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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)

Dr. R. Buesen (Study Director)
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STUDY COMPLETED ON

03 Jan 2018

TEST FACILITY

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

TEST FACILITY PROJECT IDENTIFICATION

Project No. 31C0343/09S076

SPONSOR

BASF SE
67056 Ludwigshafen, Germany

SPONSOR IDENTIFICATION NUMBER

AP study ID 405222

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PART I OF III (REPORT SECTION AND SUMMARY TABLES)

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Report; Project No.: 31C0343/09S078

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STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

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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).

table (0.97), 377dbe49-0600-4830-bf68-70649e396e3e

Submitter: Date:

Typed Name of Signer:

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



Report: Project No.: 31C0343/09S078

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.

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Date: 03 Jan 2018

Study Director:

Date:

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BASF SE
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FLAGGING CRITERIA

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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.

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Typed Name of Company: BASF Corporation, Agricultural Products
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Prof. Dr. rer. nat. B. van Ravenzwaay

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STATEMENT OF THE QUALITY ASSURANCE UNIT

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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.

table (0.97), 22d4bd23-baa4-4c30-8423-dfbd4115dbb1

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	09-13-2011
	09-21-2011	09-21-2011
Report:	09-07-2017	09-07-2017
	12-04-2017	12-04-2017

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Ludwigshafen,

03 Jan. 2018

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M.AB

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GLP CERTIFICATE (FROM THE COMPETENT AUTHORITY)

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GUTE LABORPRAXIS – GOOD LABORATORY PRACTICE
GLP-BESCHEINIGUNG
STATEMENT OF GLP COMPLIANCE
gemäß/according to § 19b Abs. 1 Chemikaliengesetz

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Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt. 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 Zeit 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 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 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 the GLP Certificate becomes invalid.

Unterschrift, Datum / Signature, Date

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 address of the GLP Monitoring Authority)

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Study No. 01Y0343/09Y049

Analytical Report
Homogeneity and Concentration Control Analysis of Reg.No. 5654329
in Ground Kliba maintenance diet mouse/rat "GLP" meal

Historical Control Data

THIS REPORT CONSISTS OF PART I, II AND III.

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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.



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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



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- Epithelial hypertrophy with mucification of the vagina

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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.

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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

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Test group 2: 500 ppm

(79 mg/kg bw/d in males and 96 mg/kg bw/d in females)

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Clinical Examinations and Clinical Pathology

- No treatment-related, adverse effects were observed.

Pathology

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

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Test group 1: 100 ppm

(15 mg/kg bw/d in males and 22 mg/kg bw/d in females)

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Clinical Examinations, Clinical Pathology and Pathology

- No treatment related, adverse effects were observed.

heading_3 (0.40), cb701f39-c8f4-4274-9370-9c748e2d2539

1.4. CONCLUSION

text_block (1.00), 8dde5a68-842a-4d33-a44a-2b87c02ad803

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.

footer (1.00), b3b64e2d-b2eb-471d-b163-f9e2b06ef019

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heading_1 (0.58), 755cc661-df7a-456c-a620-c7eb81c0575e

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.

heading_2 (0.53), 68e80f48-292a-49ea-a09f-7546ffa62128

2.2. SELECTION OF DOSES/ CONCENTRATIONS

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

left_right_mapping (0.96), bd12cee2-a5c7-4cce-8616-9e023ede70db

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.

heading_3 (0.64), 7d54b08f-7b42-45da-b4ba-d78bcd576e70

2.3. TEST GUIDELINES

The study was conducted according to the following test guidelines:

- Commission Regulation (EC) No 440/2006 of 30 May 2006 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



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heading_2 (0.39), edf2cc34-1756-4539-9340-15798e762d0b

2.4. STUDY DATES

text_block (1.00), 87214aaa-effb-46dc-b89a-38b5ddd28a49

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

table (1.00), fca62581-0498-4f6e-8bd6-ec28df0ae5ee

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	

text_block (0.99), 341c9257-f8d4-4632-9727-e351d461a53f

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

heading_3 (0.69), e61fb937-fe39-409e-bf5a-ce2869b75fe3

2.5. RETENTION OF RECORDS

text_block (0.95), ac6118c5-4b19-47b3-bf99-f203e352be56

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.

heading_3 (0.74), 395b3791-a5c4-4a01-9f00-63487a78e799

2.6. ANIMAL WELFARE

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



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heading_1 (0.44), f5bc8359-ea5e-41ca-9405-29f6d304b1c4

3. MATERIAL AND METHODS

heading_2 (0.29), ef628b63-f56b-472b-8333-c813cb9c83eb

3.1 TEST ITEM

text_block (0.99), 49c47d67-964d-44bb-9cff-4f2857c22acf

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.

left_right_mapping (1.00), 07f5baab-29b5-467c-b525-a8eb63a0dc28

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.

heading_2 (0.39), 2a818b88-1b60-4c18-8942c-20e898612e7e

ADDITIONAL TEST SUBSTANCE INFORMATION

left_right_mapping (0.99), b867c7d7-7c98-481b-8315-c4ba353092af

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



heading_1 (0.39), 7e1cdf51-eb88-44ef-8134-70cce0e3fd0b

3.2. TEST SYSTEM

left_right_mapping (0.98), 9bd2a655-f87e-4984-b056-d5b52e763d4c

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)

heading_2 (0.38), a2b4458f-07e3-4733-b3db-6d0d7729a464

3.3. HOUSING AND DIET

text_block (1.00), 6ad5a509-1d4a-4baa-8a67-52b2d16debe8

The animals were housed together (5 animals per cage) in polycarbonate cages type M III (floor area about 800 cm²). 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 disinfectant ("AUTEX", fully automatic, formalin-ammonia-based terminal disinfectant). 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

table (0.99), d8afa8a0-8679-44d2-96d9-a1d54abedc3a

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

heading_4 (0.21), 8589b274-0db0-4720-ad5a-b37161988040

3.5. TEST SUBSTANCE PREPARATIONS AND PREPARATION FREQUENCY

text_block (1.00), 324b56e2-5605-40e8-8605-bb8387f00d3e

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.



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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).



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3.7. EXPERIMENTAL PROCEDURE

text_block (1.00), 59755d2d-50de-420d-b287-b27e0d29f1c0

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.

heading_3 (0.50), 02cfa323-aa6a-45dd-85a7-ab6a1f341880

3.8. CLINICAL EXAMINATIONS

heading_3 (0.60), 60688337-e1d3-419e-a4f2-55e4dee5ac27

3.8.1. Mortality

text_block (1.00), e47f0c40-0dc9-4732-bfa1-277d0ae48815

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.

heading_3 (0.89), 0923402f-ec3b-4995-8e74-80c0be55c445

3.8.2. Clinical observations

text_block (0.99), 9e0b42d6-9c16-4a8d-aefb-03a55ea31ef4

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

heading_3 (0.85), f513f2f4-9381-409b-adcc-2f67238c6050

3.8.3. Detailed clinical observations

text_block (0.99), 4748ac4f-eb61-4554-8271-4c5242744a48

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:

non_continuous_text_block (0.99), 787a7613-3d15-40c1-82f9-1a773d0adc42

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

text_block (1.00), d79c07fd-87a9-44cd-9b8c-df95d7820ab5

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.

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.

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.

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

$$\frac{FC_x \times C}{BW_x}$$

= test substance intake for study day x

$$BW_x = \text{body weight on study day } x \text{ [g]}$$

$$FC_x = \text{mean daily food consumption on study day } x \text{ [g]}$$

$$C = \text{concentration in the diet on study day } x \text{ [mg/kg]}$$



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heading_2 (0.51), aaa9aff0-c018-4bc2-a513-c0118de9ca46
3.8.8. Statistics of clinical examinations

ext_block (0.99), d699cca1-c008-480a-8d5b-788724b46943
 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-K₃ 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: <u>hemoglobin</u> erythrocytes	
Mean corpuscular hemoglobin concentration (MCHC)	mmol/L	calculation: <u>hemoglobin</u> 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	



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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.

heading_3 (0.60), e0ff7d22-9536-4203-8b52-4c7abefe03e4

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".
Aspartate aminotransferase (AST) (L-aspartate: 2-oxoglutarate aminotransferase; EC 2.6.1.1.)	µkat/L	kinetic UV test, 340 nm; 37°C	J. Clin. Chem. Clin. Biochem. <u>8</u> , 658-660 (1970); J. Clin. Chem. Clin. Biochem. <u>9</u> , 464-465 (1971); J. Clin. Chem. Clin. Biochem. <u>10</u> , 182-192 (1972)
Alkaline phosphatase (ALP) (orthophosphoric acid monoester phosphohydrolase; EC 3.1.3.1.)	µkat/L	kinetic color test, 415 nm, 37°C	Roche working instructions
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. <u>12</u> , 228 (1974) Roche working instructions



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table (0.99), 7d7bd834-91da-4429-b46e-54b90d148ad8

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. <u>20</u> , 155 (1967); Roche working instructions
Urea (UREA)	mmol/L	enzymatic determination with the urease/ glutamate dehydrogenase 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 <u>37</u> , 193 (1972); Roche working instructions
Glucose (GLUC)	mmol/L	hexokinase/glucose-6-phosphate dehydrogenase method	Schmidt, F.H., Klin. Wschr. <u>39</u> , 1244-1247 (1961); Roche working instructions
Total bilirubin (TBIL)	µmol/L	DPD method	Wahlefeld, A.W. et al., Scand. J. Clin. Lab. Invest. <u>29</u> , Suppl. 126 (1972) Abstract 11.12; Roche working instructions
Total protein (TPROT)	g/L	biuret method	Weichselbaum, T.E., Amer. J. Clin. Path. <u>10</u> , 40 (1946); Roche working instructions
Albumin (ALB)	g/L	bromocresol green method	Doumas et al., Clin. Chim. Acta <u>31</u> , 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. <u>19</u> , 838 (1981); Roche working instructions
Magnesium (MG)	mmol/L	xylidylblue method	Mann, C.K. and Yoe, J.H., Anal. Chem. <u>28</u> , 202-205 (1956) Bohnon, C., Clin. Chim. Acta <u>7</u> , 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, <u>35</u> , 159 – 164 (1989); Randox working instruction

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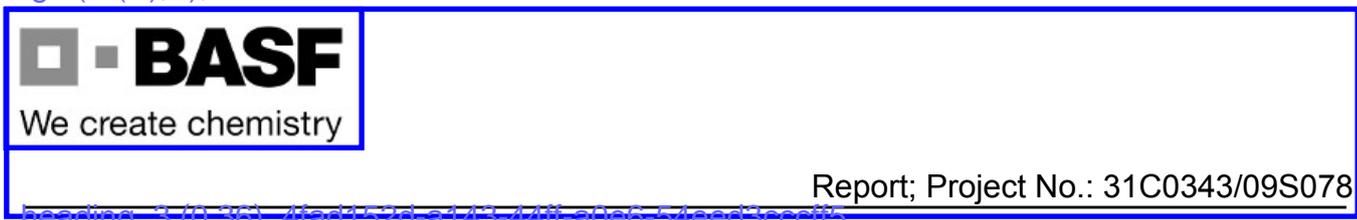
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3.9.3. Statistics of clinical pathology

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



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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



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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

text_block (0.99), a130cdf8-c23d-4370-bda0-43e89f9c22a0

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.



heading_2 (0.38), fa5beec5-22e5-400e-adf8-df8e55160955

3.10.4. Histopathology

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

table (1.00), a8018374-b0e0-48ac-a07b-ca41ecad3f94

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

footer (1.00), acfd0408-7560-4830-97d7-17c205c955a4



table(0.99), be6cd553-94d8-4381-b36a-7a569a896fec

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

text_block(0.98), 69cee9c2-97c6-4c31-8eb2-0c3654223708

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

heading_4(0.45), a29a5fc6-7fda-4714-9700-67ede7a990ca

Thymus:
 run_continuous_text_block(0.94), e6c5c345-da44-48e3-9972-78e535f4fae2

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

heading_4(0.42), 38bec37b-a699-4270-b4fd-8bbb43a61e8c

Spleen:
 reference(0.41), e5775263-db7d-4467-b59e-4c4bc1a010db

- 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

reference(0.80), 4dcd5854-9a06-4012-a65e-7b4f8aaa2dc4

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

reference(0.42), b16911b9-4b42-4fa8-8cbl-ff71291498a5

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

footer(1.00), 1717a14c-18ad-4841-aae1-f8e6dcf9127e



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text_block (0.99), 45528bbb-f8f9-4e91-a863-709028a85955

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.

heading_3 (0.46), 2bf5bccc-fbfb-4dd0-839f-450e1ba51bf9

3.10.5. Statistics of pathology

text_block (0.99), 744f4c7e-ca66-4f45-9c37-0413168d32a3

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 ≤ 0.05 ** for p ≤ 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

footer (1.00), 11aa34cc-34b4-4c3c-bcc3-d45f65a39ef5



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heading_3 (0.36), 731c9f10-2474-4d1e-a593-a426ae5325c5

4. RESULTS

text_block (1.00), cfeebaf1-55fa-4a0c-bcf2-9778a5bfa3ec

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.

heading_3 (0.57), 88acc22f-3513-4c2c-a0af-faf62cce6be0

4.1. ANALYSES

heading_3 (0.61), 46155f83-1aed-4ae3-90ed-cf10564d32f4

4.1.1. Stability analyses

text_block (0.99), 0c65ded3c-3075-47fa-8a90-8cd60df20493

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).

heading_3 (0.77), e534c35a-ceed-4d66-8d14-89cceff3bf89

4.1.2. Homogeneity control analyses

text_block (0.99), 410b90af-1823-4821-be76-75438c019294

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.

heading_3 (0.83), 94a7cb37-2635-4d6d-9f4a-2d8d844a7f8e

4.1.3. Concentration control analyses

text_block (1.00), a5ef8dc3-5c93-439d-9ab1-d7009d258a85

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).

heading_3 (0.78), 5be7d2f8-1e38-4bc9-8294-40a0dd234a58

4.1.4. Food analyses

text_block (1.00), 2559a9a9-e85e-4b98-8bec-8d0f56d9e27c

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.

heading_3 (0.65), b8895049-b20e-4f09-9fbc-5e1abc54950c

4.1.5. Drinking water analyses

text_block (1.00), 29e3162e-8ff8-482b-9585-88f30843b09c

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.

ooter (1.00), 1fa2470f-8475-4941-ae65-8e4d5bd34d68



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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.



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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)

text_block (1.00), 4d57ef6f-84ff-4e59-958d-6151c6271915

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.

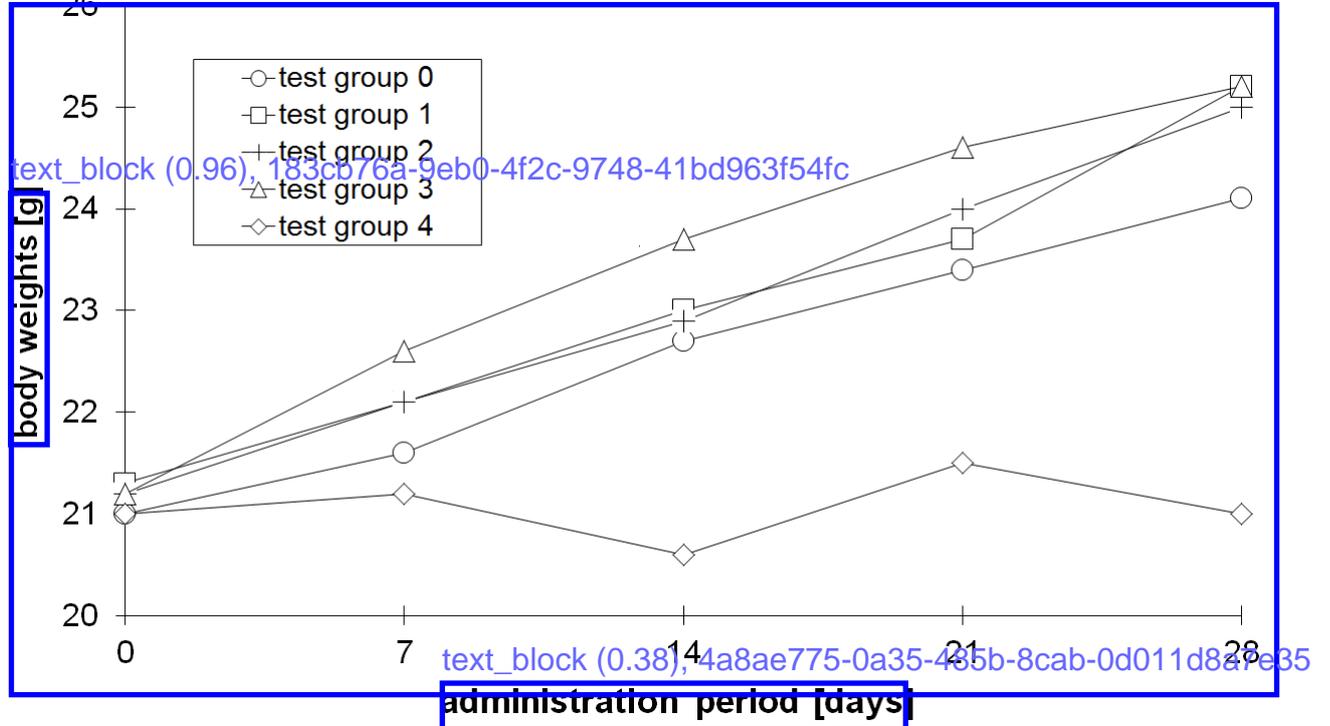
In test group 4 (1500 ppm), body weight loss was observed in male animals on study days 14 and 28 and in female animals on study day 7. Mean body weights were significantly decreased in male animals from study day 14 onwards with a maximum of -13% on study day 28. In female animals mean body weights 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

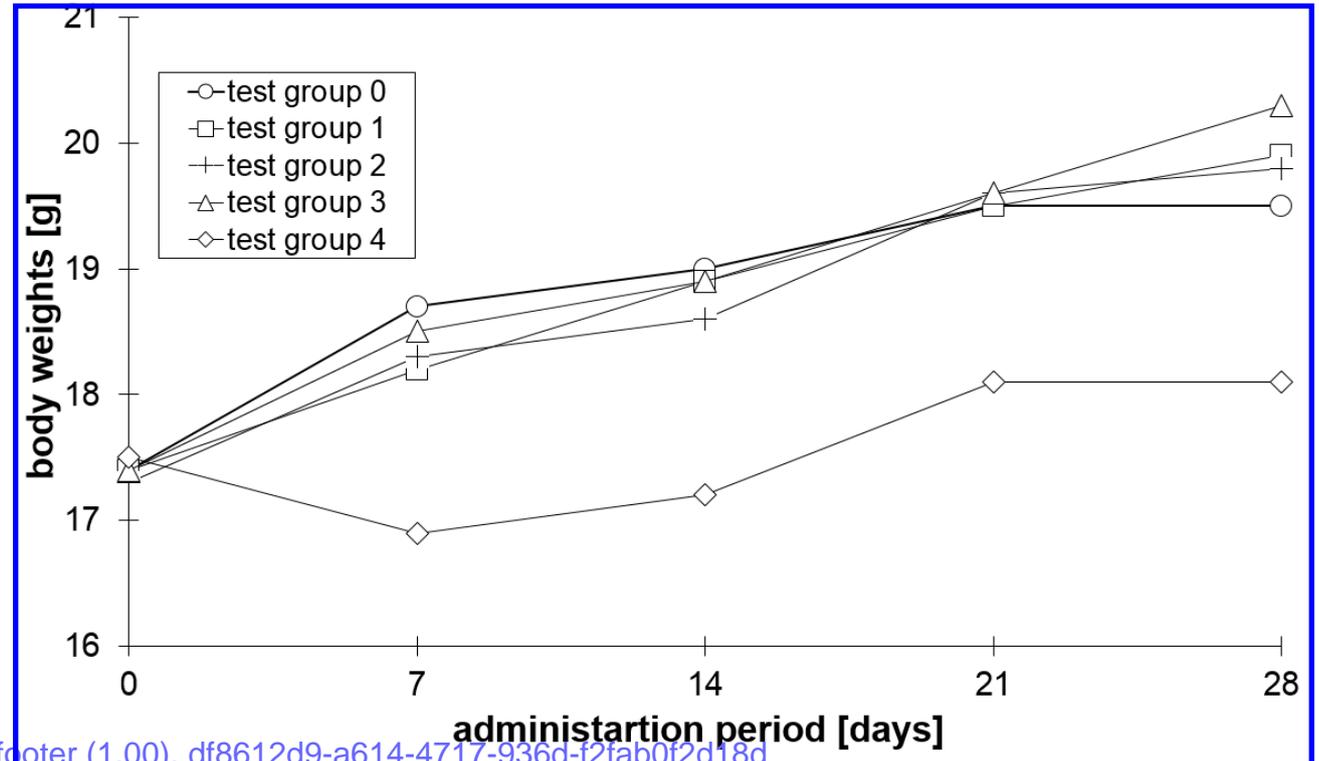
figure (0.99), e95410a4-6947-445e-a5ef-d6225e716758



text_block (0.94), dd3d280c-17d0-4304-a362-4a5ce8779aa1

Figure 4.2.5.2.: Mean body weights of female animals

figure (0.99), dde33b67-ec6f-40d0-90f7-0ec021a74f65





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heading (1.00), e9e61914-634b-4f46-8236-77d82a71b986
text_block (0.99), 7c39f517-1aea-4671-875d-56c4bede51d
4.2.6. Intake of test substance

(Tables IA 11 - IA 12)

text_block (0.99), a2b9e934-ba98-46dd-b7e9-6f9564fbbeb9
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:

table (1.00), afa6a4dd-1a99-4976-bf47-28a915465dec

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):

Test group (ppm)	Male animals				Female animals			
	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%				

*: $p \leq 0.05$; **: $p \leq 0.01$

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):

Test group (ppm)	Male animals				Female animals			
	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%				

*: $p \leq 0.05$; **: $p \leq 0.01$

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



reference (0.52), fe814d9c-375a-4c2e-b792-a18fd5c81a28
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.

reference (0.87), bdd28181-ef99-4f34-adce-76adff717414

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.

heading_3 (0.64), d81fa83d-cbae-42c7-a7ab-d1b136ff9c7f

4.4.2. Gross lesions
(Table IC-9)

text_block (0.99), 71bc8718-eacf-4a75-b26e-5ec86653b275

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

heading_3 (0.61), 2456e6d3-7ae7-4fdf-ae04-15576cac6db3

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

text_block (0.99), 3d50a0a9-8da6-4e20-89ae-c78f16ab8f80

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

footer (1.00), e9068256-91a1-4a5b-92c0-6ed0515ba54a



text_block (1.00), 944a74eb-6088-4f7a-8db7-e04efbc52535

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:

table (1.00), bf5eef8e-a43c-4016-8b41-0bc2f0be5cb5

Liver	Male animals				Female animals			
	1 (100)	2 (500)	3 (1000)	4 (1500)	1 (100)	2 (500)	3 (1000)	4 (1500)
Test group (ppm)								
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

text_block (1.00), 9990c7ef-f2cd-4afb-a6b7-01876042e72d

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.



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heading_4 (0.34), c109233e-564c-4ac1-8a9e-5091a7cb66f2
 text_block (1.00), 1f989890-957a-42c1-89d0-3bfbf862effd
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:

table (1.00), 2a0ba685-9369-428b-b887-3ab719dc9a13

Kidneys	Male animals					Female animals				
	0 (0)	1 (100)	2 (500)	3 (1000)	4 (1500)	0 (0)	1 (100)	2 (500)	3 (1000)	4 (1500)
Test group (ppm)										
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.

heading_3 (0.62), 66a736db-637a-4a39-aa56-388e1fba412a
 text_block (0.99), 8cccc31-57f1-449e-8344-e0c5cbd5aba9

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).

table (0.99), f5db8405-0945-43ad-9fc0-0d7ddaba14d7

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

text_block (0.99), 361c584a-35c9-41d7-936a-1b6e6d96fe3f

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

heading_3 (0.41), 4f42c9ec-d30f-4500-8716-a7bb43881681
 text_block (0.89), a62f0c6e-5b75-41a0-9469-3b6b0bab8b94

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:

footer (1.00), cf0c96c6-95c5-4cdc-a430-7c479b75d2e



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table (0.99), e75c6689-af7c-4da1-9c1d-6b90bec5d26e

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

text_block (0.99), 530a1da5-dc99-4ef3-934b-aa772bc20748

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

heading_2 (0.41), 4727f7ca-47ef-421a-a1b1-d5f16297b1f1

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

table (0.99), 70a92d9c-6807-4618-8368-e987357dcd2d

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

text_block (1.00), 472e2cb2-dff3-4c82-b3b0-02d431e2d8d0

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.

footer (1.00), f24d4959-6046-43a0-ad1d-5b49b1ab8634

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heading_4 (0.54), 5b1fd9ac-c447-4591-b814-cbd127dfcc36

text_block (1.00), e3dc04bd-b528-41ca-b855-f58ce7baf406

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.

table (0.99), 0d36ad71-d834-45c6-a399-9844f3116f82

Spleen	Female animals				
	0 (0)	1 (100)	2 (500)	3 (1000)	4 (1500)
Test group (ppm)	0	1	2	3	4
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	

heading_4 (0.48), 7684ae1a-76bb-4bc8-918b-776f5a2c812c

text_block (0.99), 4d905592-0531-4d18-877a-ce1f8745bf89

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.

text_block (0.98), c4737242-f43b-417b-b570-167b167c9f5c

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.



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heading_1 (0.41), 7aceb5ec-81a3-4a04-add7-a131be1cbe9e

5. DISCUSSION

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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.

text_block (0.94), 1ca256c7-1614-4686-9bae-b5dc8b693526

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).

text_block (0.99), cc91157c-b888-4d66-8d41-6483e2f6b90a

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.

text_block (0.92), 3f5c01a7-471c-4741-b663-89c72667505c

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.

text_block (0.99), 6b71f1e2-e9a5-4bbe-a237-c26a0a90aea8

~~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.

footer (1.00), 77969244-bbfd-4eb3-9377-9a83dd32912a

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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.

heading_2 (0.37), 2477cbce-69f6-4f49-81e9-b61d5ba3cbe1

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.

text_block (1.00), 634fd2ba-e261-4c7e-b2a9-121e91142db7

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.

heading_3 (0.56), d725cf1b-9b8c-4735-9ebe-433d4ffd75e5

6. CONCLUSION

text_block (1.00), 82c7688b-fe41-4856-b339-5238fac53ee4

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.

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heading_1 (0.41), 9737e275-c929-4411-a507-4623577ae2a2

7. REFERENCES

text_block (0.53), 62079c2d-333f-48fa-acd1-e887a31f2895

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2. Ruehl-Fehlert C, Kittel B, Morawietz G, Deslex P, Keenan C, Mahrt CR, Nolte T, Robinson M, Stuart BP, Deschl U (2003) Revised guides for organ sampling and trimming in rats and mice - Part 1. *Exp Toxicol Pathol* 55: 91–106
3. Kittel B, Ruehl-Fehlert C, Morawietz G, Klapwijk J, Elwell MR, Lenz B, O'Sullivan MG, Roth DR, Wadsworth PF (2004) Revised guides for organ sampling and trimming in rats and mice - Part 2. *Exp Toxicol Pathol* 55: 413–431
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6. OECD (2009) Guidance Document for Histopathologic Evaluation of Endocrine and Reproductive Tests in Rodents. ENV/JM/MONO(2009)11. pp 97-98



heading_1 (0.57), df31a81b-23e3-4e13-8600-8c9097a05646

8. APPENDIX

text_block (1.00), f5e99042-3e53-4c74-ad92-cb0581507318

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.

heading_4 (0.41), b6b5f9a9-5c5b-4bd5-86f2-676cda657e3e

8.1. LIST OF ABBREVIATIONS USED IN TABLES CLINICAL EXAMINATIONS

left_right_mapping (0.99), 535e0051-0a83-4f00-adf2-7ed06e93ebec

%	=	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



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heading_4 (0.55), b12cc9c0-d8c5-41a5-87e7-0af0694cc607

8.2. LIST OF ABBREVIATIONS USED IN TABLES CLINICAL PATHOLOGY

text_block (0.75), 44951ffd-5089-49b0-8503-5c1e7fa1ed75

CLINICAL PATHOLOGY:

left_right_mapping (0.97), 52993e2b-4557-4125-b3da-89d66ac9a273

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

text_block (0.91), e5cf5fd7-6515-4d7c-a2ae-e8b3ac916541

HEMATOLOGY:

left_right_mapping (0.99), 9dee90e8-6559-4b0a-baff-28db4f5f76f8

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

heading_4 (0.47), 7c8c1728-734a-45d5-8469-a1ffe82208eb

CLINICAL CHEMISTRY:

left_right_mapping (0.99), b0bcd1d4-0318-4b53-8a1a-78f7719f36d7

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

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left_right_mapping (0.99), 1b23e625-3350-47d1-bf50-d04bbecdd858

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

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UNITS:

left_right_mapping (0.98), 65a9503e-2d82-4a0a-a792-a707fe65caeb

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

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8.3. LIST OF ABBREVIATIONS USED IN TABLES PATHOLOGY

left_right_mapping (0.93), 9256a3b9-dac9-4e44-8cb4-197c8ec4e571

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/m ³	=	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



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% = 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

heading_2 (0.40), 75fcaa81-4b6d-4b94-ada6-4ebc289d2094

Codes for the status at necropsy:

off_right_mapping (0.99), 88cb2928-212e-4b72-8e75-0af110a8eeab

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

heading_4 (0.40), 6461b2b6-0fec-4ba2-bfc6-56da95033814

Codes used at finding level:

text_block (0.99), 02f229c1-04a4-4e03-9de2-f8605f84e152

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

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



BASF
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IA 1
08-Aug-2017 11:17
ToxData© System 3.0

	0/M	1/M	2/M	3/M	4/M
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

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Study 31C0343/09S078

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 text_block(0.99), a80c8583-3f8a-4be2-91c6-1b5887fbc1cb

Summary - Clinical Observations

Sex: Male - Phase: In-life

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IA 2
08-Aug-2017 11:17
ToxData© System 3.0

	0/F	1/F	2/F	3/F	4/F
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

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Study 31C0343/09S078

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Summary - Clinical Observation
Sex: Female - Phase: In-life

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Report; Project No.: 31C0343/09S078

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IA 3
08-Aug-2017 13:45
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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

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

d = day

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IA 5
08-Aug-2017 13:48
ToxData@ System 3.0

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

d = day

text_block (0.99), 1a916ff9-08b6-4d6c-a751-7bf7e9ec38b0

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text_block (0.99), 8606f950-8914-42dc-9306-1208e4af90cc



We create chemistry

Report; Project No.: 31C0343/09S078

non_continuous_table(0.99), d6e1d161-31c7-4845-a823-48d3c67c076

IA 6
08-Aug-2017 13:48
ToxData@ System 3.0

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

d = day

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BASF
We create chemistry

Report; Project No.: 31C0343/09S078

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IA 7
08-Aug-2017 13:58
ToxData@ System 3.0

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

text_block (1.00), 1aa6c573-bf36-4b8b-b847-abfe80991546

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We create chemistry

Report; Project No.: 31C0343/09S078

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IA 8
08-Aug-2017 13:58
ToxData@ System 3.0

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	17.4 n 0.4 5	17.4 0.8 5	17.3 0.6 5	17.4 0.6 5	17.5 0.5 5
		0.1	-0.8	-0.2	0.7
day 7	18.7 n 0.5 5	18.2 0.5 5	18.3 0.7 5	18.5 0.7 5	16.9* 1.8 5
		-2.3	-1.9	-1.0	-9.5
day 14	19.0 n 0.5 5	18.9 0.3 5	18.6 1.2 5	18.9 0.5 5	17.2** 1.0 5
		-0.5	-1.8	-0.2	-9.4
day 21	19.5 n 0.8 5	19.5 0.5 5	19.6 0.7 5	19.6 0.5 5	18.1* 1.3 5
		-0.1	0.3	0.5	-7.4
day 28	19.5 n 0.9 5	19.9 0.2 5	19.8 0.7 5	20.3 0.8 5	18.1 1.4 5
		1.7	1.1	4.0	-7.3

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

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We create chemistry

Report; Project No.: 31C0343/09S078

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IA 9
08-Aug-2017 14:05
ToxData@ System 3.0

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, *** p <= 0.001, X = Group excluded from statistics
d = day; n=DUNNETT



We create chemistry

Report; Project No.: 31C0343/09S078

non_continuous_table(0.99), 69c09b7a-5253-4e82-81e3-ae720d27b931

IA 10
08-Aug-2017 14:05
ToxData@ System 3.0

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

Sex: Female - Phase: In-life

	0/F	1/F	2/F	3/F	4/F
d0 -> 7	Mean 1.2n S.d. 0.3 N 5	0.8 0.5 5 -35.5	1.0 0.4 5 -17.7	1.1 0.4 5 -11.3	-0.7** 1.3 5 -153.2
d0 -> 14	Mean 1.5n S.d. 0.6 N 5	1.4 0.6 5 -7.8	1.3 0.7 5 -13.0	1.5 0.3 5 0.0	-0.4** 0.6 5 -123.4
d0 -> 21	Mean 2.1n S.d. 0.6 N 5	2.0 0.9 5 -1.9	2.3 0.2 5 9.6	2.2 0.5 5 6.7	0.5** 1.0 5 -75.0
d0 -> 28	Mean 2.1n S.d. 0.6 N 5	2.4 0.7 5 15.1	2.5 0.3 5 17.0	2.9 0.6 5 38.7	0.6** 1.1 5 -72.6

Statistic Profile = Dunnett test (two-sided); p <= 0.05; ** p <= 0.01; *** p <= 0.001; **** p <= 0.0001; NS = Group excluded from statistics
d = day; n=DUNNETT

Study 31C0343/09S078

text_block(1.00), 3c8d4239-2f7d-49df-b8a8-b3567771db6a

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We create chemistry

Report; Project No.: 31C0343/09S078

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IA 11
08-Aug-2017 14:21
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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	15.5	81.6	135.4	228.1
	Mean			
	S.d.			
	N	1	1	1
d 7 -> 14	15.0	79.7	161.5	213.3
	Mean			
	S.d.			
	N	1	1	1
d 14 -> 21	14.7	74.2	148.3	233.8
	Mean			
	S.d.			
	N	1	1	1
d 21 -> 28	14.5	79.0	149.6	221.8
	Mean			
	S.d.			
	N	1	1	1
Mean [mg/kg/Day]	14.9	78.6	148.7	224.2

d = day

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We create chemistry

Report; Project No.: 31C0343/09S078

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IA 12
08-Aug-2017 14:21
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	1/F	2/F	3/F	4/F
d 0 -> 7	21.8	93.8	187.7	238.6
Mean				
S.d.				
N	1	1	1	1
d 7 -> 14	21.9	96.3	192.8	278.6
Mean				
S.d.				
N	1	1	1	1
d 14 -> 21		95.1	197.7	256.9
Mean				
S.d.				
N	0	1	1	1
d 21 -> 28	23.1	98.5	198.1	271.7
Mean				
S.d.				
N	1	1	1	1
Mean [mg/kg/Day]	22.3	95.9	194.1	261.4

d = day

Study 31C0343/09S078

Summary Substance Intake (mg/kg/Day)

Sex: Female - Phase: In-life

text_block (1.00), 0906c8723e200-4013-47833659-267a2e8a83b4

text_block (1.00), 75e880b6-1e16-41b6-a6f1-948d8980c5a6



We create chemistry

Report; Project No.: 31C0343/09S078

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Study 31C0343/09S078

IB 1

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Red blood cell parameters

text_block (0.99), 73ced902-1040-4cea-87f2-4c38c32f714f

Sex: Male - Phase: In-life

table (1.00), 59a832d0-fae8-46df-8504-93751ec6c5fe

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

text_block (0.98), e6b0789f-c11a-4f8b-bc8b-e1b0ecd60970

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



Report; Project No.: 31C0343/09S078

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Study 31C0343/09S078

IB 2
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Red blood cell parameters

text_block (0.99), 72a3d705-c9aa-4206-943a-3b14ab1f6965

Sex: Female - Phase: In-life

table (1.00), 4c39c68f-93a5-40b4-8f3b-2a9bae6c9e75

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

text_block (0.98), 9ee7e789-7724-4f52-a269-5bb0cd51c374

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



Report; Project No.: 31C0343/09S078

non_continuous_text_block

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Study 31C0343/09S078

IB 3
06-Dec-2011 16:15
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White blood cell parameters 7221c7f7-1616-4abe-8404-eb7454a55810

Sex: Male Phase: In life

table (1.00), 9e944499-8dd6-4d4d-a988-269ad797e023

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

text_block (0.99), f70ff4d7-ce39-4d94-a5ab-e8de61ac1e0c

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



Report; Project No.: 31C0343/09S078

non_continuous_text_block

text_block (0.99), db83b974-709b-424b-ad52-69ca0f8bd2a8

Study 31C0343/09S078

IB 4
06-Dec-2011 16:15
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text_block (0.97), 48a40daa-15ef-476f-b36a-ac6f71fbd8a1

White blood cell parameters

text_block (0.99), 811ac144-4795-4549-b85f-a68d277cdf03

Sex: Female - Phase: In-life

table (1.00), 1d8302f5-b262-4a51-96d9-93bcfcb401b4

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

text_block (0.99), 5345a4fa-2ef7-46b9-af48-f626c3cb31ad

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



We create chemistry

Report; Project No.: 31C0343/09S078

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text_block (0.99), c7c61595-5825-4baa-a1f4-a3e744173c8c

Study 31C0343/09S078

IB 5
 06-Dec-2011 16:16
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text_block (0.94), 8e0e09ad-65e0-408a-865d-df6bf85e2a69

Enzyme:

text_block (0.99), ab3c8fac-e7a3-46b6-98d9-55c407eb74a7

Sex: Male - Phase: In-life

table (1.00), 264df791-ca6f-48e2-b476-919f6ba11a2a

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

text_block (0.98), 7153dc98-54eb-4e8c-8af4-73b057922be1

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



Report; Project No.: 31C0343/09S078

non_continuous_text_blo

text_block (0.99), 5f3c1223-a759-4701-87f6-2d37f1e58c5b

Study 31C0343/09S078

IB 6
06-Dec-2011 16:16
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text_block (0.94), ebb05b5f-5014-48f2-917b-24446e5819c5

Enzyme:

text_block (0.99), 928bf27d-1581-4b81-9598-0f66b44c2e0c

Sex: Female - Phase: In-life

table (1.00), b5f6954e-84c1-4ad3-b36f-e1454b148bd5

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

text_block (0.97), 27af01d2-ad22-4321-b317-38abb0d84201

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



Report; Project No.: 31C0343/09S078

non_continuous_text_block

text_block (0.99), cdd01ba0-e822-4cbc-a2b4-e2128b5cff0c

Study 31C0343/09S078

IB 7
15-Sep-2017 12:12
Ascentos™ 1.3

text_block (0.95), 3b761a9ea-58c5-4bf0-93f8-e7064aa5443e7

Substrate:

text_block (0.99), 5cea6559-d362-416c-8aa2-841f9eeee30c

Sex: Male - Phase: In-life

table (1.00), b8eea92b-7fe4-4a3f-9568-d2cd34403c2f

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

text_block (0.98), 0311b1c8d-9beb-4775-9de0-c9af198cb210

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



Report; Project No.: 31C0343/09S078

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text_block (0.99), e58bad69-3ef1-47e4-84ef-04f3b6b92734

Study 31C0343/09S078

IB 8
15-Sep-2017 12:12
Ascentos™ 1.3

text_block (0.96), 951db5ab-1686-407a-b4e1-69da0f598175

Substrates

text_block (0.99), e03542b9-3298-4288-9427-11caee6ec2dc

Sex: Female - Phase: In-life

table (1.00), f6510aee-a34f-415e-9ecb-da06f2239836

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

text_block (0.98), 9f145db6-e09a-46fd-92e4-da2ecb693796

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



Report; Project No.: 31C0343/09S078

text_block (0.99), c05acce7bad-4c85-8116-e96b63413e90

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Study 31C0343/09S078

IB 9
06-Dec-2011 16:18
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text_block (0.98), 463c9ce3-da3c-4881-922f-ae54eaab76d

Electrolytes + minerals

text_block (0.99), b9a693db-e7f6-474c-a472-1003c763831a

Sex: Male - Phase: In-life

table (1.00), 640ced85-d3a2-4b0a-9b22-1f0e5324041f

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

text_block (0.98), ac7e8413-9b15-4a0a-931d-b4487aa93d0f

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



Report; Project No.: 31C0343/09S078

non_continuous_text_block

text_block (0.99), 854502bd-4ef5-486f-8c57-dca2d9251ed6

Study 31C0343/09S078

IB 10
06-Dec-2011 16:18
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text_block (0.97), 88ef164a3987-4b1c-a235-0d60ec61eb7e

Electrolytes + minerals

text_block (0.99), ea7ea3b5-e550-4d3b-b801-cd35a45f7942

Sex: Female - Phase: In-life

table (1.00), f7895b33-873c-4014-9581-9cfc72a833bd

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

text_block (0.98), 21ab1c3c-4284-405f-8b9f-a199547bcc31

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



IC 1/14
31C0343/09S078
05.Jan.2012 MAHU

PATHOLOGY REPORT

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

Sacrifice	Sex	Group	F1		F0		F1		F0		
			M	F	M	F	M	F	M	F	
terminal body weight	g	M	20.64	21.62	21.28	21.8	21.8	18.66	*	18.66	*
	% dev		100	105	103	106	106	90		90	
	SD		0.68	1.052	0.786	0.828	0.828	1.303		1.303	
	n		5	5	5	5	5	5		5	
Adrenal glands	mg	M	4.6	5.8	5.2	4.6	4.6	5.6		5.6	
	% dev		100	145	130	115	115	140		140	
	SD		1.414	1.095	1.095	0.894	0.894	1.517		1.517	
	n		5	5	5	5	5	5		5	
Brain	mg	M	450.9	449.6	457.0	448.6	448.6	433.2		433.2	
	% dev		100	100	101	100	100	96		96	
	SD		9.88	15.837	23.033	15.05	15.05	13.535		13.535	
	n		5	5	5	5	5	5		5	
Thyroidaloids	mg	M	55.2	55.4	57.8	58.2	58.2	51.0		51.0	
	% dev		100	100	105	105	105	92		92	
	SD		3.033	8.081	3.768	8.167	8.167	9.22		9.22	
	n		5	5	5	5	5	5		5	
Heart	mg	M	117.6	123.6	128.0	126.4	126.4	116.4		116.4	
	% dev		100	105	109	107	107	99		99	
	SD		10.037	19.731	4.637	13.297	13.297	16.041		16.041	
	n		5	5	5	5	5	5		5	
Kidneys	mg	M	291.0	284.8	297.2	298.4	298.4	287.0		287.0	
	% dev		100	98	102	102	102	98		98	
	SD		11.567	15.897	18.807	18.622	18.622	24.99		24.99	
	n		5	5	5	5	5	5		5	
Liver	mg	M	866.8	846.6	959.4	959.4	959.4	995.6		995.6	
	% dev		100	98	111	111	129	115		115	
	SD		33.237	60.533	41.343	72.799	72.799	154.281		154.281	
	n		5	5	5	5	5	5		5	
Prostate	mg	M	46.4	46.6	44.6	52.4	52.4	40.2		40.2	
	% dev		100	100	96	113	113	87		87	
	SD		4.722	8.792	9.813	7.797	7.797	10.826		10.826	
	n		5	5	5	5	5	5		5	
Seminal vesicle	mg	M	152.6	155.4	168.4	165.0	165.0	91.6		91.6	*
	% dev		100	102	110	108	108	60		60	
	SD		19.269	14.741	18.461	25.288	25.288	41.495		41.495	
	n		5	5	5	5	5	5		5	

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



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PATHOLOGY REPORT

BASF
 Repeated-dose 28-day toxicity study in C57BL/6 JRJ mice
 Administration via the diet

ABSOLUTE WEIGHTS - MEAN VALUES (MALE)

Sacrifice	F1	M	0	1	2	3	4
Group	38.2	100	100	38.2	100	100	38.2
mg	44.0	115	117	44.8	112	112	42.6
% dev	6.782	5	5	7.396	4.278	5	5
SD	5	5	5	5	5	5	5
n	180.0	102	107	189.0	105	107	188.4
Testes	176.8	11.189	13.172	7.211	7.896	7.896	56.221
% dev	38.8	5	5	36.6	5	5	5
SD	125	4.604	3.435	5	5	5	5
n	310	2915	2915	310	2915	2915	310
Thymus	310	100	100	36.6	37.6	37.6	21.2
% dev	100	5	5	118	121	121	68
SD	5	5	5	5	5	5	5
n	188.4	107	107	188.4	107	107	188.4

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



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PATHOLOGY REPORT

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

MEAN VALUES (FEMALE)

Parameter	F1		F0		F1		F0	
	g	% dev						
Terminal body weight	16.76	100	16.84	100	16.72	100	17.1	100
Adrenal glands	7.2	100	7.2	100	8.2	114	8.8	122
Pituitary	44.2	100	45.2	101	43.8	99	45.5	102
Heart	108.2	100	111.2	103	106.4	98	110.0	101
Kidneys	249.4	100	254.0	102	240.2	96	253.0	101
Liver	781.0	100	733.2	94	807.2	103	956.4	122
Ovaries	15.8	100	13.6	86	13.6	86	14.2	90
Spleen	47.2	100	48.4	103	46.2	98	48.6	103
Thymus	39.2	100	46.8	119	44.0	112	44.4	113

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



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PATHOLOGY REPORT

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

ABSOLUTE WEIGHTS - MEAN VALUES (FEMALE)

Sacrifice Sex Group	F1 F 0	mg			
		0	1	2	3
Uterus	M	70.2	76.4	84.4	81.6
	% dev	100	109	120	116
	SD	25.825	21.267	42.618	23.037
	n	5	5	5	5

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

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PATHOLOGY REPORT

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

Relative Weights - Mean Values (Male)	Group 1		Group 2		Group 3		Group 4	
	M	n	M	n	M	n	M	n
Terminal body weight	100.0	5	100.0	5	100.0	5	100.0	5
% dev	0.055		0.124		0.102		0.058	
SD	0.006		0.004		0.005		0.004	
n	5		5		5		5	
Adrenal glands	0.019	5	0.027	5	0.024	5	0.021	5
% dev	1.38		1.38		1.27		1.09	
SD	0.006		0.004		0.005		0.004	
n	5		5		5		5	
Brain	2.184	5	2.083	5	2.149	5	2.058*	5
% dev	0.055		0.124		0.102		0.058	
SD	0.006		0.004		0.005		0.004	
n	5		5		5		5	
Epididymides	0.268	5	0.256	5	0.272	5	0.267	5
% dev	1.02		1.02		1.02		1.00	
SD	0.022		0.03		0.024		0.019	
n	5		5		5		5	
Heart	0.569	5	0.57	5	0.602	5	0.579	5
% dev	1.06		1.06		1.06		1.02	
SD	0.035		0.067		0.028		0.047	
n	5		5		5		5	
Kidneys	1.412	5	1.318*	5	1.397	5	1.369	5
% dev	0.055		0.055		0.08		0.074	
SD	0.05		0.055		0.08		0.074	
n	5		5		5		5	
Liver	4.202	5	3.914*	5	4.508**	5	5.144**	5
% dev	1.07		1.07		1.07		1.22	
SD	0.167		0.155		0.071		0.218	
n	5		5		5		5	
Prostate	0.225	5	0.216	5	0.209	5	0.241	5
% dev	0.025		0.04		0.039		0.042	
SD	0.025		0.04		0.039		0.042	
n	5		5		5		5	
Seminal vesicle	0.742	5	0.72	5	0.794	5	0.758	5
% dev	1.07		1.07		1.07		1.02	
SD	0.118		0.076		0.106		0.117	
n	5		5		5		5	

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

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PATHOLOGY REPORT

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

RELATIVE WEIGHTS - MEAN VALUES (MALE)

Sacrifice	F1	1	2	3	4
Sex	M				
Group	0				
%	M 0.185	0.203	0.21	0.195	0.181
% dev	100	110	113	105	97
SD	0.812	0.024	0.031	0.017	0.025
n	5	5	5	5	5
%	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
%	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

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PATHOLOGY REPORT

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

F1 Sex Group	RELATIVE WEIGHTS - MEAN VALUES (FEMALE)			
	0	1	2	3
Terminal body weight	% M 100.0 % dev 100 n 5	100.0 100 5	100.0 100 5	100.0 100 5
Adrenal glands	% M 0.043 % dev 100 SD 0.005 n 5	0.043 99 0.008 5	0.049 114 0.007 5	0.057 131 0.012 5
Brain	% M 2.654 % dev 100 SD 0.176 n 5	2.675 101 0.125 5	2.62 99 0.077 5	2.554 96 0.049 5
Heart	% M 0.644 % dev 100 SD 0.057 n 5	0.66 102 0.062 5	0.637 99 0.026 5	0.643 100 0.09 5
Kidneys	% M 1.487 % dev 100 SD 0.075 n 5	1.509 101 0.096 5	1.437 97 0.054 5	1.48 99 0.098 5
Liver	% M 4.667 % dev 100 SD 0.283 n 5	4.355 93 0.422 5	4.83 103 0.147 5	5.592** 120 0.245 5
Ovaries	% M 0.094 % dev 100 SD 0.01 n 5	0.081 86 0.01 5	0.081 86 0.01 5	0.083 88 0.015 5
Spleen	% M 0.281 % dev 100 SD 0.033 n 5	0.288 102 0.034 5	0.275 98 0.036 5	0.284 101 0.042 5
Thymus	% M 0.234 % dev 100 SD 0.009 n 5	0.278 119 0.027 5	0.264 113 0.027 5	0.26 111 0.036 5

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



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PATHOLOGY REPORT

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

RELATIVE WEIGHTS - MEAN VALUES (FEMALE)

F1 Sex Group	Relative Weights (Mean Values)			
	1	2	3	4
% M	0.453	0.501	0.479	0.467
% dev	108	120	115	112
SD	0.121	0.241	0.245	0.245
n	5	5	5	5

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

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PATHOLOGY REPORT

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

INCIDENCE OF ALL MICROSCOPIC FINDINGS

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



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PATHOLOGY REPORT

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

MICROSCOPIC FINDINGS TARGET ORGANS

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



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PATHOLOGY REPORT

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

MICROSCOPIC FINDINGS TARGET ORGANS

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

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STUDY TITLE

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Report

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

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TEST FACILITY

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Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

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TEST FACILITY PROJECT IDENTIFICATION

Project No. 31C0343/09S078

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**PART II OF III
(TABLES SECTION, INDIVIDUAL VALUES)**

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CONTENTS OF PART II (TABLES SECTION; INDIVIDUAL VALUES)

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PATHOLOGY

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Study 31C0343/09S078

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

Sex: Male - Phase: In-life

Group	Cage	Animals	d0 -> 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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ToxData© System 3.0

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	029, 028, 030, 026, 027		3.6	3.8	3.8	4.1
1/F	034, 032, 033, 031, 035		3.9	4.1	0.50L	4.5
2/F	038, 036, 039, 040, 037		3.3	3.6	3.6	3.9
3/F	042, 044, 045, 041, 043		3.4	3.6	3.8	4.0
4/F	049, 050, 048, 046, 047		2.7	3.2	3.0	3.3

d = day, OL = Outlier

Study 31C0343/09S078

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BASF
We create chemistry

Report; Project No.: 31C0343/09S078

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IIA 23
08-Aug-2017 11:14
ToxData@ System 3.0

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

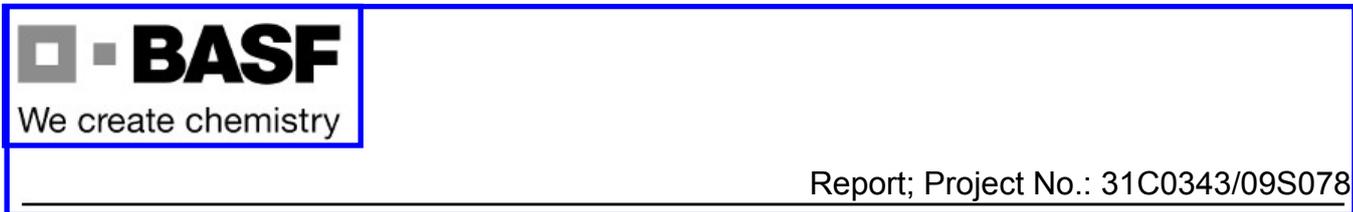
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Report; Project No.: 31C0343/09S078

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IIA 24
08-Aug-2017 11:14
ToxData© System 3.0

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

Study 31C0343/09S078

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BASF
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Report; Project No.: 31C0343/09S078

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IIA 25
08-Aug-2017 11:15
ToxData@ System 3.0

Study 31C0343/09S078

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



BASF
We create chemistry

Report; Project No.: 31C0343/09S078

non_continuous table (0.99), e72a8271-5217-4117-8139-ff187736a735

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
	031	18.3	18.8	19.3	20.2	20.2
	032	16.9	17.6	18.7	19.7	19.8
1/F	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
	036	17.1	18.3	18.5	19.2	19.8
	037	17.2	18.8	18.8	19.6	20.0
2/F	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
	041	17.7	18.5	19.0	19.5	19.8
	042	16.5	17.3	18.5	19.4	19.7
3/F	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
	046	17.3	15.1	16.0	16.2	16.1
	047	16.9	15.1	16.3	17.3	17.2
4/F	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

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BASF
We create chemistry

Report; Project No.: 31C0343/09S078

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IIB 1
06-Dec-2011 16:03
ToxData© System 3.0

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
0/M	002	10.22	8.6	0.456	44.6	0.84	18.93	2.5	1.460
0/M	003	9.16	7.6	0.400	43.6	0.84	19.20	2.7	1.644
0/M	004	9.72	8.2	0.432	44.5	0.84	18.84	2.7	1.520
0/M	005	11.00	9.4	0.480	43.6	0.85	19.50	2.6	1.390
0/M	006	10.12	8.8	0.472	46.7	0.86	18.44	2.7	1.740
0/M	007	6.92	8.4	0.308	44.6	1.21	27.22	2.3	1.888
0/M	008	9.04	7.6	0.398	44.1	0.84	19.05	2.4	1.426
0/M	009	10.74	9.2	0.480	44.6	0.86	19.26	2.7	1.576
0/M	010	9.64	8.2	0.430	44.5	0.84	18.93	3.1	1.424
0/M	011	8.72	7.2	0.390	44.9	0.83	18.52	2.6	1.810
0/M	012	10.72	9.2	0.486	45.3	0.86	19.01	2.8	1.578
2/M	013	10.26	9.0	0.452	44.1	0.87	19.82	2.6	1.540
2/M	014	9.72	8.2	0.430	44.3	0.85	19.11	2.4	1.582
2/M	015	9.98	8.4	0.448	44.9	0.85	18.91	2.4	1.670
2/M	016	10.22	8.6	0.458	44.7	0.84	18.83	2.7	1.860
2/M	017	10.00	8.6	0.444	44.5	0.86	19.25	2.6	1.922
2/M	018	10.26	8.6	0.450	43.9	0.83	18.89	2.3	1.610
2/M	019	10.56	8.8	0.464	43.9	0.83	18.96	2.2	1.846
2/M	020	10.46	9.0	0.456	43.5	0.86	19.74	2.4	1.804
2/M	021	7.48	6.0	0.330	44.2	0.79	17.87	2.6	1.742
2/M	022	8.50	7.2	0.384	45.1	0.85	18.88	3.4	812
2/M	023	9.36	7.8	0.408	43.7	0.83	19.08	2.1	1.816
2/M	024	6.94	6.0	0.318	45.8	0.85	18.62	4.6	738
2/M	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: Male Phase: In-life

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IIB 2
06-Dec-2011 16:03
ToxData@ System 3.0

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	2.88
	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
	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
1/F	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	8.74
	035	10.46	9.4	0.474	45.4	0.91	19.99	2.3	1.224
	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
2/F	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	1.302
	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	1.500
	043	9.14	8.0	0.418	45.6	0.88	19.20	2.6	1.368
3/F	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
	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
4/F	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	9.74

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Study 31C0343/09S078

Red blood cell parameters

Sex, Form, Phase, In, Lif

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IIB 3
06-Dec-2011 16:06
ToxData@ System 3.0

Study 31C0343/09S078

White blood cell parameters

Sex: Male -Phase: In-life

Dose Group	Animal Number	WBC [giga/L]		NEUTA [giga/L]		LYMPHA [giga/L]		MONOA [giga/L]		EOSA [giga/L]		BASOA [giga/L]		LUCA [giga/L]		NEUT [%]		LYMPH [%]		MONO [%]		EOS [%]		BASO [%]		LUC [%]		
		day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29
0/M	001	5.70	0.38	2.72	0.02	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	14.0	83.9	0.7	1.0	0.3	0.1	0.5	0.1	0.5	0.1	0.5	0.1	0.5
	002	4.78	0.36	4.36	0.02	0.04	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.00	0.02	7.3	89.6	0.2	0.4	0.0	0.0	0.4	0.0	0.4	0.0	0.4	0.0	0.5
	003	4.42	0.34	4.04	0.02	0.00	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	7.7	91.4	0.5	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2
	004	3.00	0.30	2.66	0.00	0.02	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	10.2	88.5	0.2	0.6	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.4
	005	3.50	0.36	3.10	0.02	0.02	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	10.0	88.7	0.5	0.4	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.3
1/M	006	5.80	0.58	5.14	0.02	0.02	0.00	0.04	0.00	0.04	0.00	0.00	0.00	0.04	9.9	88.6	0.3	0.4	0.0	0.3	0.4	0.0	0.3	0.4	0.0	0.3	0.7	
	007	4.22	0.26	3.92	0.02	0.02	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.04	6.2	92.8	0.4	0.3	0.1	0.2	0.1	0.2	0.1	0.2	0.1	0.2	0.1	0.2
	008	6.68	0.28	6.32	0.02	0.02	0.00	0.04	0.00	0.04	0.00	0.00	0.00	0.04	4.1	94.6	0.4	0.4	0.4	0.4	0.4	0.0	0.0	0.0	0.0	0.0	0.5	0.5
	009	3.14	0.22	2.90	0.00	0.00	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	7.0	92.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.4	0.4
	010	4.56	0.30	4.20	0.04	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	6.5	91.7	0.7	0.7	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.3	0.3
	011	4.06	0.32	3.68	0.00	0.04	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.02	8.1	90.5	0.2	0.8	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.3
2/M	012	4.90	0.26	4.58	0.02	0.02	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	5.2	93.5	0.4	0.3	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.6	0.6
	013	2.34	0.18	2.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	7.3	91.7	0.2	0.3	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.4	0.4
	014	5.56	0.42	5.08	0.02	0.02	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	7.4	91.3	0.3	0.6	0.1	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
	015	3.78	0.66	5.04	0.04	0.04	0.00	0.04	0.00	0.02	0.00	0.00	0.00	0.02	11.3	87.3	0.6	0.3	0.0	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
	016	3.32	0.36	5.88	0.02	0.04	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	5.7	93.0	0.3	0.6	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.4	0.4
3/M	017	6.02	0.58	5.34	0.02	0.04	0.00	0.02	0.00	0.04	0.00	0.00	0.00	0.04	9.5	88.8	0.4	0.7	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.5	0.5
	018	3.32	0.16	3.10	0.02	0.02	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.00	4.9	93.8	0.4	0.6	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2
	019	3.30	0.18	3.06	0.02	0.02	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.00	5.7	92.8	0.4	0.4	0.0	0.0	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
	020	2.78	0.36	2.34	0.02	0.04	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	12.9	83.8	0.9	1.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.9	0.9
	021	4.58	1.36	3.06	0.06	0.02	0.00	0.06	0.00	0.02	0.00	0.00	0.00	0.08	29.8	66.7	1.3	0.6	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	1.6	1.6
4/M	022	6.04	0.42	5.48	0.02	0.04	0.00	0.04	0.00	0.02	0.00	0.00	0.00	0.04	7.1	90.9	0.5	0.6	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.8	0.8
	023	1.48	0.34	1.04	0.02	0.06	0.00	0.02	0.00	0.06	0.00	0.00	0.00	0.02	22.7	70.6	1.0	3.8	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	1.8	1.8
	024	3.00	0.38	2.58	0.00	0.02	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	12.4	86.3	0.3	0.5	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.3
	025																											



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06-Dec-2011 16:06
ToxData@ System 3.0

Study 31C0343/09S078

White blood cell parameters

Sex: Female, Phase: In-life

Dose Group	Animal Number	SWBC [giga/L]		NEUTA [giga/L]		LYMPHA [giga/L]		MONOA [giga/L]		EOSA [giga/L]		BASOA [giga/L]		LUCA [giga/L]		NEUT [%]		LYMPH [%]		MONO [%]		EOS [%]		BASO [%]		LUC [%]			
		day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	day 29	
0/F	026	2.42	0.32	0.22	0.22	2.06	0.02	0.02	0.02	0.00	0.00	0.00	0.00	0.02	0.02	13.5	84.9	84.9	0.8	0.8	0.1	0.3	0.4	0.4	0.0	0.0	0.0	0.1	
	027	2.02	0.22	1.78	0.22	2.06	0.02	0.02	0.02	0.00	0.00	0.00	0.00	0.00	0.00	11.0	87.5	87.5	0.8	0.8	0.5	0.2	0.2	0.0	0.0	0.0	0.0	0.1	
	028	2.70	0.54	2.10	0.04	2.10	0.04	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	20.1	78.0	78.0	1.1	1.1	0.6	0.0	0.0	0.1	0.0	0.0	0.0	0.1	
	029	4.32	0.66	3.58	0.02	3.58	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	15.3	83.0	83.0	0.4	0.4	0.7	0.3	0.3	0.3	0.3	0.3	0.3	0.3	
	030	5.10	0.54	4.46	0.02	4.46	0.02	0.04	0.02	0.04	0.02	0.02	0.02	0.02	0.02	10.7	87.6	87.6	0.3	0.3	0.8	0.1	0.1	0.6	0.6	0.6	0.6	0.6	
	031	4.72	0.34	4.26	0.04	4.26	0.04	0.02	0.02	0.08	0.02	0.02	0.02	0.02	0.02	7.4	90.2	90.2	0.7	0.7	1.1	0.3	0.4	0.4	0.4	0.4	0.4	0.4	
1/F	032	5.18	0.42	4.62	0.00	4.62	0.00	0.06	0.00	0.06	0.00	0.00	0.00	0.02	0.04	8.0	89.2	89.2	0.5	0.5	1.4	0.2	0.2	0.6	0.6	0.6	0.6	0.6	
	033	4.22	0.24	3.90	0.00	3.90	0.00	0.06	0.00	0.06	0.00	0.00	0.00	0.02	0.02	5.7	92.5	92.5	0.2	0.2	1.3	0.0	0.0	0.3	0.3	0.3	0.3	0.3	
	034	5.92	0.36	3.46	0.04	3.46	0.04	0.04	0.00	0.04	0.00	0.00	0.00	0.02	0.02	9.2	88.5	88.5	0.8	0.8	1.0	0.1	0.1	0.4	0.4	0.4	0.4	0.4	
	035	4.70	0.46	4.16	0.02	4.16	0.02	0.02	0.00	0.02	0.00	0.00	0.00	0.02	0.02	9.7	88.6	88.6	0.5	0.5	0.5	0.0	0.0	0.6	0.6	0.6	0.6	0.6	
	036	3.24	0.40	2.76	0.02	2.76	0.02	0.04	0.00	0.04	0.00	0.00	0.00	0.02	0.02	12.2	85.1	85.1	0.6	0.6	1.3	0.1	0.1	0.8	0.8	0.8	0.8	0.8	
	037	3.04	0.42	2.58	0.02	2.58	0.02	0.02	0.00	0.02	0.00	0.00	0.00	0.02	0.02	13.6	84.9	84.9	0.4	0.4	0.6	0.1	0.1	0.4	0.4	0.4	0.4	0.4	
2/F	038	2.46	0.30	2.12	0.02	2.12	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.02	12.4	85.9	85.9	0.7	0.7	0.3	0.1	0.1	0.6	0.6	0.6	0.6	0.6	
	039	3.54	0.44	2.98	0.06	2.98	0.06	0.06	0.00	0.06	0.00	0.00	0.00	0.00	0.00	12.5	83.9	83.9	1.8	1.8	1.6	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2
	040	1.50	0.24	1.24	0.00	1.24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	15.4	82.9	82.9	0.3	0.3	0.6	0.6	0.2	0.2	0.2	0.2	0.2	0.2	
	041	5.86	0.66	5.08	0.02	5.08	0.02	0.06	0.00	0.06	0.00	0.00	0.00	0.02	0.02	11.4	86.5	86.5	0.4	0.4	1.1	0.2	0.2	0.4	0.4	0.4	0.4	0.4	
	042	2.62	0.20	2.40	0.00	2.40	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	0.02	7.4	91.4	91.4	0.1	0.1	0.6	0.1	0.1	0.4	0.4	0.4	0.4	0.4	
3/F	043	3.78	0.34	3.38	0.02	3.38	0.02	0.02	0.00	0.02	0.00	0.00	0.00	0.02	0.02	8.7	89.4	89.4	0.8	0.8	0.7	0.1	0.1	0.3	0.3	0.3	0.3	0.3	0.3
	044	6.42	0.44	5.88	0.02	5.88	0.02	0.04	0.00	0.04	0.00	0.00	0.00	0.02	0.02	6.9	91.7	91.7	0.2	0.2	0.8	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2
	045	2.26	0.16	1.06	0.00	1.06	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.00	0.00	12.6	84.3	84.3	0.5	0.5	1.8	0.8	0.8	0.0	0.0	0.0	0.0	0.0	0.0
	046	2.32	0.20	2.06	0.02	2.06	0.02	0.02	0.00	0.02	0.00	0.00	0.00	0.00	0.00	8.8	88.8	88.8	0.9	0.9	0.9	0.2	0.2	0.4	0.4	0.4	0.4	0.4	0.4
	047	3.94	0.32	3.58	0.02	3.58	0.02	0.02	0.00	0.02	0.00	0.00	0.00	0.00	0.00	7.9	91.1	91.1	0.3	0.3	0.4	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2
4/F	048	4.90	0.54	4.26	0.02	4.26	0.02	0.04	0.00	0.04	0.00	0.00	0.00	0.02	0.02	11.1	86.9	86.9	0.2	0.2	1.0	0.1	0.1	0.6	0.6	0.6	0.6	0.6	0.6
	049	4.18	0.26	3.86	0.00	3.86	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.02	0.02	6.4	92.6	92.6	0.1	0.1	0.4	0.1	0.1	0.4	0.4	0.4	0.4	0.4	0.4
	050	1.48	0.20	1.26	0.00	1.26	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.00	0.00	12.8	85.2	85.2	0.3	0.3	0.8	0.5	0.5	0.3	0.3	0.3	0.3	0.3	0.3



We create chemistry

Report; Project No.: 31C0343/09S078

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06-Dec-2011 16:07
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Study 31C0343/09S078

Enzymes

Sex: Male Phase: In-life

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text_block(0.83), 8d472224-3ca0-41a8-ac17-19016778b91a

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



BASF
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Report; Project No.: 31C0343/09S078

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06-Dec-2011 16:07
ToxData© System 3.0

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

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Study 31C0343/09S078

Enzymes
Sex: Female - Phase: In-life

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

Substrates

Sex Female Phase NC1016

Dose Group	Animal Number	UREA	CREA	GLUC	TBIL	TBA	TPROT	ALB	GLOB	CHOL	TRIG
		[mmol/L] day 29	[μmol/L] day 29	[mmol/L] day 29	[μmol/L] day 29	[μmol/L] day 29	[g/L] day 29	[g/L] day 29	[g/L] day 29	[mmol/L] day 29	[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
1/F	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
	031	11.07	37.4	10.09	1.95	8.0	50.84	36.83	14.01	2.15	0.61
2/F	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
3/F	035	7.49	19.1	1.99	2.70	NM	NM	NM	NM	NM	NM
	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
4/F	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	8.25	45.0	8.45	1.61	14.8	48.27	34.48	13.79	2.18	0.57
4/F	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
	046	10.56	21.6	4.44	4.36	5.0	29.99	7.37	22.62	0.58	0.25
4/F	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

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06-Dec-2011 16:31
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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	2.02	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

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Study 31C0343/09S078

Electrolytes + minerals

Sex: Female - Phase: In-life

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NM = Not measured



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BASF

PATHOLOGY REPORT

JIC 1/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
Sacrifice	F1					
Sex	M					
Group	0					
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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Report; Project No.: 31C0343/09S078

text_block (0.99), 223fc417-6bff-4ea9-b09b-729854038619e-d535-4a77-8df8-3601s24e2b1dcd (1.00)

BASF **PATHOLOGY REPORT** **IIC 2/72**
31C0343/09S078
05.Jan.2012 MAHU

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

text_block (0.99), 8d575bb9-2832-11f7-8862-2307ba269a (0.76), a746f68e-32d3-4700-b9b2-4a28

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
Sacrifice	F1					
Sex	M					
Group	0					
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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PATHOLOGY REPORT

IIS 3/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
Sacrifice	F1					
Sex	M					
Group	1					
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



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PATHOLOGY REPORT

IIC 4/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS AND INDIVIDUAL VALUES

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
Sacrifice	F1					
Sex	M					
Group	1					
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



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PATHOLOGY REPORT

IIG 5/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
Sacrifice	F1					
Sex	M					
Group	2					
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



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05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	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



Report; Project No.: 31C0343/09S078

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

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ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
Sacrifice	F1					
Sex	M					
Group	3					
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



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 31C0343/09S078
 05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
Sacrifice	F1					
Sex	M					
Group	3					
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



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IIC 9/72
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05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS AND INDIVIDUAL VALUES

	Term. body weight g	Adrenal glands mg	Brain mg	Epididymides mg	Heart mg	Kidneys mg
Sacrifice	F1					
Sex	M					
Group	4					
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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Report; Project No.: 31C0343/09S078

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

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ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Liver mg	Prostate mg	Seminal vesicle mg	Spleen mg	Testes mg	Thymus mg
Sacrifice	F1					
Sex	M					
Group	4					
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



Report; Project No.: 31C0343/09S078

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PATHOLOGY REPORT

IIC 11/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS INDIVIDUAL VALUES -040140042c90

	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



Report; Project No.: 31C0343/09S078

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PATHOLOGY REPORT

ILIC 12/72
31C0343/09S078
05.Jan.2012 MAHU

Repeated-dose 28-day toxicity study in C57BL/6 JRj mice
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	



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IIC 13/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES - Zinc

	Term. body weight g	Adrenal glands mg	Brain mg	Heart mg	Kidneys mg	Liver mg
Sacrifice	F1					
Sex	F					
Group	1					
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



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PATHOLOGY REPORT

LIC 14/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS - INDIVIDUAL VALUES

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
Sacrifice	F1			
Sex	F			
Group	1			
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



Report; Project No.: 31C0343/09S078

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PATHOLOGY REPORT

IIC 15/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Term. body weight g	Adrenal glands mg	Brain mg	Heart mg	Kidneys mg	Liver mg
Sacrifice	F1					
Sex	F					
Group	2					
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



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Report; Project No.: 31C0343/09S078

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PATHOLOGY REPORT

ITC 16/72
31C0343/09S078
05.Jan.2012 MAHU

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

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ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
Sacrifice	F1			
Sex	F			
Group	2			
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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PATHOLOGY REPORT

LLC 17/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS INDIVIDUAL VALUES 31c0343/09s078

	Term. body weight g	Adrenal glands mg	Brain mg	Heart mg	Kidneys mg	Liver mg
Sacrifice	F1					
Sex	F					
Group	3					
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



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Report; Project No.: 31C0343/09S078

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PATHOLOGY REPORT

IIC 18/72
 31C0343/09S078
 05.Jan.2012 MAHU

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

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ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
Sacrifice	F1			
Sex	F			
Group	3			
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



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PATHOLOGY REPORT

IIC 19/72
31C0343/09S078
05.Jan.2012 MAHU

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

ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Term. body weight g	Adrenal glands mg	Brain mg	Heart mg	Kidneys mg	Liver mg
Sacrifice	F1					
Sex	F					
Group	4					
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	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



Report; Project No.: 31C0343/09S078

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PATHOLOGY REPORT

IIC 20/72
 31C0343/09S078
 05.Jan.2012 MAHU

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

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ABSOLUTE WEIGHTS INDIVIDUAL VALUES

	Ovaries mg	Spleen mg	Thymus mg	Uterus mg
Sacrifice	F1			
Sex	F			
Group	4			
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



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PATHOLOGY REPORT

IIS 22/72
31C0343/09S078
05.Jan.2012 MAHU

Repeated-dose 28-day toxicity study in C57BL/6 JRj mice
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



Report; Project No.: 31C0343/09S078

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PATHOLOGY REPORT

LIC 23/72
31C0343/09S078
05.Jan.2012 MAHU

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

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RELATIVE WEIGHTS INDIVIDUAL VALUES -32a0d4232269

	Term. body weight %	Adrenal glands %	Brain %	Epididymides %	Heart %	Kidneys %
Sacrifice	F1					
Sex	M					
Group	1					
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



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PATHOLOGY REPORT

IIC 24/72
31C0343/09S078
05.Jan.2012 MAHU

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

text_block (0.99), a458ed07-d1ff-4f77-60d12-02a5fa2846
RELATIVE WEIGHTS AND INDIVIDUAL VALUES - 51447fcc1c84

	Liver %	Prostate %	Seminal vesicle %	Spleen %	Testes %	Thymus %
Sacrifice	F1					
Sex	M					
Group	1					
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



text_block (0.99), f7a03409-d516e448cbk (0.98), 52b15259f3-4d45-4064-d0616-0001e001e000 (1.00)

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PATHOLOGY REPORT

LIC 25/72
31C0343/09S078
05.Jan.2012 MAHU

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

text_block (0.99), e1ca860a-0a9e-1d0e-ki42-0b9c-117d1123d (0.74), 15cf3a54-4af9-4070-a5ff-35100e

RELATIVE WEIGHTS OF INDIVIDUAL ORGANS

	Term. body weight %	Adrenal glands %	Brain %	Epididymides %	Heart %	Kidneys %
Sacrifice	F1					
Sex	M					
Group	2					
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



text_block (0.99), cf4c01a3-6c6e4ef-block (0.68), 4d11b3a0-3cd8-4079-ad411d105934066a5 (1.00)

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PATHOLOGY REPORT

IIC 26/72

31C0343/09S078

05.Jan.2012 MAHU

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

RELATIVE WEIGHTS INDIVIDUAL VALUES

	Liver %	Prostate %	Seminal vesicle %	Spleen %	Testes %	Thymus %
Sacrifice	F1					
Sex	M					
Group	2					
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



Report; Project No.: 31C0343/09S078

text_block (0.99), cc8c81c5-4219-4b71-8004-067af2711585022e-4878-814719703546a179b (1.00)

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PATHOLOGY REPORT

IIC 27/72
 31C0343/09S078
 05.Jan.2012 MAHU

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

text_block (0.99), 16594812-fc8a-4f48-969a-b4042a822747 (0.74), 11359ec6-9897-47e0-8c9f-cbd4

RELATIVE WEIGHTS INDIVIDUAL VALUES

	Term. body weight %	Adrenal glands %	Brain %	Epididymides %	Heart %	Kidneys %
Sacrifice	F1					
Sex	M					
Group	3					
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



text_block (0.99), b39af0fb-270849f1b02e-09677edc239-f3fd-40ca-920114081c858e00

BASF

PATHOLOGY REPORT

EIC 28/72
31C0343/09S078
05.Jan.2012 MAHU

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

RELATIVE WEIGHTS AND INDIVIDUAL VALUES - 67f3366c3102

	Liver %	Prostate %	Seminal vesicle %	Spleen %	Testes %	Thymus %
Sacrifice	F1					
Sex	M					
Group	3					
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



We create chemistry

Report; Project No.: 31C0343/09S078

text_block (0.99), f6bcc0c0-1533e449bc30(0.98), 2cf80696-f6d0-47e2-832e1d5e71e2d822

BASF

PATHOLOGY REPORT

IIC 29/72

31C0343/09S078

05.Jan.2012 MAHU

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

text_block (0.99), 2e56e26a-b05f4b2b01ac6172806dc2

RELATIVE WEIGHTS OF INDIVIDUAL ORGANS - 70cc69bb9008

	Term. body weight %	Adrenal glands %	Brain %	Epididymides %	Heart %	Kidneys %
Sacrifice	F1					
Sex	M					
Group	4					
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



We create chemistry

Report; Project No.: 31C0343/09S078

text_block (0.99), 1bcd551-3f74e4c0aa13e58242e60815-ffbd-49ee-850ndue29ef680

BASF

PATHOLOGY REPORT

IIC 30/72
 31C0343/09S078
 05.Jan.2012 MAHU

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

text_block (0.99), 807066be-3000-4520-8710-21-0af-21886(0.74), a40805ee-ae80-4787-9607-aa4

RELATIVE WEIGHTS INDIVIDUAL VALUES

	Liver %	Prostate %	Seminal vesicle %	Spleen %	Testes %	Thymus %
Sacrifice	F1					
Sex	M					
Group	4					
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



Report; Project No.: 31C0343/09S078

text_block (0.99), 3af42f5f-0ede4023b71e (0.93), f8638152f9-92f8-4875-8c91e830e1486280ck (1.00)

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PATHOLOGY REPORT

LTC 31/72
31C0343/09S078
05.Jan.2012 MAHU

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

RELATIVE WEIGHTS INDIVIDUAL VALUES T-0 44344c8456

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



Report; Project No.: 31C0343/09S078

text_block (0.99), 9d89739f-d6c4e12b8d5-708271a05a3-bf5d-4406920b67704852c15

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PATHOLOGY REPORT

ILC 32/72
31C0343/09S078
05.Jan.2012 MAHU

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

RELATIVE WEIGHTS INDIVIDUAL VALUES

	Ovaries %	Spleen %	Thymus %	Uterus %
Sacrifice	F1			
Sex	F			
Group	0			
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



Report; Project No.: 31C0343/09S078

text_block (0.99), 9c3a32e8-2501e4c0a4b1(0.98), 4374e9a8-73a7-4c96-9d1f7050e25610c (1.00)

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PATHOLOGY REPORT

LIC 33/72
31C0343/09S078
05.Jan.2012 MAHU

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

RELATIVE WEIGHTS INDIVIDUAL VALUES

	Term. body weight %	Adrenal glands %	Brain %	Heart %	Kidneys %	Liver %
Sacrifice	F1					
Sex	F					
Group	1					
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



text_block (0.99), ff936e07-6265461b16ac80e98a4890a106-ce1d-4011-90f91d4e85f6a207

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PATHOLOGY REPORT

IIC 34/72
31C0343/09S078
05.Jan.2012 MAHU

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

RELATIVE WEIGHTS INDIVIDUAL VALUES

	Ovaries %	Spleen %	Thymus %	Uterus %
Sacrifice	F1			
Sex	F			
Group	1			
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



We create chemistry

Report; Project No.: 31C0343/09S078

text_block (0.99), d3cbaae9-7a3e-4f5e-9106-97a72634a268b084-4e3a-950e1b0c8e62476 (1.00)

BASF **PATHOLOGY REPORT** **IIC 35/72**
31C0343/09S078
05.Jan.2012 MAHU

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

text_block (0.99), ead53b51-b875-4b53-8af7-cfb822e4103f (0.74), 5db08332-1dce-4358-a69f-bc77

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



text_block (0.99), cf0e7a30-0041e40b19c6(0.99), 662f55773b81b-410e-881f-481650bed1d2

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PATHOLOGY REPORT

IIS 36/72

31C0343/09S078

05.Jan.2012 MAHU

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

text_block (0.99), 12a702da-0f3f4d8-651d0cc-d643888a
RELATIVE WEIGHTS INDIVIDUAL VALUES 8-76879f638bed

	Ovaries %	Spleen %	Thymus %	Uterus %
Sacrifice	F1			
Sex	F			
Group	2			
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



text_block (0.99), 38489d2f-0821e4d95d06(0.96), 243d8790-725f-4f1a-84809b0e75d48688

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PATHOLOGY REPORT

IIS 37/72
31C0343/09S078
05.Jan.2012 MAHU

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

text_block (0.99), f6611705-ba7b04d57-8602-f7e01e-445dc(0.74), f646f619-068b-4790-83a2-069b5

RELATIVE WEIGHTS AND INDIVIDUAL VALUES F0920f430109a

	Term. body weight %	Adrenal glands %	Brain %	Heart %	Kidneys %	Liver %
Sacrifice	F1					
Sex	F					
Group	3					
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



text_block (0.99), f493440b-e51d48bdc8-0-983b7472d626-5c22-4259-9704a01517e3ab1d (1.00)

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PATHOLOGY REPORT

IIC 38/72

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05.Jan.2012 MAHU

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

text_block (0.99), 7651be1315bd4570584f30084c866a (0.73), 286dcf76-4f9b-4e0b-a4d1-b0840

RELATIVE WEIGHTS INDIVIDUAL VALUES 4-C/a6115c4327

	Ovaries %	Spleen %	Thymus %	Uterus %
Sacrifice	F1			
Sex	F			
Group	3			
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



We create chemistry

Report; Project No.: 31C0343/09S078

text_block (0.99), 16a87bf3-db71e22de938(0.28), 8769487bb-2dcc-40aa-c558-171a3e26437ak (1.00)

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PATHOLOGY REPORT

IIC 39/72
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Repeated-dose 28-day toxicity study in C57BL/6 JRj mice
 Administration via the diet

text_block (0.99), 617ab0de-135b-4cfe-8f0d-02cc1172884k (0.74), 0be830b6-504b-4cd9-b3b0-6c1c

RELATIVE WEIGHTS INDIVIDUAL VALUES - Zlf23e7b876c

	Term. body weight %	Adrenal glands %	Brain %	Heart %	Kidneys %	Liver %
Sacrifice	F1					
Sex	F					
Group	4					
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



Report; Project No.: 31C0343/09S078

text_block (0.99), ed6d77f4-0b2de48369b0 (0.98), 3e7668d5-542d-46bb-d0eb-c0537e7792

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PATHOLOGY REPORT

IIC 40/72
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05.Jan.2012 MAHU

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

text_block (0.99), adf4310-5724-42a9-88-1-25013286424 (50.73), 925a3db7-2fe1-456a-aafef8631

RELATIVE WEIGHTS INDIVIDUAL VALUES

	Ovaries %	Spleen %	Thymus %	Uterus %
Sacrifice	F1			
Sex	F			
Group	4			
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



text_block (0.99), f12aa381-3d30e11804(0.49), 90760095-8adc-40c9-901a-99e2f6e2 text_block (0.99)

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PATHOLOGY REPORT

JIC 41/72
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05.Jan.2012 MAHU

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

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), 0d50bcfd-0915-4fd7-b

Sacrifice	F1
Sex	M
Group	0
Animal	1

text_block (0.98), d06217e9-76a3-44e7-93dd-1a54a337e806

left_right_mapping (1.00), 3fd69304-a09d-4ab1-bea6-c6b3c99cadc8

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

non_continuous_text_block (0.99), b330f0f2-47c1-41b0-b2a6-b9dde61e0d06

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.

left_right_mapping (0.99), 738ce4c8-b6e1-46c4-

text_block (0.98), b9668ae9-a9af-4698-a99b-f7f4b37a4876

Animal 2

left_right_mapping (1.00), f09a742b-75f0-41f1-8aab-ce5b9e1ac0f0

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

non_continuous_text_block (0.98), 43bd2a17-78d6-4595-831b-856a1b7d2183

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.



Report; Project No.: 31C0343/09S078

text_block (0.99), 12776ebf-800b-4498-90b5-29158922a464-8d78-40ed-818a30eb4e7354f1

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PATHOLOGY REPORT

IIC 42/72
31C0343/09S078

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

05.Jan.2012 MAHU

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), 2451697a-69b9-40a3-

Sacrifice	F1
Sex	M
Group	0
Animal	3

text_block (0.98), 57c80c46-16c3-4c05-b054-b2da61ec95b0

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

non_continuous_text_block (0.99), 0bf94462-180f-459e-ae79-14de3afa74c3

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.

left_right_mapping (0.97), 90062b9d-99a7-4add-

text_block (0.98), 4903ba78-0f3d-49a5-86cb-7672005a307

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

non_continuous_text_block (0.96), 499179f5-fcd1-4e3c-8783-c66434028ce6

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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text_block (0.99), db6bd7f4-218e4d51bc78(0.99), f2642e32-336d-4109-b90b1ad23b1b8b2156c (0.99)

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PATHOLOGY REPORT

TIC 43/72
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Repeated-dose 28-day toxicity study in C57BL/6 JRj mice
Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), bfdc0d95-7ea5-4c3b-b06d-c

Sacrifice	F1
Sex	M
Group	0
cont. Animal	4

non_continuous_text_block (0.98), e82d0ae3-2da2-4507-810e-e52c61ad25ee

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

text_block (0.99), d3cdf20a-60aa-4366-8ea6-56af-2998d50

left_right_mapping (1.00), 5665b0fe-3dad-4b10-b7b3-62b7d4a6d8a0

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

non_continuous_text_block (0.96), abe47e88-4828-4b59-8bea-c917f6fd8614

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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text_block (0.99), 6be745f1-4cfc482910c3-0297, 07d87243-870a-408eca00ba-062ed2b26k (0.99)

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left_right_mapping (1.00), cdc23c8f-4700-4a84-9

Sacrifice F1
Sex M
Group 1
Animal 6

text_block (0.98), 31d13d4e-7f82-4e37-8432-a16c2fac0526

left_right_mapping (1.00), 85e396fa-df71-40a5-8c8e-8dac0a6789c7

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

non_continuous_text_block (1.00), 0c1d355d-9896-4169-a48a-19ca63884516

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.

left_right_mapping (0.97), 99d28b4d-25c6-4cf7-

text_block (0.98), c34230a9-f7ed-4533-b549-d4581cedb082

Animal 7

left_right_mapping (1.00), acd96484-113f-4d12-a29d-4d683183c563

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

non_continuous_text_block (0.99), f8dbb479-0902-498b-8352-2917ae6d471a

Macroscopic findings

Animal without particular findings.

non_continuous_text_block (0.99), 0eedd6b7-da04-482c-9b58-a8920ccce01d

Microscopic findings

Kidneys

Tubules, basophilic, (multi)focal, unilateral, grade 1

Liver

Vacuolar change reduced, grade 1.

All other organs examined without microscopic findings.

left_right_mapping (0.98), 76b462b8-31bb-47b0-

text_block (0.98), d6a3915c-10d4-41a4-8b9b-84689438bc81

Animal 8

left_right_mapping (1.00), 3cc911bc-da14-4c8a-8f79-439ac9d0f845

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

footer (1.00), d41225e9-c17a-41a8-9cf8-d53c99e61ec5



text_block (0.99), fbd976f9-1dbb1e45b19d6109291e8b3e2b6-6dd4-48bd-dc91b6033e3592dbk (0.99)

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left_right_mapping (1.00), 118faeab-c0ad-46b9-aaf9-3

Sacrifice	F1
Sex	M
Group	1
cont. Animal	8

non_continuous_text_block (0.99), da31fa3013bc-4921-ab40-fa6f0ea7e3e9

Macroscopic findings
Animal without particular findings

Microscopic findings
All organs examined without pathologic findings

left_right_mapping (0.98), b9b0ac4c-1f43-48d5-8

text_block (0.99), a9fc6fb8-a01e-46cb-a949-d995-207d52e
Animal 9

General information (0.99), 8f035a24-ac9f-40f6-8f76-81e5005aa91a

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

non_continuous_text_block (0.99), 450b8215-faf7-4ee8-ad55-e458c4c36bf5

Macroscopic findings
Liver
All other organs without macroscopic findings.

non_continuous_text_block (0.99), 8884ac5c-fcd0-4051-a5f3-a5010f74c90e

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.

left_right_mapping (0.99), f184f9c9-4c02-425b-8

text_block (0.98), 8d3763ca-c945-4c02-a0f0-27e31b345c9
Animal 10

General information (1.00), cf8f9e48-b877-4349-83df-e1605f258c2c

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



text_block (0.99), 5834b110-1f53e1deaf7(0.99), 3e18342b5-e403-40d7-90176-a5b5-9af1a30c (0.99)

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left_right_mapping (1.00), adf8458b-31be-49a4-8c3a-e

Sacrifice	F1
Sex	M
Group	1
cont. Animal	10

non_continuous_text_block (1.00), e595a1e7-086e-46cd-a5b5-afe505d87aad

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (1.00), 2117cf58-d2f9-42d8-a99f-91167266888a

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.



text_block (0.99), 84d39576-016e410a570-99f5632e57b4-ed20-4002-090184017cbe541b0e (0.99)

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left_right_mapping (1.00), 878f65cf-1624-431f-90

Sacrifice	F1
Sex	M
Group	2
Animal	11

text_block (0.98), 0064780e-08e0-4e9e-925f-21b428350ad7

left_right_mapping (1.00), 2ef32fb4-6c35-41d3-a10f-0270e93e6b8a

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

non_continuous_text_block (0.99), ac52cfd6-7c3e-4e58-8dd8-322ee91beda1

Macroscopic findings

Animal without particular findings.

non_continuous_text_block (1.00), 866d2e59-b86e-4fb2-abc8-e9e9f93be058

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

left_right_mapping (0.96), e961366-0fc8-403a-8

text_block (0.98), 5482869f-2b3c-47db-850b-59ac40670f59

Animal 12

left_right_mapping (0.99), d13af43c-5f0a-4684-abf4-64fc0aa4563c

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

non_continuous_text_block (0.99), 45c12731-baed-40b4-9222-864534ea3def

Macroscopic findings

Animal without particular findings.

non_continuous_text_block (0.99), db80c084-a3b4-4120-8f1d-82da8be75037

Microscopic findings

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

left_right_mapping (0.97), 17871ada-a1b1-4d20

text_block (0.98), 83bb4ba4-e264-4cd3-871f-5152674dc706

Animal 13

left_right_mapping (1.00), 30a488db-68e3-4138-aded-8435e9cd7a95

General information

Sex : Male
Group : 2 (500 ppm)
Sacrifice : Final sacrifice group
Necropsy status : Planned sacrifice
Date of death : 21.Sep.2011
28 days after start of exposure

footer (1.00), 03ee0f2f-fa56-4e11-a645-4c52886de071



text_block (0.99), 7642b5ba-abcb-4057-92c9-263045-4142-46d7ca708b68510c810c (0.99)

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left_right_mapping (1.00), b80d8b02-29c1-4708-af2e-4

Sacrifice F1
Sex M
Group 2
Animal 13

text_block (0.99), 60f8ab25-75dc-4412-b1b8-d027390ee17d

non_continuous_text_block (1.00), 5627225c-1534-4003-a7f5-4fd3b24c32ae

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.

left_right_mapping (0.98), abb5a940-2902-4a1f-

text_block (0.99), bd8decac-43a1-412a-b596-9ae97e2af09c

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

non_continuous_text_block (0.99), f0cc5a00-833b-456f-b1b7-c42c74aebb1e

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), 70c1248c-a253-4b37-a5fe-6fdd684ffb9d

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.

left_right_mapping (0.97), 216db92b-12df-4732-9

text_block (0.98), 225148a6-d05d-45b8-acb4-6c3e3a4e154e

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

footer (1.00), 0521a9cf-a4e3-4a89-8652-9aa837dccb6a



We create chemistry

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text_block (0.99), e5b0e537-1211e-42b0-939-996-956e6a152ddb7-4001-c57a-0ab07e4747b1

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left_right_mapping (1.00), b31fad4c-8efa-43b0-939e-a

Sacrifice	F1
Sex	M
Group	2
cont. Animal	15

non_continuous_text_block (1.00), 1cde4e7a-9c0c-4a1b-ba7d-ad306f077250

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (1.00), 917364e2-8ad4-401c-a6ab-55ca998d7f80

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.



We create chemistry

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text_block (0.99), e95b98c2-b9cfe46ed90c(0.99), 782295f5-1c32-48a8-810m1270a7_d6x7b8

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left_right_mapping (1.00), 11be2b26-80d4-44f5-

Sacrifice	F1
Sex	M
Group	3
Animal	16

text_block (0.98), 911b2bd0-6ec0-482c-867c-dbf30fab4828

left_right_mapping (1.00), ca82db61-4152-4111-9881-2a90c1569685

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

non_continuous_text_block (0.99), 61cc009-eb77-4a6d-a466-39e41a41bb40

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.

left_right_mapping (0.98), 16d062c6-af1e-4d45-

text_block (0.98), f7273ec9-3f89-485e-aec1-4e7199749e16

left_right_mapping (1.00), 043c9875-a8ad-477f-9ce3-dddbf8e0dbe5

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

non_continuous_text_block (0.99), 401db6a7-a190-4fb2-94dc-369d5c0a7e89

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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text_block (0.99), 44acc404-6a21e4db7eak (0.99), 109d163e5-0dd3-4019e8081u238f400d1d0c (0.99)

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left_right_mapping (1.00), 525ff38e-6568-4f37-8

Sacrifice	F1
Sex	M
Group	3
Animal	18

text_block (0.98), 9e9bfcf1-a0d8-4efd-b96f-3480920873ad

left_right_mapping (1.00), 75eda0b4-e579-4732-b9c9-5721e0de8093

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

non_continuous_text_block (1.00), a7b80b18-3952-4ee3-8200-2d432656fc0e

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), a12e1f5a-df22-4a97-ac9d-f8baef573f68

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.

left_right_mapping (0.99), 3911f5b6-de90-48ad-

text_block (0.99), 568c050e-96da-4573-8b4f-80df413593465

Animal 19

left_right_mapping (1.00), 2c093119-eb09-45e0-9785-c9f60b71b71b

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

non_continuous_text_block (0.99), 4dce0f0c-b80b-4c1a-a506-3f7d07f6795d

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), 0a163e32-8e0d-4abb-8d43-c9db54a8e778

Microscopic findings

Liver
 Hypertrophy, centrilobular, grade 2.
 Vacuolar change reduced, grade 2.
 All other organs examined without microscopic findings.



text_block (0.99), 3e3d7f51-7578e4b85eak7(0.99), 8280975e-6ac7-4nd9-067612aa8cfe9196

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left_right_mapping (1.00), 17e7724a-da90-41c0-

Sacrifice	F1
Sex	M
Group	3
Animal	20

text_block (0.98), 2a0faeb5-6555-44ab-b092-cff8576e137

left_right_mapping (1.00), 61b97643-9181-4661-8359-fb1072aa8fc2

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

non_continuous_text_block (1.00), 4e23ad3d-4475-4d9a-8e59-d9ef6d1ab35f

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), 24dc3f6f-7f7c-4d09-aba1-6dbdbd49ae24

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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text_block (0.99), 2a6628e2-481e-409b-9939-731bd4698-eb29-4079-d048-824e-941b1b1c (0.99)

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left_right_mapping (1.00), e9615c93-f5c8-4746-9

Sacrifice	F1
Sex	M
Group	4
Animal	21

text_block (0.98), 96284c06-eac0-449d-b550-409d9884377

left_right_mapping (1.00), 6a6501a6-a2a6-409f-af2e-8693303f0933

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

non_continuous_text_block (1.00), 32f0d6b9-2117-48e7-8d42-58d17b8e2265

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), c13ad826-9287-45be-9932-ae64729dad6d

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.

left_right_mapping (0.99), acb9fc98-cf23-42f1-a

text_block (0.98), 42390e13-26c6-4156-ac43-af7d96a0fe2a

Animal 22

left_right_mapping (1.00), 5fd2bdf2-40c1-4917-966e-b3348d681bc3

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

non_continuous_text_block (0.98), dc030b78-c832-48ad-a037-6469b5a433ab

Macroscopic findings

Thymus
 Organ size reduced, severe.
 All other organs without macroscopic findings.



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text_block (0.99), d4a819bb-c011e480-9b50-2a3f0659847d-14f9-48e1-8089-80e40506a19b60 (0.99)

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Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), 37895540-8d60-47c8-82d2-

Sacrifice	F1
Sex	M
Group	4
cont. Animal	22

non_continuous_text_block (0.97), d2c0e7d1-3496-4eb2-a4c4-8bb8e97c2ab6

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.

left_right_mapping (0.98), 0fafcc25-adcf-46d5-9-

text_block (0.99), 1a81e757-3f32-4ae4-b975-a8e1-2171ae0

Animal 23

General information (1.00), 5f3e94f8-cd34-45eb-ad7d-b4af014e3eb8

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

non_continuous_text_block (0.90), e69b6db5-ec7b-432b-ac1d-d46ba8152842

Macroscopic findings
Animal without particular findings



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text_block (0.99), fc7b145e-2ebf4d71a08a0989816cb2db-7ca2-48e3-c774-2030-4e2668e0ek (0.99)

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left_right_mapping (1.00), fee19397-a14d-4a7c-9c0f-c

Sacrifice	F1
Sex	M
Group	4
cont. Animal	23

non_continuous_text_block (0.99), 50b5c7dc-1bd4-4240-99a5-0d8c-68b6f335

Microscopic findings

Coagulating glands
No or insufficient 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.

left_right_mapping (0.99), 79289f74-3e7e-423e-

text_block (0.97), 754169f2-2a6b-4fc5-84ff-c04e780643b2

Animal 24

General information (1.00), cf55a726-74a1-47dd-9658-30385525f03d

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

non_continuous_text_block (0.94), 9ac960d5-9a61-464e-b423-12edcd3d891a

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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text_block (0.99), 3872fd09-bb80e146a9(0.99), f27079481c-cfdc-405f-b922ib0b89ef616a block (0.99)

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 Administration via the diet

SINGLE ANIMAL SHEET
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left_right_mapping (1.00), a843cecc-8ec6-4278-b5cd-

Sacrifice	F1
Sex	M
Group	4
cont. Animal	24

non_continuous_text_block (0.67), 4397f945-c382-4b5e-9dec-2f0da5570e96

non_continuous_text_block (1.00), 3f1c5f0b-09c0-428c-a0ef-665839bef278

Spleen
 Pigment storage, grade 1.
 Thymus
 Atrophy, diffuse, grade 3.
 Cyst(s).
 All other organs examined without microscopic findings

left_right_mapping (0.97), f364193f-51cb-4d46-a

text_block (0.98), baf89098-4b1f-46f2-b885-1acf40403773

Animal	25
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left_right_mapping (1.00), 06e4b035-6b49-4f69-aea0-afa80e23c313

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

non_continuous_text_block (0.99), db81e54d-bf8d-404d-a959-e503835b0848

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

non_continuous_text_block (0.99), 36430171-5d70-4ec7-bd66-9d3bf1d6f016

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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text_block (0.99), 64869485-9b504e1b0970-98e651bb50d7c1a-4d06-888910a147e97ad

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left_right_mapping (1.00), 4bbb4609-44f4-4aab-

Sacrifice	F1
Sex	F
Group	0
Animal	26

text_block (0.98), abd0c932-48b2-4915-9ada-b68b7ca321c7

left_right_mapping (1.00), fa2cd5dd-7045-4464-bcba-551df2028a98

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

non_continuous_text_block (1.00), 97a05edc-8ecd-48e3-85c2-ba5722dd2830

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (1.00), facbd0aa-05f7-4b42-907c-6d531b17324e

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.

left_right_mapping (0.99), e579c990-16e7-4431-

text_block (0.98), 3729c50e-0e93-469a-99f8-29ec52463b2

left_right_mapping (1.00), a18f7258-5f1d-49e4-8835-999226fa72cc

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

non_continuous_text_block (0.98), 00205499-97e8-4b4f-94c1-e9654b3d4e9d

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.98), 00361608-8b29-4f1f-bb13-59c498eb55f5

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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text_block (0.99), 27e5cea1-bb77e45b10e170-99a636d085b3a3db-454e-0d791da51f05867

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left_right_mapping (1.00), 94396824-fec6-4e13-8

Sacrifice F1
Sex F
Group 0
Animal 28

text_block (0.98), f0717e5e-39bb-44ed-9d94-898c4a300a7

left_right_mapping (1.00), 68ac694f-2c37-488c-aebd-6685b4f36450

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

non_continuous_text_block (0.99), 6b884a61-6d70-46c9-b9ed-bc36a69c9650

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), 908e9134-7a7b-4ae8-affb-2a4ee78b38b9

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.

left_right_mapping (0.99), 8d1c1590-25f1-4860-

text_block (0.98), 47807ed0-82c5-4758-9361-89e7821cc8c

left_right_mapping (1.00), 0fb542e1-c9e2-4c80-a831-3645d2d67a05

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

non_continuous_text_block (0.95), 72ccad97-16b1-49c3-ac7b-36ddbdb43f35

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), 3b65b4a7-076a-41ca-98fe-c479c9bc516b

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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text_block (0.99), 816da1bb-3b21e40bb9930-36) a18083588-ddf3-497d-b209-0b55462620cc (0.99)

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left_right_mapping (1.00), a4cd2afb-3145-4d0d-ade4-6

Sacrifice	F1
Sex	F
Group	0
Animal	29

text_block (0.96), 37c22865-3b99-40bc-adeb-90f4104a7d54

All other organs examined without microscopic findings.

left_right_mapping (0.95), 57e50ac2-dc83-47b4-9

text_block (0.98), 0ecc3a88-801d-4d31-aa9a-918510fa8d74

Animal	30
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General information (0.99), 53257167-db1a-41e1-a36f-aa15353a78a2

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

non_continuous_text_block (0.98), 73103f0c-0736-4831-9e51-101e3d584a66

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.



text_block (0.99), 3058fe1e-393e1f1b-b674099755702b5-7f6d-4bd8-82011a0d3e4188b (1.00)

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left_right_mapping (1.00), e290276c-f146-4aab-9

Sacrifice	F1
Sex	F
Group	1
Animal	31

text_block (0.98), b7ee2d04-139e-4b0d-9485-d85d1fde3d19

left_right_mapping (1.00), de3c852e-f194-4023-beda-ad132e0bde5e

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

non_continuous_text_block (0.99), 8293e4ef-e1bd-4261-9a19-053d4672ba87

Macroscopic findings

Animal without particular findings.

non_continuous_text_block (0.99), 4122daf2-b76b-4e4a-8319-39b486a9420a

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.

left_right_mapping (0.98), 68723187-6634-4641-

text_block (0.98), ac92dae8-3a82-479e-ad71-6750590e8a27

Animal 32

left_right_mapping (1.00), f5fb0e67-641c-48dd-b947-b02ed1bee379

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

non_continuous_text_block (0.98), e7a9e29c-4313-47fb-b3e2-6b2b33e421d4

Macroscopic findings

Animal without particular findings.

non_continuous_text_block (0.98), 217a542d-45f7-4902-8e75-64462c1e8843

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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text_block (0.99), b8f53727-6c0f4e11b310790b76263bae-9a51-4a01-c64a-45ba852b8ddk (0.99)

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left_right_mapping (1.00), 892647c0-9177-4c15-

Sacrifice	F1
Sex	F
Group	1
Animal	33

text_block (0.98), ead0906b-a916-4d20-a895-7cea28581429

left_right_mapping (1.00), 2bb1ade6-af00-4ee5-bd03-c58018be374b

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

non_continuous_text_block (0.99), 6096fb1e-e71b-4689-aa7f-6aa346e87e06

Macroscopic findings

Animal without particular findings. 156ebb-283c-4a27-bd4d-62d3389ae79d

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.

left_right_mapping (0.99), 1713b8cb-bd52-4b6d-

text_block (0.98), 0bb8b0e7-2ee9-45d7-9334-dc7d0e852b46

Animal 34

left_right_mapping (1.00), 45cdbba0-4b50-459d-83d6-a27436358d7a

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

non_continuous_text_block (0.98), 277b5d38-47f3-4f98-9460-edd475a524f6

Macroscopic findings

Animal without particular findings.

non_continuous_text_block (0.99), e4ac5ce0-b06f-4f5a-9962-d19853b34653

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.



text_block (0.99), 36446c94-47f5-468a-b4(0-99)86d1262f-eeed-41a2-006f-0a453def31e8

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left_right_mapping (1.00), e180a1a6-15ba-4c4c-9191-

Sacrifice	F1
Sex	F
Group	1
cont. Animal	34

non_continuous_text_block (0.99), 90f7a6f8-95f0-4bbf-905c-964a7d91b92a

Spleen
Pigment storage, grade 1.
Hematopoiesis, extramedullary, (multi)focal, grade 2.
All other organs examined without microscopic findings.

left_right_mapping (0.98), 72179a26-b6d7-4121-

Animal	35
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text_block (0.98), b08667ff-2fad-4e76-996d-72838a2af20e

General information (1.00), 338628be-9a87-42cb-85b7-76ddd880fd0f

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

non_continuous_text_block (0.99), e234276c-ee5b-4beb-9aba-500601e0aa71

Macroscopic findings

non_continuous_text_block (0.99), 9ae87c3-f881-4be0-92c9-0b3110a6e2ea

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



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text_block (0.99), b7fefbbf-265e-4689-b7e3-0007-88218372-f6f3-4900-8003-054993text_block (0.99)

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left_right_mapping (1.00), dd2053c9-ea50-4235-

Sacrifice	F1
Sex	F
Group	2
Animal	36

text_block (0.98), d5aa3a36-daf7-4a49-a411-22c5281ab856

left_right_mapping (1.00), 50780c19-b774-4ede-a148-4c6d1d00d4d3

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

non_continuous_text_block (0.99), b140c9c9-b300-4691-83cb-d27ab4e30674

Macroscopic findings

Animal without particular findings.

non_continuous_text_block (0.99), 14dbb7da-061d-44a1-8786-b39934991b02

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.

left_right_mapping (0.99), d9be4c49-a646-4bb7-

text_block (0.98), 89830c95-46dd-4c5e-9876-7d9086ebc94c

Animal 37

left_right_mapping (1.00), 001f17c6-ca8a-4050-98cb-cf8fac878ae6

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

non_continuous_text_block (0.69), 5032c190-d7ea-4290-a457-de1ebdc20a79

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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text_block (0.99), 4538aa69-09b4e4c9a5a (0.99), f1d66410ce1655-4bb2-024d3b14917e4710c (0.99)

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left_right_mapping (1.00), 239137e2-d687-4b3e-95fd-3

Sacrifice	F1
Sex	F
Group	2
cont. Animal	37

non_continuous_text_block (0.99); 7bb50372-717b-4d10-ad07-d94ec542ac5a

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.

left_right_mapping (0.97), 637724b1-85db-4f98-a

text_block (0.98), fa260d11-ad10-4603-84c3-c0e7-79597f4

Animal 38

left_right_mapping (1.00), 65a70116-baa2-467e-9924-a5ae7f59c159

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

non_continuous_text_block (0.99), c8149ab-eb5a-4eeb-a1bc-53fc14502276

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), cc9bde1-6801-43d7-9545-371808f70e9b

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.

left_right_mapping (0.99), e491d2d8-f2b9-453e-l

text_block (0.98), 5cb00707-619f-4bdd-94a5-c02613624a2a

Animal 39

left_right_mapping (1.00), 507bdfcb-572e-4c9a-97b8-f5d7d4b694e6

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

non_continuous_text_block (0.97), 5ca07756-8a4f-48ae-bfad-352f64fc24ad

Macroscopic findings
Animal without particular findings.



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Report; Project No.: 31C0343/09S078

text_block (0.99), 438bafb5-d544e11-d4c28(0.92), 7a818507-4e71-4aa2-d077-50fa8e4a31b0c (0.99)

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05.Jan.2012 MAHU

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Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), ae49f767-7fbe-4851-b07a-1

Sacrifice	F1
Sex	F
Group	2
cont. Animal	39

Macroscopic 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
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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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text_block (0.99), 4ef36e24-a561e426-c146-0592-5aa0690-ad2a-4775-8fa0-d970a7db5e

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left_right_mapping (1.00), a93da983-ae13-4d35-

Sacrifice	F1
Sex	F
Group	3
Animal	41

text_block (0.98), b289075b-26a9-4850-a11b-9798cb00a51

left_right_mapping (1.00), 1d6f7fe4-d7c3-4813-99a7-141f350218d1

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

non_continuous_text_block (0.99), 0c2c4640-486-4421-93cc-53db7ab9a137

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), 75b15a06-8864-414b-8cd1-f5ce15c455b9

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

left_right_mapping (0.99), d1266a62-1d49-4b78-

text_block (0.99), 5014a437-8d2a-4d8d-9ecc-8453ada9c9c

Animal	42
--------	----

left_right_mapping (1.00), 2ab910c9-1875-4f01-9de3-c08bb18a3d0c

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

non_continuous_text_block (0.94), 009b30c2-0a33-4ac5-82f0-475652245c68

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), 522a3e96-4b28-4d51-bb8e-60a056130812

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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Report; Project No.: 31C0343/09S078

text_block (0.99), 20309899-1d5e442ea55092e8658677-a4e3-401c-b0d9-45c5f308b098

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31C0343/09S078
05.Jan.2012 MAHU

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Administration via the diet

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), 8357c69c-625e-4586-b526-

Sacrifice	F1
Sex	F
Group	3
cont. Animal	42

non_continuous_text_block (0.99), 5ebe355f-8858-482c-80df-9b4661a01d75

Spleen

Pigment storage, grade 1.
Hematopoiesis, extramedullary, (multi)focal, grade 2.
All other organs examined without microscopic findings

left_right_mapping (0.97), 0808637f-ede5-4781-

text_block (0.98), 8d29de5e-91b0-4d58-baf8-789055a399d7

Animal 43

General information (1.00), 188a1ba0-cb30-4dca-ab52-2f2b28153e56

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

non_continuous_text_block (0.99), 2275f999-5144-48f2-a0d2-6e490f2b469f

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), 89afb9c2-fad2-4f50-9c87-2c178298e784

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

left_right_mapping (0.99), 5344fb37-86fc-4bd7-9

text_block (0.98), 5b6b958a-8b18-4d6f-8071-a2744090b447

Animal 44

left_right_mapping (1.00), 4e16f4da-c628-48d9-8172-ad0be9a9e897

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



Report; Project No.: 31C0343/09S078

text_block (0.99), 6ef9d7f4-1218ed19ac200910578078-4217-495b-b50a50c1abed2b8c (0.99)

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05.Jan.2012 MAHU

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

SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), a6fd9159-f4a5-4274-862c-7

Sacrifice	F1
Sex	F
Group	3
cont. Animal	44

non_continuous_text_block (0.99), 5d7aad43e30941d19e9c-8c9496076a3e

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.

left_right_mapping (0.99), 0e41333e-8525-4293-

Animal 45

text_block (0.99), 2e9918df-7d3b-46c5-abac-0b618a10e550

left_right_mapping (1.00), cdf9bf9e-e1fb-410c-a836-aefa9a0cd297

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

non_continuous_text_block (0.97), 07126d61-61c6-424b-a3a9-0f2dbfc9b646

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.98), 1083cd33-cb40-47da-aea8-56f81c7d5b02

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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Sacrifice	F1
Sex	F
Group	4
Animal	46

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left_right_mapping (1.00), 7aa013fa-b659-46e8-aa20-5e42e092deff

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

non_continuous_text_block (0.99), 6d8b73d9-c0a5-4d67-a30d-3e3519fa9848

Macroscopic findings

Animal without particular findings.

non_continuous_text_block (0.99), 6904ce14-6ada-4c7b-8879-97e594b95d7e

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.

left_right_mapping (0.97), 03eb5957-2624-40cb

text_block (0.98), 564384d6-d6ef-41ba-a8ac-bf96010b51f9

Animal 47

left_right_mapping (1.00), b116259d-0732-4fcc-a696-a23f46a917b8

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

footer (1.00), e8a29484-b34c-4e2e-90f4-31772f337ebd

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(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), 092084ca-db03-4b0a-a8d8-

Sacrifice	F1
Sex	F
Group	4
Animal	47

non_continuous_text_block (0.99), b03eb1bf42a7-41e0-94bf-7327a79bab26

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 insufficient tissue present on slide.
- Spleen
 - Pigment storage, grade 1.
 - Hematopoiesis, extramedullary, (multi)focal, grade 1.

All other organs examined without microscopic findings.

left_right_mapping (0.99), 81c03dba-7f80-45ab-

text_block (0.98), 63975f75-b785-4fd8-82e3-36f68b5e187b

Animal 48

left_right_mapping (1.00), 516ce03e-2a87-4058-84e9-d929a3ad7ade

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

non_continuous_text_block (0.99), 7f561619-a14c-491d-a04c-077f2c14d426

Macroscopic findings

Adrenal cortex
 Organ size reduced, moderate.
 Brain
 * Organ damaged at necropsy.
 All other organs without macroscopic findings.



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text_block (0.99), 356f31b0-3206e4890cd6-0992cda585631a-5253-40e1-822c1608286ad1b

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SINGLE ANIMAL SHEET
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Sacrifice	F1
Sex	F
Group	4
Animal	48

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non_continuous_text_block (0.93), a44a51b5-1d48-467c-ab6a-6b455569622b

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 insufficient tissue present on slide.

Spleen
Pigment storage, grade 2.

All other organs examined without microscopic findings.

left_right_mapping (0.99), d64fc216-04ea-4c7b-

text_block (0.98), 0ea0f82c-8828-421e-af2f-02333a8d487a

Animal 49

General Information (1.00), 68c327ab-1000-4197-ab6b-f2010f83023d

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

non_continuous_text_block (0.83), 4279b067-d17d-486e-9c85-079bfc6f44f

Macroscopic findings

Animal without centrilobular 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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text_block (0.99), eb346b99-ca8541d92ak(0.99), 55d256c1-c90f-4a10-89041f1a095de0ab

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Administration via the diet

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SINGLE ANIMAL SHEET
(GROSS LESIONS AND MICROSCOPIC FINDINGS)

left_right_mapping (1.00), adddbecf-6c84-429a-8d56-c

Sacrifice	F1
Sex	F
Group	4
cont. Animal	49

non_continuous_text_block (0.99), a197ce61-d31b-4798-a74c-66452bcbce74

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

left_right_mapping (0.98), 7199d89e-7f64-4fcf-88

text_block (0.98), f5184f33-65c6-4582-bde2-f643d74fc433

Animal 50

General Information (1.00), c468b3cc-8be2-4ac6-ab51-3d16c5ad350e

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

non_continuous_text_block (0.95), 6ae81797-9558-486b-8835-b1175137be01

Macroscopic findings
Animal without particular findings.

non_continuous_text_block (0.99), tee0d52-082c-43e0-bdde-79592e778170

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 insufficient 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.



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heading_4 (0.86), b4091ebd-13c0-466c-b122-30ae26c93eb2

STUDY TITLE

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Report

title (0.64), 8f705d53-5fa3-4c6c-9227-184d182b03fa

BAS 850 H

title (0.92), d2f4d941-eab3-4904-a563-ab6ae060b8be

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

heading_4 (0.76), 9c5361a2-a625-4338-bc69-4b091a770760

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non_continuous_text_block (0.53), 6354e971-3be3-471e-8e77-d8f39fd6

TEST FACILITY

BASF SE
Experimental Toxicology and Ecology
67056 Ludwigshafen, Germany

heading_4 (0.94), 2235789a-ba0e-4b8e-af22-0798bb539bfe

TEST FACILITY PROJECT IDENTIFICATION

Project No. 31C0343/09S078

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**PART III OF III
(SUPPLEMENT)**

text_block (1.00), 38765859-7661-4e6b-a853-52aa0aeb94dd

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footer (1.00), f956db97-82ca-4f1c-a55e-ac7682da49d9

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Study No. 386120_4

Certificate of Analysis BAS 850 H
Study No. 415835_2

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Analytical Report
Reg.No. 5654329
Stability Analysis in Ground Kliba maintenance diet mouse/rat "GLP" meal
Study No. 01Y0343/09Y049

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Analytical Report
Homogeneity and Concentration Control Analysis of Reg.No. 5654329
in Ground Kliba maintenance diet mouse/rat "GLP" meal

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Historical Control Data



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09/0343-9

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APR/DP - Product Characterization & Performance Management

heading_4 (0.65), 838475ad-0452-44ef-9cfe-59e71cf8e840

BASF SE - Crop Protection - Services - Customer Support - Global - Germany - 556d-1540-491a-8dd0-5bc61caf00b9

Certificate of Analysis

left_right_mapping (0.99), 02789c9d-173e-4c5f-95d3-ee3262dae3db

Reg.No. : 5654329
Substance Type : TGAI (=TC)
Date of Initial Analysis : June 28, 2011

Batch No. : COD-001484
Date of Production : June 24, 2011
Study Code : 386120_4

text_block (0.98), 14b192cf-85ec-4360-8b02-68a8725c2cdf

Purity: 99.3% (HPLC) + 1.0%

figure (0.98), 640cc62f-951b-4720-ab61-15038031a23

Chemical structure diagram and table with fields: CL-No., CAS No., Core Project (5654329), Internal (Metabolite) Code, Molecular Formula (C16H11F3N4O4S), Molecular Weight (412.3)

DPAC-Name : 1,3-dimethyl-6-methoxy-3-[2,2,7-trimethyl-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
Issued on : November 14, 2017

Study Completion Date : July 25, 2011
Issued by : J. Schalk

text_block (0.98), 9b36d919-6d5a-42fd-a184-609c950984d2

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Released July 25, 2011 by Genari, Gerhard



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Report: Project No.: 31C0343/09S078

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APR/DP - Product Characterization & Performance Management

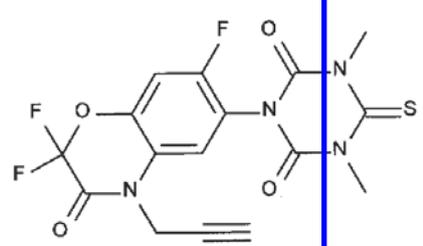
BASF SE - Crop Protection - Speyerer Strasse 2, D-67317 Umstadt, Germany

Certificate of Analysis

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

text_block (0.99), ee95810f-292b-4c37-a411-25b1c6d1eea5
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 ₃ N ₄ O ₄ S
	Molecular Weight	412.3

UPAC-Name :	1,5-dimethyl-6-thioxo-3-[2,2,7-trifluoro-3-oxo-4-(prop-2-yn-1-yl)-1,3,5-triazinane-2,4-dione]benzoxazin-6-yl
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 Completed: June 27, 2012

Issued on: June 28, 2012

Issued by: 

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STUDY TITLE

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ANALYTICAL REPORT

Reg. No. 5654329

title (0.93), d978241c-3f5e-420d-8b42-6ede6ef100ab

Stability Analysis in

Ground Kilba maintenance diet mouse/rat "GLP" meal

AUTHORS

Dr. Matthias Becker
Dr. Henniske Kamp

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STUDY COMPLETED ON

text_block (0.61), 3b9409d9-fc06-4d35-bd5f-52472173a480

16 January 2012

TEST FACILITY

Experimental Toxicology and Ecology
BASF SE
67056 Ludwigshafen, Germany

heading_4 (0.96), 7037380d-0594-40eb-b369-4af9f504e95b

TEST FACILITY PROJECT IDENTIFICATION

Project No.: 01Y0343/09S049

SPONSOR

BASF SE
67056 Ludwigshafen, Germany

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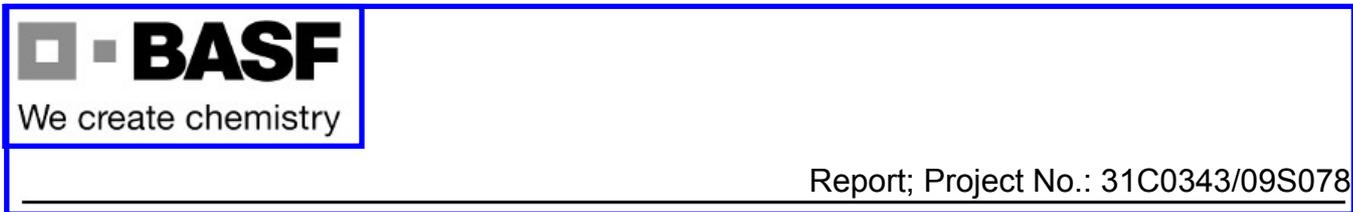
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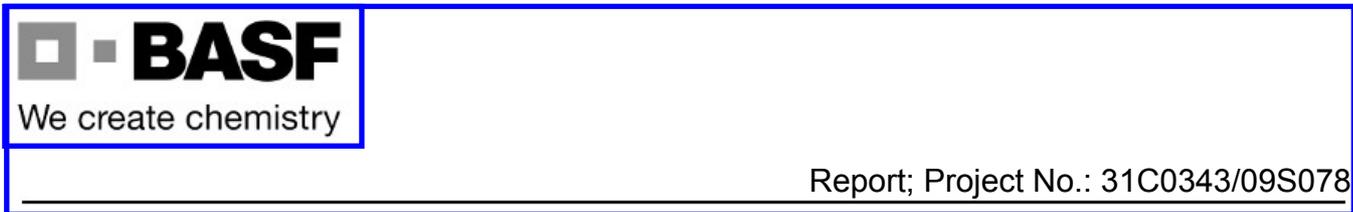
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SIGNATURE PAGE

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Study Director:

[Signature] 16 Jan 2012
Dr. Matthias Becker

Management:

[Signature] 09 Jan 2012
Dr. Hennicke Kamp

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Management:

[Signature] 09 Jan 2012
Dr. Hennicke Kamp

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STATEMENT OF THE QUALITY ASSURANCE UNIT

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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.

table (0.89), 259c1460-8d6a-43a2-b3ec-462c38914bdb

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

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Ludwigshafen,

13 January 2012

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CONTENTS

- TITLE PAGE
- BLANK PAGE
- GLP COMPLIANCE STATEMENT
- BLANK PAGE
- SIGNATURE PAGE
- STATEMENT OF THE QUALITY ASSURANCE UNIT
- GLP CERTIFICATE (FROM THE COMPETENT AUTHORITY)

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1.	INTRODUCTION
2.	RETENTION OF RECORDS
3.	TIME SCHEDULE
4.	MATERIAL AND METHODS
4.1.	TEST ITEM
4.2.	SAMPLE DATA
4.3.	TEST SUBSTANCE PREPARATION
4.4.	SAMPLE PREPARATION AND ANALYSIS
4.5.	LIST OF DEVIATIONS
4.5.1.	List of deviations from the control procedure
5.	RESULTS AND DISCUSSION
5.1.	ANALYSIS OF STABILITY
5.2.	DISCUSSION
FIGURES	
6.	APPENDIX
6.1.	CONTROL PROCEDURE 09/0343_01-02

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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.

heading_2 (0.56), 9876f2d7-dfaa-4da7-b506-e6e4c0bf0a8d

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.

heading_2 (0.48), e9fa101d-2d87-4600-8b42-1127b667b9c1

3. TIME SCHEDULE

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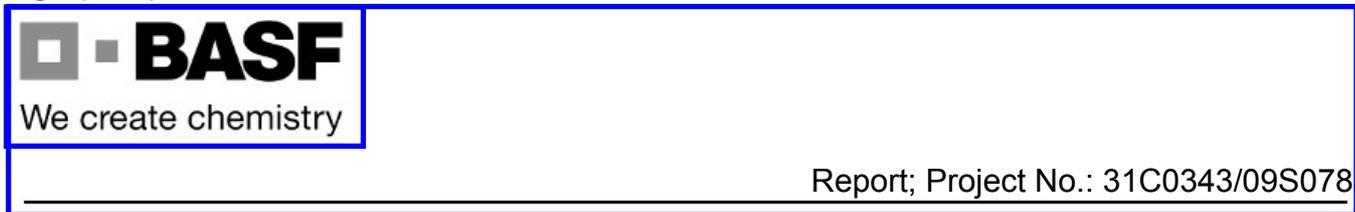
Study initiation date:	25 May 2011
Experimental starting date:	19 July 2011
Experimental completion date:	23 August 2011

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4. MATERIAL AND METHODS

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text_block (0.60), 852710ee-1b2d-4da4-b840-7b34889b7acd

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

left_right_mapping (0.99), 87c267a2-f1e0-426d-8083-68b905d897e3

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.

text_block (0.97), 6590435d-3187-4b12-941c-3bb3ba60410f

Additional Test Substance Information

left_right_mapping (0.97), bb085234-c7fa-44db-b59a-f83007d9bced

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

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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

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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.

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4.5. LIST OF DEVIATIONS

non_continuous_text_block (0.52), 210a3913-7b7c-43da-9546-5fb0afb55dd1

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.

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Report; Project No.: 01Y0343/09Y049

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5. RESULTS AND DISCUSSION

heading_4 (0.31), d6209b7d-d026-4223-96a3-ad07b686ee92

5.1 ANALYSIS OF STABILITY

text_block (0.99), 5219d100-6a7c-4209-a78e-bdc51c8231bb

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.

table (1.00), 9a076d6-3447-4f3c-9545-dbab4877e52e

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

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5.2. DISCUSSION

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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 emperature. All determined concentrations were in range between 90 % and 110 % of the nominal concentration.

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FIGURES (0.99), 16ec2cdb-107e-4f44-b5d9-086af7824df6

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

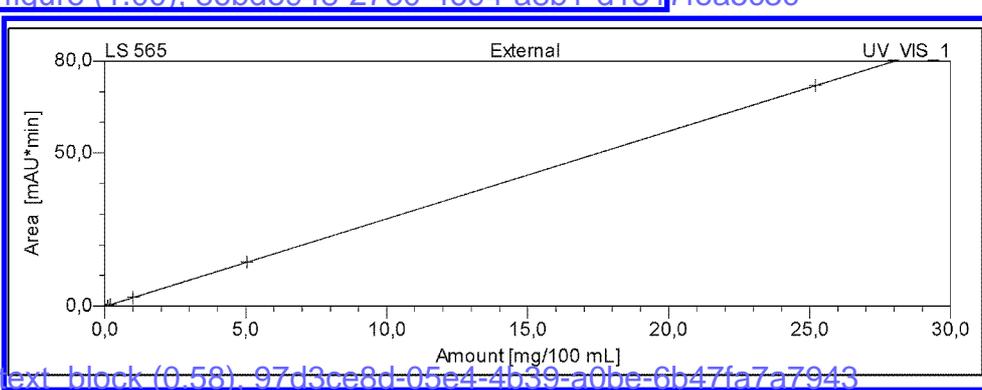
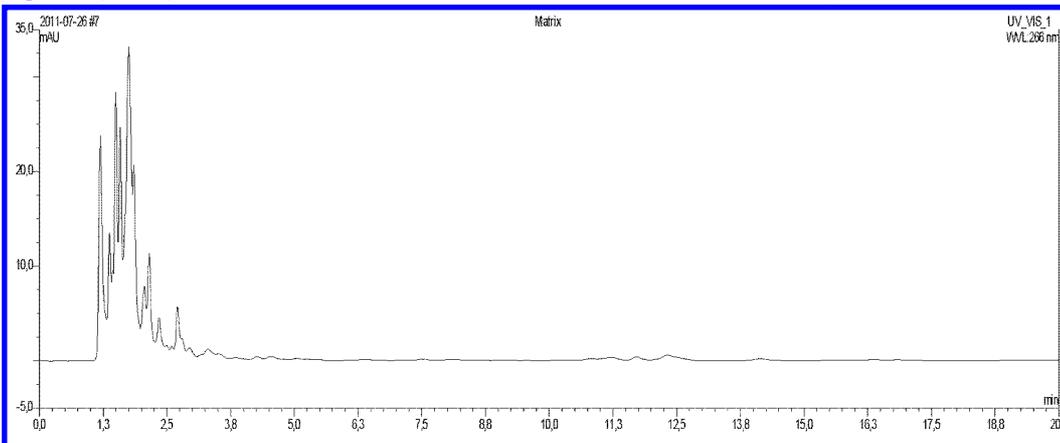


Figure 1.2: Chromatogram matrix solution (measured on 26 July 2011)



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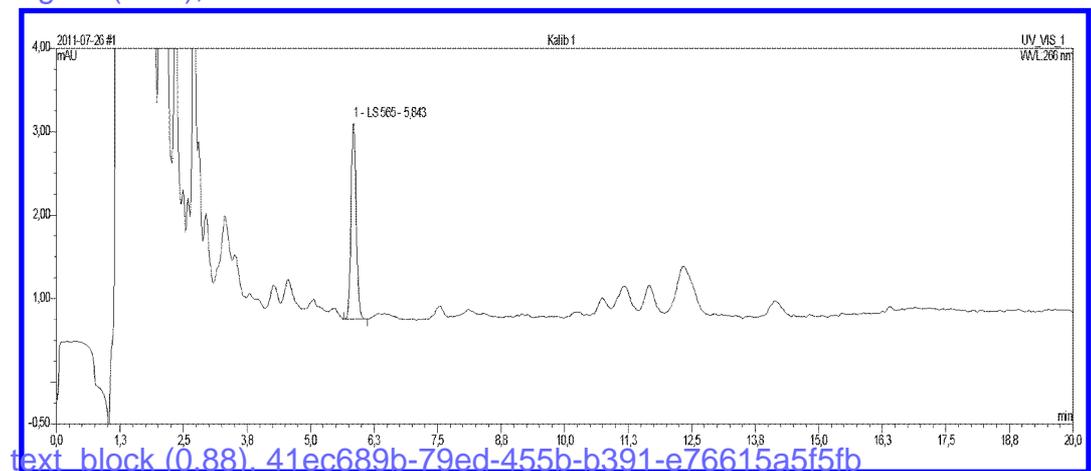


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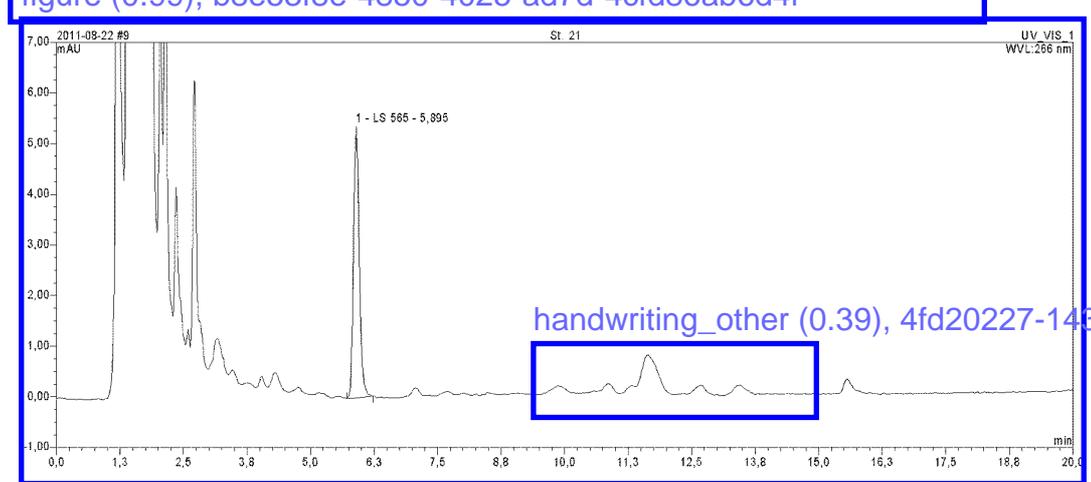
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Figure 1.3: Chromatogram calibration solution 1 (0.101 mg/100 mL, measured on 26 July 2011)



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



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6. APPENDIX

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6.1. CONTROL PROCEDURE 09/0343_01-02

BASF SE Test Facility Experiments, Methods, Quality Control, Analytical Chemistry Wuppertal, Germany			
Test substance number: 09/0343	No.: 09/0343_01-02	Effective from: 26.07.2011	
Name of test substance: Reg.No. 5664329			
Control procedure: Control of PIP / Niba in diet in isocratic HPLC			
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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Report; Project No.: 01Y0343/09Y049

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CONTROL TEST

Test substance number: 09/0343

Name of test substance: Reg.No. 6041329

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

Effective from: 26.07.2011

Page 2 of 3

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 B (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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Report; Project No.: 01Y0343/09Y049

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Experimental: Toxicology and Ecology / Analytical Chemistry

Test substance number: 09/0343
Name of test substance: Reg.No. 5654329
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"

No.: 09/0343_01-02
Effective from: 26.07.2011

Page 3 of 6

Retention time:

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

System suitability:

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

The coefficient of determination (R²) 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

$$Y = a \cdot X + b$$

Calculated calibration curve

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

Intercept

$$b = Y - a \cdot X$$

Heading 4

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

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

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Experimental Toxicology and Ecology / Analytical Chemistry

CONTROL TEST

Test substance number: 09/0343
Name of test substance: Reg.No. 5654329
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"

No.: 09/0343_01/02
Effective from: 26.07.2011
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Recovery factor: 17c59f98b-bc7e-4082-8840-9690cf8d58fc

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

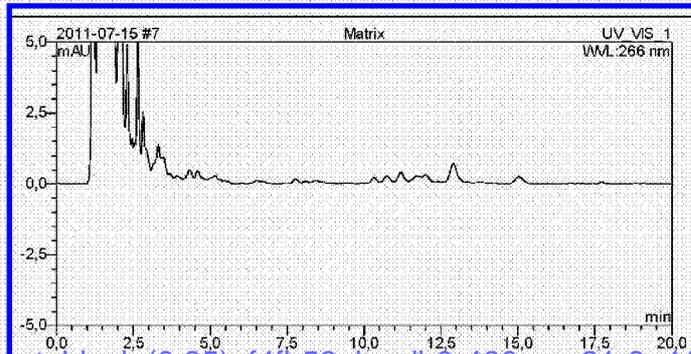
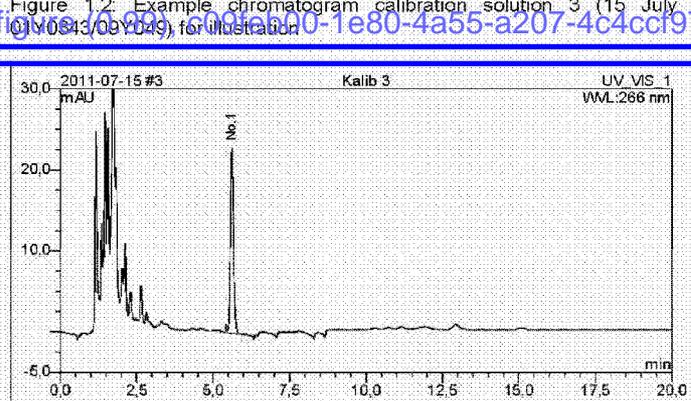


Figure 1.2: Example chromatogram calibration solution 3 (15 July 2011, Project no.: 01Y0343/09Y049) for illustration



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left-right-mapping (0.96), dd1b548d-0cb0-45d

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CONTROL TEST

Test substance number: 09/0343

Name of test substance: Reg.No. 5654329

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

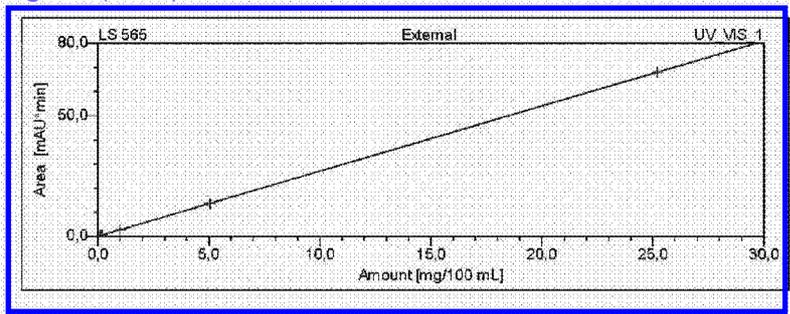
No.: 09/0343_01-BZ

Effective from: 26.07.2011

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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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title (0.64), 8801e7d0-b63c-4d54-a48d-ba83054dc52d

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

heading_1 (0.35), 3f52d8cb-8668-46c8-bd23-60644329ca0b

1. PROJECT AND TEST SUBSTANCE INFORMATION

left_right_mapping (1.00), a23cd2bd-7850-4125-b39f-2df3b969c657

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

heading_4 (0.35), 9e8972ea-345b-42b7-ae6c-178cfa868588

2. SAMPLE DATA

2.1. HOMOGENEITY AND CONCENTRATION CONTROL ANALYSIS

left_right_mapping (0.68), 9936cab8-8e7b-4592-bd4b-394a7fe81eb

Vehicle: Kliba lab diet mouse/rat "GLP"

Storage conditions of the samples until analysis: Freezer

heading_2 (0.32), a300df4f-0231-4e6b-8738-1c17b0990545

3. MATERIAL AND METHODS

heading_3 (0.37), d5d7f87d-8148-4ecf-85c4-f157845164d5

3.1. SAMPLE PREPARATION AND ANALYSIS

text_block (0.99), 91166bdc-a1dd-47f2-a3bc-d40c7a425928

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.

heading_3 (0.38), 30d61e5f-53ef-4326-affb-38ce3ed3e137

3.2. LIST OF DEVIATIONS

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



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4. RESULTS AND DISCUSSION

heading_1 (0.23), b1a7f127-8e8d-49be-8a99-50bde0361ba2

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:

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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

table (1.00), fb279dbb-9e92-4f95-bc02-43385b6d9d28

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%

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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.

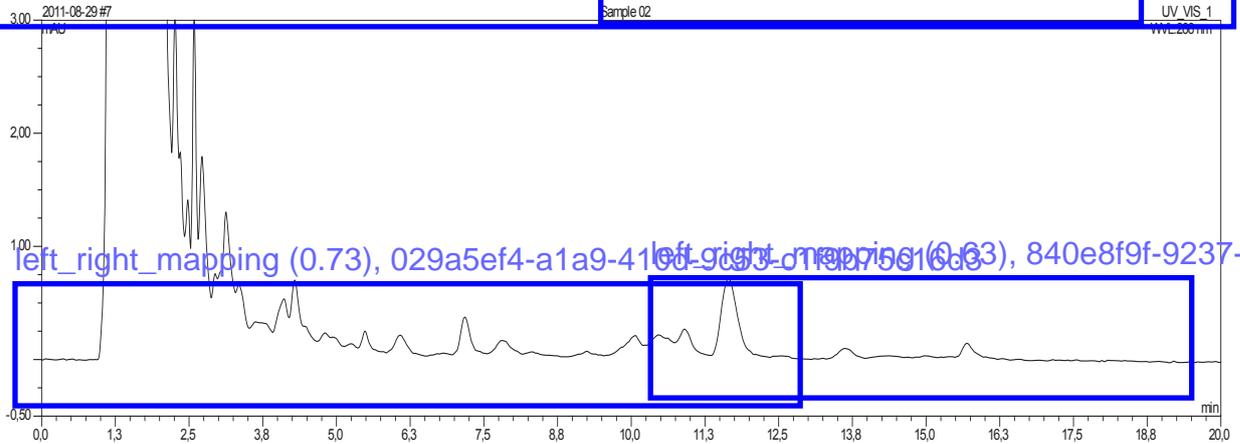


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Figure 1.1 Chromatogram of a blank sample (sample 02, measured on 29 Aug 2011)



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

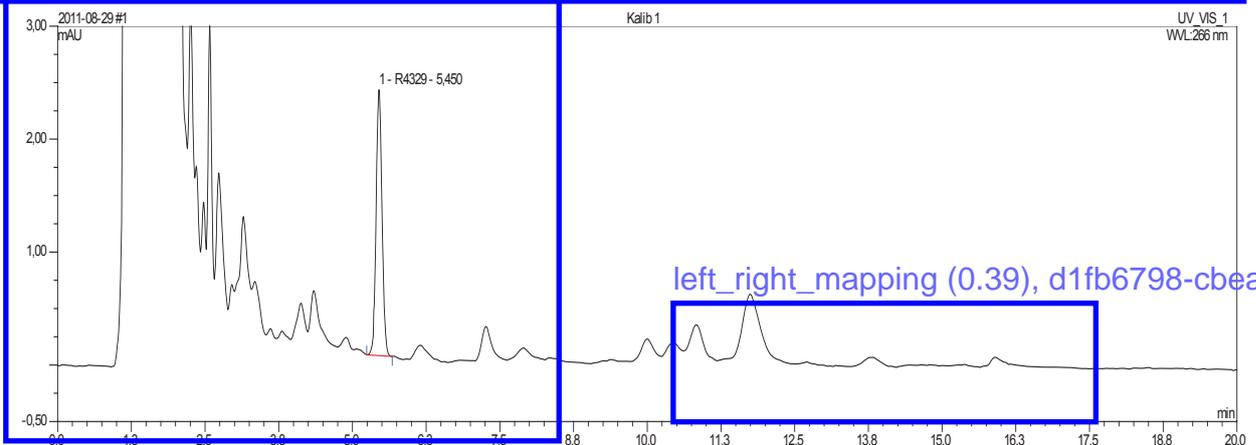
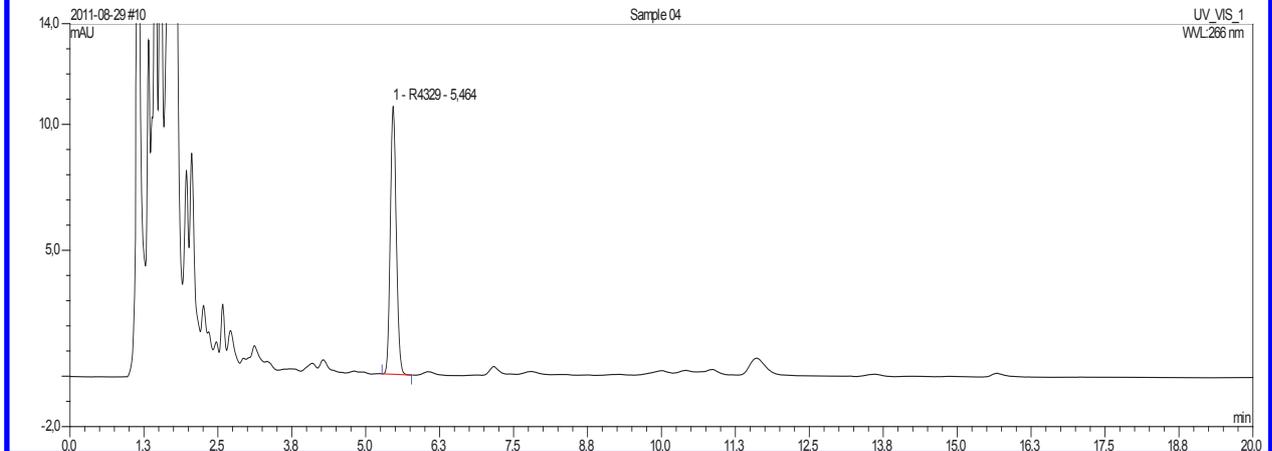


figure (0.99), 6311803a-ce00-480c-9a9c-652b9b4c468a

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



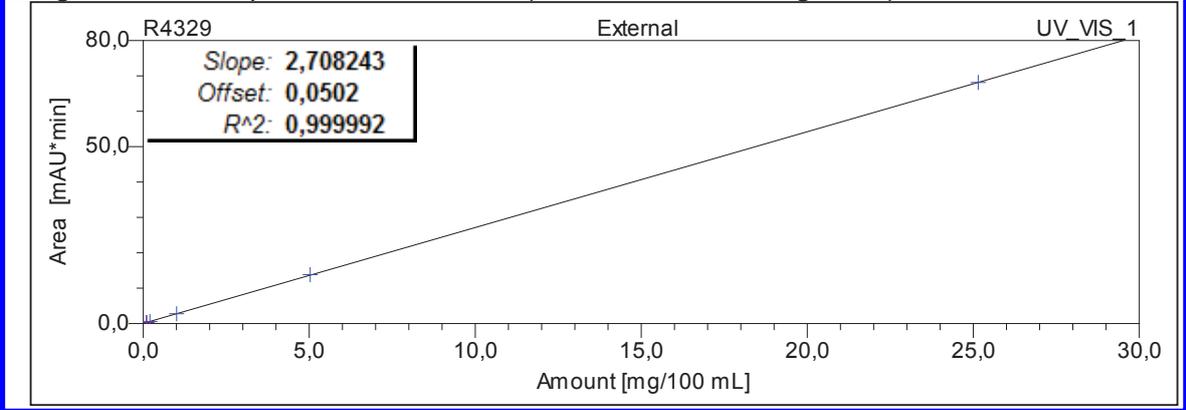


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figure (0.99), 78a74d64-bfd1-43d9-a6bc-ff1544d8d8e4
Figure 1.4 Example calibration curve (measured on 29 Aug 2011)



5. APPENDIX

5.1. CONTROL PROCEDURE 09/0343_01-02

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CONTROL TEST

Test substance number: 09/0343

Name of test substance: Reg.No. 5654329

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

No.: 09/0343_01-02
Effective from: 26.07.2011

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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

left_right_mapping (0.99), ae2295d1-2dd2-4dfe-b092-4ddb3691699e

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.

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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)

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System-suitability solution:

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

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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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Experimental Toxicology and Ecology / Analytical Chemistry

CONTROL TEST

Test substance number: 09/0343

Name of test substance: Reg.No. 5654329

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

No.: 09/0343_01-02

Effective from: 26.07.2011

Retention time:

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

System suitability:

The calculated content 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

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a = slope of calibration curve

b = intercept

Analysed concentration (C_x)

$$C_x = \frac{(Y - b) \cdot V \cdot d}{R_f}$$

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



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Report; Project No.: 31C0343/09S078

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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

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table (1.00), 7a280817-eda7-45ab-987c-e0c2d366d5a7

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



CONTROL TEST

Test substance number: 09/0343
Name of test substance: Reg.No. 5654329
Control procedure: Content (HPLC) / Kliba lab diet mouse/rat "GLP"

No.: 09/0343-01-02
Effective from: 26.07.2011

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

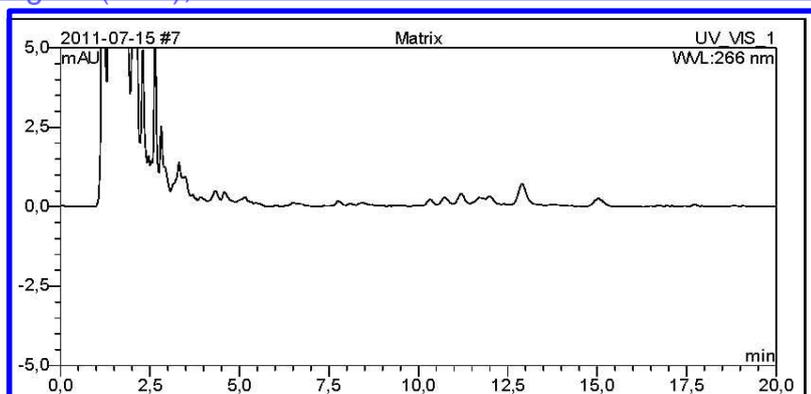
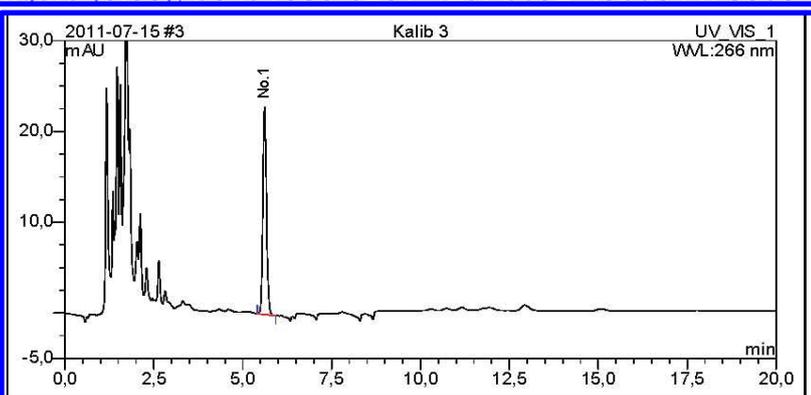


Figure 1.2: Example chromatogram calibration solution 3 (15 July 2011, Project no.: 01Y0343/09Y049) for illustration





BASF
We create chemistry

Report; Project No.: 31C0343/09S078

Historical Control Data

C57BL / 6 J Rj
Thymus - m



BASF
We create chemistry

1/1/2008 - 12/14/2017

4 weeks

Duration

Species mouse

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	5.663	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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12/14/2017