

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	WBC [giga/L] day 29	NEUTA [giga/L] day 29	LYMPHA [giga/L] day 29	MONOA [giga/L] day 29	EOSA [giga/L] day 29	BASOA [giga/L] day 29	LUCA [giga/L] day 29	NEUT [%] day 29	LYMPH [%] day 29	MONO [%] day 29	EOS [%] day 29	BASO [%] day 29	LUC [%] day 29
0/M	001	2.72	0.38	2.28	0.02	0.02	0.00	0.00	14.0	83.9	0.7	1.0	0.3	0.1
	002	5.70	0.52	5.10	0.02	0.02	0.00	0.02	9.3	89.6	0.2	0.4	0.0	0.5
	003	4.78	0.36	4.36	0.02	0.04	0.00	0.02	7.3	90.9	0.5	0.8	0.1	0.4
	004	4.42	0.34	4.04	0.02	0.00	0.00	0.02	7.7	91.4	0.5	0.1	0.1	0.2
	005	3.00	0.30	2.66	0.00	0.02	0.00	0.02	10.2	88.5	0.2	0.6	0.2	0.4
1/M	006	3.50	0.36	3.10	0.02	0.02	0.00	0.02	10.0	88.7	0.5	0.4	0.1	0.3
	007	5.80	0.58	5.14	0.02	0.02	0.00	0.04	9.9	88.6	0.3	0.4	0.0	0.7
	008	4.22	0.26	3.92	0.02	0.02	0.00	0.00	6.2	92.8	0.4	0.3	0.1	0.2
	009	6.68	0.28	6.32	0.02	0.02	0.00	0.04	4.1	94.6	0.4	0.4	0.0	0.5
	010	3.14	0.22	2.90	0.00	0.00	0.00	0.02	7.0	92.2	0.2	0.2	0.2	0.4
2/M	011	4.56	0.30	4.20	0.04	0.04	0.00	0.02	6.5	91.7	0.7	0.7	0.1	0.3
	012	4.06	0.32	3.68	0.00	0.04	0.00	0.02	8.1	90.5	0.2	0.8	0.2	0.3
	013	4.90	0.26	4.58	0.02	0.02	0.00	0.02	5.2	93.5	0.4	0.3	0.1	0.6
	014	2.34	0.18	2.14	0.00	0.00	0.00	0.00	7.3	91.7	0.2	0.3	0.1	0.4
	015	5.56	0.42	5.08	0.02	0.04	0.00	0.02	7.4	91.3	0.3	0.6	0.1	0.3
3/M	016	5.78	0.66	5.04	0.04	0.02	0.00	0.02	11.3	87.3	0.6	0.3	0.0	0.4
	017	6.32	0.36	5.88	0.02	0.04	0.00	0.02	5.7	93.0	0.3	0.6	0.1	0.4
	018	6.02	0.58	5.34	0.02	0.04	0.00	0.04	9.5	88.8	0.4	0.7	0.1	0.5
	019	3.32	0.16	3.10	0.02	0.02	0.00	0.00	4.9	93.8	0.4	0.6	0.1	0.2
	020	3.30	0.18	3.06	0.02	0.02	0.00	0.02	5.7	92.8	0.6	0.4	0.0	0.4
4/M	021	2.78	0.36	2.34	0.02	0.04	0.00	0.02	12.9	83.8	0.9	1.2	0.3	0.9
	022	4.58	1.36	3.06	0.06	0.02	0.00	0.08	29.8	66.7	1.3	0.6	0.1	1.6
	023	6.04	0.42	5.48	0.02	0.04	0.00	0.04	7.1	90.9	0.5	0.6	0.1	0.8
	024	1.48	0.34	1.04	0.02	0.06	0.00	0.02	22.7	70.6	1.0	3.8	0.2	1.8
	025	3.00	0.38	2.58	0.00	0.02	0.00	0.00	12.4	86.3	0.3	0.5	0.2	0.3

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Study 31C0343/09S078

White blood cell parameters

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	WBC [giga/L] day 29	NEUTA [giga/L] day 29	LYMPHA [giga/L] day 29	MONOA [giga/L] day 29	EOSA [giga/L] day 29	BASOA [giga/L] day 29	LUCA [giga/L] day 29	NEUT [%] day 29	LYMPH [%] day 29	MONO [%] day 29	EOS [%] day 29	BASO [%] day 29	LUC [%] day 29
0/F	026	2.42	0.32	2.06	0.02	0.00	0.00	0.02	13.5	84.9	0.8	0.1	0.3	0.4
	027	2.02	0.22	1.78	0.02	0.02	0.00	0.00	11.0	87.5	0.8	0.5	0.2	0.0
	028	2.70	0.54	2.10	0.04	0.02	0.00	0.00	20.1	78.0	1.1	0.6	0.0	0.1
	029	4.32	0.66	3.58	0.02	0.02	0.02	0.02	15.3	83.0	0.4	0.7	0.3	0.3
	030	5.10	0.54	4.46	0.02	0.04	0.00	0.02	10.7	87.6	0.3	0.8	0.1	0.6
1/F	031	4.72	0.34	4.26	0.04	0.06	0.02	0.02	7.4	90.2	0.7	1.1	0.3	0.4
	032	5.18	0.42	4.62	0.02	0.08	0.02	0.04	8.0	89.2	0.5	1.4	0.2	0.6
	033	4.22	0.24	3.90	0.00	0.06	0.00	0.02	5.7	92.5	0.2	1.3	0.0	0.3
	034	3.92	0.36	3.46	0.04	0.04	0.00	0.02	9.2	88.5	0.8	1.0	0.1	0.4
	035	4.70	0.46	4.16	0.02	0.02	0.00	0.02	9.7	88.6	0.5	0.5	0.0	0.6
2/F	036	3.24	0.40	2.76	0.02	0.04	0.00	0.02	12.2	85.1	0.6	1.3	0.1	0.8
	037	3.04	0.42	2.58	0.02	0.02	0.00	0.02	13.6	84.9	0.4	0.6	0.1	0.4
	038	2.46	0.30	2.12	0.02	0.00	0.00	0.02	12.4	85.9	0.7	0.3	0.1	0.6
	039	3.54	0.44	2.98	0.06	0.06	0.00	0.00	12.5	83.9	1.8	1.6	0.1	0.2
	040	1.50	0.24	1.24	0.00	0.00	0.00	0.00	15.4	82.9	0.3	0.6	0.6	0.2
3/F	041	5.86	0.66	5.08	0.02	0.06	0.00	0.02	11.4	86.5	0.4	1.1	0.2	0.4
	042	2.62	0.20	2.40	0.00	0.02	0.00	0.02	7.4	91.4	0.1	0.6	0.1	0.4
	043	3.78	0.34	3.38	0.02	0.02	0.00	0.02	8.7	89.4	0.8	0.7	0.1	0.3
	044	6.42	0.44	5.88	0.02	0.04	0.00	0.02	6.9	91.7	0.2	0.8	0.1	0.2
	045	1.26	0.16	1.06	0.00	0.02	0.00	0.00	12.6	84.3	0.5	1.8	0.8	0.0
4/F	046	2.32	0.20	2.06	0.02	0.02	0.00	0.00	8.8	88.8	0.9	0.9	0.2	0.4
	047	3.94	0.32	3.58	0.02	0.02	0.00	0.00	7.9	91.1	0.3	0.4	0.1	0.2
	048	4.90	0.54	4.26	0.02	0.04	0.00	0.02	11.1	86.9	0.2	1.0	0.1	0.6
	049	4.18	0.26	3.86	0.00	0.02	0.00	0.02	6.4	92.6	0.1	0.4	0.1	0.4
	050	1.48	0.20	1.26	0.00	0.02	0.00	0.00	12.8	85.2	0.3	0.8	0.5	0.3

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Study 31C0343/09S078

Enzymes

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	ALT [µkat/L] day 29	AST [µkat/L] day 29	ALP [µkat/L] day 29	GGT_C [nkat/L] day 29
0/M	001	0.94	6.31	1.65	0
	002	0.73	5.84	1.60	0
	003	0.59	3.40	1.72	0
	004	0.55	4.01	2.43	0
	005	0.73	5.43	2.33	0
1/M	006	0.68	4.90	1.94	0
	007	0.41	2.40	1.76	0
	008	0.50	3.57	1.76	0
	009	0.47	3.14	1.65	0
	010	0.45	3.30	1.96	0
2/M	011	0.60	5.12	2.07	0
	012	0.62	4.57	2.06	0
	013	0.55	3.65	1.87	0
	014	0.58	4.31	2.17	0
	015	0.52	4.41	2.03	0
3/M	016	0.53	4.66	1.70	0
	017	0.53	3.64	1.95	0
	018	0.56	3.39	1.65	0
	019	0.49	3.90	3.18	0
	020	0.54	3.55	1.88	0
4/M	021	0.94	6.86	1.58	0
	022	1.65	9.85	0.97	0
	023	1.00	3.47	1.63	0
	024	1.66	7.63	0.69	0
	025	0.74	4.54	1.70	0

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Study 31C0343/09S078

Enzymes

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	ALT [µkat/L] day 29	AST [µkat/L] day 29	ALP [µkat/L] day 29	GGT_C [nkat/L] day 29
0/F	026	1.83	10.09	2.45	0
	027	0.48	3.93	3.15	0
	028	0.98	6.22	2.55	0
	029	0.80	6.66	2.22	0
	030	0.77	4.53	2.29	0
1/F	031	0.92	5.89	2.46	0
	032	0.84	7.20	2.43	0
	033	0.70	3.85	2.84	0
	034	0.80	5.24	2.10	0
	035	1.25	12.12	2.54	0
2/F	036	0.92	5.63	2.11	0
	037	0.76	4.59	2.41	0
	038	0.70	4.47	2.31	0
	039	0.95	7.41	2.30	0
	040	0.73	5.57	2.54	0
3/F	041	1.07	5.89	1.62	0
	042	0.87	3.76	2.25	0
	043	1.02	8.38	2.34	0
	044	1.08	8.80	1.97	0
	045	0.81	4.89	2.37	0
4/F	046	1.33	5.09	1.24	0
	047	1.38	6.45	2.68	0
	048	1.14	4.81	1.94	0
	049	1.07	4.48	2.10	0
	050	1.73	7.69	0.90	0

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Study 31C0343/09S078

15-Sep-2017 12:13

Ascentos™ 1.3

Substrates

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	UREA [mmol/L] day 29	CREA [µmol/L] day 29	GLUC [mmol/L] day 29	TBIL [µmol/L] day 29	TBA [µmol/L] day 29	TPROT [g/L] day 29	ALB [g/L] day 29	GLOB [g/L] day 29	CHOL [mmol/L] day 29	TRIG [mmol/L] day 29
0/M	001	11.43	40.1	4.77	1.59	7.2	50.00	36.00	14.00	1.83	0.64
	002	10.72	39.2	6.66	2.95	4.4	51.16	35.46	15.70	2.28	0.92
	003	9.48	34.0	5.50	2.05	2.8	49.66	35.45	14.21	2.44	0.83
	004	10.51	32.3	6.52	2.03	3.8	51.31	36.04	15.27	2.55	0.72
	005	12.02	38.1	6.59	2.59	2.8	52.71	36.80	15.91	2.45	0.77
1/M	006	12.16	36.0	6.58	2.83	9.6	53.31	37.33	15.98	2.63	0.86
	007	11.49	32.6	9.73	2.67	7.0	53.67	36.97	16.70	2.65	0.90
	008	11.54	38.4	8.06	2.29	4.5	52.74	37.29	15.45	2.99	1.12
	009	10.64	36.2	6.48	1.87	4.3	51.06	35.04	16.02	2.48	0.61
	010	12.71	41.7	7.15	2.35	6.0	49.81	34.78	15.03	2.30	0.65
2/M	011	10.28	36.7	5.19	2.39	4.8	51.60	36.15	15.45	2.30	0.81
	012	9.33	37.0	6.33	3.20	3.0	51.15	35.67	15.48	2.34	1.03
	013	10.65	38.0	7.92	2.33	7.2	51.97	36.55	15.42	2.39	0.77
	014	11.52	36.8	8.12	2.65	4.7	49.97	35.09	14.88	2.00	0.57
	015	11.21	33.5	7.94	2.68	2.9	49.15	34.81	14.34	2.25	0.85
3/M	016	13.06	34.0	7.08	2.15	5.0	49.55	35.29	14.26	2.45	0.81
	017	11.19	39.8	7.07	3.95	2.4	49.59	34.57	15.02	2.52	1.13
	018	14.63	37.4	7.05	4.09	7.8	50.79	36.23	14.56	2.65	1.42
	019	9.75	37.0	7.98	3.52	2.7	52.34	37.40	14.94	2.54	1.02
	020	10.65	36.3	10.85	2.41	3.1	47.34	33.05	14.29	1.99	0.57
4/M	021	13.31	42.2	6.45	4.18	8.7	49.68	34.97	14.71	2.84	1.84
	022	10.58	30.7	4.30	2.71	91.5	43.20	30.02	13.18	2.33	1.68
	023	11.93	38.2	8.38	4.34	6.2	49.90	33.92	15.98	3.31	1.55
	024	10.54	26.7	4.44	2.03	26.5	38.70	26.93	11.77	2.32	1.70
	025	11.90	35.8	6.93	3.72	6.8	47.72	33.35	14.37	3.07	1.26

IIB 8
15-Sep-2017 12:13
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Study 31C0343/09S078

Substrates

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	UREA [mmol/L] day 29	CREA [µmol/L] day 29	GLUC [mmol/L] day 29	TBIL [µmol/L] day 29	TBA [µmol/L] day 29	TPROT [g/L] day 29	ALB [g/L] day 29	GLOB [g/L] day 29	CHOL [mmol/L] day 29	TRIG [mmol/L] day 29
0/F	026	12.60	36.4	7.87	2.38	6.8	46.22	34.71	11.51	1.55	0.84
	027	8.79	41.6	9.04	3.04	4.4	51.12	38.18	12.94	1.95	0.50
	028	11.64	35.9	8.40	1.79	7.5	48.05	36.20	11.85	1.66	0.76
	029	11.83	37.4	10.75	2.18	12.4	50.44	36.70	13.74	2.00	0.58
	030	9.63	33.4	7.32	2.31	6.0	50.25	36.53	13.72	2.22	0.76
1/F	031	11.07	37.4	10.09	1.95	8.0	50.84	36.83	14.01	2.15	0.61
	032	8.94	37.6	9.22	2.39	14.3	51.34	38.21	13.13	1.89	0.72
	033	10.20	35.8	5.29	1.45	7.7	53.09	38.99	14.10	1.96	0.50
	034	8.95	40.2	5.32	2.03	63.5	45.69	32.43	13.26	1.44	0.68
	035	7.49	19.1	1.99	2.70	NM	NM	NM	NM	NM	NM
2/F	036	8.48	33.3	8.12	2.10	9.8	46.64	35.00	11.64	2.07	1.06
	037	9.37	30.4	7.28	2.18	6.3	50.08	36.99	13.09	2.20	0.65
	038	9.55	32.6	8.55	2.11	14.7	48.75	36.47	12.28	2.10	0.65
	039	11.78	42.2	7.47	1.44	10.9	48.34	36.20	12.14	1.82	0.56
	040	10.83	37.6	9.38	1.67	6.4	49.36	36.13	13.23	1.88	0.31
3/F	041	9.80	36.6	6.76	2.60	6.9	48.90	35.65	13.25	2.50	0.94
	042	10.16	32.3	NM	2.41	NM	49.12	NM	NM	NM	NM
	043	18.25	45.0	8.45	1.61	14.8	48.27	34.48	13.79	2.18	0.57
	044	8.38	34.7	7.43	1.92	7.9	49.43	35.11	14.32	2.27	0.85
	045	11.29	33.8	7.48	1.88	9.6	51.20	36.70	14.50	2.12	0.45
4/F	046	10.56	21.6	4.44	4.36	5.0	29.99	7.37	22.62	0.58	0.25
	047	8.70	36.6	4.72	3.47	7.2	48.81	34.28	14.53	2.73	1.19
	048	8.18	32.1	6.93	2.36	6.8	48.89	34.30	14.59	3.41	2.11
	049	8.76	29.2	8.26	2.75	6.2	46.32	33.27	13.05	2.90	1.56
	050	10.15	29.9	5.06	2.82	6.6	45.15	31.32	13.83	3.50	2.57

NM = Not measured

IIB 9

06-Dec-2011 16:31

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Study 31C0343/09S078

Electrolytes + minerals

Sex: **Male** - Phase: **In-life**

Dose Group	Animal Number	NA [mmol/L] day 29	K [mmol/L] day 29	CL [mmol/L] day 29	INP [mmol/L] day 29	CA [mmol/L] day 29	MG [mmol/L] day 29
0/M	001	149.2	6.47	115.6	2.22	2.30	1.24
	002	149.5	6.79	114.4	2.47	2.43	1.24
	003	152.6	5.33	117.8	2.32	2.35	1.19
	004	149.7	6.33	115.9	2.69	2.41	1.21
	005	150.9	6.51	116.0	2.23	2.33	1.09
1/M	006	149.4	6.26	114.0	2.58	2.48	1.45
	007	149.9	5.73	113.3	2.45	2.51	1.23
	008	150.5	6.73	114.3	2.63	2.52	1.26
	009	151.0	5.46	113.6	2.54	2.45	1.28
	010	150.3	5.56	113.2	2.56	2.38	1.19
2/M	011	150.0	6.00	112.8	2.63	2.50	1.32
	012	149.4	7.37	115.5	2.81	2.45	1.28
	013	151.2	5.79	115.1	2.84	2.53	1.33
	014	151.4	5.71	117.7	2.65	2.34	1.15
	015	150.4	6.04	118.6	2.51	2.41	1.18
3/M	016	149.0	5.98	112.7	2.56	2.41	1.30
	017	150.6	6.14	115.4	3.00	2.45	1.31
	018	152.0	5.24	115.2	2.74	2.47	1.36
	019	150.3	6.53	114.8	2.65	2.52	1.20
	020	150.4	6.00	115.7	2.12	2.35	1.16
4/M	021	150.1	5.90	115.4	2.98	2.37	1.32
	022	149.9	6.52	115.1	3.30	2.26	1.26
	023	152.9	5.48	116.9	2.70	2.44	1.35
	024	155.0	6.02	120.8	3.64	2.22	1.21
	025	151.8	6.11	118.3	2.79	2.40	1.17

IIB 10
06-Dec-2011 16:31
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Study 31C0343/09S078

Electrolytes + minerals

Sex: **Female** - Phase: **In-life**

Dose Group	Animal Number	NA [mmol/L] day 29	K [mmol/L] day 29	CL [mmol/L] day 29	INP [mmol/L] day 29	CA [mmol/L] day 29	MG [mmol/L] day 29
0/F	026	148.4	6.97	114.9	3.65	2.31	1.41
	027	151.0	5.24	115.7	2.00	2.35	1.12
	028	151.8	5.48	118.5	3.04	2.38	1.20
	029	151.1	6.26	116.2	2.84	2.40	1.35
	030	150.4	5.59	116.7	2.49	2.38	1.20
1/F	031	149.9	6.31	115.1	2.92	2.44	1.35
	032	147.4	7.08	113.7	2.53	2.35	1.16
	033	153.9	4.63	117.7	3.28	2.34	1.36
	034	151.7	5.57	114.3	2.58	2.20	1.29
	035	146.8	7.99	115.9	2.69	2.15	NM
2/F	036	148.2	5.62	114.0	2.61	2.27	1.21
	037	150.8	6.30	115.9	2.71	2.40	1.27
	038	152.4	5.22	115.9	2.55	2.41	1.20
	039	150.9	6.98	116.2	2.58	2.32	1.26
	040	151.1	5.75	116.7	2.25	2.31	1.23
3/F	041	150.4	5.34	115.4	2.32	2.39	1.35
	042	153.4	5.35	117.9	2.62	2.47	NM
	043	149.9	6.57	117.3	3.24	2.37	1.31
	044	150.6	6.55	115.1	3.00	2.35	1.31
	045	153.7	5.64	119.3	2.65	2.34	1.14
4/F	046	149.9	5.26	116.4	2.50	2.51	0.05
	047	152.0	5.57	118.3	2.72	2.40	1.28
	048	150.8	5.24	117.1	2.76	2.42	1.23
	049	150.3	5.91	115.6	2.83	2.38	1.31
	050	152.3	6.11	119.3	2.60	2.27	1.09

NM = Not measured

BASF PATHOLOGY REPORT IIC 1/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 0

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
M	20.64	4.0	450.6	55.2	117.6	291.4
SD	0.68	1.414	9.788	3.033	10.237	11.567
n	5	5	5	5	5	5
1	20.6	5.0	453.0	55.0	125.0	292.0
2	20.5	3.0	440.0	59.0	111.0	276.0
3	20.8	3.0	446.0	54.0	115.0	306.0
4	19.7	3.0	448.0	57.0	106.0	285.0
5	21.6	6.0	466.0	51.0	131.0	298.0

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Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 0

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
M	866.8	46.4	152.6	38.2	176.8	31.0
SD	33.237	4.722	19.269	1.304	11.189	2.915
n	5	5	5	5	5	5
1	853.0	43.0	156.0	38.0	185.0	29.0
2	818.0	46.0	158.0	39.0	183.0	30.0
3	900.0	54.0	143.0	39.0	186.0	31.0
4	869.0	47.0	179.0	39.0	161.0	29.0
5	894.0	42.0	127.0	36.0	169.0	36.0

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31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 1

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
M	21.62	5.8	449.6	55.4	123.6	284.8
SD	1.052	1.095	15.837	8.081	19.731	15.897
n	5	5	5	5	5	5
6	19.9	4.0	441.0	47.0	100.0	266.0
7	22.0	6.0	437.0	47.0	118.0	303.0
8	21.5	6.0	477.0	58.0	115.0	288.0
9	22.7	7.0	447.0	65.0	152.0	296.0
10	22.0	6.0	446.0	60.0	133.0	271.0

BASF PATHOLOGY REPORT IIC 4/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 1

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
M	846.6	46.6	155.4	44.0	180.0	38.8
SD	60.533	8.792	14.741	6.782	13.172	4.604
n	5	5	5	5	5	5
6	749.0	39.0	151.0	39.0	175.0	32.0
7	835.0	46.0	173.0	45.0	176.0	43.0
8	864.0	61.0	167.0	38.0	202.0	43.0
9	877.0	47.0	150.0	55.0	180.0	39.0
10	908.0	40.0	136.0	43.0	167.0	37.0

BASF PATHOLOGY REPORT IIC 5/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 2

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
M	21.28	5.2	457.0	57.8	128.0	297.2
SD	0.786	1.095	23.033	3.768	4.637	18.807
n	5	5	5	5	5	5
11	22.4	6.0	449.0	54.0	124.0	292.0
12	20.4	6.0	434.0	61.0	124.0	287.0
13	20.7	6.0	448.0	58.0	127.0	277.0
14	21.6	4.0	495.0	62.0	135.0	326.0
15	21.3	4.0	459.0	54.0	130.0	304.0

BASF PATHOLOGY REPORT IIC 6/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 2

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
M	959.4	44.6	168.4	44.8	189.0	36.6
SD	41.343	9.813	18.461	7.396	7.211	3.435
n	5	5	5	5	5	5
11	1023.0	62.0	143.0	46.0	184.0	35.0
12	936.0	41.0	161.0	41.0	182.0	40.0
13	915.0	42.0	193.0	36.0	186.0	40.0
14	973.0	39.0	169.0	56.0	199.0	32.0
15	950.0	39.0	176.0	45.0	194.0	36.0

BASF PATHOLOGY REPORT IIC 7/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 3

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
M	21.8	4.6	448.6	58.2	126.4	298.4
SD	0.648	0.894	15.06	8.167	13.297	18.622
n	5	5	5	5	5	5
16	22.4	6.0	445.0	56.0	133.0	292.0
17	21.9	4.0	448.0	51.0	123.0	284.0
18	20.7	4.0	428.0	61.0	107.0	280.0
19	21.9	4.0	470.0	52.0	126.0	314.0
20	22.1	5.0	452.0	71.0	143.0	322.0

BASF PATHOLOGY REPORT IIC 8/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 3

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
M	1122.2	52.4	165.0	42.6	186.2	37.6
SD	72.799	7.797	25.288	4.278	7.396	6.878
n	5	5	5	5	5	5
16	1140.0	57.0	199.0	46.0	186.0	37.0
17	1173.0	47.0	161.0	37.0	179.0	40.0
18	1003.0	64.0	174.0	39.0	181.0	26.0
19	1110.0	47.0	162.0	45.0	198.0	42.0
20	1185.0	47.0	129.0	46.0	187.0	43.0

BASF PATHOLOGY REPORT IIC 9/72
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Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 4

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
M	18.66	5.6	433.2	51.0	116.4	287.0
SD	1.303	1.517	13.535	9.22	16.041	24.99
n	5	5	5	5	5	5
21	18.8	6.0	419.0	52.0	98.0	263.0
22	19.2	4.0	448.0	44.0	142.0	328.0
23	19.2	5.0	429.0	56.0	114.0	273.0
24	16.4	8.0	423.0	40.0	111.0	281.0
25	19.7	5.0	447.0	63.0	117.0	290.0

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Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 4

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
M	995.6	40.2	91.6	33.8	188.4	21.2
SD	154.281	10.826	41.495	5.975	56.221	10.78
n	5	5	5	5	5	5
21	994.0	43.0	89.0	29.0	190.0	27.0
22	924.0	50.0	93.0	36.0	132.0	11.0
23	1156.0	46.0	145.0	42.0	184.0	25.0
24	778.0	22.0	29.0	27.0	156.0	9.0
25	1126.0	40.0	102.0	35.0	280.0	34.0

BASF PATHOLOGY REPORT IIC 11/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 0

	Term. body weight g	Adrenal glands mg	Brain mg	Heart mg	Kidneys mg	Liver mg
M	16.76	7.2	444.2	108.2	249.4	781.0
SD	0.74	0.837	23.232	13.142	18.716	33.705
n	5	5	5	5	5	5
26	16.1	8.0	422.0	98.0	227.0	786.0
27	17.9	7.0	443.0	122.0	270.0	751.0
28	16.8	8.0	421.0	121.0	237.0	818.0
29	16.1	6.0	463.0	93.0	246.0	742.0
30	16.9	7.0	472.0	107.0	267.0	808.0

BASF PATHOLOGY REPORT IIC 12/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 0

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
M	15.8	47.2	39.2	70.2
SD	1.924	6.907	1.924	25.821
n	5	5	5	5
26	13.0	38.0	40.0	49.0
27	18.0	53.0	42.0	71.0
28	15.0	46.0	39.0	55.0
29	17.0	44.0	37.0	62.0
30	16.0	55.0	38.0	114.0

BASF PATHOLOGY REPORT IIC 13/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 1

	Term. body weight g	Adrenal glands mg	Brain mg	Heart mg	Kidneys mg	Liver mg
M	16.84	7.2	450.2	111.2	254.0	733.2
SD	0.365	1.304	14.704	11.777	13.172	69.283
n	5	5	5	5	5	5
31	17.3	8.0	446.0	119.0	248.0	777.0
32	17.1	6.0	432.0	112.0	238.0	753.0
33	16.6	9.0	472.0	100.0	255.0	706.0
34	16.8	7.0	455.0	126.0	274.0	627.0
35	16.4	6.0	446.0	99.0	255.0	803.0

BASF PATHOLOGY REPORT IIC 14/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 1

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
M	13.6	48.4	46.8	76.4
SD	1.673	5.03	4.207	21.267
n	5	5	5	5
31	14.0	43.0	47.0	103.0
32	14.0	44.0	48.0	83.0
33	16.0	53.0	42.0	78.0
34	12.0	54.0	44.0	44.0
35	12.0	48.0	53.0	74.0

BASF PATHOLOGY REPORT IIC 15/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 2

	Term. body weight g	Adrenal glands mg	Brain mg	Heart mg	Kidneys mg	Liver mg
M	16.72	8.2	437.8	106.4	240.2	807.2
SD	0.814	1.304	20.241	6.107	13.882	37.252
n	5	5	5	5	5	5
36	17.2	9.0	431.0	109.0	231.0	828.0
37	17.1	9.0	463.0	106.0	252.0	784.0
38	17.5	8.0	453.0	110.0	256.0	861.0
39	15.5	6.0	412.0	96.0	223.0	768.0
40	16.3	9.0	430.0	111.0	239.0	795.0

BASF PATHOLOGY REPORT IIC 16/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 2

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
M	13.6	46.2	44.0	84.4
SD	1.949	7.662	2.915	42.618
n	5	5	5	5
36	16.0	47.0	42.0	156.0
37	13.0	55.0	46.0	86.0
38	13.0	52.0	43.0	55.0
39	11.0	40.0	48.0	50.0
40	15.0	37.0	41.0	75.0

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Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 3

	Term. body weight g	Adrenal glands mg	Brain mg	Heart mg	Kidneys mg	Liver mg
M	17.1	8.0	436.6	110.0	253.0	956.4
SD	0.43	0.707	11.126	8.515	17.819	50.152
n	5	5	5	5	5	5
41	17.3	9.0	430.0	102.0	237.0	1016.0
42	16.6	8.0	422.0	100.0	231.0	878.0
43	16.7	7.0	436.0	119.0	268.0	964.0
44	17.6	8.0	447.0	113.0	269.0	951.0
45	17.3	8.0	448.0	116.0	260.0	973.0

BASF PATHOLOGY REPORT IIC 18/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 3

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
M	14.2	48.6	44.4	81.6
SD	2.683	7.956	6.066	23.137
n	5	5	5	5
41	12.0	41.0	41.0	70.0
42	16.0	42.0	51.0	122.0
43	13.0	47.0	36.0	64.0
44	18.0	60.0	49.0	75.0
45	12.0	53.0	45.0	77.0

BASF PATHOLOGY REPORT IIC 19/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 4

	Term. body weight g	Adrenal glands mg	Brain mg		Heart mg	Kidneys mg	Liver mg
M	15.6	8.8	415.75		97.4	245.6	981.8
SD	0.957	1.924	27.439		9.29	22.579	70.704
n	5	5	4		5	5	5
46	14.2	9.0	376.0		89.0	217.0	898.0
47	15.1	8.0	419.0		98.0	236.0	923.0
48	16.2	6.0	323.0	s	94.0	249.0	1010.0
49	16.6	10.0	435.0		93.0	247.0	1006.0
50	15.9	11.0	433.0		113.0	279.0	1072.0

BASF PATHOLOGY REPORT IIC 20/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 4

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
M	11.4	32.8	35.6	74.0
SD	3.847	6.834	14.153	40.639
n	5	5	5	5
46	8.0	24.0	26.0	28.0
47	14.0	38.0	52.0	89.0
48	12.0	36.0	35.0	118.0
49	16.0	39.0	47.0	101.0
50	7.0	27.0	18.0	34.0

BASF PATHOLOGY REPORT IIC 21/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 0

	Term. body weight	Adrenal glands	Brain	Epididymides	Heart	Kidneys
	%	%	%	%	%	%
M	100.0	0.019	2.184	0.268	0.569	1.412
SD		0.006	0.055	0.022	0.035	0.05
n	5	5	5	5	5	5
1	100.0	0.024	2.199	0.267	0.607	1.417
2	100.0	0.015	2.146	0.288	0.541	1.346
3	100.0	0.014	2.144	0.26	0.553	1.471
4	100.0	0.015	2.274	0.289	0.538	1.447
5	100.0	0.028	2.157	0.236	0.606	1.38

BASF PATHOLOGY REPORT IIC 22/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 0

	Liver	Prostate	Seminal vesicle	Spleen	Testes	Thymus
	%	%	%	%	%	%
M	4.202	0.225	0.742	0.185	0.857	0.15
SD	0.167	0.025	0.118	0.012	0.054	0.01
n	5	5	5	5	5	5
1	4.141	0.209	0.757	0.184	0.898	0.141
2	3.99	0.224	0.771	0.19	0.893	0.146
3	4.327	0.26	0.688	0.188	0.894	0.149
4	4.411	0.239	0.909	0.198	0.817	0.147
5	4.139	0.194	0.588	0.167	0.782	0.167

BASF PATHOLOGY REPORT IIC 23/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 1

	Term. body weight	Adrenal glands	Brain	Epididy-mides	Heart	Kidneys
	%	%	%	%	%	%
M	100.0	0.027	2.083	0.256	0.57	1.318
SD		0.004	0.124	0.03	0.067	0.055
n	5	5	5	5	5	5
6	100.0	0.02	2.216	0.236	0.503	1.337
7	100.0	0.027	1.986	0.214	0.536	1.377
8	100.0	0.028	2.219	0.27	0.535	1.34
9	100.0	0.031	1.969	0.286	0.67	1.304
10	100.0	0.027	2.027	0.273	0.605	1.232

BASF PATHOLOGY REPORT IIC 24/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 1

	Liver	Prostate	Seminal vesicle	Spleen	Testes	Thymus
	%	%	%	%	%	%
M	3.914	0.216	0.72	0.203	0.834	0.179
SD	0.155	0.04	0.076	0.024	0.074	0.017
n	5	5	5	5	5	5
6	3.764	0.196	0.759	0.196	0.879	0.161
7	3.795	0.209	0.786	0.205	0.8	0.195
8	4.019	0.284	0.777	0.177	0.94	0.2
9	3.863	0.207	0.661	0.242	0.793	0.172
10	4.127	0.182	0.618	0.195	0.759	0.168

BASF PATHOLOGY REPORT IIC 25/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 2

	Term. body weight	Adrenal glands	Brain	Epididymides	Heart	Kidneys
	%	%	%	%	%	%
M	100.0	0.024	2.149	0.272	0.602	1.397
SD		0.005	0.102	0.024	0.028	0.08
n	5	5	5	5	5	5
11	100.0	0.027	2.004	0.241	0.554	1.304
12	100.0	0.029	2.127	0.299	0.608	1.407
13	100.0	0.029	2.164	0.28	0.614	1.338
14	100.0	0.019	2.292	0.287	0.625	1.509
15	100.0	0.019	2.155	0.254	0.61	1.427

BASF PATHOLOGY REPORT IIC 26/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 2

	Liver	Prostate	Seminal vesicle	Spleen	Testes	Thymus
	%	%	%	%	%	%
M	4.508	0.209	0.794	0.21	0.889	0.173
SD	0.071	0.039	0.106	0.031	0.039	0.022
n	5	5	5	5	5	5
11	4.567	0.277	0.638	0.205	0.821	0.156
12	4.588	0.201	0.789	0.201	0.892	0.196
13	4.42	0.203	0.932	0.174	0.899	0.193
14	4.505	0.181	0.782	0.259	0.921	0.148
15	4.46	0.183	0.826	0.211	0.911	0.169

BASF PATHOLOGY REPORT IIC 27/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 3

	Term. body weight %	Adrenal glands %	Brain %	Epididymides %	Heart %	Kidneys %
M	100.0	0.021	2.058	0.267	0.579	1.369
SD		0.004	0.058	0.039	0.047	0.074
n	5	5	5	5	5	5
16	100.0	0.027	1.987	0.25	0.594	1.304
17	100.0	0.018	2.046	0.233	0.562	1.297
18	100.0	0.019	2.068	0.295	0.517	1.353
19	100.0	0.018	2.146	0.237	0.575	1.434
20	100.0	0.023	2.045	0.321	0.647	1.457

BASF PATHOLOGY REPORT IIC 28/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 3

	Liver	Prostate	Seminal vesicle	Spleen	Testes	Thymus
	%	%	%	%	%	%
M	5.144	0.241	0.758	0.195	0.854	0.172
SD	0.218	0.042	0.117	0.017	0.035	0.028
n	5	5	5	5	5	5
16	5.089	0.254	0.888	0.205	0.83	0.165
17	5.356	0.215	0.735	0.169	0.817	0.183
18	4.845	0.309	0.841	0.188	0.874	0.126
19	5.068	0.215	0.74	0.205	0.904	0.192
20	5.362	0.213	0.584	0.208	0.846	0.195

BASF PATHOLOGY REPORT IIC 29/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 4

	Term. body weight %	Adrenal glands %	Brain %	Epididymides %	Heart %	Kidneys %
M	100.0	0.031	2.329	0.272	0.625	1.543
SD		0.011	0.146	0.036	0.084	0.156
n	5	5	5	5	5	5
21	100.0	0.032	2.229	0.277	0.521	1.399
22	100.0	0.021	2.333	0.229	0.74	1.708
23	100.0	0.026	2.234	0.292	0.594	1.422
24	100.0	0.049	2.579	0.244	0.677	1.713
25	100.0	0.025	2.269	0.32	0.594	1.472

BASF PATHOLOGY REPORT IIC 30/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex M
Group 4

	Liver	Prostate	Seminal vesicle	Spleen	Testes	Thymus
	%	%	%	%	%	%
M	5.316	0.213	0.482	0.181	1.006	0.112
SD	0.556	0.049	0.206	0.025	0.264	0.053
n	5	5	5	5	5	5
21	5.287	0.229	0.473	0.154	1.011	0.144
22	4.813	0.26	0.484	0.188	0.688	0.057
23	6.021	0.24	0.755	0.219	0.958	0.13
24	4.744	0.134	0.177	0.165	0.951	0.055
25	5.716	0.203	0.518	0.178	1.421	0.173

BASF PATHOLOGY REPORT IIC 31/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 0

	Term. body weight	Adrenal glands	Brain	Heart	Kidneys	Liver
	%	%	%	%	%	%
M	100.0	0.043	2.654	0.644	1.487	4.667
SD		0.005	0.176	0.057	0.075	0.285
n	5	5	5	5	5	5
26	100.0	0.05	2.621	0.609	1.41	4.882
27	100.0	0.039	2.475	0.682	1.508	4.196
28	100.0	0.048	2.506	0.72	1.411	4.869
29	100.0	0.037	2.876	0.578	1.528	4.609
30	100.0	0.041	2.793	0.633	1.58	4.781

BASF PATHOLOGY REPORT IIC 32/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 0

	Ovaries %	Spleen %	Thymus %	Uterus %
M	0.094	0.281	0.234	0.418
SD	0.01	0.033	0.009	0.149
n	5	5	5	5
26	0.081	0.236	0.248	0.304
27	0.101	0.296	0.235	0.397
28	0.089	0.274	0.232	0.327
29	0.106	0.273	0.23	0.385
30	0.095	0.325	0.225	0.675

BASF PATHOLOGY REPORT IIC 33/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 1

	Term. body weight	Adrenal glands	Brain	Heart	Kidneys	Liver
	%	%	%	%	%	%
M	100.0	0.043	2.675	0.66	1.509	4.355
SD		0.008	0.125	0.062	0.096	0.422
n	5	5	5	5	5	5
31	100.0	0.046	2.578	0.688	1.434	4.491
32	100.0	0.035	2.526	0.655	1.392	4.404
33	100.0	0.054	2.843	0.602	1.536	4.253
34	100.0	0.042	2.708	0.75	1.631	3.732
35	100.0	0.037	2.72	0.604	1.555	4.896

BASF PATHOLOGY REPORT IIC 34/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 1

	Ovaries %	Spleen %	Thymus %	Uterus %
M	0.081	0.288	0.278	0.453
SD	0.01	0.034	0.027	0.121
n	5	5	5	5
31	0.081	0.249	0.272	0.595
32	0.082	0.257	0.281	0.485
33	0.096	0.319	0.253	0.47
34	0.071	0.321	0.262	0.262
35	0.073	0.293	0.323	0.451

BASF PATHOLOGY REPORT IIC 35/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 2

	Term. body weight	Adrenal glands	Brain	Heart	Kidneys	Liver
	%	%	%	%	%	%
M	100.0	0.049	2.62	0.637	1.437	4.83
SD		0.007	0.077	0.026	0.054	0.147
n	5	5	5	5	5	5
36	100.0	0.052	2.506	0.634	1.343	4.814
37	100.0	0.053	2.708	0.62	1.474	4.585
38	100.0	0.046	2.589	0.629	1.463	4.92
39	100.0	0.039	2.658	0.619	1.439	4.955
40	100.0	0.055	2.638	0.681	1.466	4.877

BASF PATHOLOGY REPORT IIC 36/72
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Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 2

	Ovaries %	Spleen %	Thymus %	Uterus %
M	0.081	0.275	0.264	0.501
SD	0.01	0.036	0.027	0.241
n	5	5	5	5
36	0.093	0.273	0.244	0.907
37	0.076	0.322	0.269	0.503
38	0.074	0.297	0.246	0.314
39	0.071	0.258	0.31	0.323
40	0.092	0.227	0.252	0.46

BASF PATHOLOGY REPORT IIC 37/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 3

	Term. body weight	Adrenal glands	Brain	Heart	Kidneys	Liver
	%	%	%	%	%	%
M	100.0	0.047	2.554	0.643	1.48	5.592
SD		0.004	0.049	0.05	0.098	0.245
n	5	5	5	5	5	5
41	100.0	0.052	2.486	0.59	1.37	5.873
42	100.0	0.048	2.542	0.602	1.392	5.289
43	100.0	0.042	2.611	0.713	1.605	5.772
44	100.0	0.045	2.54	0.642	1.528	5.403
45	100.0	0.046	2.59	0.671	1.503	5.624

BASF PATHOLOGY REPORT IIC 38/72
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Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 3

	Ovaries %	Spleen %	Thymus %	Uterus %
M	0.083	0.284	0.26	0.479
SD	0.015	0.042	0.036	0.145
n	5	5	5	5
41	0.069	0.237	0.237	0.405
42	0.096	0.253	0.307	0.735
43	0.078	0.281	0.216	0.383
44	0.102	0.341	0.278	0.426
45	0.069	0.306	0.26	0.445

BASF PATHOLOGY REPORT IIC 39/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 4

	Term. body weight	Adrenal glands	Brain	Heart	Kidneys	Liver
	%	%	%	%	%	%
M	100.0	0.057	2.692	0.625	1.574	6.295
SD		0.012	0.07	0.059	0.104	0.271
n	5	5	4	5	5	5
46	100.0	0.063	2.648	0.627	1.528	6.324
47	100.0	0.053	2.775	0.649	1.563	6.113
48	100.0	0.037	1.994s	0.58	1.537	6.235
49	100.0	0.06	2.62	0.56	1.488	6.06
50	100.0	0.069	2.723	0.711	1.755	6.742

BASF PATHOLOGY REPORT IIC 40/72
31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice 05.Jan.2012 MAHU
Administration via the diet

RELATIVE WEIGHTS - INDIVIDUAL VALUES

Sacrifice F1
Sex F
Group 4

	Ovaries %	Spleen %	Thymus %	Uterus %
M	0.073	0.21	0.228	0.467
SD	0.023	0.038	0.089	0.245
n	5	5	5	5
46	0.056	0.169	0.183	0.197
47	0.093	0.252	0.344	0.589
48	0.074	0.222	0.216	0.728
49	0.096	0.235	0.283	0.608
50	0.044	0.17	0.113	0.214

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BASF                              PATHOLOGY REPORT                  IIC       41/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        0
                                                  Animal                       1
..............................................................................
General information
  Sex               : Male
  Group             : 0 (0 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Pituitary gland
    Cyst(s), pars distalis.
  Spleen
    Pigment storage, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      2
..............................................................................
General information
  Sex               : Male
  Group             : 0 (0 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Coagulating glands
    Unilaterally investigated or present. No histopathologic findings noted.
  Kidneys
    Mineralization, papilla, (multi)focal, grade 1.
  Testes
    Degeneration, tubular, (multi)focal, grade 1.
  Thyroid glands
    Unilaterally investigated or present. No histopathologic findings noted.
  All other organs examined without microscopic findings.
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BASF                              PATHOLOGY REPORT                  IIC       42/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        0
                                                  Animal                       3
..............................................................................
General information
  Sex               : Male
  Group             : 0 (0 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Eyes with optic nerve
  * Unilaterally, lens and cornea are missing
  Kidneys
    Vacuolation increased, grade 1.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                       4
..............................................................................
General information
  Sex               : Male
  Group             : 0 (0 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Adrenal medulla
    Unilaterally investigated or present. No histopathologic findings noted.
  Coagulating glands
    Unilaterally investigated or present. No histopathologic findings noted.
  Kidneys
    Mineralization, papilla, (multi)focal, unilateral, grade 1.
    Cast, tubular, unilateral.
    Tubules, basophilic, (multi)focal, unilateral, grade 1.
    Infiltration, interstitial, lymphoid, unilateral, grade 1.
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BASF                              PATHOLOGY REPORT                  IIC       43/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        0
                                          cont.   Animal                       4
..............................................................................
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  Testes
    Degeneration, tubular, (multi)focal, unilateral, grade 1.
  Thymus
    Cyst(s).
  All other organs examined without microscopic findings.

                                                  Animal                      5
..............................................................................
General information
  Sex              : Male
  Group            : 0 (0 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Axillary lymph nodes
    Unilaterally investigated or present. No histopathologic findings noted.
  Eyes with optic nerve
  * unilaterally, the cornea is missing
  Forestomach
    Hyperplasia, squamous cell, focal, grade 1.
  * with focal mineralization
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  All other organs examined without microscopic findings.
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BASF                                PATHOLOGY REPORT                  IIC       44/72
                                                                       31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice          05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                    Sacrifice                F1
                                                    Sex                       M
                                                    Group                     1
                                                    Animal                    6
..............................................................................
General information
  Sex               : Male
  Group             : 1 (100 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  All other organs examined without microscopic findings.

                                                    Animal                    7
..............................................................................
General information
  Sex               : Male
  Group             : 1 (100 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Tubules, basophilic, (multi)focal, unilateral, grade 1.
  Liver
    Vacuolar change reduced, grade 1.
  All other organs examined without microscopic findings.

                                                    Animal                    8
..............................................................................
General information
  Sex               : Male
  Group             : 1 (100 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        1
                                         cont.    Animal                       8
..............................................................................
Macroscopic findings
  Animal without particular findings.

Microscopic findings
  All organs examined without pathologic findings.

                                                  Animal                       9
..............................................................................
General information
  Sex              : Male
  Group            : 1 (100 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Liver
    Deformation, left medial lobe.
  All other organs without macroscopic findings.

Microscopic findings
  Kidneys
    Fibrosis, (multi)focal, unilateral, grade 1.
  Liver
    No histopathologic correlate to gross lesion(s).
    Hypertrophy, centrilobular, grade 1.
  Thymus
    Cyst(s).
  All other organs examined without microscopic findings.

                                                  Animal                      10
..............................................................................
General information
  Sex              : Male
  Group            : 1 (100 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure
```

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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

	Sacrifice	F1
	Sex	M
	Group	1
cont.	Animal	10

Macroscopic findings
Animal without particular findings.

Microscopic findings
Kidneys
Cast, tubular, unilateral.
Infiltration, lymphoid cell, renal pelvis, (multi)focal, unilateral, grade 1.
Liver
Hypertrophy, centrilobular, grade 1.
Vacuolar change reduced, grade 1.
All other organs examined without microscopic findings.

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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        2
                                                  Animal                      11
..............................................................................
General information
  Sex               : Male
  Group             : 2 (500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Vacuolation increased, grade 1.
    Cast, tubular, unilateral.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      12
..............................................................................
General information
  Sex               : Male
  Group             : 2 (500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Vacuolation increased, grade 1.
    Cast, tubular, unilateral.
  All other organs examined without microscopic findings.

                                                  Animal                      13
..............................................................................
General information
  Sex               : Male
  Group             : 2 (500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        2
                                          cont.   Animal                      13
..............................................................................
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Cast, tubular, unilateral.
    Infiltration, lymphoid cell, renal pelvis, (multi)focal, unilateral, grade
    1.
    Granuloma, focal, unilateral.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      14
..............................................................................
General information
  Sex               : Male
  Group             : 2 (500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Mineralization, papilla, (multi)focal, unilateral, grade 1.
  Liver
    Hypertrophy, centrilobular, grade 1.
    Vacuolar change reduced, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      15
..............................................................................
General information
  Sex               : Male
  Group             : 2 (500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure
```

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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

	Sacrifice	F1
	Sex	M
	Group	2
cont.	Animal	15

Macroscopic findings
Animal without particular findings.

Microscopic findings
Kidneys
Cast, tubular, unilateral.
Liver
Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
All other organs examined without microscopic findings.

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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        3
                                                  Animal                      16
..............................................................................
General information
  Sex              : Male
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Hypertrophy, centrilobular, grade 2.
    Vacuolar change reduced, grade 2.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      17
..............................................................................
General information
  Sex              : Male
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Cast, tubular, unilateral.
    Infiltration, interstitial, lymphoid, unilateral, grade 1.
  Liver
    Hypertrophy, centrilobular, grade 1.
    Vacuolar change reduced, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
    Infiltration, mixed cell, (multi)focal, grade 1.
  All other organs examined without microscopic findings.
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        3
                                                  Animal                      18
..............................................................................
General information
  Sex              : Male
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Vacuolation increased, grade 1.
    Cast, tubular, unilateral.
  Liver
    Hypertrophy, centrilobular, grade 2.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
    Infiltration, mixed cell, (multi)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      19
..............................................................................
General information
  Sex              : Male
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Hypertrophy, centrilobular, grade 2.
    Vacuolar change reduced, grade 2.
  All other organs examined without microscopic findings.
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                    Sacrifice                F1
                                                    Sex                       M
                                                    Group                     3
                                                    Animal                   20
..............................................................................
General information
  Sex              : Male
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Tubules, basophilic, (multi)focal, unilateral, grade 1.
  Liver
    Hypertrophy, centrilobular, grade 2.
    Vacuolar change reduced, grade 2.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  All other organs examined without microscopic findings.
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BASF                              PATHOLOGY REPORT                  IIC       53/72
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        4
                                                  Animal                      21
..............................................................................
General information
  Sex               : Male
  Group             : 4 (1500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Vacuolation increased, grade 2.
    Mineralization, papilla, (multi)focal, unilateral, grade 1.
  Liver
    Multinucleated hepatocytes increased, grade 1.
    Hypertrophy, diffuse, grade 2.
    Vacuolar change reduced, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Pituitary gland
    Cyst(s), pars distalis.
  All other organs examined without microscopic findings.

                                                  Animal                      22
..............................................................................
General information
  Sex               : Male
  Group             : 4 (1500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Thymus
    Organ size reduced, severe.
  All other organs without macroscopic findings.
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        4
                                        cont.     Animal                      22
..............................................................................
Microscopic findings
  Axillary lymph nodes
    Unilaterally investigated or present.
  Coagulating glands
    Unilaterally investigated or present. No histopathologic findings noted.
  Kidneys
    Vacuolation increased, grade 2.
    Mineralization, papilla, (multi)focal, grade 1.
  Liver
    Necrosis, coagulative, randomly distributed, grade 3.
    Multinucleated hepatocytes increased, grade 1.
    Hypertrophy, diffuse, grade 2.
    Vacuolar change reduced, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 2.
  Seminal vesicle
    Reduced content, grade 1.
  * dilation in contralateral organ
  Spleen
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  Testes
    Degeneration, tubular, (multi)focal, grade 2.
  * grade 1 in contralateral organ
  Thymus
    Gross lesion(s) evaluated histopathologically.
    Atrophy, diffuse, grade 3, correlates to gross lesion Organ size reduced.
  All other organs examined without microscopic findings.

                                                  Animal                      23
..............................................................................
General information
  Sex              : Male
  Group            : 4 (1500 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          M
                                                  Group                        4
                                         cont.    Animal                      23
..............................................................................
Microscopic findings
  Coagulating glands
    No or insufficent tissue present on slide.
  Kidneys
    Vacuolation increased, grade 1.
    Mineralization, papilla, (multi)focal, grade 1.
    Cast, tubular.
  Liver
    Necrosis, coagulative, randomly distributed, grade 1.
    Hypertrophy, diffuse, grade 2.
    Vacuolar change reduced, grade 2.
    Vacuolar change, macrovesicular, centrilobular, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Lungs
    Infiltrates, interstitial, mononuclear, diffuse, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      24
..............................................................................
General information
  Sex               : Male
  Group             : 4 (1500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Eyes with optic nerve
  * unilaterally, the cornea is missing
  Kidneys
    Vacuolation increased, grade 2.
    Mineralization, papilla, (multi)focal, unilateral, grade 1.
    Cast, tubular, unilateral.
    Tubules, basophilic, (multi)focal, grade 1.
    Granuloma, focal, unilateral.
  Liver
    Multinucleated hepatocytes increased, grade 2.
    Hypertrophy, diffuse, grade 2.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 2.
  Seminal vesicle
    Reduced content, grade 3.
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
-------------------------------------------------------------------------------
                                                    Sacrifice                  F1
                                                    Sex                         M
                                                    Group                       4
                                           cont.    Animal                     24
...............................................................................
  Spleen
    Pigment storage, grade 1.
  Thymus
    Atrophy, diffuse, grade 3.
    Cyst(s).
  All other organs examined without microscopic findings.

                                                    Animal                     25
...............................................................................
General information
  Sex               : Male
  Group             : 4 (1500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Testes
    Enlarged, left side, moderate.
  All other organs without macroscopic findings.

Microscopic findings
  Eyes with optic nerve
  * unilaterally, the cornea is missing
  Kidneys
    Vacuolation increased, grade 2.
  Liver
    Hypertrophy, diffuse, grade 2.
    Vacuolar change reduced, grade 2.
    Vacuolar change, macrovesicular, centrilobular, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  Testes
    Gross lesion(s) evaluated histopathologically.
    Dilation, tubular, diffuse, grade 3, correlates to gross lesion Enlarged.
    Degeneration, tubular, (multi)focal, unilateral, grade 1.
  All other organs examined without microscopic findings.
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        0
                                                  Animal                      26
..............................................................................
General information
  Sex              : Female
  Group            : 0 (0 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Cast, tubular, unilateral.
    Tubules, basophilic, (multi)focal, grade 1.
    Fibrosis, (multi)focal, unilateral, grade 1.
  Spleen
    Pigment storage, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      27
..............................................................................
General information
  Sex              : Female
  Group            : 0 (0 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 3.
  Thymus
    Cyst(s).
  All other organs examined without microscopic findings.
```

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BASF                              PATHOLOGY REPORT                  IIC       58/72
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        0
                                                  Animal                      28
..............................................................................
General information
  Sex              : Female
  Group            : 0 (0 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Tubules, basophilic, (multi)focal, unilateral, grade 1.
  Lungs
    Histiocytosis, alveolar, (multi)focal with pigment storage in macrophages,
    grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      29
..............................................................................
General information
  Sex              : Female
  Group            : 0 (0 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Heart
    Mineralization, (multi)focal, grade 1.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Lungs
    Histiocytosis, alveolar, (multi)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        0
                                         cont.    Animal                      29
..............................................................................
  All other organs examined without microscopic findings.

                                                  Animal                      30
..............................................................................
General information
  Sex              : Female
  Group            : 0 (0 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Glandular stomach
    Dilation, fundic gland, (multi)focal.
  Kidneys
    Vacuolation increased, grade 1.
    Mineralization, papilla, (multi)focal, unilateral, grade 1.
    Mineralization, tubular, (multi)focal, unilateral, grade 1.
    Tubules, basophilic, (multi)focal, unilateral, grade 1.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.
```

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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        1
                                                  Animal                      31
..............................................................................
General information
  Sex               : Female
  Group             : 1 (100 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Tubules, basophilic, (multi)focal, unilateral, grade 1.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      32
..............................................................................
General information
  Sex               : Female
  Group             : 1 (100 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Tubules, basophilic, (multi)focal, unilateral, grade 1.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  All other organs examined without microscopic findings.
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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        1
                                                  Animal                      33
..............................................................................
General information
  Sex               : Female
  Group             : 1 (100 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 3.
  All other organs examined without microscopic findings.

                                                  Animal                      34
..............................................................................
General information
  Sex               : Female
  Group             : 1 (100 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Adrenal cortex
    Accessory cortical tissue, unilateral.
  Kidneys
    Vacuolation increased, grade 1.
    Mineralization, papilla, (multi)focal, unilateral, grade 1.
    Infiltration, lymphoid cell, renal pelvis, (multi)focal, unilateral, grade
    1.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Ovaries
    Unilaterally investigated or present. No histopathologic findings noted.
```

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BASF                                PATHOLOGY REPORT                 IIC       62/72
                                                                      31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice          05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        1
                                          cont.   Animal                      34
..............................................................................
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.

                                                  Animal                      35
..............................................................................
General information
  Sex              : Female
  Group            : 1 (100 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  All other organs examined without microscopic findings.
```

```
BASF                              PATHOLOGY REPORT                  IIC       63/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        2
                                                  Animal                      36
..............................................................................
General information
  Sex              : Female
  Group            : 2 (500 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Kidneys
    Vacuolation increased, grade 1.
    Cast, tubular, unilateral.
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.

                                                  Animal                      37
..............................................................................
General information
  Sex              : Female
  Group            : 2 (500 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Liver
    Focus, between left medial lobe and right medial lobe, diameter 2.0 mm,
    yellow.
  All other organs without macroscopic findings.

Microscopic findings
  Adrenal cortex
    Advanced involution of X-zone, grade 1.
  Liver
    Gross lesion(s) evaluated histopathologically.
    Vacuolar change reduced, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 2.
```

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BASF                                PATHOLOGY REPORT                  IIC       64/72
                                                                       31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice          05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        2
                                          cont.   Animal                      37
..............................................................................
    Cyst(s), biliary, correlates to gross lesion Focus.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 3.
  All other organs examined without microscopic findings.

                                                  Animal                      38
..............................................................................
General information
  Sex               : Female
  Group             : 2 (500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 2.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.

                                                  Animal                      39
..............................................................................
General information
  Sex               : Female
  Group             : 2 (500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.
```

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BASF                              PATHOLOGY REPORT                  IIC       65/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        2
                                         cont.    Animal                      39
..............................................................................
Microscopic findings
  Liver
    Vacuolar change reduced, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      40
..............................................................................
General information
  Sex               : Female
  Group             : 2 (500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Vacuolar change reduced, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.
```

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BASF                              PATHOLOGY REPORT                  IIC       66/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice          05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        3
                                                  Animal                      41
..............................................................................
General information
  Sex              : Female
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Adrenal cortex
    Advanced involution of X-zone, grade 1.
  Kidneys
    Vacuolation increased, grade 1.
    Fibrosis, capsule, unilateral, grade 1.
  Liver
    Hypertrophy, centrilobular, grade 1.
    Vacuolar change, macrovesicular, centrilobular, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.

                                                  Animal                      42
..............................................................................
General information
  Sex              : Female
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Hypertrophy, centrilobular, grade 1.
    Vacuolar change reduced, grade 2.
    Vacuolar change, macrovesicular, centrilobular, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
```

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BASF                              PATHOLOGY REPORT                  IIC       67/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        3
                                          cont.   Animal                      42
..............................................................................
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.

                                                  Animal                      43
..............................................................................
General information
  Sex              : Female
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Liver
    Hypertrophy, centrilobular, grade 1.
    Vacuolar change reduced, grade 1.
    Vacuolar change, macrovesicular, centrilobular, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.

                                                  Animal                      44
..............................................................................
General information
  Sex              : Female
  Group            : 3 (1000 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure
```

```
BASF                              PATHOLOGY REPORT                  IIC       68/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        3
                                          cont.   Animal                      44
..............................................................................
Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Adrenal cortex
    Advanced involution of X-zone, grade 1.
  Adrenal medulla
    Unilaterally investigated or present. No histopathologic findings noted.
  Kidneys
    Vacuolation increased, grade 1.
    Tubules, basophilic, (multi)focal, grade 1.
  Liver
    Hypertrophy, centrilobular, grade 1.
    Vacuolar change, macrovesicular, centrilobular, grade 1.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 3.
  All other organs examined without microscopic findings.

                                                  Animal                      45
..............................................................................
General information
  Sex               : Female
  Group             : 3 (1000 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Adrenal cortex
    Advanced involution of X-zone, grade 2.
  Kidneys
    Cast, tubular, unilateral.
  Liver
    Hypertrophy, centrilobular, grade 2.
    Vacuolar change reduced, grade 2.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 2.
  All other organs examined without microscopic findings.
```

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BASF                                PATHOLOGY REPORT                  IIC       69/72
                                                                       31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                    Sacrifice                  F1
                                                    Sex                         F
                                                    Group                       4
                                                    Animal                     46
..............................................................................
General information
  Sex               : Female
  Group             : 4 (1500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Adrenal cortex
    Advanced involution of X-zone, grade 2.
  Eyes with optic nerve
  * unilaterally, the cornea is missing
  Kidneys
    Vacuolation increased, grade 2.
    Mineralization, papilla, (multi)focal, unilateral, grade 1.
    Cast, tubular, unilateral.
  Liver
    Hypertrophy, diffuse, grade 2.
    Vacuolar change reduced, grade 2.
    Vacuolar change, macrovesicular, centrilobular, grade 3.
  Lungs
    Infiltrates, interstitial, mononuclear, diffuse, grade 1.
  Ovaries
    Hyperplasia/hypertrophy, interstitial cell, grade 3.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  Uterus
    Atrophy, diffuse, grade 3.
  Vagina
    Epithelial hypertrophy with mucification, grade 3.
  All other organs examined without microscopic findings.

                                                    Animal                     47
..............................................................................
General information
  Sex               : Female
  Group             : 4 (1500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure
```

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BASF                              PATHOLOGY REPORT                  IIC       70/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        4
                                          cont.   Animal                      47
..............................................................................
Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Adrenal cortex
    Advanced involution of X-zone, grade 1.
  Axillary lymph nodes
    Unilaterally investigated or present. No histopathologic findings noted.
  Kidneys
    Vacuolation increased, grade 1.
    Mineralization, papilla, (multi)focal, unilateral, grade 1.
  Liver
    Hypertrophy, diffuse, grade 1.
    Vacuolar change reduced, grade 1.
    Vacuolar change, macrovesicular, centrilobular, grade 2.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 2.
  Ovaries
    Hyperplasia/hypertrophy, interstitial cell, grade 2.
  Sciatic nerve
    No or insufficent tissue present on slide.
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      48
..............................................................................
General information
  Sex               : Female
  Group             : 4 (1500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Adrenal cortex
    Organ size reduced, moderate.
  Brain
  * Organ damaged at necropsy.
  All other organs without macroscopic findings.
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BASF                              PATHOLOGY REPORT                  IIC       71/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        4
                                         cont.    Animal                      48
..............................................................................
Microscopic findings
  Adrenal cortex
    No histopathologic correlate to gross lesion(s).
    Advanced involution of X-zone, grade 1.
  Kidneys
    Vacuolation increased, grade 2.
  Liver
    Hypertrophy, diffuse, grade 1.
    Vacuolar change reduced, grade 1.
    Vacuolar change, macrovesicular, centrilobular, grade 2.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 1.
  Ovaries
    Hyperplasia/hypertrophy, interstitial cell, grade 1.
  Pituitary gland
    No or insufficent tissue present on slide.
  Spleen
    Pigment storage, grade 2.
  All other organs examined without microscopic findings.

                                                  Animal                      49
..............................................................................
General information
  Sex               : Female
  Group             : 4 (1500 ppm)
  Sacrifice         : Final sacrifice group
  Necropsy status   : Planned sacrifice
  Date of death     : 21.Sep.2011
                      29 days after start of exposure
                      1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Axillary lymph nodes
    Unilaterally investigated or present. No histopathologic findings noted.
  Eyes with optic nerve
  * unilaterally, the lens is missing
  Kidneys
    Vacuolation increased, grade 1.
    Cast, tubular.
  Liver
    Hypertrophy, diffuse, grade 1.
    Vacuolar change reduced, grade 1.
    Vacuolar change, macrovesicular, centrilobular, grade 2.
    Infiltration, lymphoid and/or presence of Kupffer cell i)focal, grade 2.
```

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BASF                              PATHOLOGY REPORT                  IIC       72/72
                                                                     31C0343/09S078
Repeated-dose 28-day toxicity study in C57BL/6 JRj mice           05.Jan.2012 MAHU
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)
-------------------------------------------------------------------------------
                                                  Sacrifice                   F1
                                                  Sex                          F
                                                  Group                        4
                                          cont.   Animal                      49
...............................................................................
  Spleen
    Pigment storage, grade 1.
    Hematopoiesis, extramedullary, (multi)focal, grade 1.
  All other organs examined without microscopic findings.

                                                  Animal                      50
...............................................................................
General information
  Sex              : Female
  Group            : 4 (1500 ppm)
  Sacrifice        : Final sacrifice group
  Necropsy status  : Planned sacrifice
  Date of death    : 21.Sep.2011
                     29 days after start of exposure
                     1 day after end of exposure

Macroscopic findings
  Animal without particular findings.

Microscopic findings
  Adrenal cortex
    Advanced involution of X-zone, grade 2.
  Kidneys
    Vacuolation increased, grade 2.
  Liver
    Hypertrophy, diffuse, grade 2.
    Vacuolar change reduced, grade 1.
    Vacuolar change, macrovesicular, centrilobular, grade 3.
  Ovaries
    Hyperplasia/hypertrophy, interstitial cell, grade 2.
  Pituitary gland
    No or insufficent tissue present on slide.
  Spleen
    Pigment storage, grade 1.
  Thymus
    Atrophy, diffuse, grade 2.
  Uterus
    Atrophy, diffuse, grade 1.
  Vagina
    Epithelial hypertrophy with mucification, grade 3.
  All other organs examined without microscopic findings.
```

STUDY TITLE

Report

BAS 850 H

Repeated dose 28-day oral toxicity study in C57BL/6 J Rj mice
Administration via the diet

TEST FACILITY

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

TEST FACILITY PROJECT IDENTIFICATION

Project No. 31C0343/09S078

PART III OF III
(SUPPLEMENT)

CONTENTS OF PART III (SUPPLEMENT)

09/0343-9
added 14.11.17 TS

BASF
The Chemical Company

BASF SE

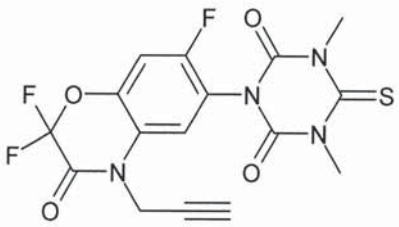
APR/DP - Product Characterization & Performance Management

BASF SE - Crop Protection - Speyerer Strasse 2, D-67117 Limburgerhof, Germany

Certificate of Analysis

Reg.No. :	**5654329**	**Batch No. :**	**COD-001484**
Substance Type :	TGAI (=TC)	**Date of Production :**	June 24, 2011
Date of Initial Analysis :	June 28, 2011	**Study Code :**	386120_4

Purity : 99.3 % (tolerance ± 1.0%)



CL-No.	
CAS No.	
Core Project	5654329
Internal (Metabolite) Code	
Molecular Formula	$C_{16}H_{11}F_3N_4O_4S$
Molecular Weight	412.3

IUPAC-Name :	1,5-dimethyl-6-thioxo-3-[2,2,7-trifluoro-3-oxo-4-(prop-2-yn-1-yl)-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1,3,5-triazinane-2,4-dione
Determination by :	HPLC
Homogeneity :	given

Additional Information

Storage Advice :	keep at ambient temperature (+5 to +30 °C)
Expiration Date :	July 01, 2012

Recipients should ensure that the label information on the corresponding substance container(s) correspond(s) with that on this Certificate of Analysis

Study Director : Genari, Gerhard

Study Completion Date : July 25, 2011

Issued on : November 14, 2017

Issued by : T. Schalk

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Released July 25, 2011 by Genari, Gerhard

09/0343-9
erg. 28.06.12 RS

BASF
The Chemical Company

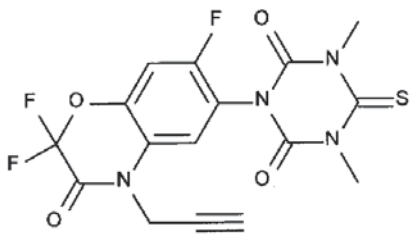
BASF SE
APR/DP - Product Characterization & Performance Management

BASF SE - Crop Protection - Speyerer Strasse 2, D-67117 Limburgerhof, Germany

Certificate of Analysis

BAS Code :	**BAS 850 H**		
Reg.No. :	**5654329**	**Batch No. :**	**COD-001484**
Substance Type :	TGAI (=TC)	**Date of Production :**	June 24, 2011
Date of Initial Analysis :	June 28, 2011	**Study Code :**	386120_4
Date of Reanalysis :	June 19, 2012	**Study Code :**	415835_2

Purity : 99.3 % (tolerance ± 1.0%)



CL-No.	
CAS No.	1258836-72-4
Core Project	850H
Internal (Metabolite) Code	
Molecular Formula	$C_{16}H_{11}F_3N_4O_4S$
Molecular Weight	412.3

IUPAC-Name :	1,5-dimethyl-6-thioxo-3-[2,2,7-trifluoro-3-oxo-4-(prop-2-yn-1-yl)-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1,3,5-triazinane-2,4-dione
Determination by :	HPLC
Homogeneity :	given

Additional Information

Storage Advice :	keep at ambient temperature (+5 to +30 °C)
Expiration Date :	July 01, 2013

Recipients should ensure that the label information on the corresponding substance container(s) correspond(s) with that on this Certificate of Analysis

Study Director : Genari, Gerhard

Study Completion Date : June 27, 2012

Issued on : June 28, 2012

Issued by : T. Gualk

This document has been computer generated and is based on the GLP-studies cited above
Released June 27, 2012 by Genari, Gerhard

The Chemical Company

STUDY TITLE

ANALYTICAL REPORT

Reg.No. 5654329

Stability Analysis in

Ground Kliba maintenance diet mouse/rat "GLP" meal

AUTHOR

Dr. Matthias Becker
Dr. Hennicke Kamp

STUDY COMPLETED ON

16 January 2012

Test Facility

Experimental Toxicology and Ecology
BASF SE
67056 Ludwigshafen, Germany

TEST FACILITY PROJECT IDENTIFICATION

Project No.: 01Y0343/09Y049

SPONSOR

BASF SE
67056 Ludwigshafen, Germany

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Report; Project No.: 01Y0343/09Y049

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with the OECD Principles of Good Laboratory Practice and the GLP Principles of the German "Chemikaliengesetz" (Chemicals Act) which meet the United States Environmental Protection Agency Good Laboratory Practice Standards [40 CFR Part 160 (FIFRA) and Part 792 (TSCA)], with the exception that recognized differences exist between the GLP Principles/Standards of OECD and the Principles/Standards of FIFRA and TSCA.

Study Director M. Becker
Dr. M. Becker

16 Jan 2012
Date

The Chemical Company

Report; Project No.: 01Y0343/09Y049

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Report; Project No.: 01Y0343/09Y049

SIGNATURE PAGE

Study Director: 16 Jan 2012
Dr. Matthias Becker

Management: 09 Jan 2012
Dr. Hennicke Kamp

BASF
The Chemical Company

STATEMENT OF THE QUALITY ASSURANCE UNIT

The Quality Assurance Unit (QAU) inspected the study and reported any inspection results to the Study Director and to Management.

The final report reflects the raw data.

Phase of study	Date of inspection (mm-dd-yyyy)	Reported to Study Director and to Management (mm-dd-yyyy)
Study Plan:	05-25-2011	05-25-2011
Conduct of study:	07-19-2011	07-19-2011
Report:	01-04-2012	01-04-2012

Ludwigshafen, 13 January 2012

Zachmann

GLP CERTIFICATE (FROM THE COMPETENT AUTHORITY)

RheinlandPfalz

Gute Laborpraxis / Good Laboratory Practice

GLP-Bescheinigung / Statement of GLP Compliance
(gem. /according to § 19 Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung und der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at::

Prüfeinrichtung / Test facility

BASF SE
Experimentelle Toxikologie und Ökologie
67056 Ludwigshafen

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

Prüfung nach Kategorien / Areas of Expertise
(gem. / according ChemVwV-GLP Nr. 5.3/OECD guidance)
1,2,3,4,5,8,9
Kat. 9 – Biochemische und pathologische Untersuchungen zu Wirkmechanismen / Biochemical and pathological examinations concerning mode of action

Datum der Inspektion / Date of Inspection
(Tag.Monat Jahr / day.month year)
19.05.2009 & 06. bis 08.07.2009

Die genannte Prüfeinrichtung befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können.
Eine erneute behördliche Überprüfung der Einhaltung der GLP-Grundsätze durch die Prüfeinrichtung ist so rechtzeitig zu beantragen, dass die Folgeinspektion spätestens vier Jahre nach dem Beginn der o.g. Inspektion stattfinden kann. Ohne diesen Antrag wird die Prüfeinrichtung nach Ablauf der Frist aus dem deutschen GLP-Überwachungsprogramm genommen und diese GLP-Bescheinigung verliert ihre Gültigkeit.

Based on the inspection report it can be confirmed, that the test facility is able to conduct the aforementioned studies in compliance with the Principles of GLP.

Verification of the compliance of the test facility with the Priciples of the GLP has to be applied for in time to allow for a follow-up inspection to take place within four years after commencing the above mentioned inspection. Elapsing this term, the test facility will be taken out of the German GLP-Monitoring Programme and this GLP Certificate becomes invalid.

Unterschrift, Datum / Signature, Date

22.10.2009

Dr. Pia Hirsch - stellv. Präsidentin -
(Name und Funktion der verantwortlichen Person / name and function of responsible person)

Siegel

Landesamt für Umwelt, Wasserwirtschaft und Gewerbeaufsicht
Kaiser-Friedrich-Straße 7
55116 Mainz

(Name und Adresse der GLP-Überwachungsbehörde / Name and adress of the GLP Monitoring Authority)

Landesamt für Umwelt, Wasserwirtschaft und Gewerbeaufsicht

The Chemical Company

Report; Project No.: 01Y0343/09Y049

CONTENTS

The Chemical Company

Report; Project No.: 01Y0343/09Y049

1. INTRODUCTION

In the context of toxicological studies the stability of the test substance Reg.No. 5654329 in the vehicle Ground Kliba maintenance diet mouse/rat "GLP" meal has to be verified. The results of these analyses are reported and discussed.

2. RETENTION OF RECORDS

GLP-relevant records and materials are stored at BASF SE for at least the period of time specified in the GLP principles. Details concerning responsibilities or locations of archiving can be seen from the respective SOPs and from the raw data.

3. TIME SCHEDULE

Study initiation date:	25 May 2011
Experimental starting date:	19 July 2011
Experimental completion date:	23 August 2011

4. MATERIAL AND METHODS

4.1. TEST ITEM

The analyses of the test item (= test substance) were carried out at the test facility Crop Protection - Ecology and Environmental Analytics of BASF SE, Speyerer Straße 2, 67117 Limburgerhof, Germany.

Name of test substance:	Reg.No. 5654329
Test substance No.:	09/0343-9
Batch identification:	COD-001484
CAS No.:	unknown
Purity:	99.3 % (tolerance ± 1.0%) (according to project no: 386120_4)
Homogeneity:	homogeneous
Storage stability:	stable until: 01 Jul 2012 The stability of the test substance under storage conditions over the test period was guaranteed by the manufacturer, and the manufacturer holds this responsibility.

Additional Test Substance Information

Date of production:	24 Jun 2011
Physical state/ Appearance:	solid / beige
Storage conditions	ambient

4.2. SAMPLE DATA

Sponsor:	Ph.D. Buesen
Vehicle:	Ground Kliba maintenance diet mouse/rat “GLP” meal
Target concentration:	50 ppm
Duration of the stability test period:	34 days
Storage conditions of the samples during the stability period:	ambient

4.3. TEST SUBSTANCE PREPARATION

50.5 mg of the test substance was mixed with 1 kg Ground Kliba maintenance diet mouse/rat "GLP" meal. The final nominal concentration was 50.4 ppm.

4.4. SAMPLE PREPARATION AND ANALYSIS

The sample preparation and analysis of the test substance was carried out according to the valid control procedures 09/0343_01-01 and 09/0343_01-02.

A detailed description of the control procedure is given in the appendix of this report.
Due to the correction of non quality relevant orthographical failures, the latest version (09/0343_01-02) of the control procedure is described in the appendix.

4.5. LIST OF DEVIATIONS

4.5.1. List of deviations from the control procedure

There was no deviation from the described control procedures 09/0343_01-01 and 09/0343_01-02.

5. RESULTS AND DISCUSSION

5.1. ANALYSIS OF STABILITY

The results obtained for the stability of the test substance in Ground Kliba maintenance diet mouse/rat "GLP" meal are summarized in the following table.

Initial content [ppm]	Time after starting [days]	Analytical value [ppm]		Initial content [%]		
		Individual samples	Mean		Mean	RSD
50.4	0	49.78; 47.04; 51.88; 49.32; 48.39	49.28	98.8; 93.3; 102.9; 97.9; 96.0	97.8	3.6
50.4	7	46.26; 49.09; 57.54; 46.37; 53.73	50.60	91.8; 97.4; 114.2; 92.0; 106.6	100.4	9.7
50.4	10	50.85; 51.11; 50.51; 45.47; 47.70	49.13	100.9; 101.4; 100.2; 90.2; 94.6	97.5	5.0
50.4	14	51.72; 47.48; 49.65; 43.96	48.20	102.6; 94.2; 98.5; 87.2	95.6	6.9
50.4	34	47.42; 56.54; 53.99; 57.14; 53.70	53.76	94.1; 112.2; 107.1; 113.4; 106.6	106.7	7.2

5.2. DISCUSSION

Based on the analytical results it is concluded, that Reg.No. 5654329 is stable in Ground Kliba maintenance diet mouse/rat "GLP" meal over a period of 34 days at ambient temperature. All determined concentrations were in range between 90 % and 110 % of the nominal concentration.

FIGURES

Figure 1.1: Calibration curve (measured on 26 July 2011)

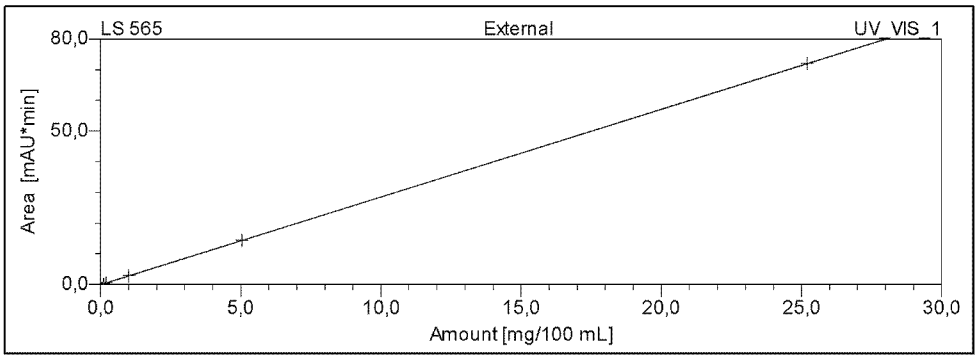


Figure 1.2: Chromatogram matrix solution (measured on 26 July 2011)

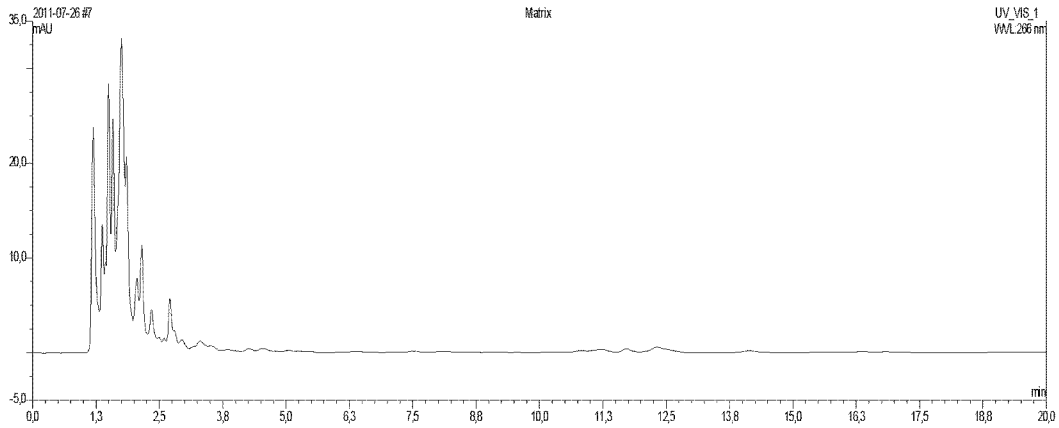


Figure 1.3: Chromatogram calibration solution 1 (0.101 mg/100 mL, measured on 26 July 2011)

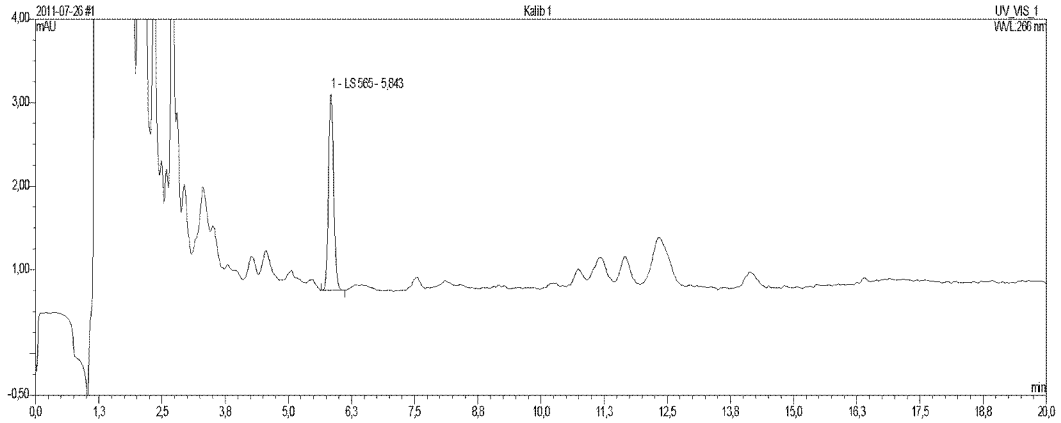
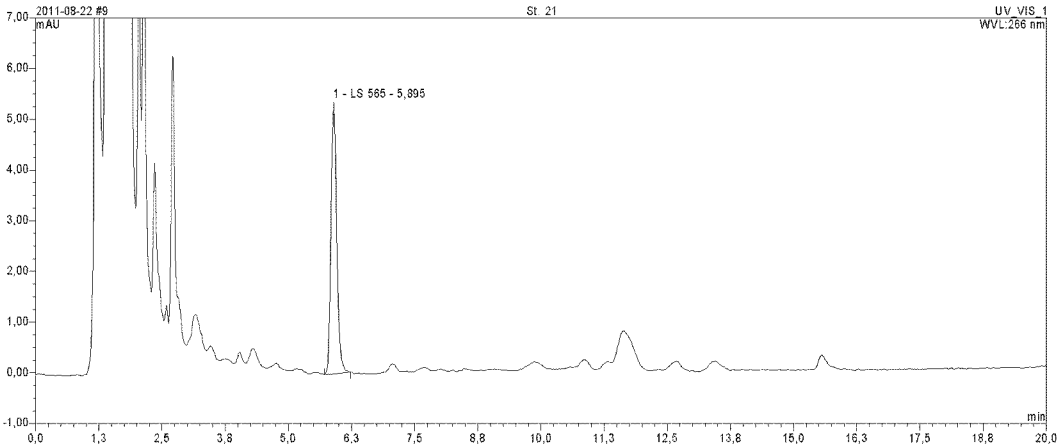


Figure 1.4: Chromatogram sample solution day 34 (measured on 22 August 2011)



6. APPENDIX

6.1. CONTROL PROCEDURE 09/0343_01-02

BASF SE
Test Facility
Experimental Toxicology and Ecology / Analytical Chemistry

BASF
The Chemical Company

CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 1 of 6

Technique	HPLC
System:	Agilent 1100 with autosampler, DAD, Dionex Chromeleon – Software (Dionex), or equivalent system
Column:	Length: 250 mm Inner diameter: 4.6 mm
Stationary Phase:	Gemini 5 µm C18, Phenomenex or equivalent
Mobile Phase A:	1000 mL of acetonitrile are mixed with 1 mL formic acid
Mobile Phase B:	1000 mL of water are mixed with 1 mL formic acid

Isocratic:

Time (min)	Mobile Phase A (%)	Mobile Phase B (%)
	65	35

Injection volume:	5 µL
Flow rate:	1.4 mL/min
Detection:	266 nm
Column temperature:	ambient
Run time:	approx. 20 min

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CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 2 of 6

Sample solution: extraction solvent: acetonitrile / water 1+1 (v/v)

Concentration range (50 – 6250 ppm)
5 g of the samples are weighed into a 50 mL Polypropylene centrifuge tube with a screw cap. Extract the samples 3 times with 30 mL extraction solvent for 30 minutes using a lab shaker. After centrifugation at 4500 rpm for 2 min, the supernatants are collected in a 100 mL volumetric flask. The combined extracts are diluted with acetonitrile to 100 mL.

The samples are filtered (cellulose filter, 0.2 µm) prior HPLC analysis.

Annotation: If the amount of test substance in the sample solution is outside the calibration range (calibration solutions 1 – 5), an adequate dilution step with matrix solution has to be performed to match the described concentration range.

Matrix solution: The preparation of the matrix solution has to be performed according to the procedure described for sample solution preparation

Stock solution: Approx. 50 mg test substance is dissolved to a final volume of 100 mL with extraction solvent (50 mg/100 mL).

Calibration solution 1: 0.1 mL stock solution are diluted with matrix solution to 50 mL (0.1 mg/100 mL)
Calibration solution 2: 0.1 mL stock solution are diluted with matrix solution to 25 mL (0.2 mg/100 mL)
Calibration solution 3: 0.1 mL stock solution are diluted with matrix solution to 5 mL (1.0 mg/100 mL)
Calibration solution 4: 0.5 mL stock solution are diluted with matrix solution to 5 mL (5.0 mg/100 mL)
Calibration solution 5: 2.5 mL stock solution are diluted with matrix solution to 5 mL (25.0 mg/100 mL)

System-suitability solution:
System-suitability solution is prepared with a second independent weighing according to calibration solution 3 (1.0 mg/100 mL)

Procedure: After conditioning the HPLC system, sample solutions, matrix solution, calibration solutions and system-suitability solution are injected according to the sequence described in the raw data. All solutions are injected at least once.

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CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 3 of 6

Retention time:

Test substance: Reg.No. 5654329:
approx. 5.6 min

System suitability:

The calculated contend of the system-suitability solution, has to be in the range from 95 % to 105 %.

The coefficient of determination (R^2) has to be ≥ 0.990. If the correlation coefficient (R) is used, this value has to be ≥ 0.995.

Calculation:

The concentration control measurements are based on external calibration (calibration solutions 1 – 5).

The calculation of the content as well as the recovery in percent of test substance in Kliba lab diet mouse/rat "GLP" is performed electronically (e.g. Dionex Chromeleon – Software, Microsoft Excel). Basic formulas for calculations are described below.

Formulas:

Calibration curve

$Y = a \cdot x + b$

a = slope of calibration curve
b = intercept

Analysed concentration (C_A)

$$C_A = \frac{(Y-b)}{a} \bullet \frac{V \bullet d}{w} \bullet Rf$$

w = weight sample
V = final sample volume
d = dilution factor
Rf = recovery factor (see recovery factor table below)

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CONTROL TEST

Test substance number: 09/0343 — No.: 09/0343_01-02

Name of test substance: Reg.No. 5654329 — Effective from: 26.07.2011

Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP" —

Recovery factor

Concentration [ppm]	Recovery [%]	Mean [%] RSD [%]	Recovery-factor
50.5	89.4; 91.5; 100.1; 94.9	94.0 4.9	1.06
250.3	99.6; 95.5; 92.9; 97.0; 98.8	96.8 2.8	1.03
1250	97.7; 93.3; 95.9; 97.2; 89.0	94.6 3.7	1.06

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CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 5 of 6

Figure 1.1: Example chromatogram matrix solution (15 July 2011, Project no.: 01Y0343/09Y049) for illustration

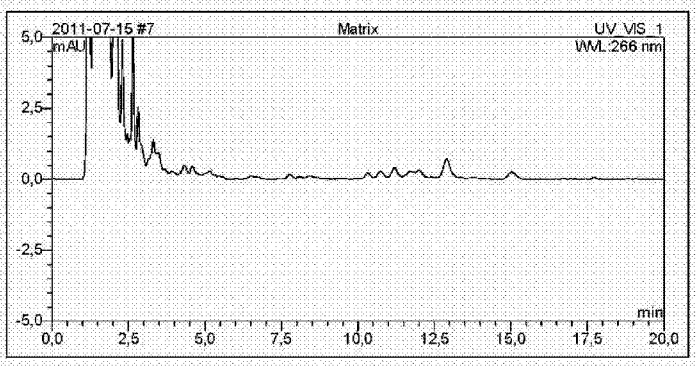
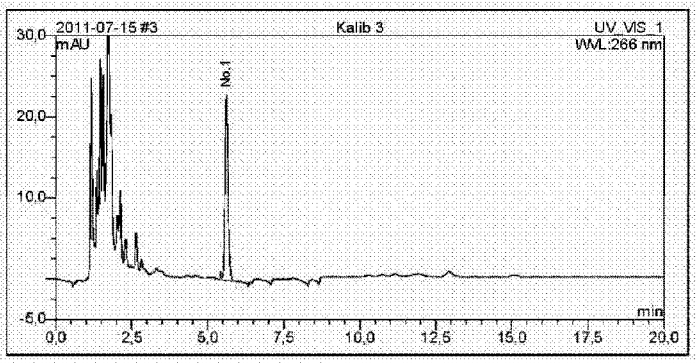


Figure 1.2: Example chromatogram calibration solution 3 (15 July 2011, Project no.: 01Y0343/09Y049) for illustration



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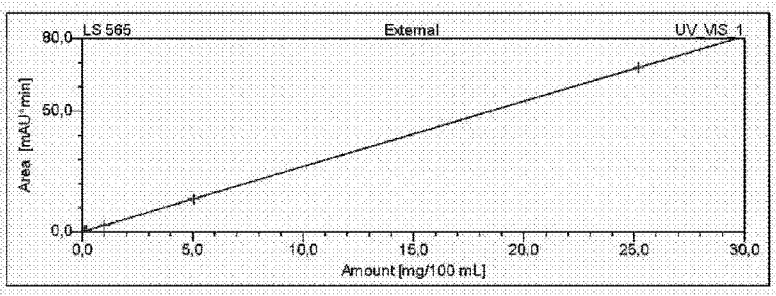
CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 6 of 6

Figure 1.3: Example calibration curve (15 July 2011 concentration range: 0.101 – 25.20 mg/100 mL, Project no.: 01Y0343/09Y049) for illustration



Homogeneity and Concentration Control Analysis of BAS 850 H in Kliba lab diet mouse/rat “GLP”

1. PROJECT AND TEST SUBSTANCE INFORMATION

Project No.:	31C0343/09S078
Test item (= test substance):	BAS 850 H
Batch No.:	COD-001484
Synonym:	Reg.No. 5654329

2. SAMPLE DATA

2.1. HOMOGENEITY AND CONCENTRATION CONTROL ANALYSIS

Vehicle:	Kliba lab diet mouse/rat “GLP”
Storage conditions of the samples until analysis:	Freezer

3. MATERIAL AND METHODS

3.1. SAMPLE PREPARATION AND ANALYSIS

The sample preparation and analysis of the test substance was carried out according to the valid control procedure 09/0343_01-02.

A detailed description of the control procedure is given in the appendix of this report.

3.2. LIST OF DEVIATIONS

3.2.1. List of deviations from the control procedure

There was no deviation from the described control procedure 09/0343_01-02.

4. RESULTS AND DISCUSSION

4.1. HOMOGENEITY AND CONCENTRATION CONTROL ANALYSIS

The results obtained for the homogeneity and concentration control analysis of BAS 850 H in Kliba lab diet mouse/rat “GLP” are summarized in the following table:

Date of sample preparation:	**21 Aug 2011**
Date of sampling:	**21 Aug 2011**
Date of receipt of sample in analytical laboratory:	**21 Aug 2011**
Starting date of analytical determination:	**29 Aug 2011**

Name	Amount	Nominal Conc	Nominal Conc	Mean	RSD
	ppm	ppm	%	%	%
Sample 03	88.535	100	88.5%		
Sample 04	93.930	100	93.9%		
Sample 05	98.532	100	98.5%	93.7%	5.3%
Sample 06	471.076	500	94.2%		
Sample 07	1023.468	1000	102.3%		
Sample 08	1487.685	1500	99.2%		
Sample 09	1623.864	1500	108.3%		
Sample 10	1566.904	1500	104.5%	104.0%	4.4%

Considering the low relative standard deviation in the homogeneity analysis, it can be concluded that BAS 850 H was distributed homogeneously in Kliba lab diet mouse/rat “GLP”.

The mean values (samples 3 – 5 and samples 8 – 10) and single values (samples 6 and 7) of BAS 850 H in Kliba lab diet mouse/rat “GLP” were found to be in the range of 90 % – 110 % of the nominal concentrations.

These results demonstrated the correctness of the concentrations of BAS 850 H in Kliba lab diet mouse/rat “GLP”.

Figures of the calibration curve and examples of chromatograms will follow within this report.

Figure 1.1 Chromatogram of a blank sample (sample 02, measured on 29 Aug 2011)

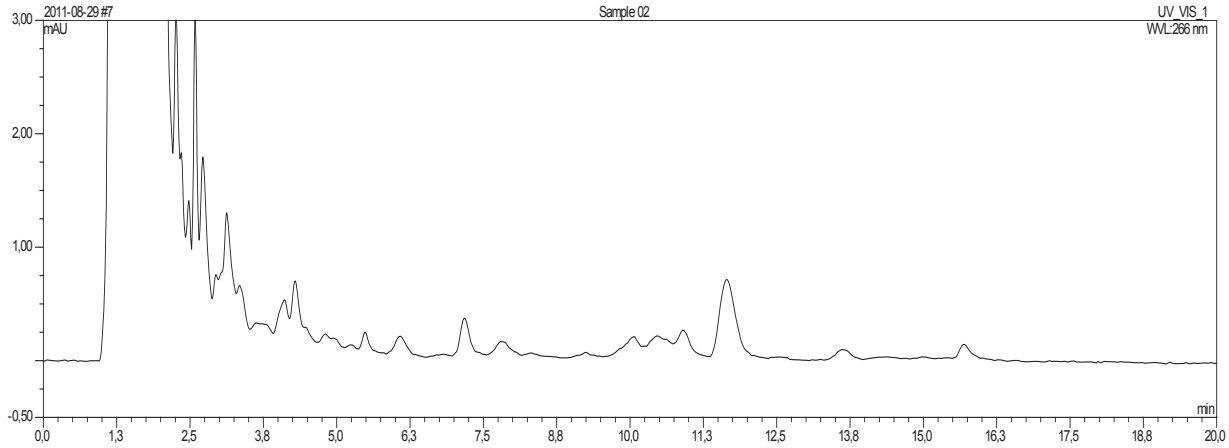


Figure 1.2 Chromatogram of calibration solution 1 (0.101 mg/100 mL, measured on 29 Aug 2011)

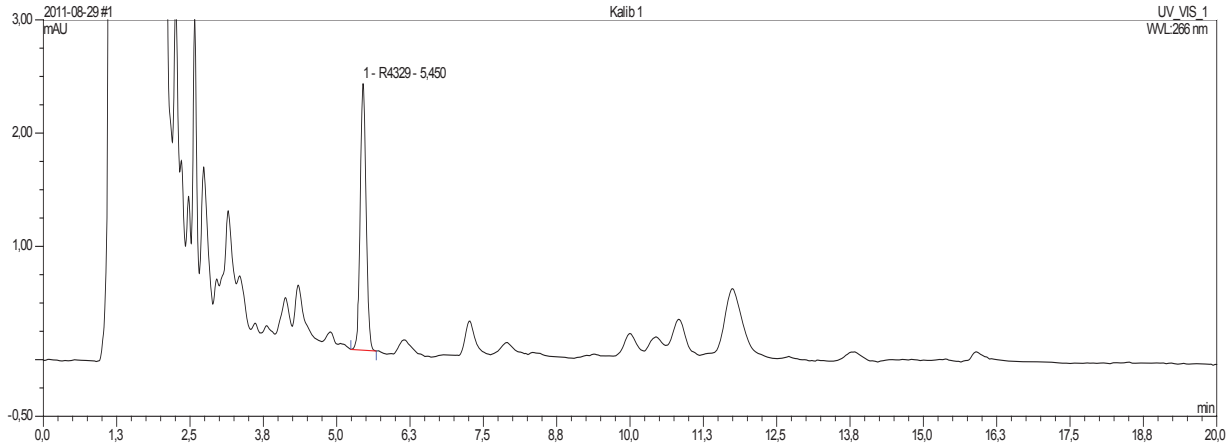


Figure 1.3 Chromatogram of a sample (sample 04, measured on 29 Aug 2011)

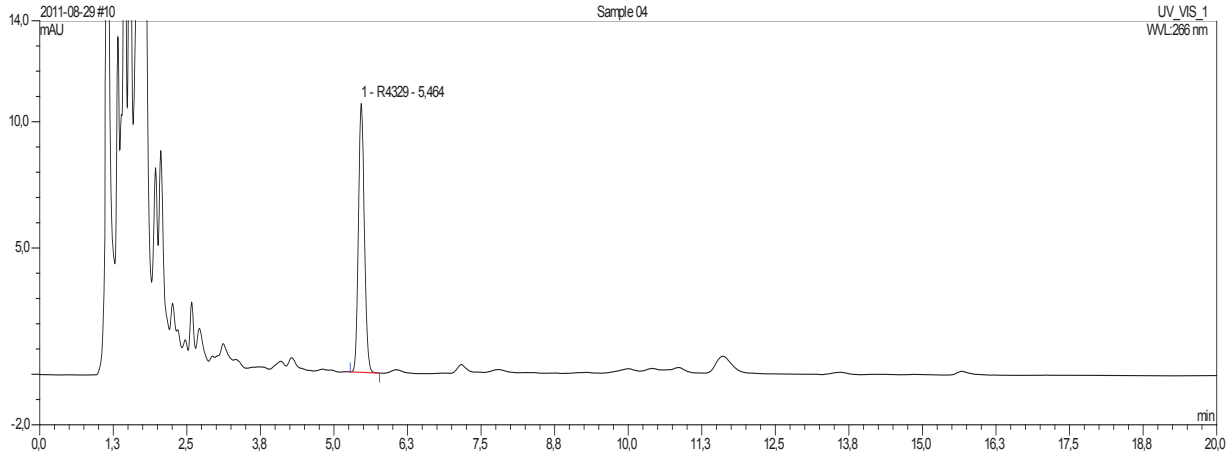
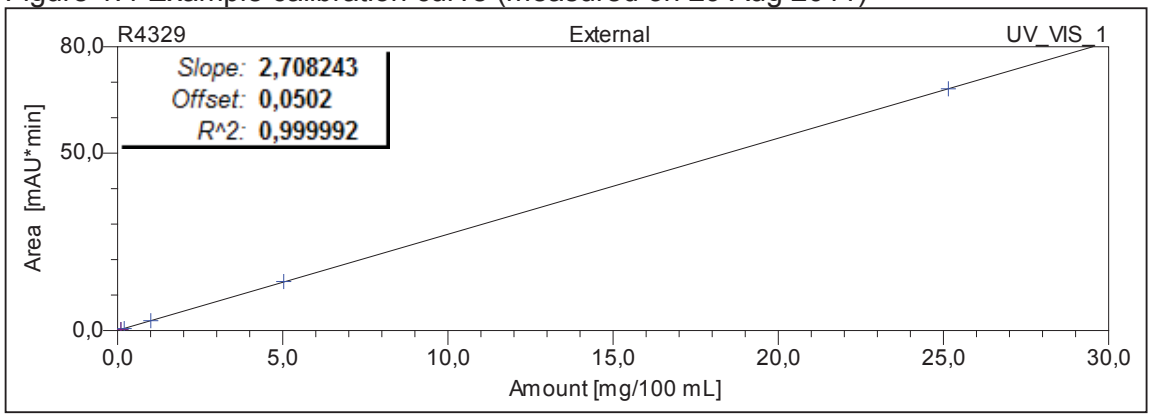


Figure 1.4 Example calibration curve (measured on 29 Aug 2011)



5. APPENDIX

5.1. CONTROL PROCEDURE 09/0343_01-02

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CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 1 of 6

Technique	HPLC
System:	Agilent 1100 with autosampler, DAD, Dionex Chromeleon – Software (Dionex), or equivalent system
Column:	Length: 250 mm Inner diameter: 4.6 mm
Stationary Phase:	Gemini 5 µm C18, Phenomenex or equivalent
Mobile Phase A:	1000 mL of acetonitrile are mixed with 1 mL formic acid
Mobile Phase B:	1000 mL of water are mixed with 1 mL formic acid

Isocratic:

Time (min)	Mobile Phase A (%)	Mobile Phase B (%)
	65	35

Injection volume:	5 µL
Flow rate:	1.4 mL/min
Detection:	266 nm
Column temperature:	ambient
Run time:	approx. 20 min

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The Chemical Company

CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 2 of 6

Sample solution: extraction solvent: acetonitrile / water 1+1 (v/v)

Concentration range (50 – 6250 ppm)
5 g of the samples are weighed into a 50 mL Polypropylene centrifuge tube with a screw cap. Extract the samples 3 times with 30 mL extraction solvent for 30 minutes using a lab shaker. After centrifugation at 4500 rpm for 2 min, the supernatants are collected in a 100 mL volumetric flask. The combined extracts are diluted with acetonitrile to 100 mL.

The samples are filtered (cellulose filter, 0.2 µm) prior HPLC analysis.

Annotation: If the amount of test substance in the sample solution is outside the calibration range (calibration solutions 1 – 5), an adequate dilution step with matrix solution has to be performed to match the described concentration range.

Matrix solution: The preparation of the matrix solution has to be performed according to the procedure described for sample solution preparation

Stock solution: Approx. 50 mg test substance is dissolved to a final volume of 100 mL with extraction solvent (50 mg/100 mL).

Calibration solution 1: 0.1 mL stock solution are diluted with matrix solution to 50 mL (0.1 mg/100 mL)
Calibration solution 2: 0.1 mL stock solution are diluted with matrix solution to 25 mL (0.2 mg/100 mL)
Calibration solution 3: 0.1 mL stock solution are diluted with matrix solution to 5 mL (1.0 mg/100 mL)
Calibration solution 4: 0.5 mL stock solution are diluted with matrix solution to 5 mL (5.0 mg/100 mL)
Calibration solution 5: 2.5 mL stock solution are diluted with matrix solution to 5 mL (25.0 mg/100 mL)

System-suitability solution:
System-suitability solution is prepared with a second independent weighing according to calibration solution 3 (1.0 mg/100 mL)

Procedure After conditioning the HPLC system, sample solutions, matrix solution, calibration solutions and system-suitability solution are injected according to the sequence described in the raw data. All solutions are injected at least once.

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The Chemical Company

CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 3 of 6

Retention time:

Test substance: Reg.No. 5654329:
approx. 5.6 min

System suitability:

The calculated contend of the system-suitability solution, has to be in the range from 95 % to 105 %.

The coefficient of determination (R^2) has to be ≥ 0.990. If the correlation coefficient (R) is used, this value has to be ≥ 0.995.

Calculation:

The concentration control measurements are based on external calibration (calibration solutions 1 – 5).

The calculation of the content as well as the recovery in percent of test substance in Kliba lab diet mouse/rat "GLP" is performed electronically (e.g. Dionex Chromeleon – Software, Microsoft Excel). Basic formulas for calculations are described below.

Formulas:

Calibration curve

$Y = a \cdot x + b$

a = slope of calibration curve
b = intercept

Analysed concentration (C_A)

$$C_A = \frac{(Y-b)}{a} \bullet \frac{V \bullet d}{w} \bullet Rf$$

w = weight sample
V = final sample volume
d = dilution factor
Rf = recovery factor (see recovery factor table below)

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Test Facility
Experimental Toxicology and Ecology / Analytical Chemistry

BASF
The Chemical Company

CONTROL TEST

Test substance number: 09/0343 No.: 09/0343_01-02

Name of test substance: Reg.No. 5654329 Effective from: 26.07.2011

Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP" Page 4 of 6

Recovery factor

Concentration [ppm]	Recovery [%]	Mean [%] RSD [%]	Recovery-factor
50.5	89.4; 91.5; 100.1; 94.9	94.0 4.9	1.06
250.3	99.6; 95.5; 92.9; 97.0; 98.8	96.8 2.8	1.03
1250	97.7; 93.3; 95.9; 97.2; 89.0	94.6 3.7	1.06

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Experimental Toxicology and Ecology / Analytical Chemistry

The Chemical Company

CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 5 of 6

Figure 1.1: Example chromatogram matrix solution (15 July 2011, Project no.: 01Y0343/09Y049) for illustration

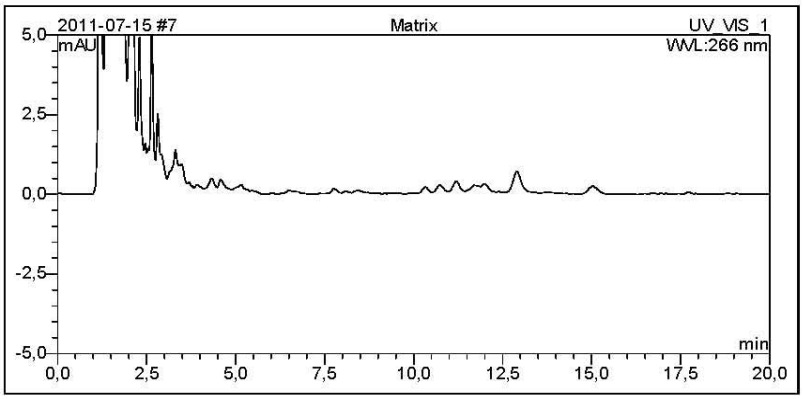
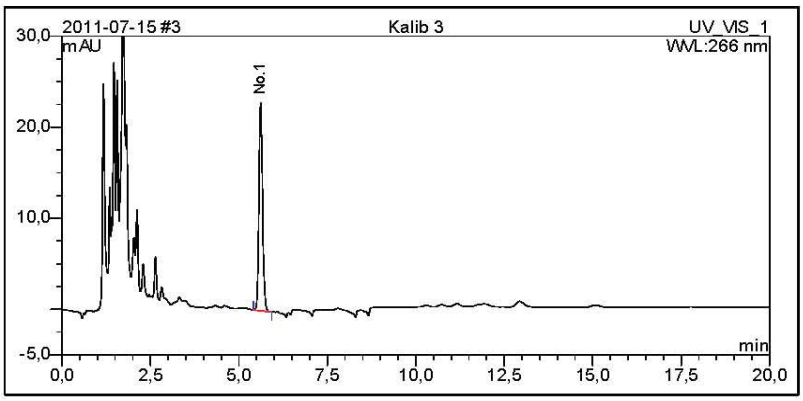


Figure 1.2: Example chromatogram calibration solution 3 (15 July 2011, Project no.: 01Y0343/09Y049) for illustration



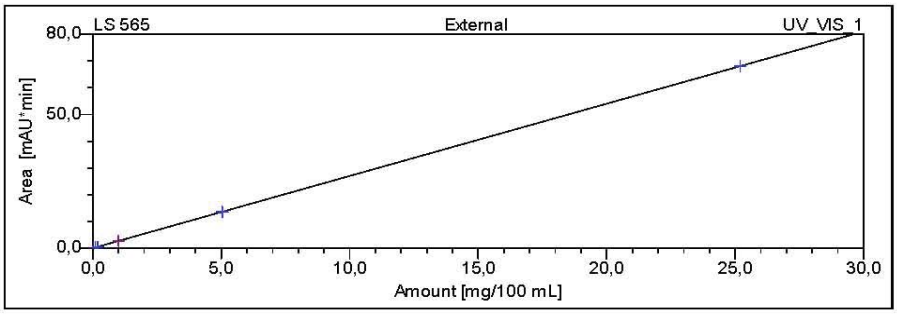
BASF SE
Test Facility
Experimental Toxicology and Ecology / Analytical Chemistry

The Chemical Company

CONTROL TEST

Test substance number: 09/0343	No.: 09/0343_01-02
Name of test substance: Reg.No. 5654329	Effective from: 26.07.2011
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"	Page 6 of 6

Figure 1.3: Example calibration curve (15 July 2011 concentration range: 0.101 – 25.20 mg/100 mL, Project no.: 01Y0343/09Y049) for illustration



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Historical Control Data

C57BL / 6 J Rj

Thymus - m

1/1/2008 - 12/14/2017

Species mouse **Duration** 4 weeks

study	application	study start	study end	No	abs. in mg	SD abs. in mg	rel.wght	SD rel.wght	age	supplier
01S002	feeding	2/1/2010	3/1/2010	8	25.500	4.309	0.131	0.026	5-7 weeks (35-49 days)	Janvier
02S032	feeding	7/1/2014	8/1/2014	5	27.000	3.674	0.130	0.018	5-7 weeks (35-49 days)	Janvier
07C014	feeding	8/1/2010	9/1/2010	5	37.600	4.336	0.168	0.016	5-7 weeks (35-49 days)	Janvier
07S015	feeding	8/2/2010	8/30/2010	5	33.400	1.342	0.158	0.009	5-7 weeks (35-49 days)	Janvier
08C009	feeding	7/1/2010	8/1/2010	5	32.400	5.683	0.146	0.027	5-7 weeks (35-49 days)	Janvier
11C201	feeding	1/1/2013	2/1/2013	5	32.840	3.863	0.157	0.017	5-7 weeks (35-49 days)	Janvier
11S214	feeding	5/1/2013	6/1/2013	5	30.800	7.294	0.154	0.036	5-7 weeks (35-49 days)	Janvier
11S218	feeding	5/1/2013	6/1/2013	5	32.200	5.805	0.158	0.025	5-7 weeks (35-49 days)	Janvier
12S072	feeding	12/1/2012	1/1/2013	5	47.080	6.380	0.205	0.024	5-7 weeks (35-49 days)	Janvier
14C011	feeding	5/1/2014	6/1/2014	5	28.000	8.000	0.121	0.036	5-7 weeks (35-49 days)	Janvier
96S001	feeding	9/1/2010	10/1/2010	8	29.125	6.010	0.133	0.028	5-7 weeks (35-49 days)	Janvier

total no of animals	**61**	**max abs. wght.**	**47.080 mg**	**max rel. wght.**	**0.205 %**
total no of studies	**11**	**min abs. wght.**	**25.500 mg**	**min rel. wght.**	**0.121 %**
		mean abs. wght.	**32.359 mg**	**mean rel. wght.**	**0.151 %**

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