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3-MONTH SUBCHRONIC DIETARY TOXICITY STUDY IN BEAGLE DOGS

Test No. 943128

CGA 329351 tech.

FINAL REPORT

Study Director: Dr. med. vet. 5.1.2.e Woo

Testing Facility: CIBA-GEIGY Limited
Short-/Long-term Toxicology
4332 Stein / Switzerland

Test Guideline: OECD No. 409
FIFRA Subdivision F, 82-1
MAFF Japan

Study completed: August 7, 1995

Sponsor: CIBA-GEIGY Limited
Crop Protection Division
4002 Basle / Switzerland

This report contains: 377 pages

0.1. Reserved Page for Proprietary Information or Statement of No Data Confidentiality Claims

0.2. Certification of Good Laboratory Practices

This study has been performed in compliance with Good Laboratory Practice (GLP) in Switzerland, Procedures and Principles, March 1986 (Verfahren und Grundsaetze der Guten Laborpraxis (GLP) in der Schweiz), issued by the Swiss Federal Department of the Interior and the Intercantonal Office for the Control of Medicaments. These procedures are in essence consistent with:

- OECD Principles of Good Laboratory Practice (Council Decision 81/30, adopted on May 12, 1981, and the OECD Recommendation 89/87 concerning the 'Compliance with Principles of Good Laboratory Practice', adopted on October 2, 1989).

- United States Environmental Protection Agency, Title 40 Code of Federal Regulations Part 160 (FIFRA); Federal Register, August 17, 1989.

- United States Environmental Protection Agency, Title 40 Code of Federal Regulations Part 792 (TSCA); Federal Register, August 17, 1989.

- Japan Ministry of Agriculture, Forestry and Fisheries, NohSan, Notification No. 3850, Agricultural Production Bureau, August 10, 1984.

Study Director: Dr. med. vet. [redacted]

.....

date: August 7, 1995

Facility Management: [redacted] Ph.D.
D.A.B.T., A.T.S.

.....

date: 7 August 1995

For the Sponsor: [redacted]

.....

date: 8 August 1995

0.3. Reserved Page for Flagging Statements

0.4. Signatures

This report presents the results of the investigations as compiled by the undersigned.

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Quality Assurance Statement

Ciba-Geigy Ltd., GLP Quality Assurance Product Safety, 4002 Basel

Project	943128
Test Substance	CGA 329351 tech.
Study Title	3-Month Subchronic Dietary Toxicity Study in Beagle Dogs
Study Director	Dr. [redacted]
QA-Inspector	[redacted]

I hereby certify that the following Quality Assurance activities were performed:

Activity	Performed	Reported
Facility Inspection	October 04, 1994	October 10, 1994
Protocol Audit	November 17, 1994	November 17, 1994
Study Related Inspection	December 12, 1994	December 14, 1994
Study Related Inspection	February 14, 1995	February 15, 1995
Facility Inspection	March 16, 1995	March 22, 1995
Study Related Inspection	March 20, 1995	March 20, 1995
Final Report Audit	July 11, 1995	July 13, 1995

August 7, 1995

Date

Form. QSSTAT12

[redacted]

Inspector Quality Assurance

0.5. Quality Assurance Statement

Ciba-Geigy Ltd., GLP Quality Assurance Product Safety, 4002 Basel

Project	943128
Test Substance	CGA 329351 tech.
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Final Report Audit	July 11, 1995	July 13, 1995

August 7, 1995

Date

[redacted]

Inspector Quality Assurance

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1. SUMMARY AND CONCLUSION

A total of 40 pedigree Beagle dogs was used (4 males and 4 females per dose group). The test article CGA 329351 tech. was administered orally in the diet for a period of 13 weeks at concentrations of 0, 50, 125, 250 and 1250 ppm.

Dose levels

Based on the analytically determined concentration of the test article in the diet, the calculated mean daily intake of CGA 329351 tech. was 1.57, 4.07, 7.25 and 38.6 mg/kg body weight for males and 1.56, 4.33, 7.93 and 39.5 mg/kg body weight for females.

Mortality

None of the animals died or had to be sacrificed during the course of this study.

In-life observations

There were not clinical signs related to treatment with the test article.

Body weight development

Body weight development was not affected by treatment.

Food consumption

In either sex food consumption was similar in all treated and control groups.

Food consumption ratios

Food consumption ratios of treated animals were comparable to those of the controls.

Eye examinations

The results of ophthalmoscopic examinations revealed no reaction to the treatment.

Hematology

No treatment-related changes in hematologic parameters were observed.

Blood chemistry

Increased alkaline phosphatase activities were noted in males and females of the high dose group (1250 ppm) after 7 and 13 weeks of treatment.

Urine analysis

Treatment had no influence on urine parameters investigated.

Organ weights

Mean absolute and relative liver weights were increased in males and and females of group 5 (1250 ppm).

Pathology

Macroscopical and microscopical examination showed the usual spectrum of changes occurring spontaneously in our colony of dogs. There were no findings attributable to treatment with the test article.

Conclusion

Under the conditions of this study, CGA 329351 tech. was well tolerated up to concentrations in feed of 1250 ppm, corresponding to daily intakes of 38.6 and 39.5 mg/kg in males and females, respectively.

The slight increases in liver weight and alkaline phosphatase activity indicate a hepatotropic effect of the test article.

Based on the results of this study, 250 ppm is considered to represent a no-observed-effect level (NOEL). This concentration corresponds to a daily intake of CGA 329351 tech. of 7.25 mg/kg in males and 7.93 mg/kg in females.

2. INTRODUCTION

Purpose

This toxicity study in dogs was conducted in order to determine the potential toxicity of the test article CGA 329351 tech. upon daily dietary administration for a period of 13 weeks and to estimate a "no observable effect level" of exposure.

Good laboratory practice

The study was carried out in accordance with the principles of Good Laboratory Practice as set forth in "Verfahren und Grundsaetze der Guten Laborpraxis (GLP) in der Schweiz", Swiss Federal Department of the Interior and Intercantonal Office for the Control of Medicaments (IKS), March 1986.
These procedures are in essence consistent with:

- OECD Principles of Good Laboratory Practice (Council Decision 81/30, adopted on May 12, 1981, and the OECD Recommendation 89/87 concerning the 'Mutual Recognition of Compliance with Good Laboratory Practice', adopted on October 2, 1989).

- United States Environmental Protection Agency, Title 40 Code of Federal Regulations Part 160 (FIFRA); Federal Register, August 17, 1989.

- United States Environmental Protection Agency, Title 40 Code of Federal Regulations Part 792 (TSCA); Federal Register, August 17, 1989.

- Japan Ministry of Agriculture, Forestry and Fisheries, Notification No. 3850, Agricultural Production Bureau, August 10, 1984.

The study was subjected to periodic internal quality assurance evaluation.

Analytical investigations, performed at RCC Umweltchemie AG, was inspected by the Quality Assurance Unit of RCC Research and Consulting Company AG, 4452 Itingen / Switzerland.

Basis of the study

This study was carried out according to:

- FIFRA, Pesticide Assessment Guidelines, Subdivision F: Hazard Evaluation, Human and Domestic Animals (November 1982); Section 82-1: Subchronic oral toxicity, 90-day study.

- OECD Guideline for testing of chemicals Nr. 409: "Subchronic Oral Toxicity - Non-rodent: 90-day Study", adopted May 12, 1981.

- Notification of Director-General, Agricultural Production Bureau, Ministry of Agriculture, Forestry and Fisheries (MAFF), Japan, 59 NohSan No. 4200, dated January 28, 1985: "Guidance on Toxicology Study data for Application of Agricultural Chemical Registration".

Testing facility

All in-life testing and necropsy was performed at the Sisseln facility:

CIBA-GEIGY Limited
Short-/Long-term Toxicology
4332 Stein / Switzerland

Histopathology was performed at the Rosental facility:

CIBA-GEIGY Limited
Short-/Long-term Toxicology
Toxicological Pathology
4002 Basle / Switzerland

Chemical analysis was performed by:

RCC Umweltchemie AG
4452 Itingen / Switzerland

Personnel and responsible scientists

The following scientists, professionals and supervisory personnel were involved in the conduct of the study:

Study director:	Dr. med. vet. [redacted]
Technical assistant:	[redacted]
Laboratory investigations:	Dr. med. vet. [redacted] FVH Clinical chemistry
Clinical laboratory assistant:	[redacted]
Pathology services:	Mrs. [redacted], dipl. med. vet.
Pathology:	Dr. med. vet. [redacted] FVH Pathology Head of Toxicologic Pathology
	[redacted], MVDr, C.Sc. FVH Pathology Study pathologist
Analytics:	[redacted]
Statistics:	[redacted], dipl. stat.

The job descriptions and the summaries of training and professional experience of personnel participating in this study are filed in the archives of CIBA-GEIGY Limited.

The job descriptions and the summaries of training and professional experience of the analysts are archived at RCC Umweltchemie AG, Switzerland.

Archivation

Archives are located at CIBA-GEIGY Limited, Werk Stein WST 460, 4332 Stein, Switzerland. Raw data, protocol and report, specimens and raw data of laboratory investigations are stored at this location.

Raw data of the analytical determinations are stored in the archives of RCC Umweltchemie AG, 4452 Itingen, Switzerland.

Raw data of the histopathological examination and specimens (wet tissues, tissue blocks or histological slides) are stored in the archives of Toxicological Pathology of Short-/Long-term Toxicology, CIBA-GEIGY Limited, 4002 Basel, Switzerland.

Distribution

This report was distributed to:

Dr. [redacted] (Sponsor)
Archive (Original)

3. MATERIALS AND METHODS

3.1. Test article

Code No:	CGA 329351 tech.
Batch No:	OP.4
Description:	viscous liquid
Content of active ingredient:	97.1 %
Date of receipt:	October 10, 1994
Stability:	guaranteed by the sponsor until reanalysis date April 1998
Storage conditions:	room temperature

3.2. Experimental animals and housing

Species

Pedigree Beagle dogs, dewormed, vaccinated against rabies, distemper, leptospirosis, canine hepatitis and parvovirus infection.

Source

Animal production CIBA-GEIGY Limited, 4332 Stein/Switzerland

Initial body weight range (at week -1)

males	8.7 to 11.1 kg
females	8.7 to 11.1 kg

Initial age range (at week -1)

males	24 to 28 weeks
females	28 to 33 weeks

Identification

The dogs were identified with tattoo-numbers on the lobe of the ear and with individual neckchain numbers (1-40).

Husbandry

Two dogs were housed together in a kennel. Each dog was fastened with a chain during the feeding period, thereafter indoor and outdoor runs were available for the dogs. The kennels were provided with heating to give a minimum room temperature of 15° C throughout the year.

Room temperature and humidity of air were monitored continuously and the recordings are filed with the raw data.

Lighting: Daylight, supplemented by artificial light when necessary to ensure light during 12 hours/day.

Music was broadcasted for about 8 hours daily during the lighting phase.

Diet

Certified pelleted standard diet NAFAG 9405 Tox, 350 g/animal daily.

All batches of diet were assayed for composition and contaminant levels by the manufacturer. Analytical results are available at the animal supply office (CIBA-GEIGY Limited, Pharmaceuticals Division).

Water

Tap water was given ad libitum. The drinking water quality fulfilled in the critical parameters the specifications of the "Schweizerisches Lebensmittelbuch" (Edition 1972). Results of the routine chemical examination of water at source (Grundwasserfassung Stein) as conducted periodically by the water authority (Baudepartement des Kantons Aargau, Abteilung Gewaesserschutz) are available to CIBA-GEIGY Limited, as well as the results of in house chemical analysis by the analytical laboratories of the Pharmaceuticals Division, CIBA-GEIGY Limited.

3.3. Procedure

A protocol was prepared prior to the initiation of the study.

Number of dogs/group

4 males and 4 females

Acclimatization period

An acclimatization period of 32 days was allowed between delivery and the start of treatment.

Animal distribution

Immediately after delivery, the animals were distributed into groups. In order to avoid litter effects and initially different body weights, animals were assigned to different groups by means of a randomized complete block design, generated by SAS/STAT procedure PLAN <1>.

The general outline of the experiment is presented in the following animal distribution table.

Dose (ppm)	Group 1 0	Group 2 50	Group 3 125	Group 4 250	Group 5 1250
Males	1-4	5-8	9-12	13-16	17-20
Females	21-24	25-28	29-32	33-36	37-40

Dose levels

0, 50, 125, 250 and 1250 ppm (= mg/kg diet)

<1> SAS/STAT User's Guide, Version 6, Fourth Edition, Volume 2, Cary, NC: SAS Institute Inc., 1989. pp 1221 - 1240.

Rationale for dose selection

The doses were selected based on the results of the studies performed with a structurally similar product which was tested for 90 days and 6 months. In the 90-day study, it was given at concentrations of 50, 250 and 1250 ppm. The no-observable-effect level (NOEL) was 250 ppm (6.3 mg/kg). Accordingly, in this 3-month study dose levels of 50, 250 and 1250 of CGA 329351 tech. are chosen.

Low doses of 50 and 125 ppm were expected to result in a daily intake of about 1.7 and 4.2 mg/kg and are included to cover the possibility that there could be a greater sensitivity compared to structurally similar products.

A dose of 250 ppm (8.3 mg/kg) was expected to be a no-observable-effect level for a 3-month dosing period.

A high dose of 1250 ppm was expected to result in a daily intake of about 41.7 mg/kg and to cause evidence of systemic toxicity without fatalities.

Study schedule

Study initiation (protocol date)	November 3, 1994
Start of acclimatisation	October 20, 1994
Start of administration	November 21, 1994
Termination of administration	February 19 to 22, 1995
Date of sacrifice	February 20 to 23, 1995
Duration of treatment	91 to 94 days
Date of completion (report date)	August 7, 1995

3.4. Compound administration and preparation

Route of administration

orally, admixed to the diet

Frequency of administration

once/day, 7 days a week

Preparation of the test article for administration

For each concentration an appropriate amount of test article was dissolved in acetone (about 160 g in 1000 g) and the solution added to a fixed amount of bolus alba. Acetone was evaporated at room temperature and the bolus alba premix was blended with a predefined amount of pulverized food. From this premix 1, a predefined amount was added to a further portion of pulverised food and thorough mixing, a homogeneous premix 2 was obtained for each of the concentrations. To these premixes diet was added to attain the nominal concentrations, blended homogeneously and pelleted.
Diet was prepared at about monthly intervals and stored in paper bags or stainless steal containers at room temperature.

Control diet

The diet for control animals was prepared similarly using equal amounts of bolus alba and acetone but without adding test article.

Analysis of test article in the diet

Samples of the pelleted diet containing the test article were analysed for concentration, homogeneity and stability of CGA 329351 tech.

Analyses were done with the first (mixture 1) and the third mixture (mixture 3).

The analyses were carried out by the Analytical Laboratory of RCC Umweltchemie AG, 4452 Itingen, Switzerland.

The results of the analysis (RCC Project 386234) are given in the result and appendix sections of this report.

3.5. Observations and records

Mortality

All animals were checked daily (a.m. and p.m. on working days, a.m. on weekends and holidays), in order to record mortalities and to allow dead or moribund animals to be submitted to necropsy as soon as possible.

In-life observations

In order to detect changes in state of health or behaviour, or any other reactions to treatment, examination was carried out daily.

Body weight

The weight of all animals was recorded individually at weekly weighing sessions.

Food consumption

daily (reported as weekly means)

Unit: g/animal/day

Food was offered as a constant amount of 350 g/animal/day with access being limited to about 3 hours.

Food consumption ratios

Food consumption ratio (FCR) was calculated according to the following formula:

$$FCR = \frac{\text{weekly food consumption (g)}}{\text{body weight (kg) x 7}}$$

Unit: g food/kg body weight/day

Test article intake

Mean test article intake (TAInom) was calculated on a weekly basis according to the following formula:

$$TAInom = \frac{FCR \times Cnom}{1000}$$

Unit: mg/kg body weight/day

Cnom = nominal concentration of test article in food (ppm)

The overall mean test article intake value was subsequently corrected for the analytically determined test article content. Effective mean test article intake (TAIeff) was calculated as follows:

$$TAIeff = \frac{TAInom \times Ceff}{100}$$

Unit: mg/kg body weight/day

Ceff = mean effective concentration of test article in food (in % of Cnom) as determined analytically

Eye examinations

Eye examinations were performed in all animals at pretest and towards the end of the treatment period. After external inspection, the lens, the iris and the fundus were examined with an ophthalmoscope. The appearance of the fundus was documented photographically. Mydriaticum™ (Dispersa AG) was applied to induce mydriasis. The pupillary reflex was checked in all animals and the third eyelid was examined after local anesthesia using Novesin™ 0.4% (Dispersa AG).

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3.6. Laboratory investigations

Laboratory investigations (hematology, blood chemistry and urine analysis) were carried out on all surviving animals of each dose group at:

pretest:	November 14/17, 1994
week 7:	January 4/5, 1995
week 13:	February 15/16, 1995

To reduce the biological variability due to circadian rhythms, blood sampling was performed in the morning. Blood was removed from the jugular vein. The following anticoagulants were used: EDTA for performing the complete blood count, 3.8% sodium citrate for coagulation testing and heparin for blood chemistry investigations. Food was withheld for at least 16 hours prior to blood collection.

Urine for analysis was obtained by catheterization.

The parameters and methods used are listed in the following tables.

3.6.1. Parameters and methods used in hematology

Parameters determined by the Technicon H*1 (Method code: M0002) <1>

Red blood cell parameters	Abbreviation	SI Unit<2>
Erythrocyte count	RBC	T/l
Hemoglobin	Hb	mmol/l
Hematocrit	Hct	1
Mean corpuscular volume	MCV	fl
Red cell volume distribution width<3>	RDW	1
Mean corpuscular hemoglobin	MCH	fmol
Mean corpuscular hemoglobin concentration	MCHC	mmol/l
Hemoglobin concentration distribution width<4>	HDW	mmol/l
White blood cell parameters		
Leukocyte count	WBC	G/l
Differential leukocyte count		rel. abs.
Neutrophils	Neut	1 G/l
Eosinophils	Eos	1 G/l
Basophils	Baso	1 G/l
Lymphocytes	Lympho	1 G/l
Monocytes	Mono	1 G/l
Large unstained cells	Luc	1 G/l
Blood platelets		
Thrombocyte Count	Plt	G/l
Prothrombin time		
Photometric assay using chromogenic substrate on a Cobas Bio centrifugal analyser (Method code: M0001)	PT (CS)	sec
Reticulocyte count		
Reticulocytes were stained with Thiazole Orange and determined by FACSCAN flow cytometer as a percentage of total erythrocytes (Method code: M0003)	Reti	1

<1> Method code is used for assignment of valid reference values (see Appendix D)
<2> A table which lists SI units, conventional units and factors to convert data from SI units to conventional units is given in Appendix D
<3> RDW is derived as a coefficient of variation of the volume histogram
<4> HDW is derived as the standard deviation of the hemoglobin concentration histogram

3.6.2. Parameters and methods used in blood chemistry

Parameter	Method of analysis (Method code) Instrument	Abbre-viation	Unit
Glucose	Hexokinase/G6P-DH (M0001) HITACHI 737	Gluc	mmol/l
Urea	Urease/GLDH (M0001) HITACHI 737	Urea	mmol/l
Creatinine	Enzymatic colorimetric test (M0001) HITACHI 737	Creat-e	umol/l
Total bilirubin	Reaction with 2,5-Di-chlorophenyldiazonium salt (M0001) HITACHI 737	Bili-tot	umol/l
Total protein	Biuret reaction (M0001) HITACHI 737	Prot	g/l
Albumin	Bromcresol green method (M0001) HITACHI 737	Alb	g/l
Globulin	Calculated value (M0001) (Total Protein minus Albumin)	Glob	g/l
A/G Ratio	Calculated value (M0001) (Albumin/Globulins)	A/G	1
Cholesterol	Enzymatic, CHOD/PAP (M0001) HITACHI 737	Chol	mmol/l
Triglycerides	Glycerol-Kinase GPO/PAP method (M0001) HITACHI 737	Trigly	mmol/l
Phospho-lipids	Phospholipase-Cholin-oxidase-Peroxidase-reaction (M0001) HITACHI 737	Phos-Lip	mmol/l

Parameter	Method of analysis (Method code) Instrument	Abbre-viation	Unit
Sodium	Ion selective electrode (M0001) HITACHI 737	Na+	mmol/l
Potassium	Ion selective electrode (M0001) HITACHI 737	K+	mmol/l
Calcium	o-Cresolphthalein complexone method (M0001) HITACHI 737	Ca++	mmol/l
Chloride	Ion selective electrode (M0001) HITACHI 737	Cl-	mmol/l
Phosphorus inorganic	Phosphomolybdate reaction (M0001) HITACHI 737	PO4-in	mmol/l
Aspartate amino-transferase EC 2.6.1.1	MDH/NADH coupled reaction method (M0001) HITACHI 737	ASAT (GOT)	U/l
Alanine amino-transferase EC 2.6.1.2	LDH/NADH coupled reaction method (M0001) HITACHI 737	ALAT (GPT)	U/l
Alkaline phosphatase EC 3.1.3.1	p-Nitrophenyl-phosphate as substrate (M0001) HITACHI 737	AlP	U/l
Gamma-glutamyl transpeptidase EC 2.3.2.2	Substrate: L-gamma-glutamyl-3-carboxy-4-nitroanilide (M0001) HITACHI 737	GGT	U/l
Creatine kinase EC 2.7.3.2	HK/ATP and G6P-DH/NADPH coupled reaction method (M0001) HITACHI 737	CK	U/l

3.6.3. Parameters and methods used in urinalysis

Physical and chemical examination

Chemical urine components, pH and relative density were estimated by an automated urine analyser Clinitek Auto 2000 (Ames) using solid-phase reagent systems combined with reflectance spectroscopy (chemical constituents and pH), and applying the falling drop method (relative density).

The results of the semiquantitative estimates were classified in the following categories:

0 normal range
\+ trace
++ small amount
+++ large amount

Parameter	Abbreviation	Method of analysis
Relative density	Rel dens	Falling drop method Clinitek Auto 2000 (M0001)
pH-value	pH	Clinitek Auto 2000 (M0001)
Urine color	Color N = normal C = colorless YB = yellow-brown YG = yellow-green R = red B = brown RB = red-brown	Visual inspection
Protein	Prot	Clinitek Auto 2000
Glucose	Gluc	Clinitek Auto 2000
Ketones	Keto	Clinitek Auto 2000
Bilirubin	Bili	Clinitek Auto 2000
Blood	Blood	Clinitek Auto 2000
Urobilinogen	UBG	Clinitek Auto 2000

Microscopic examination

After centrifugation of the urine specimen, the sediment was stained with a modified Sternheimer-Malbin stain and examined microscopically. Results of microscopic estimates for formed elements (cells, casts, crystals) are classified in the following categories:

	0	no abnormalities observed
	+	few
	++	moderate number
	+++	many
Cells:	RBC	Erythrocytes
	WBC	Leukocytes
	Epi-squa	Squamous epithelial cells
	Epi-tr	Transitional epithelial cells
	Epi-ren	Renal epithelial cells
Casts:	Cst-Hyal	Hyaline casts
	Cst-Gran	Granular casts
	Cst-Wax	Waxy casts
	Cst-RBC	Erythrocyte casts
	Cst-WBC	Leukocyte casts
	Cst-Epi	Epithelial cell casts
Crystals:	Cry-PO4	Triple phosphate crystals
	Cry-Caox	Calcium oxalate crystals
	Cry-UrAc	Uric acid crystals
	Cry-Uram	Amorphous urate crystals
	Cry-Tyr	Tyrosine crystals
	Cry-Cys	Cystine crystals
	Cry-CaPhos	Di-calcium phosphate crystals
	Cry-Unid	Unidentified crystals

3.7. Pathology

3.7.1. Macroscopical examination

At scheduled sacrifice all controls and treated animals were anesthetised by intravenous injection of T 61 (Hoechst), exsanguinated and subjected to detailed necropsy.

At necropsy the following weights were recorded from all animals:

body (exsanguinated)
brain
heart
liver
kidneys
adrenals
thymus
ovaries/testes
spleen
thyroid gland (including parathyroids)

The following organs and tissues were preserved in neutral buffered 4% formalin:

skin
mammary area
spleen
cervical lymph node
mesenteric lymph node
popliteal lymph node
sternum with bone marrow
rib with cartilage
skeletal muscle (semimembranosus)
trachea
lung
heart
aorta
submandibular salivary gland (both)
liver
gall bladder
pancreas
esophagus
stomach
small intestine (duodenum, jejunum and ileum)
large intestine (cecum, colon and rectum)
kidney (both)
urinary bladder
prostate
testis (both)
epididymis (both)
vagina

uterus
ovary (both)
pituitary gland
adrenal gland (both)
thyroid with parathyroid gland
thymus
peripheral nerve (sciatic nerve)
brain
spinal cord
eye with optic nerve (both)
lacrimal gland (both)
any tissue with gross lesions

3.7.2. Microscopical examination

After the fixation, organ samples listed above were taken, embedded in paraplast, sectioned at 3-5 microns, stained with hematoxylin and eosin, and subjected to a microscopical examination.

3.7.3. Presentation of pathology data

Where practicable, gross lesions were identified by a capital letter, e.g. A, B, C, etc. at necropsy.

At the subsequent histopathological evaluation the diagnosis or diagnoses corresponding to the macroscopically identified lesions were given the same alphabetical label in order to correlate the microscopical findings with the changes seen at necropsy.

In compiling the incidence tables of microscopical findings, an animal presenting with a primary process (e.g. a rapidly growing tumor) that caused a biological response considered to be secondary (e.g. pressure atrophy) was counted in the summary tables as an animal presenting with the primary process. Secondary changes are mentioned among the individual findings.

The relationship between primary and secondary diagnosis was indicated by an arrow, e.g. A -> B, specifying that the diagnosis "A" was secondary to the diagnosis recognized as "B".

When no descriptor was ascribed at necropsy the histopathologist marked diagnoses by the symbols Z', Y', X' etc. in order to draw relationships between diagnoses.

The histopathological findings were assessed with respect to their severity, as well as their incidence (number of affected individuals per group). The degree of severity was defined according to the following criteria:
Grade "+" : minimal (slight) = histopathological change is a noticeable but not prominent feature of the tissue.
Grade "++" : moderate = histopathological change is a prominent but not dominant feature of the tissue.
Grade "+++" : marked = histopathological change is a dominant feature of the tissue.

In paired organs, the findings of uneven severity were graded as follows:

Grade +/++ = Grade ++ (bilateral)
Grade +/+++ = Grade ++ (bilateral)
Grade ++/+++ = Grade +++ (bilateral)

The "Summary tables of microscopical findings" presented in this report show the incidence of microscopical lesions, while the severity of each particular finding (with exceptions specified by the standard operating procedures) is described with the individual findings. Likewise, the unilateral/bilateral occurrence of findings in paired organs is explained in detail with the individual findings, while summary tables indicate only if one of both paired organs was missing or could not be examined.

3.8. Statistical analysis

For each time point and parameter an univariate statistical analysis was performed. Nonparametric methods were applied, to allow for non normal as well as normal data distribution.

Each treated group was compared to the control group by Wilcoxon's two-sample test <1> and tested for increasing or decreasing trends from control up to the respective dose group by Jonckheere's test for ordered alternatives <1,2>.

Two-sided asymptotic p-values are reported in the "statistics" tables. Flags for significant differences between groups (*) or trends over groups (+ or -) are given in the "means" tables according to the specified significance level. Statistical tests and flags used are indicated in the header of each table.

Statistical significance does not necessarily imply biological relevance. Hence, the responsible scientist may not comment on statistically significant values lying within the physiological range and on the other hand may comment on values, which differ substantially from the expected normal values although this difference was not statistically significant.

References

<1> E.L. Lehmann, Nonparametrics: Statistical Methods Based on Ranks. Holden-Day (1975): pp. 5-31, 232-238

<2> A.R. Jonckheere, Biometrika (1954) 41: pp. 133-145

Explanation of statistics and flags

N	the number of observations on which the calculations are based
Mean	the sum of the observed values divided by N
Median	the 50th percentile
Min, Max	the smallest value, the largest value
p_W	p-value, the probability of an outcome being greater than or equal to the absolute value of Wilcoxon's standardized test statistic, if the null hypothesis is true (two-sided, with correction for ties). Not given, if sample sizes too small
	*, significant difference in location between treated group and control at the level specified in the header of the table
p_J	p-value, the probability of an outcome being greater than or equal to the absolute value of Jonckheere's standardized test statistic, if the null hypothesis is true (two-sided, no correction for ties). Not given, if sample sizes too small
	+ or -, significant positive or negative trend from control up to the respective dose group at the level specified in the header of the table

3.9. Deviations from the protocol

Amended

Study title was changed.

Not amended

As of May 1, 1995 Facility management changed from Dr. [redacted] to [redacted], Ph.D.

On May 15, 1995 Mrs. [redacted] was set in charge for pathology services.

After the start of the study responsibility for study pathologist changed from Dr. [redacted] to Dr. [redacted].

Initial age of one female was slightly higher than proposed in the protocol.

The above mentioned deviations are considered to have no impact on the validity of the study.

There were no known circumstances that could have affected the quality and/or integrity of the data.

4. RESULTS

4.1. Dietary levels

4.1.1. Analytical results

Stability

CGA 329351 tech. was stable at room temperature in pelleted dog diet for at least 42 days.
For details see table on the next page.

Homogeneity

The diet mixtures can be considered homogeneous. The homogeneity varied in the range from -6 % to +6 % of the mean concentrations (see table next page).

Content

The content of active ingredient in all samples was found to be in agreement with the nominal concentrations. Overall mean concentrations, expressed as a percentage of the nominal concentrations were calculated to be 93.9, 101.2, 91.4 and 91.7% for dose groups 2 (50 ppm), 3 (125 ppm), 4 (250 ppm) and 5 (1250 ppm), respectively.

For details see appendix section (RCC Project 386234).

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Test material content, homogeneity and stability

	Group 2	Group 3	Group 4	Group 5
Nominal (ppm)	50	125	250	1250
Analytical (% of Nominal)				
Mixture 1				
Sample A	91.4	92.7	92.5	91.2
Sample B	87.9	93.0	92.7	91.2
Sample C	91.0	93.7	93.2	91.4
Mean	90.1	93.1	92.8	91.3
Stability	89.5	87.0	96.5	96.4
Mixture 3				
Sample B	97.6	109.3	90.0	92.1
Mean (%)	93.9	101.2	91.4	91.7

A: Beginning)
B: Middle) of discharge from the pelleting machine
C: End)

Mixture 1: prepared on November 15, 1994
Mixture 3: prepared on January 12, 1995

Test article content in group 1 diet (control) was always below analytical detectability.

4.1.2. Test article intake

For each dose level, the mean test article intake (in mg/kg body weight per day) is presented in the following tables.

Weekly mean test article intakes were calculated based on food consumption, body weight and nominal test article concentration. Listed values for weeks 1 to 13 were corrected to 2 decimal places. However, overall mean values were calculated by unrounded values. Overall means were calculated and corrected for the mean amount of test article in the diet according to the results of analytical determination of test article concentration.

Rounded to 3 meaningful digits, the mean daily intake of CGA 329351 tech. was 1.57, 4.07, 7.25 and 38.6 mg/kg body weight for males, and 1.56, 4.33, 7.93 and 39.5 mg/kg body weight for females.

Daily intake (means) : males
(mg/kg body weight/day)

Dose(ppm)	group 2 50	group 3 125	group 4 250	group 5 1250
week:				
1	1.81	4.30	8.50	45.71
2	1.81	4.31	8.44	45.13
3	1.77	4.22	8.30	44.20
4	1.74	4.16	8.17	43.40
5	1.69	4.05	8.00	42.46
6	1.68	4.03	7.89	41.90
7	1.66	4.00	7.86	41.61
8	1.64	3.94	7.73	41.00
9	1.62	3.90	7.63	40.61
10	1.61	3.87	7.65	40.38
11	1.60	3.83	7.64	40.10
12	1.58	3.82	7.68	40.40
13	1.59	3.83	7.62	40.28
Overall mean nominal	1.68	4.02	7.93	42.09
Overall mean effective*	1.57	4.07	7.25	38.60

* corrected for analytical content

Daily intake (means) : females
(mg/kg body weight/day)

Dose(ppm)	group 2 50	group 3 125	group 4 250	group 5 1250
week:				
1	1.74	4.43	9.00	44.70
2	1.74	4.45	9.13	44.70
3	1.71	4.40	8.98	44.10
4	1.70	4.29	8.88	43.86
5	1.67	4.30	8.71	42.82
6	1.67	4.29	8.64	42.58
7	1.65	4.27	8.61	42.59
8	1.63	4.25	8.52	42.58
9	1.63	4.11	8.47	42.19
10	1.63	4.27	8.50	42.50
11	1.63	4.25	8.46	42.18
12	1.62	4.19	8.46	42.29
13	1.63	4.19	8.47	42.38
Overall mean nominal	1.66	4.28	8.68	43.03
Overall mean effective*	1.56	4.33	7.93	39.46

* corrected for analytical content

4.2. Mortality

Individual mortality data including fate and days on test are presented in Appendix B of this report.

None of the animals died or had to be sacrificed during the course of this study.

4.3. In-life observations

The summary of antemortem findings is presented below, individual signs are presented in Appendix B of this report.

No toxicologically relevant clinical signs or changes in behavior were observed at any time during the study.

Diarrhea of a variable degree occurred intermittently for control and treated animals. However, no relationship to treatment could be established (see Appendix B).

Antemortem findings (incidence)

Dose (ppm)	group 1 0		group 2 50		group 3 125		group 4 250		group 5 1250	
Sex	m	f	m	f	m	f	m	f	m	f
hair loss, back	1	-	-	-	-	-	-	-	-	-
wound, neck	-	-	-	1	-	-	-	-	-	-
scab, neck	-	-	-	1	-	-	-	-	-	-

4.4. Body weight

Mean body weight values are presented in the following tables and plots. Individual body weight values collected during the investigation and their statistics are presented in Appendices A and B of this report.

Body weight development in both sexes was comparable to that of the controls.

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

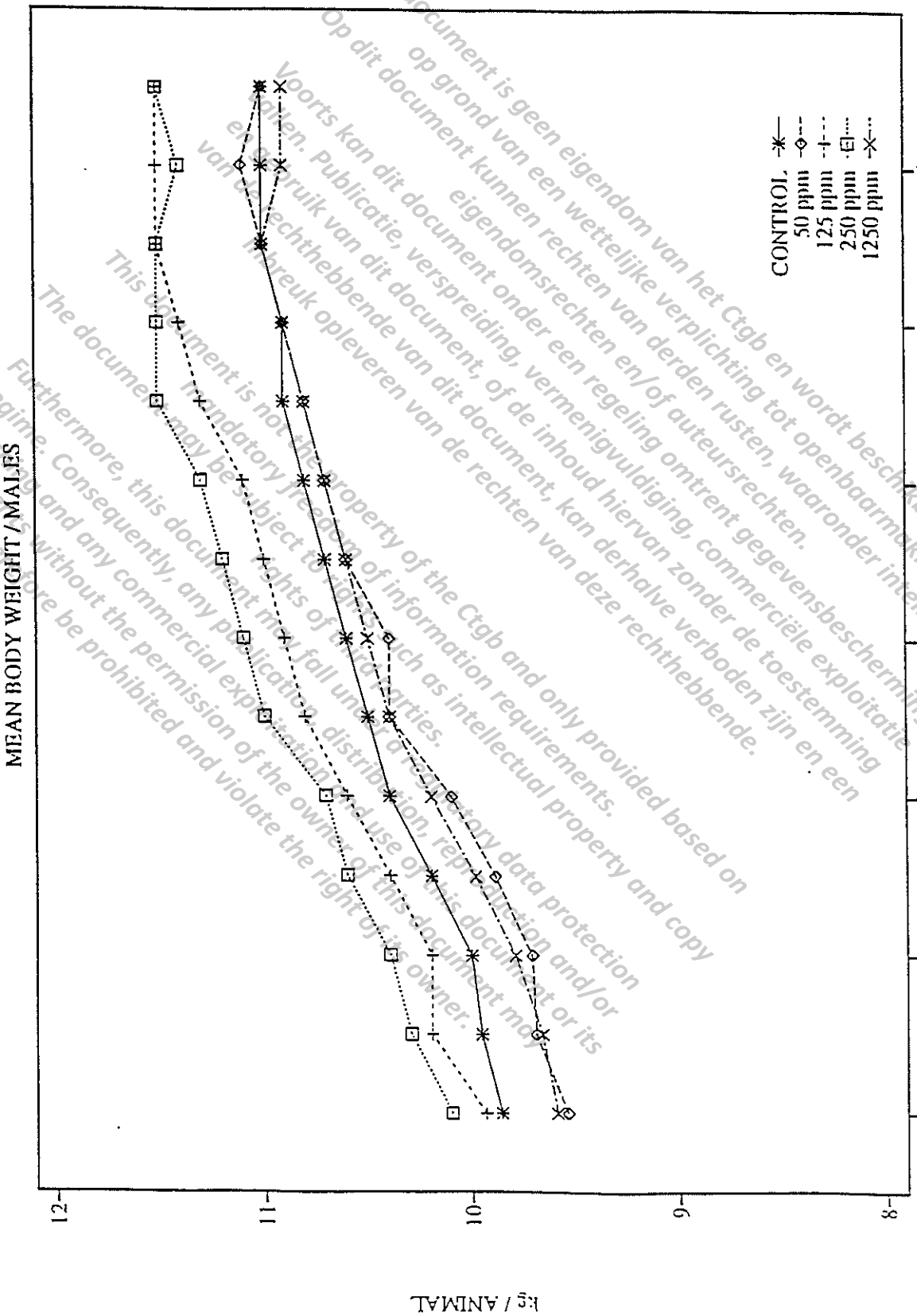
Body weight (means) : males
(kg/animal)

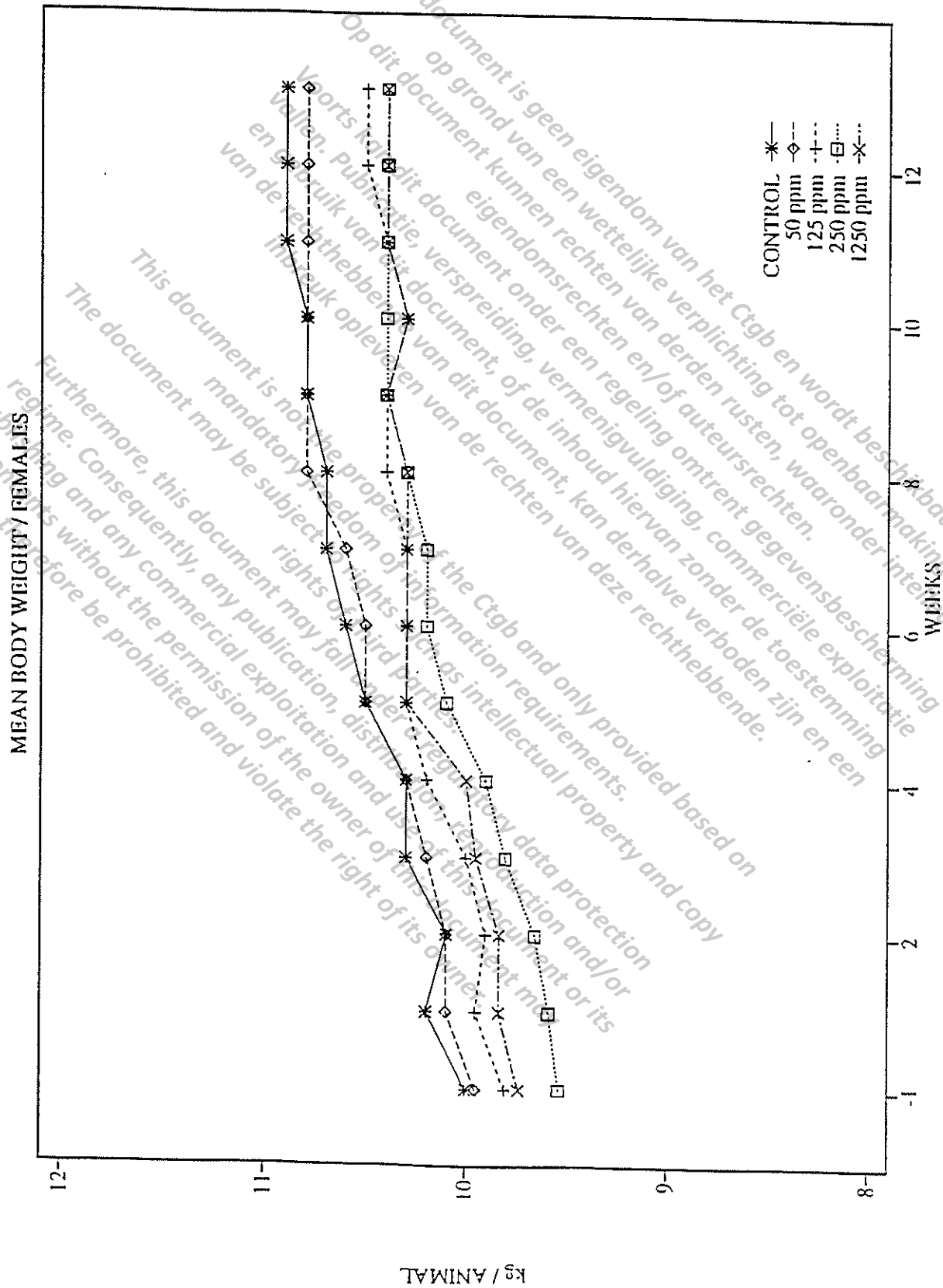
Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	9.850	9.525	9.925	10.08	9.575
1	9.950	9.675	10.20	10.30	9.650
2	10.00	9.700	10.18	10.38	9.775
3	10.18	9.875	10.40	10.55	9.975
4	10.38	10.05	10.55	10.73	10.15
5	10.50	10.35	10.83	10.95	10.38
6	10.58	10.43	10.90	11.10	10.50
7	10.70	10.55	10.98	11.15	10.58
8	10.80	10.68	11.13	11.33	10.73
9	10.88	10.83	11.25	11.48	10.83
10	10.93	10.90	11.35	11.45	10.90
11	11.00	10.98	11.45	11.48	10.98
12	10.95	11.05	11.50	11.40	10.90
13	11.03	11.03	11.45	11.50	10.93

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Body weight (means) : females
(kg/animal)

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	10.00	9.950	9.800	9.525	9.725
1	10.18	10.10	9.950	9.575	9.825
2	10.10	10.10	9.900	9.650	9.825
3	10.25	10.23	10.00	9.800	9.950
4	10.33	10.33	10.18	9.900	10.00
5	10.50	10.50	10.25	10.10	10.25
6	10.63	10.48	10.28	10.15	10.30
7	10.68	10.63	10.33	10.23	10.30
8	10.73	10.75	10.35	10.33	10.30
9	10.83	10.78	10.43	10.40	10.40
10	10.80	10.78	10.33	10.35	10.33
11	10.85	10.78	10.38	10.40	10.40
12	10.85	10.83	10.53	10.40	10.38
13	10.88	10.78	10.53	10.40	10.35





4.5. Food consumption

Mean food consumption values are presented in the following tables and plots. Individual food consumption values collected during the investigation and their statistics are presented in Appendices A and B of this report.

Mean food consumption for all groups and both sexes was comparable to that of the controls.

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

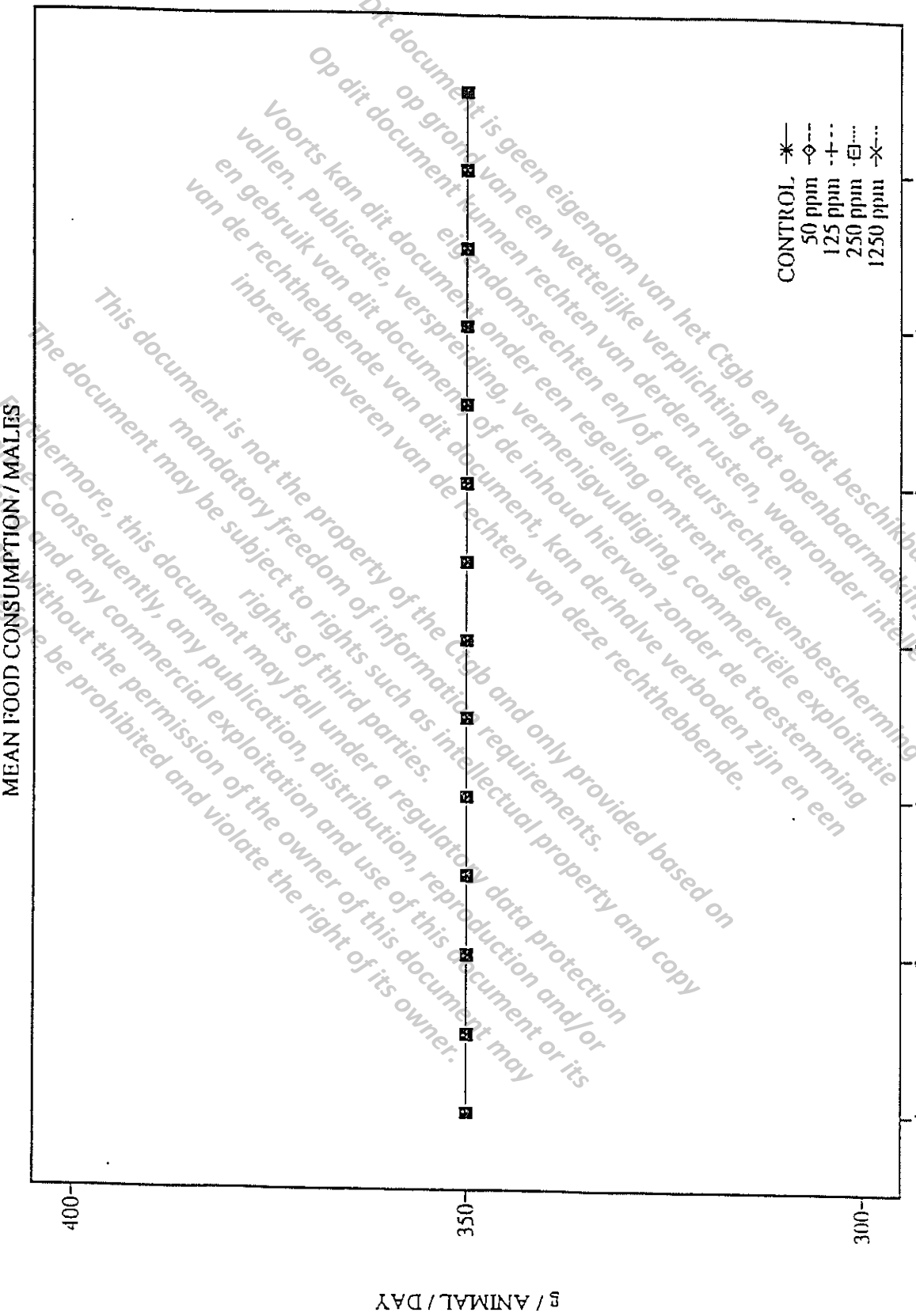
Food consumption (means) : males
(g/animal/day)

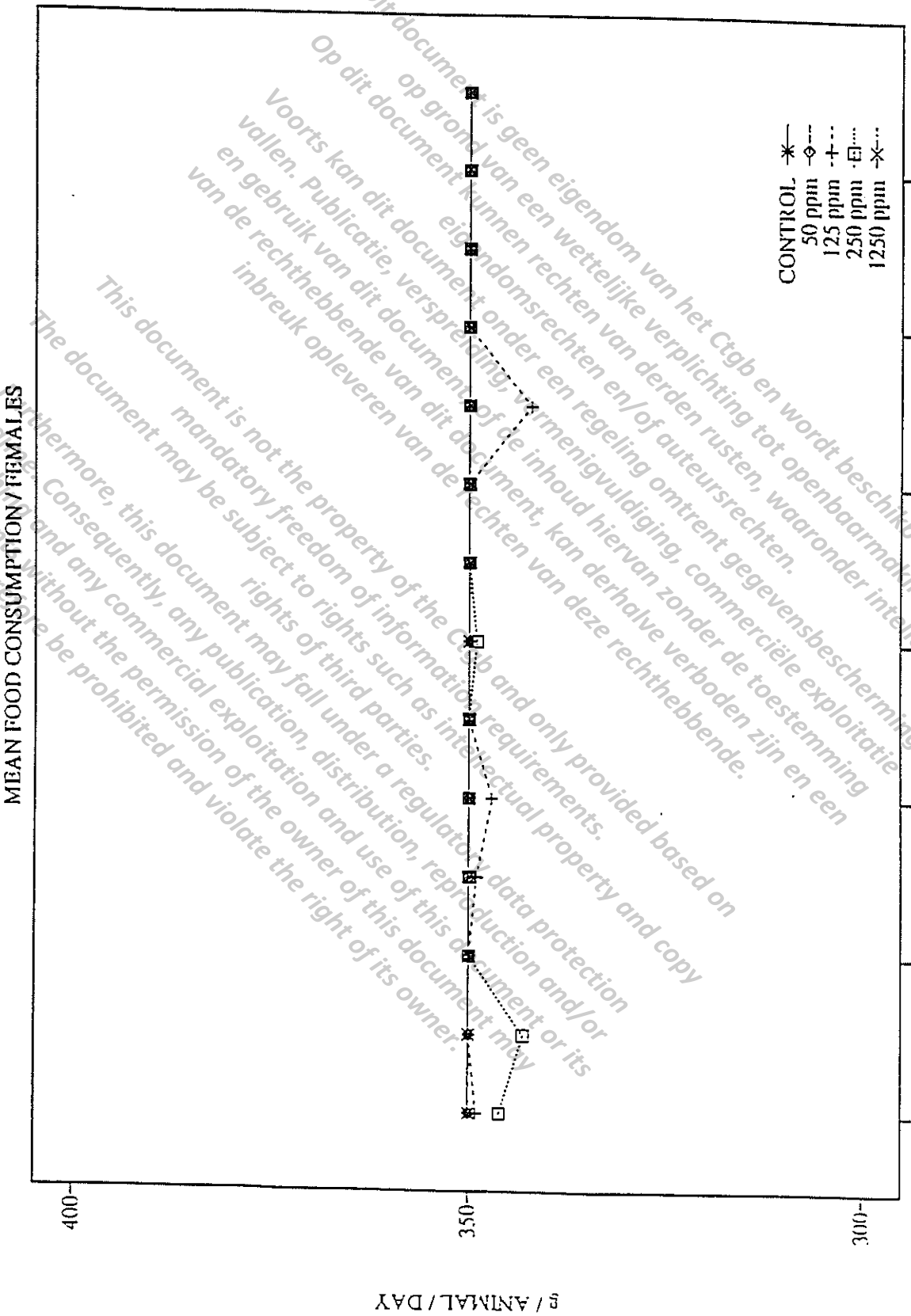
Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	350.0	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0	350.0

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Food consumption (means) : females
(g/animal/day)

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	350.0	350.0	348.9	346.4	350.0
1	350.0	350.0	350.0	342.9	350.0
2	350.0	350.0	350.0	350.0	350.0
3	350.0	350.0	349.3	350.0	350.0
4	350.0	350.0	346.8	350.0	350.0
5	350.0	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	348.9	350.0
7	350.0	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0	350.0
9	350.0	350.0	341.8	350.0	350.0
10	350.0	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0	350.0





4.6. Food consumption ratios

Mean food consumption ratios are presented in the following tables and plots.

No consistent difference in mean food consumption ratios was observed between groups.

No statistical tests performed

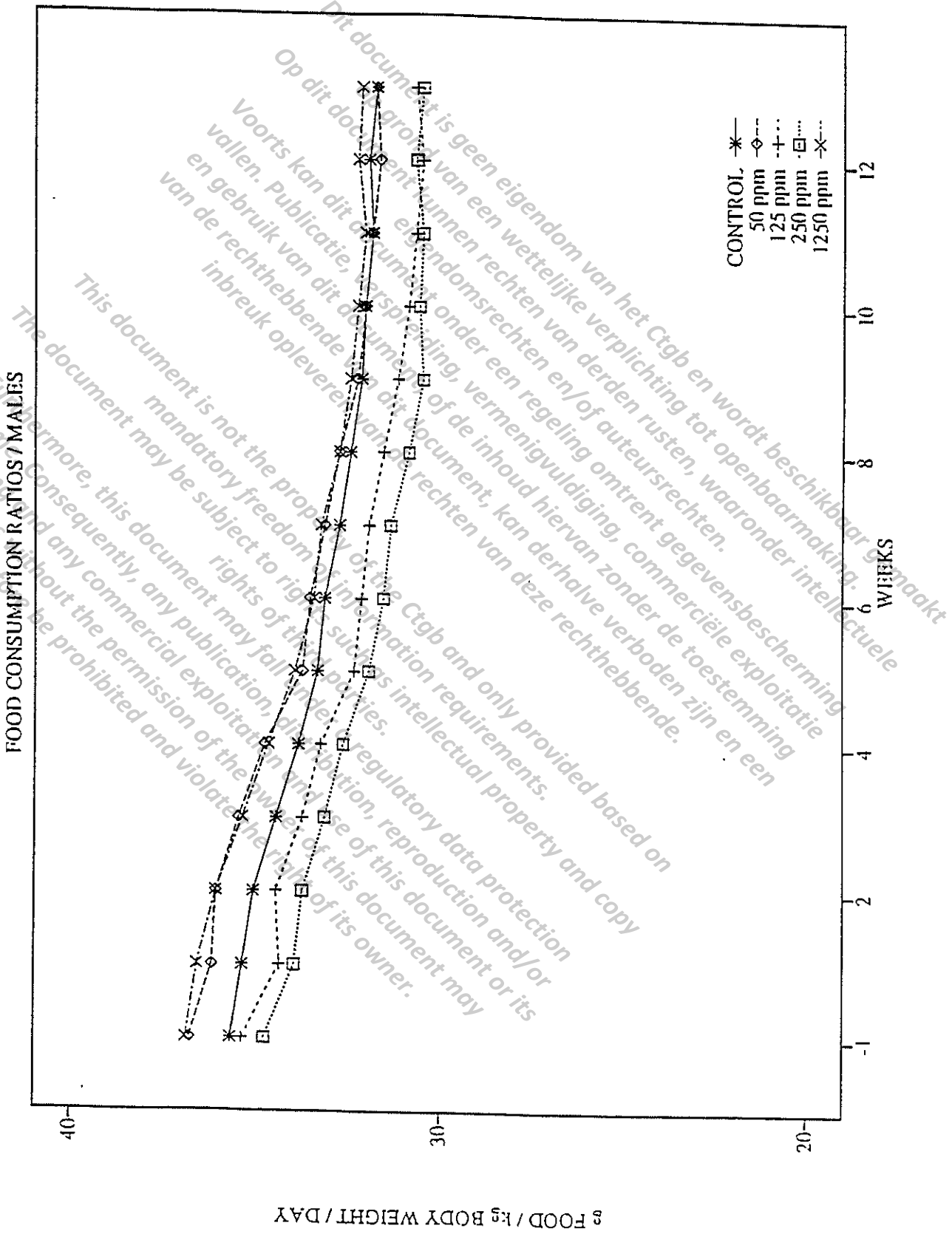
Food consumption ratios (means) : males
(g food/kg body weight/day)

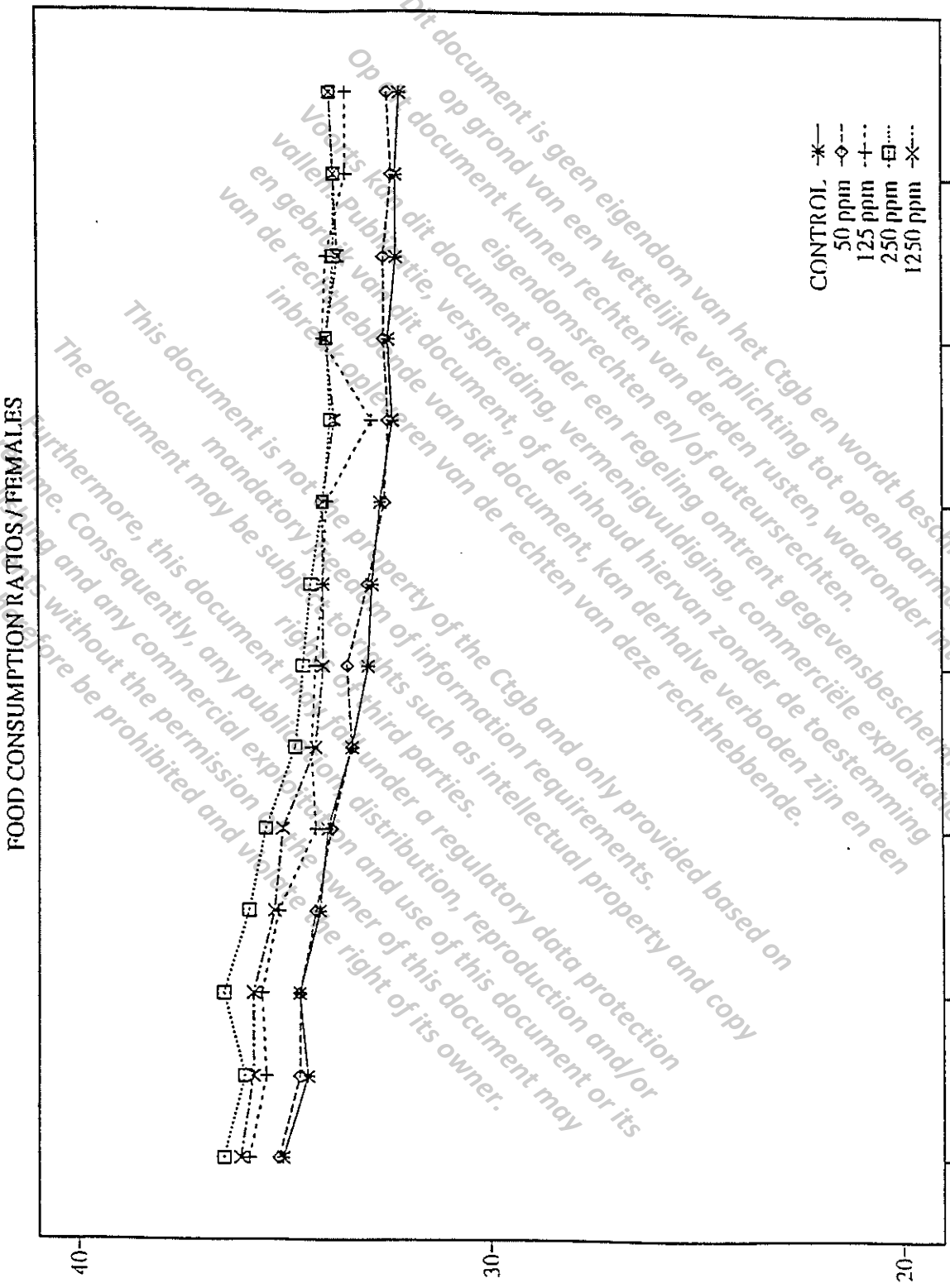
Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	35.75	36.80	35.38	34.78	36.85
1	35.37	36.22	34.40	34.00	36.57
2	35.14	36.12	34.51	33.77	36.10
3	34.52	35.48	33.75	33.20	35.36
4	33.85	34.85	33.28	32.66	34.72
5	33.43	33.83	32.44	31.98	33.97
6	33.18	33.59	32.20	31.55	33.52
7	32.79	33.19	31.98	31.42	33.29
8	32.48	32.80	31.55	30.92	32.80
9	32.23	32.35	31.21	30.53	32.49
10	32.09	32.13	30.93	30.59	32.30
11	31.87	31.91	30.65	30.54	32.08
12	31.99	31.69	30.52	30.73	32.32
13	31.77	31.77	30.65	30.48	32.22

No statistical tests performed

Food consumption ratios (means) : females
(g food/kg body weight/day)

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	35.09	35.21	35.92	36.54	36.13
1	34.48	34.72	35.46	35.98	35.76
2	34.73	34.70	35.60	36.50	35.76
3	34.21	34.27	35.17	35.93	35.28
4	33.98	33.94	34.30	35.53	35.09
5	33.41	33.36	34.39	34.83	34.26
6	33.00	33.45	34.29	34.57	34.06
7	32.85	32.99	34.12	34.43	34.07
8	32.69	32.62	34.03	34.07	34.06
9	32.38	32.55	32.91	33.86	33.75
10	32.45	32.55	34.14	34.00	34.00
11	32.31	32.55	34.00	33.83	33.74
12	32.31	32.40	33.52	33.83	33.83
13	32.24	32.55	33.48	33.87	33.90





4.7. Eye examinations

The findings in individual dogs are listed in Appendix B of this report.

The examination of conjunctiva, sclera, cornea, lens, and fundus did not reveal any treatment-related findings.

No alterations of the pupillary reflex could be seen in control and treated dogs.

Detailed examination of the third eyelid under local anesthesia revealed conjunctivitis follicularis in all male and female dogs of the control and treated groups at pretest and at week 13. There was no difference in the intensity of the lesion between treated and control animals. This finding is, therefore, considered to be of no experimental relevance.

4.8. Hematology

Mean values are presented in the following tables. Individual values and their statistics are given in the Appendices A and B of this report. Reference values from previous studies are given in Appendix D.

No treatment-related changes in hematologic parameters were observed.

Values recorded in treated dogs were similar to those of controls and to pretest values with only few statistically significant differences. However, also in these cases an effect of the treatment was considered to be unlikely because the deviations did not show any relation to the administered doses or to the duration of the treatment. In addition, all individual values remained within the range of reference values. The findings were therefore attributed to normal biological variation.

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Hematology (means) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
RBC (T/l)					
week: -1	6.193	6.178	6.273	5.633*	5.743
7	6.321	6.445	6.460	6.005	5.973
13	6.423	6.483	6.408	6.110	6.063
Hb (mmol/l)					
week: -1	8.775	8.750	9.025	7.925*	8.125*
7	8.850	9.075	9.175	8.425	8.375
13	9.000	9.200	9.125	8.500	8.550
Hct (1)					
week: -1	0.410	0.415	0.430	0.374*	0.387
7	0.424	0.437	0.441	0.403	0.406
13	0.422	0.429	0.426	0.399	0.402
MCV (fl)					
week: -1	66.20	67.15	68.50	66.45	67.40
7	67.15	67.83	68.30	67.15	68.05
13	65.83	66.18	66.40	65.23	66.28
RDW (1)					
week: -1	0.144	0.139	0.145	0.146	0.146
7	0.136	0.132	0.133	0.138	0.137
13	0.134	0.129	0.131	0.134	0.137
MCH (fmol)					
week: -1	1.423	1.418	1.438	1.413	1.418
7	1.403	1.410	1.423	1.403	1.403
13	1.405	1.418	1.423	1.390	1.410
MCHC (mmol/l)					
week: -1	21.48	21.09	20.98	21.25	21.03*
7	20.86	20.76	20.84	20.90	20.57
13	21.35	21.44	21.44	21.31	21.31

Hematology (means) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
HDW (mmol/l)					
week: -1	1.108	1.048	1.083	1.055	1.175
7	1.184	1.158	1.145	1.223	1.140
13	1.130	1.093	1.140	1.100	1.070
Reti (1)					
week: -1	0.022	0.025	0.028	0.020	0.022
7	0.018	0.019	0.019	0.020	0.019
13	0.019	0.018	0.019	0.016	0.017
WBC (G/l)					
week: -1	10.59	10.80	10.64	9.965	9.883
7	10.85	10.79	12.41*	12.15	10.64
13	9.670	10.45	11.16	10.04	9.173
Neut (1)					
week: -1	0.572	0.537	0.491*	0.514	0.503
7	0.571	0.533	0.559	0.564	0.537
13	0.569	0.560	0.577	0.558	0.541
Eos (1)					
week: -1	0.027	0.022	0.033	0.027	0.026
7	0.026	0.025	0.028	0.032	0.024
13	0.022	0.022	0.022	0.017	0.016
Baso (1)					
week: -1	0.005	0.006	0.006	0.005	0.005
7	0.003	0.005	0.005	0.003	0.004
13	0.004	0.004	0.004	0.004	0.003
Lympho (1)					
week: -1	0.343	0.375	0.421	0.395	0.397
7	0.347	0.375	0.352	0.337	0.364
13	0.347	0.350	0.332	0.353	0.377

Hematology (means) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Mono (1)					
week: -1	0.049	0.056	0.044	0.054	0.064
7	0.050	0.058	0.054	0.060	0.068
13	0.050	0.059	0.057	0.061	0.054
Luc (1)					
week: -1	0.005	0.005	0.005	0.005	0.005
7	0.003	0.004	0.004	0.005	0.004
13	0.009	0.007	0.008	0.008	0.008
Neut (G/l)					
week: -1	6.093	5.803	5.223	5.135	5.005
7	6.183	5.783	6.928	6.983	5.725
13	5.605	5.908	6.468	5.588	4.963
Eos (G/l)					
week: -1	0.290	0.243	0.353	0.268	0.265
7	0.280	0.273	0.340	0.343	0.253
13	0.208	0.218	0.238	0.180	0.148
Baso (G/l)					
week: -1	0.053	0.058	0.065	0.050	0.048
7	0.036	0.048	0.058	0.038	0.035
13	0.038	0.038	0.043	0.035	0.028
Lympho (G/l)					
week: -1	3.585	4.033	4.470*	3.925	3.883
7	3.780	4.023	4.370	4.005	3.865
13	3.263	3.608	3.695	3.550	3.465
Mono (G/l)					
week: -1	0.523	0.610	0.480	0.543	0.638
7	0.544	0.623	0.665	0.735	0.720
13	0.478	0.605	0.628	0.600	0.500

Hematology (means) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Luc (G/l)					
week: -1	0.045	0.055	0.053	0.048	0.050
7	0.031	0.043	0.040	0.053*	0.043
13	0.080	0.073	0.090	0.083	0.068
Plt (G/l)					
week: -1	287.0	270.5	303.3	263.5	294.8
7	313.5	293.5	313.5	303.8	331.0
13	287.8	293.3	286.5	289.0	326.0
PT(CS) (sec)					
week: -1	30.52	31.11	33.34	34.53	33.99
7	31.39	32.92	35.36	35.07	34.54
13	29.34	32.10	33.15	34.17*	33.38*

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Hematology (means) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
RBC (T/l)					
week: -1	6.683	6.755	6.614	6.745	6.785
7	7.058	7.100	6.708	7.035	6.785
13	6.665	6.893	6.570	6.830	6.610
Hb (mmol/l)					
week: -1	9.400	9.538	9.400	9.550	9.375
7	9.825	9.975	9.475	9.825	9.325
13	9.425	9.775	9.400	9.700	9.325
Hct (1)					
week: -1	0.448	0.459	0.448	0.453	0.452
7	0.472	0.477	0.449	0.472	0.448
13	0.443	0.455	0.435	0.453	0.436
MCV (fl)					
week: -1	66.98	67.95	67.64	67.24	66.50
7	66.93	67.20	66.93	67.23	66.13
13	66.48	66.10	66.18	66.25	66.05
RDW (1)					
week: -1	0.140	0.147	0.142	0.143	0.147
7	0.135	0.136	0.133	0.136	0.138
13	0.130	0.135	0.133	0.134	0.136
MCH (fmol)					
week: -1	1.405	1.411	1.423	1.418	1.383
7	1.393	1.403	1.410	1.400	1.373
13	1.413	1.420	1.433	1.420	1.408
MCHC (mmol/l)					
week: -1	20.97	20.83	21.01	21.07	20.76
7	20.79	20.89	21.08*	20.82	20.72
13	21.26	21.47	21.65*	21.46	21.33

Hematology (means) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
HDW (mmol/l)					
week: -1	1.103	1.104	1.064	1.069	1.098
7	1.165	1.185	1.128	1.143	1.118
13	1.090	1.110	1.090	1.090	1.100
Reti (1)					
week: -1	0.021	0.023	0.023	0.019	0.022
7	0.021	0.020	0.017	0.016*	0.020
13	0.017	0.016	0.016	0.015	0.015
WBC (G/l)					
week: -1	9.613	13.06	9.445	9.834	10.51
7	12.26	11.24	9.238	9.283	11.07
13	10.86	10.56	9.308	9.230	10.70
Neut (1)					
week: -1	0.524	0.616	0.544	0.524	0.569
7	0.565	0.611	0.569	0.521	0.607
13	0.599	0.625	0.589	0.580	0.612
Eos (1)					
week: -1	0.030	0.019	0.025	0.033	0.031
7	0.027	0.021	0.024	0.052	0.027
13	0.022	0.018	0.020	0.030	0.029
Baso (1)					
week: -1	0.006	0.005	0.005	0.005	0.006
7	0.005	0.006	0.004*	0.005	0.004
13	0.005	0.005	0.004	0.004	0.004
Lympho (1)					
week: -1	0.395	0.302	0.377	0.391	0.345
7	0.353	0.323	0.356	0.366	0.316
13	0.325	0.305	0.336	0.335	0.307

Hematology (means) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Mono (1)					
week: -1	0.042	0.054	0.046	0.043	0.045
7	0.046	0.036	0.046	0.054	0.044
13	0.043	0.040	0.044	0.046	0.043
Luc (1)					
week: -1	0.004	0.004	0.004	0.005	0.005
7	0.004	0.004	0.003	0.003	0.003
13	0.007	0.007	0.007	0.005*	0.006
Neut (G/l)					
week: -1	5.043	8.399	5.154	5.103	5.945
7	7.143	6.948	5.280	4.773	6.708
13	6.588	6.653	5.563	5.400	6.520
Eos (G/l)					
week: -1	0.293	0.226	0.228	0.315	0.318
7	0.335	0.215	0.213	0.450	0.295
13	0.245	0.193	0.178	0.243	0.313
Baso (G/l)					
week: -1	0.058	0.053	0.045	0.048	0.065
7	0.063	0.058	0.030*	0.045	0.043
13	0.045	0.053	0.038	0.035	0.043
Lympho (G/l)					
week: -1	3.778	3.558	3.559	3.908	3.663
7	4.085	3.565	3.263	3.503	3.498
13	3.435	3.160	3.063	3.095	3.300
Mono (G/l)					
week: -1	0.413	0.770	0.424	0.418	0.470
7	0.593	0.408	0.425	0.485	0.490
13	0.465	0.430	0.408	0.405	0.458

Hematology (means) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Luc (G/l)					
week: -1	0.040	0.055	0.041	0.046	0.050
7	0.048	0.043	0.025*	0.030	0.033
13	0.078	0.078	0.065	0.053	0.063
Plt (G/l)					
week: -1	285.8	296.3	223.6*	257.0	278.3
7	305.5	328.0	244.0*	305.3	321.0
13	299.5	295.8	245.0*	303.5	318.3
PT(CS) (sec)					
week: -1	32.83	32.69	32.59	31.45	31.75
7	31.09	32.61	31.45	30.13	29.06
13	31.20	32.15	32.39	30.74	30.96

4.9. Blood chemistry

Mean values are presented in the following tables. Individual values and their statistics are given in the Appendices A and B of this report. Reference values from previous studies are given in Appendix D.

Increased alkaline phosphatase activities were noted in males and females of group 5 (1250 ppm) after 7 and 13 weeks of treatment. No further changes of toxicological relevance were seen in any of the blood chemistry parameters investigated.

The mean plasma concentrations of cholesterol and phospholipids in males of group 4 (250 ppm) and group 5 (1250 ppm) were below the control values already at pretest and remained stable over the treatment period. These differences could therefore not be attributed to the treatment. In the same dose groups minimally reduced calcium concentrations were noted after 13 weeks. The magnitude of these changes was judged to be too small to be toxicologically relevant. This conclusion is supported by the absence of any corroborative changes indicating toxicity. Among the females, minimally increased sodium levels were recorded after 7 weeks of treatment in groups 3, 4 and 5 (125, 250, 1250 ppm). However, the observation was not reproduced after 13 weeks and the values remained within the range of reference values. An influence of the treatment was therefore considered to be unlikely. Other minimal deviations occurred without any relation to the dose administered. Also these findings were therefore not attributed to the treatment.

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Blood chemistry (means) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Gluc (mmol/l)					
week: -1	5.673	5.955	6.075*	5.713	5.865
7	5.700	5.710	6.293*	5.528	5.933
13	5.820	5.655	5.888	5.570	5.525
Urea (mmol/l)					
week: -1	3.270	3.093	3.328	3.388	4.060
7	3.483	3.213	3.323	3.648	3.480
13	3.945	3.625	3.710	4.120	3.968
Creat-e (umol/l)					
week: -1	66.05	69.60	73.83	67.53	75.33*
7	64.18	71.88*	76.03 +	67.93	73.50
13	73.90	77.90	74.90	72.60	77.25
Bili-tot (umol/l)					
week: -1	1.858	2.380	2.500*	2.380	2.020
7	2.385	2.753	2.935*	2.875	2.508
13	2.693	2.938	2.938	2.998	2.878
Prot (g/l)					
week: -1	54.24	55.35	54.59	52.75	54.47
7	55.49	57.03	57.29	54.80	54.33
13	57.72	59.73	58.78	57.27	56.76
Alb (g/l)					
week: -1	31.18	30.93	31.82	29.85	30.68
7	31.48	32.21	33.17	31.78	30.83
13	32.88	32.98	34.28	32.55	32.27
Glob (g/l)					
week: -1	23.07	24.42	22.78	22.90	23.78
7	24.01	24.82	24.12	23.03	23.50
13	24.85	26.76	24.50	24.72	24.49

Blood chemistry (means) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
A/G (1)					
week: -1	1.358	1.275	1.403	1.310	1.290
7	1.315	1.298	1.380	1.380	1.315
13	1.330	1.240	1.403	1.320	1.320
Chol (mmol/l)					
week: -1	4.390	4.088	3.688	3.455*	3.390*-
7	4.578	3.880	3.866	3.475*	3.285*-
13	4.293	4.023	3.743	3.575	3.513*
Trigly (mmol/l)					
week: -1	0.430	0.423	0.494	0.343	0.363
7	0.408	0.320	0.303	0.315	0.308
13	0.293	0.261	0.298	0.273	0.275
Phos-Lip (mmol/l)					
week: -1	5.116	4.888	4.508	4.203*	4.048*-
7	5.090	4.535	4.571	4.168*	4.110*-
13	4.923	4.841	4.623	4.343	4.383
Na+ (mmol/l)					
week: -1	147.6	145.9	147.2	147.2	146.7
7	147.1	146.4	147.6	146.2	146.5
13	147.5	148.0	147.8	147.1	146.1
K+ (mmol/l)					
week: -1	4.595	4.880	4.815	4.485	4.720
7	4.580	4.445	4.655	4.578	4.653
13	4.735	4.835	4.720	4.560	4.580
Ca++ (mmol/l)					
week: -1	2.825	2.795	2.830	2.745*	2.743
7	2.933	2.940	2.955	2.833	2.845
13	2.783	2.753	2.773	2.665*	2.633*-

Blood chemistry (means) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Cl- (mmol/l)					
week: -1	109.7	109.9	108.8	110.8	109.6
7	108.1	107.7	107.7	109.7	110.2
13	113.4	113.2	111.8	114.5	113.4
PO4-in (mmol/l)					
week: -1	2.215	2.225	2.220	2.310	2.090
7	1.983	1.885	2.006	1.973	1.803*
13	1.668	1.625	1.725	1.830*	1.583
ASAT (GOT) (U/l)					
week: -1	18.79	24.06	21.13	19.73	21.13
7	23.03	24.70	25.30	24.98	21.13
13	20.95	20.98	23.00	21.45	19.88
ALAT (GPT) (U/l)					
week: -1	50.01	49.63	42.75	39.43	41.48
7	66.90	47.75	44.98	41.09	41.30
13	73.40	49.08	49.05	47.20	42.93
AlP (U/l)					
week: -1	92.65	107.0	126.4*	104.3	107.5
7	80.46	93.38	107.3	87.68	150.1*
13	65.00	76.98	84.58	79.23	135.2*+
GGT (U/l)					
week: -1	4.000	3.825	3.675	3.350	3.975
7	1.275	2.050	0.800	2.675	3.500
13	4.125	3.650	3.175	3.675	4.325
CK (U/l)					
week: -1	187.6	223.4	225.0	216.0	212.6
7	178.9	173.1	289.9	214.9	191.4
13	148.2	172.2	203.5*	181.5	170.1

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Blood chemistry (means) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Gluc (mmol/l)					
week: -1	5.743	5.370	6.003	5.875	5.500
7	5.875	5.660	6.268	5.728	5.788
13	5.505	5.463	5.858	5.570	5.310
Urea (mmol/l)					
week: -1	4.020	3.808	4.210	3.798	4.013
7	3.730	3.915	4.330	4.330	3.723
13	4.075	4.220	4.258	4.185	4.158
Creat-e (umol/l)					
week: -1	79.10	75.75	79.90	79.03	76.70
7	79.23	73.73	80.65	77.05	75.40
13	78.38	74.43	82.95	80.90	77.88
Bili-tot (umol/l)					
week: -1	2.440	2.618	2.260	2.345	2.530
7	2.755	2.755	2.693	2.755	2.570
13	2.755	3.490	3.245	3.120	2.570
Prot (g/l)					
week: -1	55.08	54.97	53.98	54.59	55.73
7	55.45	54.74	53.32	54.38	54.95
13	57.43	57.97	58.48	56.75	57.58
Alb (g/l)					
week: -1	32.27	33.31*	32.69	32.71	33.30*
7	32.43	33.20	32.91	33.02	32.81
13	33.24	34.25	34.52	33.96	33.43
Glob (g/l)					
week: -1	22.81	21.67	21.29	21.89	22.43
7	23.02	21.54	20.41*	21.37*	22.14
13	24.19	23.72	23.96	22.80	24.15

Blood chemistry (means) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
A/G (1)					
week: -1	1.420	1.545	1.535	1.498	1.488
7	1.413	1.575	1.613*	1.548*	1.490
13	1.380	1.448	1.443	1.493	1.390
Chol (mmol/l)					
week: -1	3.918	3.734	3.963	4.140	4.035
7	4.078	3.678	3.848	4.363	3.745
13	4.056	3.633	3.923	4.433	3.690
Trigly (mmol/l)					
week: -1	0.430	0.470	0.373	0.465	0.380
7	0.330	0.390	0.284	0.360	0.375
13	0.265	0.280	0.220	0.285	0.273
Phos-Lip (mmol/l)					
week: -1	4.563	4.616	4.508	4.698	4.843
7	4.688	4.438	4.430	5.003	4.635
13	4.699	4.480	4.608	5.023	4.633
Na+ (mmol/l)					
week: -1	147.6	148.5	148.8	148.0	149.2
7	145.3	145.5	147.5*	148.0*+	148.0*+
13	147.7	147.6	148.6	149.1	148.4
K+ (mmol/l)					
week: -1	4.304	4.368	4.318	4.388	4.415
7	4.178	4.329	4.098	4.223	4.055
13	4.045	4.228	4.078	4.075	3.998
Ca++ (mmol/l)					
week: -1	2.720	2.755	2.773*	2.780*	2.843*+
7	2.865	2.905	2.845	2.923	2.878
13	2.645	2.675	2.673	2.645	2.678

Blood chemistry (means) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Cl- (mmol/l)					
week: -1	110.8	110.3	110.1	111.0	110.9
7	111.1	109.2	108.4	108.1	109.2
13	114.7	113.4*	114.5	115.2	114.1
PO4-in (mmol/l)					
week: -1	1.918	1.990	2.048	2.083*	1.940
7	1.830	1.994	1.763	1.978	1.598*
13	1.425	1.600	1.505	1.525	1.533
ASAT (GOT) (U/l)					
week: -1	18.05	21.90	20.80	23.45	24.23*
7	17.80	24.70	19.73	23.15	21.63
13	17.54	24.55	18.25	18.65	20.50
ALAT (GPT) (U/l)					
week: -1	43.65	46.64	45.73	50.90	52.05
7	44.63	44.25	48.50	49.05	42.55
13	47.38	47.40	48.15	48.50	45.93
AlP (U/l)					
week: -1	82.55	106.8*	76.51	91.70	93.95*
7	78.33	89.38	64.80	90.65	173.0*+
13	64.10	70.83	59.43	76.90	165.9*+
GGT (U/l)					
week: -1	3.025	3.525	2.838	1.900	3.650*
7	1.425	0.625	1.875	1.600	3.425
13	2.700	2.850	2.225	3.475	2.700
CK (U/l)					
week: -1	189.0	208.6	215.2	242.0	264.7
7	125.4	194.5*	140.2	250.0	171.7
13	114.3	170.9*	124.8	136.7	130.6*

4.10. Urine analysis

Mean values are presented in the following tables. Individual values and their statistics are given in the Appendices A and B of this report. Reference values from previous studies are given in Appendix D.

Treatment had no influence on urine parameters investigated.

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Urine analysis (means) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Rel dens (1)					
week: -1	1.034	1.026	1.040	1.021	1.031
7	1.018	1.025	1.031	1.013	1.017
13	1.029	1.030	1.031	1.022	1.021
pH (1)					
week: -1	6.250	6.000	7.375	5.875	5.875
7	5.750	5.625	6.250	5.750	5.125
13	6.188	6.250	6.375	6.125	6.000

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Urine analysis (means) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Rel dens (1)					
week: -1	1.039	1.024	1.021	1.027	1.023
7	1.020	1.022	1.025	1.016	1.016
13	1.035	1.029	1.024	1.019*	1.029
pH (1)					
week: -1	6.375	6.250	6.125	6.938	7.000
7	5.875	6.375	6.500	6.250	6.750
13	6.500	6.625	7.667	7.750*	6.750

No statistical tests performed

Urine analysis (incidence) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Color (choice)					
week: -1	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4
13	0/4	0/4	0/4	0/4	0/4
Prot (score)					
week: -1	2/4	1/4	3/4	0/4	1/4
7	1/4	0/4	1/4	0/4	1/4
13	0/4	0/4	1/4	1/4	0/4
Gluc (score)					
week: -1	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4
13	0/4	0/4	0/4	0/4	0/4
Keto (score)					
week: -1	2/4	0/4	1/4	1/4	1/4
7	0/4	0/4	2/4	0/4	2/4
13	2/4	2/4	4/4	2/4	3/4
Bili (score)					
week: -1	1/4	0/4	0/4	1/4	0/4
7	1/4	2/4	1/4	0/4	1/4
13	3/4	3/4	2/4	1/4	1/4
Blood (score)					
week: -1	0/4	1/4	0/4	0/4	0/4
7	0/4	0/4	0/4	1/4	0/4
13	0/4	0/4	0/4	1/4	0/4
UBG (score)					
week: -1	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4
13	0/4	0/4	0/4	0/4	0/4

Urine analysis (incidence) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
RBC (score)					
week: 13	1/4	0/4	0/4	0/4	0/4
WBC (score)					
week: 7	1/4	0/4	0/4	1/4	0/4
13	0/4	1/4	1/4	1/4	0/4
Epi-squa (score)					
week: -1	3/4	3/4	1/4	3/4	0/4
13	1/4	0/4	0/4	0/4	0/4
Epi-tr (score)					
week: -1	2/4	1/4	1/4	3/4	3/4
7	1/4	2/4	4/4	4/4	1/4
13	3/4	4/4	4/4	3/4	3/4
Cst-Gran (score)					
week: 13	0/4	1/4	0/4	0/4	0/4
Cry-PO4 (score)					
week: -1	1/4	1/4	3/4	0/4	1/4
7	2/4	1/4	2/4	1/4	0/4
13	1/4	2/4	2/4	1/4	0/4
Cry-Caox (score)					
week: 13	1/4	0/4	0/4	0/4	0/4

No statistical tests performed

Urine analysis (incidence) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Color (choice)					
week: -1	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4
13	0/4	0/4	0/3	0/4	0/4
Prot (score)					
week: -1	2/4	0/4	1/4	2/4	1/4
7	1/4	1/4	1/4	0/4	0/4
13	3/4	2/4	1/3	2/4	1/4
Gluc (score)					
week: -1	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4
13	0/4	0/4	0/3	0/4	0/4
Keto (score)					
week: -1	3/4	1/4	2/4	2/4	2/4
7	4/4	4/4	2/4	2/4	3/4
13	4/4	4/4	1/3	0/4	3/4
Bili (score)					
week: -1	1/4	0/4	0/4	0/4	0/4
7	1/4	0/4	0/4	0/4	0/4
13	1/4	0/4	0/3	0/4	0/4
Blood (score)					
week: -1	0/4	0/4	0/4	0/4	1/4
7	0/4	0/4	1/4	1/4	0/4
13	2/4	3/4	1/3	1/4	1/4
UBG (score)					
week: -1	0/4	0/4	0/4	0/4	0/4
7	0/4	0/4	0/4	0/4	0/4
13	0/4	0/4	0/3	0/4	0/4

Urine analysis (incidence) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
RBC (score)					
week: 7	0/4	0/4	1/4	1/4	0/4
13	0/4	1/4	2/3	1/4	0/4
WBC (score)					
week: 7	1/4	0/4	1/4	0/4	0/4
13	2/4	3/4	0/3	0/4	1/4
Epi-squa (score)					
week: 7	0/4	0/4	1/4	1/4	0/4
Epi-tr (score)					
week: -1	2/4	1/4	2/4	1/4	2/4
7	1/4	2/4	2/4	2/4	1/4
13	3/4	3/4	3/3	2/4	4/4
Cry-PO4 (score)					
week: -1	3/4	0/4	1/4	1/4	2/4
7	1/4	3/4	2/4	0/4	2/4
13	0/4	1/4	2/3	1/4	2/4

4.11. Organ weights and ratios

Mean organ weights and ratios are presented in the following summary tables. Individual organ weights and ratios and their statistics are presented in Appendices A and B of this report.

Mean absolute and relative liver weights were increased in both sexes of group 5.

Mean thyroid to body weight ratio was increased for group 5 males (1250 ppm). However individual absolute weights were within the expected biological range and in the absence of any histopathological alterations, this deviation was not considered to be toxicologically relevant. Other organ weight changes reaching a level of statistical significance are not considered to be substance-related, either because they represent normal physiological variation or because of a lack in dose-relationship.

4.11.1. Organ weights (means)

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Organ weights (means): males week 14

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Body (kg)	10.31	10.44	10.89	10.78	10.36
Brain (g)	83.93	83.99	80.93	90.15*	80.87
Heart (g)	99.50	98.21	95.05	93.10	97.61
Liver (g)	325.4	343.6	349.4	336.5	407.1*+
Kidney (both) (g)	52.36	51.80	52.18	54.02	52.42
Adrenal (both) (g)	1.074	1.057	1.153	1.119	1.160
Thymus (g)	6.612	7.122	7.675	7.481	7.705
Testis (both) (g)	18.25	16.45	17.90	17.08	16.48
Spleen (g)	22.92	35.39*	31.07	38.36*	32.89
Thyroid gland (g)	0.778	0.866	0.956*	0.901	0.947

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Organ weights (means): females week 14

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Body (kg)	10.18	10.10	9.825	9.625	9.775
Brain (g)	83.32	83.40	81.74	81.36	82.54
Heart (g)	103.0	87.44*	91.16	95.25	92.72*
Liver (g)	302.9	288.8	297.5	293.7	387.3*
Kidney (both) (g)	48.86	48.18	40.67*	43.15	47.01
Adrenal (both) (g)	1.228	1.051*	1.255	1.181	1.217
Thymus (g)	9.680	7.465	9.256	8.584	7.168
Ovary (both) (g)	0.880	0.717	1.409	1.290	1.172
Spleen (g)	46.68	29.93	43.22	29.77	34.10
Thyroid gland (g)	0.770	0.897	0.741	0.757	0.766

4.11.2. Organ to body weight ratios (means)

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Organ to body weight ratios (means): males week 14

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Brain (o/oo)	8.146	8.055	7.440*	8.364	7.843
Heart (o/oo)	9.653	9.416	8.742	8.637*-	9.465
Liver (o/oo)	31.57	32.99	32.12	31.25	39.41*
Kidney (both) (o/oo)	5.080	4.979	4.793	5.014	5.062
Adrenal (both) (o/oo)	0.104	0.101	0.106	0.104	0.112
Thymus (o/oo)	0.645	0.678	0.704	0.690	0.754
Testis (both) (o/oo)	1.769	1.576	1.646	1.587	1.597
Spleen (o/oo)	2.221	3.380	2.840	3.591	3.121
Thyroid gland (o/oo)	0.076	0.083	0.088	0.084	0.091*

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Organ to body weight ratios (means): females week 14

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Brain (o/oo)	8.184	8.255	8.327	8.474	8.443
Heart (o/oo)	10.12	8.680*	9.273	9.939	9.496
Liver (o/oo)	29.77	28.55	30.36	30.45	39.72*+
Kidney (both) (o/oo)	4.813	4.782	4.151	4.496	4.815
Adrenal (both) (o/oo)	0.121	0.104	0.128	0.123	0.124
Thymus (o/oo)	0.946	0.737	0.941	0.873	0.729
Ovary (both) (o/oo)	0.087	0.072	0.141	0.130	0.119
Spleen (o/oo)	4.547	2.942	4.352	3.071	3.445
Thyroid gland (o/oo)	0.076	0.088	0.075	0.078	0.078

4.12. Pathology

The results and the tabulated summaries of the gross pathological and histopathological examination are presented below.

Detailed findings for individual animals are presented in Appendix B.

4.12.1. Macroscopical findings

Only a few macroscopical findings were observed in some control and treated animals. They were similar to those occurring spontaneously in our colony of dogs and their distribution among the groups did not indicate a relationship to treatment. Thus no toxicological relevance was attributed to these findings.

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Summary tables of macroscopical findings

(all observed findings)

SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Removal code : all Observation period : all

Selected experimental group(s): all

Selected animals: all

Selected findings : all

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Treatment ended in observation period, selected	4	4	4	4	4
Examined macroscopically					
S1	4	4	4	4	4
Total	4	4	4	4	4
Examined microscopically	4	4	4	4	4

Abbreviations used in pathology tables

S1, S2....	scheduled sacrifice(s)
MS	moribund sacrifice
FD	found dead
AD	accidental death

SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
SKIN					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
MAMMARY AREA					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SPLEEN					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
CERVICAL LYMPH NODE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
MESENTERIC LYMPH NODE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
POPLITEAL LYMPH NODE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
STERNUM WITH BONE MARROW					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
RIB WITH CARTILAGE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SKELETAL MUSCLE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
TRACHEA					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
LUNG					
NODULE (<.5 CM)					
S1	0	0	0	1	0
Total	0	0	0	1	0
MOTTLED					
S1	1	0	1	0	1
Total	1	0	1	0	1
NO CHANGES OBSERVED					
S1	3	4	3	3	3
Total	3	4	3	3	3
HEART					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
AORTA					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
SUBMANDIBULAR SALIVARY GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
LIVER					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
GALL BLADDER					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
PANCREAS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
OESOPHAGUS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
STOMACH					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SMALL INTESTINE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
LARGE INTESTINE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
KIDNEY					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
URINARY BLADDER					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
PROSTATE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
TESTIS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
EPIDIDYMIS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
PITUITARY GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
ADRENAL GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
THYROID WITH PARATHYROID GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
THYMUS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
PERIPHERAL NERVE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
BRAIN					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SPINAL CORD					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
EYE WITH OPTIC NERVE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
LACRIMAL GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES

Removal code : all Observation period : all

Selected experimental group(s): all

Selected animals: all

Selected findings : all

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Treatment ended in observation period, selected	4	4	4	4	4
Examined macroscopically					
S1	4	4	4	4	4
Total	4	4	4	4	4
Examined microscopically	4	4	4	4	4

Abbreviations used in pathology tables

S1, S2....	scheduled sacrifice(s)
MS	moribund sacrifice
FD	found dead
AD	accidental death

SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
SKIN					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
MAMMARY AREA					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SPLEEN					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
CERVICAL LYMPH NODE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
MESENTERIC LYMPH NODE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
POPLITEAL LYMPH NODE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
STERNUM WITH BONE MARROW					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
RIB WITH CARTILAGE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SKELETAL MUSCLE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
TRACHEA					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
LUNG					
MOTTLED					
S1	1	0	0	0	0
Total	1	0	0	0	0
NO CHANGES OBSERVED					
S1	3	4	4	4	4
Total	3	4	4	4	4
HEART					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
AORTA					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SUBMANDIBULAR SALIVARY GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
LIVER					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
GALL BLADDER					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
PANCREAS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
OESOPHAGUS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
STOMACH					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SMALL INTESTINE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
LARGE INTESTINE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
KIDNEY					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
URINARY BLADDER					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
VAGINA					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
UTERUS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
OVARY					
NO CHANGES OBSERVED					
S1	4	4	3	4	4
Total	4	4	3	4	4
CYST					
S1	0	0	1	0	0
Total	0	0	1	0	0
PITUITARY GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
ADRENAL GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
THYROID WITH PARATHYROID GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
THYMUS					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
PERIPHERAL NERVE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
BRAIN					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
SPINAL CORD					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
EYE WITH OPTIC NERVE					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4
LACRIMAL GLAND					
NO CHANGES OBSERVED					
S1	4	4	4	4	4
Total	4	4	4	4	4

4.12.2. Microscopical findings

A variety of different lesions found in this study commonly occurs in our colony of dogs and neither their morphological features, nor their distribution among the groups indicated a relationship to the treatment.

Summary tables of microscopical findings

(main diagnoses only)

SUMMARY OF MICROSCOPICAL FINDINGS IN MALES

Removal code : all Observation period : all

Selected experimental group(s): all

Selected animals: all

Selected findings : all

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Treatment ended in observation period, selected	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
Examined microscopically					
S1	4	4	4	4	4
Total	4	4	4	4	4

Abbreviations used in pathology tables

S1, S2....	scheduled sacrifice(s)
MS	moribund sacrifice
FD	found dead
AD	accidental death

SUMMARY OF MICROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined microscopically	4	4	4	4	4
SKIN					
INFLAMMATORY CELL INFILTRATION					
S1	1	0	0	0	0
Total	1	0	0	0	0
SKIN HAIR FOLLICLE					
PARASITIC GRANULOMA					
S1	0	0	0	1	1
Total	0	0	0	1	1
INFLAMMATORY CELL INFILTRATION					
S1	0	0	1	0	0
Total	0	0	1	0	0
LYMPHOCYTIC INFILTRATION					
S1	0	1	0	1	0
Total	0	1	0	1	0
BONE MARROW					
FATTY ATROPHY					
S1	4	4	4	4	4
Total	4	4	4	4	4
SPLEEN					
CONGESTION					
S1	2	3	2	2	3
Total	2	3	2	2	3
HAEMOSIDEROSIS					
S1	3	1	3	0	1
Total	3	1	3	0	1
SPLENIC WHITE PULP LYMPHATIC FOLLICLE					
HYPERPLASIA					
S1	1	0	0	0	0
Total	1	0	0	0	0

SUMMARY OF MICROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined microscopically	4	4	4	4	4
BRONCHUS					
FOREIGN BODY					
S1	0	0	1	0	0
Total	0	0	1	0	0
LUNG					
ACUTE BRONCHOPNEUMONIA					
S1	0	0	1	0	1
Total	0	0	1	0	1
FIBROSIS					
S1	0	0	0	1	0
Total	0	0	0	1	0
HAEMOSIDEROSIS					
S1	0	0	1	0	0
Total	0	0	1	0	0
LUNG BLOOD VESSEL					
DILATATION					
S1	1	0	0	0	0
Total	1	0	0	0	0
LIVER					
INFLAMMATORY CELL INFILTRATION					
S1	4	2	1	0	1
Total	4	2	1	0	1
FATTY CHANGE					
S1	1	1	1	0	1
Total	1	1	1	0	1
ORGANIZING NECROSIS					
S1	0	1	0	1	0
Total	0	1	0	1	0
DUODENAL MUCOSA					
CYSTIC DILATATION					
S1	0	0	0	1	0
Total	0	0	0	1	0

SUMMARY OF MICROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined microscopically	4	4	4	4	4
RENAL PAPILLA					
CALCIFICATION					
S1	4	4	4	4	4
Total	4	4	4	4	4
URINARY BLADDER					
INFLAMMATORY OEDEMA					
S1	0	0	1	0	0
Total	0	0	1	0	0
PROSTATE					
CHRONIC INFLAMMATION					
S1	0	1	1	0	0
Total	0	1	1	0	0
LYMPHOCYTIC INFILTRATION					
S1	0	1	0	0	0
Total	0	1	0	0	0
PROSTATIC GLANDULAR TISSUE					
ATROPHY					
S1	1	0	0	1	0
Total	1	0	0	1	0
TESTIS SPERMATOGENIC EPITHELIUM					
SPERMATIC GIANT CELL					
S1	0	0	0	1	0
Total	0	0	0	1	0
EPIDIDYMIS					
SPERMATIC GRANULOMA					
S1	0	0	0	0	1
Total	0	0	0	0	1
EPIDIDYMIS ARTERY					
POLYARTERITIS					
S1	0	0	0	1	0
Total	0	0	0	1	0

SUMMARY OF MICROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined microscopically	4	4	4	4	4
PITUITARY GLAND					
No exam. for technical reason	0	0	0	0	1
ADENOHYPOPHYSIS					
DEVELOPMENTAL CYST					
S1	0	1	1	1	0
Total	0	1	1	1	0
ADRENAL GLAND					
DEVELOPMENTAL MALFORMATION					
S1	0	0	1	0	0
Total	0	0	1	0	0
ADRENAL CORTEX					
FATTY CHANGE					
S1	0	0	1	0	1
Total	0	0	1	0	1
THYROID GLAND					
DEVELOPMENTAL CYST					
S1	0	0	1	0	1
Total	0	0	1	0	1
C-CELL OF THYROID					
HYPERPLASIA					
S1	0	2	0	0	0
Total	0	2	0	0	0
PARATHYROID GLAND					
DEVELOPMENTAL CYST					
S1	1	2	0	0	0
Total	1	2	0	0	0
THYMUS					
LYMPHOID HYPERPLASIA					
S1	1	0	0	0	0
Total	1	0	0	0	0

SUMMARY OF MICROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined microscopically	4	4	4	4	4
THYMIC MEDULLA					
HYPERPLASIA					
S1	0	1	0	1	0
Total	0	1	0	1	0
CHOROID PLEXUS					
INFLAMMATORY CELL INFILTRATION					
S1	1	0	0	1	0
Total	1	0	0	1	0
LYMPHOCYTIC INFILTRATION					
S1	1	0	0	0	0
Total	1	0	0	0	0

SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES

Removal code : all Observation period : all

Selected experimental group(s): all

Selected animals: all

Selected findings : all

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Treatment ended in observation period, selected	4	4	4	4	4
Examined macroscopically	4	4	4	4	4
Examined microscopically					
S1	4	4	4	4	4
Total	4	4	4	4	4

Abbreviations used in pathology tables

S1, S2....	scheduled sacrifice(s)
MS	moribund sacrifice
FD	found dead
AD	accidental death

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SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined microscopically	4	4	4	4	4
SKIN					
INFLAMMATORY CELL INFILTRATION					
S1	1	0	0	1	1
Total	1	0	0	1	1
EPIDERMIS					
ACANTHOSIS					
S1	1	0	0	0	1
Total	1	0	0	0	1
SKIN HAIR FOLLICLE					
CHRONIC INFLAMMATION					
S1	0	1	1	0	0
Total	0	1	1	0	0
PARASITIC GRANULOMA					
S1	0	1	0	0	0
Total	0	1	0	0	0
INFLAMMATORY CELL INFILTRATION					
S1	0	0	0	0	1
Total	0	0	0	0	1
BONE MARROW					
FATTY ATROPHY					
S1	4	4	4	4	4
Total	4	4	4	4	4
SPLEEN					
CONGESTION					
S1	3	1	2	1	1
Total	3	1	2	1	1
HAEMOSIDEROSIS					
S1	2	4	3	3	3
Total	2	4	3	3	3

SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES

Group		1	2	3	4	5
Exposure : ppm		0	50	125	250	1250
Animals initially in study		4	4	4	4	4
Examined microscopically		4	4	4	4	4
BRONCHUS						
FOREIGN BODY						
	S1	1	0	0	0	0
	Total	1	0	0	0	0
FOREIGN BODY GRANULOMA						
	S1	1	0	0	0	0
	Total	1	0	0	0	0
LUNG						
CHRONIC BRONCHOPNEUMONIA						
	S1	1	0	0	0	0
	Total	1	0	0	0	0
HEART ARTERY						
CHRONIC NECROTIZING INFLAMMATION						
	S1	1	0	0	0	0
	Total	1	0	0	0	0
LIVER						
INFLAMMATORY CELL INFILTRATION						
	S1	0	0	1	3	0
	Total	0	0	1	3	0
FATTY CHANGE						
	S1	1	1	2	2	2
	Total	1	1	2	2	2
RENAL PAPILLA						
INFLAMMATORY CELL INFILTRATION						
	S1	0	1	0	0	0
	Total	0	1	0	0	0
CALCIFICATION						
	S1	4	4	4	4	4
	Total	4	4	4	4	4

SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined microscopically	4	4	4	4	4
VAGINA					
LYMPHOCYTIC INFILTRATION					
S1	0	0	0	2	0
Total	0	0	0	2	0
OVARY					
CORPUS LUTEUM CYST					
S1	0	0	1	0	0
Total	0	0	1	0	0
OVARIAN FOLLICLE					
HYPERCELLULARITY					
S1	2	1	0	0	1
Total	2	1	0	0	1
ADENOHYPOPHYSIS					
DEVELOPMENTAL CYST					
S1	1	4	0	1	1
Total	1	4	0	1	1
ADRENAL CORTEX					
FATTY CHANGE					
S1	0	0	0	1	1
Total	0	0	0	1	1
THYROID GLAND					
DEVELOPMENTAL CYST					
S1	1	0	0	0	0
Total	1	0	0	0	0
C-CELL OF THYROID					
HYPERPLASIA					
S1	0	0	0	1	1
Total	0	0	0	1	1

SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Examined microscopically	4	4	4	4	4
PARATHYROID GLAND					
DEVELOPMENTAL CYST					
S1	0	2	1	0	0
Total	0	2	1	0	0
LACRIMAL GLAND					
One organ,no exam.tech.reasons	(0)	(1)	(1)	(0)	(0)

5. APPENDIX A: STATISTICAL DATA

5.1. Body weight (statistics)

Statistical tests and flags used:
* if p_W < 0.05
+- if p_J < 0.01

Body weight (statistics) : males
(kg/animal)

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	N	4	4	4	4	4
	Mean	9.850	9.525	9.925	10.08	9.575
	Median	9.950	9.550	10.00	10.20	9.150
	Min	8.700	9.100	9.100	9.500	8.900
	Max	10.80	9.900	10.60	10.40	11.10
	p_W		0.375	1.000	0.564	0.772
	p_J			0.942	0.427	0.921
week: 1	N	4	4	4	4	4
	Mean	9.950	9.675	10.20	10.30	9.650
	Median	10.10	9.650	10.30	10.40	9.250
	Min	8.800	9.300	9.400	9.900	8.900
	Max	10.80	10.10	10.80	10.50	11.20
	p_W		0.386	0.559	0.561	0.773
	p_J			0.510	0.191	0.842
week: 2	N	4	4	4	4	4
	Mean	10.00	9.700	10.18	10.38	9.775
	Median	10.15	9.650	10.20	10.45	9.450
	Min	9.000	9.400	9.400	9.900	8.900
	Max	10.70	10.10	10.90	10.70	11.30
	p_W		0.306	0.773	0.468	0.564
	p_J			0.884	0.283	0.974
week: 3	N	4	4	4	4	4
	Mean	10.18	9.875	10.40	10.55	9.975
	Median	10.35	9.850	10.45	10.50	9.600
	Min	9.200	9.500	9.600	10.30	9.200
	Max	10.80	10.30	11.10	10.90	11.50
	p_W		0.309	0.773	0.554	0.663
	p_J			0.770	0.243	0.894
week: 4	N	4	4	4	4	4
	Mean	10.38	10.05	10.55	10.73	10.15
	Median	10.55	10.00	10.60	10.65	9.800
	Min	9.400	9.800	9.700	10.40	9.400
	Max	11.00	10.40	11.30	11.20	11.60
	p_W		0.306	0.663	0.468	0.663
	p_J			0.826	0.243	0.894

Body weight (statistics) : males
(kg/animal)

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	5 N	4	4	4	4	4
	Mean	10.50	10.35	10.83	10.95	10.38
	Median	10.65	10.35	10.75	10.90	9.950
	Min	9.600	10.10	10.10	10.70	9.700
	Max	11.10	10.60	11.70	11.30	11.90
	p_W		0.309	0.663	0.191	0.773
	p_J			0.942	0.191	0.894
week:	6 N	4	4	4	4	4
	Mean	10.58	10.43	10.90	11.10	10.50
	Median	10.75	10.40	10.85	11.10	10.10
	Min	9.700	10.20	10.20	10.70	9.900
	Max	11.10	10.70	11.70	11.50	11.90
	p_W		0.306	0.564	0.180	0.773
	p_J			0.826	0.176	0.842
week:	7 N	4	4	4	4	4
	Mean	10.70	10.55	10.98	11.15	10.58
	Median	10.80	10.50	10.95	11.00	10.20
	Min	9.900	10.30	10.30	10.90	9.900
	Max	11.30	10.90	11.70	11.70	12.00
	p_W		0.468	0.564	0.189	0.663
	p_J			0.770	0.148	0.842
week:	8 N	4	4	4	4	4
	Mean	10.80	10.68	11.13	11.33	10.73
	Median	10.95	10.60	11.10	11.30	10.35
	Min	10.00	10.50	10.40	11.00	10.10
	Max	11.30	11.00	11.90	11.70	12.10
	p_W		0.465	0.564	0.102	0.773
	p_J			0.714	0.123	0.790
week:	9 N	4	4	4	4	4
	Mean	10.88	10.83	11.25	11.48	10.83
	Median	11.05	10.75	11.15	11.45	10.40
	Min	10.20	10.60	10.60	11.10	10.30
	Max	11.20	11.20	12.10	11.90	12.20
	p_W		0.663	0.564	0.080	0.772
	p_J			0.714	0.112	0.790

Body weight (statistics) : males
(kg/animal)

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 10 N	4	4	4	4	4
Mean	10.93	10.90	11.35	11.45	10.90
Median	11.10	10.80	11.30	11.45	10.50
Min	10.20	10.70	10.70	11.00	10.20
Max	11.30	11.30	12.10	11.90	12.40
p_W		0.659	0.561	0.189	0.661
p_J			0.608	0.148	0.894
week: 11 N	4	4	4	4	4
Mean	11.00	10.98	11.45	11.48	10.98
Median	11.15	10.90	11.40	11.50	10.50
Min	10.30	10.70	10.80	10.90	10.40
Max	11.40	11.40	12.20	12.00	12.50
p_W		0.661	0.564	0.191	0.772
p_J			0.608	0.191	0.947
week: 12 N	4	4	4	4	4
Mean	10.95	11.05	11.50	11.40	10.90
Median	11.00	10.95	11.40	11.45	10.40
Min	10.50	10.80	10.90	10.90	10.30
Max	11.30	11.50	12.30	11.80	12.50
p_W		1.000	0.559	0.245	0.243
p_J			0.464	0.243	0.816
week: 13 N	4	4	4	4	4
Mean	11.03	11.03	11.45	11.50	10.93
Median	11.00	10.90	11.40	11.50	10.50
Min	10.60	10.80	10.80	10.90	10.30
Max	11.50	11.50	12.20	12.10	12.40
p_W		0.882	0.468	0.191	0.245
p_J			0.510	0.176	0.921

Statistical tests and flags used:
* if p_W < 0.05
+- if p_J < 0.01

Body weight (statistics) : females
(kg/animal)

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1 N	4	4	4	4	4
Mean	10.00	9.950	9.800	9.525	9.725
Median	10.15	9.800	9.650	9.450	9.700
Min	9.200	9.700	8.800	8.700	8.900
Max	10.50	10.50	11.10	10.50	10.60
p_W		0.661	0.773	0.309	0.564
p_J			0.608	0.327	0.388
week: 1 N	4	4	4	4	4
Mean	10.18	10.10	9.950	9.575	9.825
Median	10.30	10.10	9.800	9.450	9.800
Min	9.400	9.500	9.000	8.800	9.000
Max	10.70	10.70	11.20	10.60	10.70
p_W		0.770	0.663	0.248	0.468
p_J			0.608	0.191	0.245
week: 2 N	4	4	4	4	4
Mean	10.10	10.10	9.900	9.650	9.825
Median	10.30	10.00	9.750	9.600	9.800
Min	9.300	9.700	9.100	8.800	9.000
Max	10.50	10.70	11.00	10.60	10.70
p_W		0.773	0.661	0.468	0.561
p_J			0.608	0.304	0.319
week: 3 N	4	4	4	4	4
Mean	10.25	10.23	10.00	9.800	9.950
Median	10.45	10.15	9.850	9.800	9.950
Min	9.500	9.800	9.100	8.900	9.200
Max	10.60	10.80	11.20	10.70	10.70
p_W		0.773	0.468	0.468	0.564
p_J			0.510	0.327	0.335
week: 4 N	4	4	4	4	4
Mean	10.33	10.33	10.18	9.900	10.00
Median	10.50	10.25	10.00	9.800	10.00
Min	9.500	9.900	9.300	9.100	9.300
Max	10.80	10.90	11.40	10.90	10.70
p_W		0.772	0.772	0.384	0.381
p_J			0.661	0.350	0.273

Body weight (statistics) : females
(kg/animal)

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	5 N	4	4	4	4	4
	Mean	10.50	10.50	10.25	10.10	10.25
	Median	10.65	10.45	10.10	10.15	10.25
	Min	9.700	10.20	9.300	9.200	9.400
	Max	11.00	10.90	11.50	10.90	11.10
	p_W		0.884	0.468	0.468	0.564
	p_J			0.464	0.350	0.425
week:	6 N	4	4	4	4	4
	Mean	10.63	10.48	10.28	10.15	10.30
	Median	10.75	10.35	10.15	10.20	10.30
	Min	9.900	10.10	9.300	9.200	9.600
	Max	11.10	11.10	11.50	11.00	11.00
	p_W		0.663	0.386	0.468	0.384
	p_J			0.421	0.304	0.319
week:	7 N	4	4	4	4	4
	Mean	10.68	10.63	10.33	10.23	10.30
	Median	10.85	10.55	10.25	10.25	10.25
	Min	9.900	10.20	9.300	9.300	9.600
	Max	11.10	11.20	11.50	11.10	11.10
	p_W		1.000	0.468	0.468	0.468
	p_J			0.510	0.375	0.352
week:	8 N	4	4	4	4	4
	Mean	10.73	10.75	10.35	10.33	10.30
	Median	10.90	10.65	10.30	10.40	10.30
	Min	10.00	10.30	9.300	9.400	9.600
	Max	11.10	11.40	11.50	11.10	11.00
	p_W		1.000	0.465	0.375	0.245
	p_J			0.510	0.350	0.232
week:	9 N	4	4	4	4	4
	Mean	10.83	10.78	10.43	10.40	10.40
	Median	10.95	10.75	10.45	10.50	10.40
	Min	10.20	10.30	9.300	9.400	9.600
	Max	11.20	11.30	11.50	11.20	11.20
	p_W		0.766	0.561	0.538	0.372
	p_J			0.661	0.455	0.406

Body weight (statistics) : females
(kg/animal)

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 10 N	4	4	4	4	4
Mean	10.80	10.78	10.33	10.35	10.33
Median	10.90	10.75	10.40	10.45	10.25
Min	10.20	10.20	9.100	9.400	9.600
Max	11.20	11.40	11.40	11.10	11.20
p_W		1.000	0.564	0.375	0.381
p_J			0.510	0.327	0.288
week: 11 N	4	4	4	4	4
Mean	10.85	10.78	10.38	10.40	10.40
Median	11.00	10.75	10.45	10.45	10.35
Min	10.20	10.20	9.100	9.500	9.700
Max	11.20	11.40	11.50	11.20	11.20
p_W		0.884	0.561	0.375	0.297
p_J			0.510	0.350	0.303
week: 12 N	4	4	4	4	4
Mean	10.85	10.83	10.53	10.40	10.38
Median	10.95	10.80	10.65	10.45	10.40
Min	10.20	10.30	9.200	9.500	9.600
Max	11.30	11.40	11.60	11.20	11.10
p_W		0.773	0.770	0.468	0.243
p_J			0.770	0.427	0.232
week: 13 N	4	4	4	4	4
Mean	10.88	10.78	10.53	10.40	10.35
Median	10.95	10.80	10.65	10.40	10.40
Min	10.20	10.20	9.300	9.400	9.600
Max	11.40	11.30	11.50	11.40	11.00
p_W		0.885	0.770	0.468	0.191
p_J			0.661	0.427	0.219

5.2. Food consumption (statistics)

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Food consumption (statistics) : males
(g/animal/day)

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week: 1	N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week: 2	N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week: 3	N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week: 4	N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000

Food consumption (statistics) : males
(g/animal/day)

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	5 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week:	6 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week:	7 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week:	8 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week:	9 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week:	10 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000

Food consumption (statistics) : males
(g/animal/day)

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 11 N	4	4	4	4	4
Mean	350.0	350.0	350.0	350.0	350.0
Median	350.0	350.0	350.0	350.0	350.0
Min	350.0	350.0	350.0	350.0	350.0
Max	350.0	350.0	350.0	350.0	350.0
p_W		1.000	1.000	1.000	1.000
p_J			1.000	1.000	1.000
week: 12 N	4	4	4	4	4
Mean	350.0	350.0	350.0	350.0	350.0
Median	350.0	350.0	350.0	350.0	350.0
Min	350.0	350.0	350.0	350.0	350.0
Max	350.0	350.0	350.0	350.0	350.0
p_W		1.000	1.000	1.000	1.000
p_J			1.000	1.000	1.000
week: 13 N	4	4	4	4	4
Mean	350.0	350.0	350.0	350.0	350.0
Median	350.0	350.0	350.0	350.0	350.0
Min	350.0	350.0	350.0	350.0	350.0
Max	350.0	350.0	350.0	350.0	350.0
p_W		1.000	1.000	1.000	1.000
p_J			1.000	1.000	1.000

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Food consumption (statistics) : females
(g/animal/day)

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: -1	N	4	4	4	4	4
	Mean	350.0	350.0	348.9	346.4	350.0
	Median	350.0	350.0	350.0	347.1	350.0
	Min	350.0	350.0	345.7	341.4	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	0.317	0.131	1.000
	p_J			0.558	0.161	0.550
week: 1	N	4	4	4	4	4
	Mean	350.0	350.0	350.0	342.9	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	321.4	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	0.317	1.000
	p_J			1.000	0.575	0.790
week: 2	N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week: 3	N	4	4	4	4	4
	Mean	350.0	350.0	349.3	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	347.1	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	0.317	1.000	1.000
	p_J			0.558	0.852	1.000
week: 4	N	4	4	4	4	4
	Mean	350.0	350.0	346.8	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	337.1	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	0.317	1.000	1.000
	p_J			0.558	0.852	1.000

Food consumption (statistics) : females
(g/animal/day)

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	5 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week:	6 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	348.9	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	345.7	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	0.317	1.000
	p_J			1.000	0.575	0.790
week:	7 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week:	8 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000
week:	9 N	4	4	4	4	4
	Mean	350.0	350.0	341.8	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	317.1	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	0.317	1.000	1.000
	p_J			0.558	0.852	1.000
week:	10 N	4	4	4	4	4
	Mean	350.0	350.0	350.0	350.0	350.0
	Median	350.0	350.0	350.0	350.0	350.0
	Min	350.0	350.0	350.0	350.0	350.0
	Max	350.0	350.0	350.0	350.0	350.0
	p_W		1.000	1.000	1.000	1.000
	p_J			1.000	1.000	1.000

Food consumption (statistics) : females
(g/animal/day)

Dose(ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 11 N	4	4	4	4	4
Mean	350.0	350.0	350.0	350.0	350.0
Median	350.0	350.0	350.0	350.0	350.0
Min	350.0	350.0	350.0	350.0	350.0
Max	350.0	350.0	350.0	350.0	350.0
p_W		1.000	1.000	1.000	1.000
p_J			1.000	1.000	1.000
week: 12 N	4	4	4	4	4
Mean	350.0	350.0	350.0	350.0	350.0
Median	350.0	350.0	350.0	350.0	350.0
Min	350.0	350.0	350.0	350.0	350.0
Max	350.0	350.0	350.0	350.0	350.0
p_W		1.000	1.000	1.000	1.000
p_J			1.000	1.000	1.000
week: 13 N	4	4	4	4	4
Mean	350.0	350.0	350.0	350.0	350.0
Median	350.0	350.0	350.0	350.0	350.0
Min	350.0	350.0	350.0	350.0	350.0
Max	350.0	350.0	350.0	350.0	350.0
p_W		1.000	1.000	1.000	1.000
p_J			1.000	1.000	1.000

5.3. Hematology (statistics)

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
RBC (T/l)					
week: -1 N	4	4	4	4	4
Mean	6.193	6.178	6.273	5.633	5.743
Median	6.120	6.165	6.285	5.635	5.785
Min	5.930	6.090	5.860	5.320	5.430
Max	6.600	6.290	6.660	5.940	5.970
p_W		0.773	0.773	0.043 *	0.083
p_J			0.558	0.093	0.020
week: 7 N	4	4	4	4	4
Mean	6.321	6.445	6.460	6.005	5.973
Median	6.313	6.450	6.435	5.945	5.875
Min	6.160	6.140	6.170	5.760	5.530
Max	6.500	6.740	6.800	6.370	6.610
p_W		0.564	0.386	0.149	0.248
p_J			0.421	0.207	0.058
week: 13 N	4	4	4	4	4
Mean	6.423	6.483	6.408	6.110	6.063
Median	6.395	6.430	6.405	6.060	6.050
Min	5.990	6.160	6.160	5.920	5.700
Max	6.910	6.910	6.660	6.400	6.450
p_W		0.885	1.000	0.248	0.149
p_J			1.000	0.135	0.028
Hb (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	8.775	8.750	9.025	7.925	8.125
Median	8.750	8.750	9.100	7.900	8.150
Min	8.400	8.700	8.400	7.500	7.800
Max	9.200	8.800	9.500	8.400	8.400
p_W		1.000	0.381	0.029 *	0.029 *
p_J			0.306	0.135	0.014

Hematology (statistics) : males

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	8.850	9.075	9.175	8.425	8.375
	Median	8.800	9.000	9.050	8.500	8.200
	Min	8.700	8.500	9.000	7.800	7.800
	Max	9.100	9.800	9.600	8.900	9.300
	p_W		0.559	0.106	0.180	0.245
	p_J			0.164	0.401	0.119
week: 13	N	4	4	4	4	4
	Mean	9.000	9.200	9.125	8.500	8.550
	Median	9.000	9.250	9.150	8.650	8.450
	Min	8.700	8.700	8.800	7.800	8.200
	Max	9.300	9.600	9.400	8.900	9.100
	p_W		0.557	0.468	0.080	0.110
	p_J			0.608	0.148	0.024
Hct (1)						
week: -1	N	4	4	4	4	4
	Mean	0.410	0.415	0.430	0.374	0.387
	Median	0.409	0.415	0.436	0.375	0.389
	Min	0.392	0.411	0.398	0.357	0.371
	Max	0.431	0.421	0.451	0.391	0.400
	p_W		0.386	0.248	0.021 *	0.059
	p_J			0.107	0.225	0.043
week: 7	N	4	4	4	4	4
	Mean	0.424	0.437	0.441	0.403	0.406
	Median	0.424	0.438	0.435	0.405	0.399
	Min	0.417	0.410	0.429	0.380	0.381
	Max	0.432	0.464	0.465	0.423	0.447
	p_W		0.248	0.083	0.083	0.248
	p_J			0.124	0.375	0.144
week: 13	N	4	4	4	4	4
	Mean	0.422	0.429	0.426	0.399	0.402
	Median	0.418	0.429	0.426	0.407	0.400
	Min	0.406	0.407	0.404	0.369	0.383
	Max	0.447	0.450	0.447	0.412	0.424
	p_W		0.564	0.885	0.149	0.083
	p_J			0.826	0.176	0.028

Hematology (statistics) : males

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
MCV (fl)						
week: -1	N	4	4	4	4	4
	Mean	66.20	67.15	68.50	66.45	67.40
	Median	65.65	67.10	67.70	66.40	67.30
	Min	65.30	66.40	67.30	63.60	66.70
	Max	68.20	68.00	71.30	69.40	68.30
	p_W		0.248	0.149	0.663	0.149
	p_J			0.057	0.484	0.370
week: 7	N	4	4	4	4	4
	Mean	67.15	67.83	68.30	67.15	68.05
	Median	66.40	67.85	68.10	67.40	67.95
	Min	65.60	66.80	67.10	64.40	67.40
	Max	70.20	68.80	69.90	69.40	68.90
	p_W		0.386	0.248	1.000	0.248
	p_J			0.213	0.608	0.425
week: 13	N	4	4	4	4	4
	Mean	65.83	66.18	66.40	65.23	66.28
	Median	65.15	66.00	66.30	65.40	66.10
	Min	64.30	65.20	65.00	62.30	65.70
	Max	68.70	67.50	68.00	67.80	67.20
	p_W		0.386	0.564	0.564	0.248
	p_J			0.464	0.926	0.690
RDW (1)						
week: -1	N	4	4	4	4	4
	Mean	0.144	0.139	0.145	0.146	0.146
	Median	0.142	0.138	0.145	0.145	0.145
	Min	0.139	0.132	0.143	0.141	0.137
	Max	0.153	0.147	0.147	0.154	0.155
	p_W		0.309	0.384	0.386	0.773
	p_J			0.558	0.283	0.245
week: 7	N	4	4	4	4	4
	Mean	0.136	0.132	0.133	0.138	0.137
	Median	0.137	0.131	0.134	0.136	0.137
	Min	0.129	0.129	0.129	0.131	0.133
	Max	0.142	0.137	0.135	0.148	0.141
	p_W		0.237	0.189	0.772	1.000
	p_J			0.341	0.963	0.445

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250	
week: 13 N	4	4	4	4	4	
Mean	0.134	0.129	0.131	0.134	0.137	
Median	0.135	0.130	0.133	0.133	0.136	
Min	0.129	0.125	0.127	0.129	0.134	
Max	0.138	0.132	0.133	0.140	0.140	
p_W		0.144	0.465	0.885	0.306	
p_J			0.661	0.815	0.104	
MCH (fmol)						
week: -1 N	4	4	4	4	4	
Mean	1.423	1.418	1.438	1.413	1.418	
Median	1.405	1.415	1.435	1.420	1.420	
Min	1.390	1.390	1.430	1.350	1.400	
Max	1.490	1.450	1.450	1.460	1.430	
p_W		0.770	0.245	0.772	0.557	
p_J			0.164	0.484	0.790	
week: 7 N	4	4	4	4	4	
Mean	1.403	1.410	1.423	1.403	1.403	
Median	1.380	1.400	1.410	1.420	1.405	
Min	1.370	1.390	1.410	1.320	1.380	
Max	1.480	1.450	1.460	1.450	1.420	
p_W		0.243	0.234	0.772	0.375	
p_J			0.057	0.243	0.486	
week: 13 N	4	4	4	4	4	
Mean	1.405	1.418	1.423	1.390	1.410	
Median	1.395	1.410	1.410	1.405	1.410	
Min	1.350	1.380	1.410	1.320	1.390	
Max	1.480	1.470	1.460	1.430	1.430	
p_W		0.655	0.442	1.000	0.554	
p_J			0.464	0.852	0.842	
MCHC (mmol/l)						
week: -1 N	4	4	4	4	4	
Mean	21.48	21.09	20.98	21.25	21.03	
Median	21.43	21.09	21.13	21.18	21.04	
Min	21.21	20.75	20.28	21.09	20.92	
Max	21.86	21.45	21.39	21.56	21.12	
p_W		0.149	0.083	0.248	0.021	*
p_J			0.079	0.262	0.036	

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Hematology (statistics) : males

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	20.86	20.76	20.84	20.90	20.57
	Median	20.89	20.74	20.84	20.95	20.63
	Min	20.60	20.51	20.67	20.55	20.14
	Max	21.06	21.05	21.00	21.16	20.90
	p_W		0.386	0.773	0.773	0.149
	p_J			0.770	0.709	0.406
week: 13	N	4	4	4	4	4
	Mean	21.35	21.44	21.44	21.31	21.31
	Median	21.47	21.39	21.51	21.19	21.33
	Min	20.90	21.24	21.09	21.06	21.14
	Max	21.58	21.75	21.66	21.79	21.45
	p_W		0.772	0.564	0.773	0.309
	p_J			0.770	0.674	0.425
HDW (mmol/l)						
week: -1	N	4	4	4	4	4
	Mean	1.108	1.048	1.083	1.055	1.175
	Median	1.085	1.050	1.090	1.060	1.110
	Min	1.010	0.970	0.990	0.990	1.080
	Max	1.250	1.120	1.160	1.110	1.400
	p_W		0.309	0.885	0.564	0.564
	p_J			0.884	0.674	0.507
week: 7	N	4	4	4	4	4
	Mean	1.184	1.158	1.145	1.223	1.140
	Median	1.203	1.160	1.135	1.215	1.140
	Min	1.110	1.100	1.050	1.160	1.080
	Max	1.220	1.210	1.260	1.300	1.200
	p_W		0.306	0.564	0.564	0.248
	p_J			0.421	0.575	0.715
week: 13	N	4	4	4	4	4
	Mean	1.130	1.093	1.140	1.100	1.070
	Median	1.130	1.100	1.145	1.095	1.090
	Min	1.060	1.040	1.100	1.030	0.990
	Max	1.200	1.130	1.170	1.180	1.110
	p_W		0.309	0.884	0.386	0.149
	p_J			0.826	0.641	0.163

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Reti (1)					
week: -1 N	4	4	4	4	4
Mean	0.022	0.025	0.028	0.020	0.022
Median	0.025	0.027	0.028	0.020	0.023
Min	0.015	0.019	0.020	0.014	0.016
Max	0.025	0.028	0.034	0.024	0.026
p_W		0.146	0.146	0.189	0.559
p_J			0.048	0.779	0.618
week: 7 N	4	4	4	4	4
Mean	0.018	0.019	0.019	0.020	0.019
Median	0.019	0.020	0.017	0.020	0.019
Min	0.015	0.016	0.014	0.016	0.014
Max	0.021	0.021	0.027	0.024	0.023
p_W		0.642	0.884	0.457	1.000
p_J			0.826	0.641	0.842
week: 13 N	4	4	4	4	4
Mean	0.019	0.018	0.019	0.016	0.017
Median	0.019	0.019	0.018	0.014	0.018
Min	0.016	0.014	0.013	0.011	0.013
Max	0.023	0.021	0.027	0.025	0.018
p_W		0.770	0.884	0.306	0.137
p_J			0.714	0.243	0.232
WBC (G/l)					
week: -1 N	4	4	4	4	4
Mean	10.59	10.80	10.64	9.965	9.883
Median	10.82	10.93	10.63	9.805	10.20
Min	8.870	8.570	10.15	8.830	7.730
Max	11.86	12.79	11.16	11.42	11.41
p_W		0.773	0.773	0.564	0.386
p_J			1.000	0.513	0.303
week: 7 N	4	4	4	4	4
Mean	10.85	10.79	12.41	12.15	10.64
Median	10.75	10.87	12.43	11.08	10.59
Min	10.07	9.980	11.31	9.740	9.120
Max	11.83	11.45	13.46	16.72	12.27
p_W		1.000	0.043 *	0.773	0.773
p_J			0.040	0.225	0.894

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	9.670	10.45	11.16	10.04	9.173
Median	9.300	10.41	11.12	10.32	9.465
Min	7.870	9.110	9.610	7.730	7.770
Max	12.21	11.89	12.80	11.78	9.990
p_W		0.564	0.248	1.000	0.564
p_J			0.188	0.641	0.507
Neut (1)					
week: -1 N	4	4	4	4	4
Mean	0.572	0.537	0.491	0.514	0.503
Median	0.567	0.558	0.489	0.522	0.488
Min	0.532	0.443	0.454	0.444	0.470
Max	0.622	0.588	0.531	0.569	0.567
p_W		0.386	0.021 *	0.248	0.083
p_J			0.028	0.076	0.063
week: 7 N	4	4	4	4	4
Mean	0.571	0.533	0.559	0.564	0.537
Median	0.582	0.561	0.572	0.544	0.539
Min	0.475	0.421	0.510	0.517	0.516
Max	0.646	0.590	0.580	0.650	0.555
p_W		0.386	0.248	0.773	0.248
p_J			0.421	0.427	0.195
week: 13 N	4	4	4	4	4
Mean	0.569	0.560	0.577	0.558	0.541
Median	0.571	0.563	0.587	0.558	0.537
Min	0.467	0.472	0.488	0.525	0.508
Max	0.666	0.641	0.647	0.591	0.583
p_W		0.773	1.000	0.564	0.564
p_J			0.884	0.641	0.319
Eos (1)					
week: -1 N	4	4	4	4	4
Mean	0.027	0.022	0.033	0.027	0.026
Median	0.029	0.020	0.031	0.029	0.026
Min	0.018	0.017	0.020	0.014	0.015
Max	0.034	0.030	0.048	0.036	0.038
p_W		0.146	0.564	0.772	0.773
p_J			0.714	0.674	0.868

Hematology (statistics) : males

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	0.026	0.025	0.028	0.032	0.024
	Median	0.029	0.026	0.029	0.016	0.023
	Min	0.016	0.022	0.015	0.013	0.017
	Max	0.031	0.027	0.039	0.083	0.032
	p_W		0.245	0.773	0.309	0.773
	p_J			0.770	0.262	0.335
week: 13	N	4	4	4	4	4
	Mean	0.022	0.022	0.022	0.017	0.016
	Median	0.020	0.020	0.023	0.017	0.016
	Min	0.017	0.018	0.009	0.014	0.011
	Max	0.029	0.028	0.033	0.022	0.023
	p_W		0.885	0.885	0.306	0.191
	p_J			0.884	0.455	0.153
Baso (1)						
week: -1	N	4	4	4	4	4
	Mean	0.005	0.006	0.006	0.005	0.005
	Median	0.005	0.005	0.005	0.005	0.005
	Min	0.004	0.004	0.003	0.003	0.004
	Max	0.006	0.009	0.012	0.006	0.006
	p_W		1.000	1.000	0.752	0.752
	p_J			0.884	0.709	0.715
week: 7	N	4	4	4	4	4
	Mean	0.003	0.005	0.005	0.003	0.004
	Median	0.003	0.004	0.004	0.003	0.003
	Min	0.002	0.003	0.003	0.002	0.002
	Max	0.004	0.007	0.007	0.004	0.006
	p_W		0.375	0.180	0.765	0.882
	p_J			0.242	0.852	0.550
week: 13	N	4	4	4	4	4
	Mean	0.004	0.004	0.004	0.004	0.003
	Median	0.004	0.004	0.004	0.004	0.003
	Min	0.003	0.003	0.003	0.002	0.002
	Max	0.005	0.004	0.005	0.005	0.004
	p_W		0.874	0.647	1.000	0.278
	p_J			0.608	0.744	0.425

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Lympho (1)					
week: -1 N	4	4	4	4	4
Mean	0.343	0.375	0.421	0.395	0.397
Median	0.352	0.358	0.413	0.384	0.424
Min	0.273	0.325	0.365	0.343	0.313
Max	0.393	0.461	0.493	0.468	0.429
p_W		0.564	0.083	0.248	0.149
p_J			0.079	0.135	0.153
week: 7 N	4	4	4	4	4
Mean	0.347	0.375	0.352	0.337	0.364
Median	0.343	0.357	0.335	0.348	0.362
Min	0.271	0.321	0.319	0.269	0.323
Max	0.431	0.464	0.420	0.383	0.409
p_W		0.564	0.564	0.773	0.773
p_J			0.661	0.575	0.974
week: 13 N	4	4	4	4	4
Mean	0.347	0.350	0.332	0.353	0.377
Median	0.351	0.357	0.307	0.352	0.377
Min	0.256	0.270	0.270	0.327	0.334
Max	0.431	0.417	0.445	0.380	0.422
p_W		0.773	0.773	0.885	0.564
p_J			0.826	0.779	0.288
Mono (1)					
week: -1 N	4	4	4	4	4
Mean	0.049	0.056	0.044	0.054	0.064
Median	0.045	0.054	0.048	0.054	0.062
Min	0.038	0.046	0.026	0.046	0.053
Max	0.068	0.070	0.055	0.062	0.079
p_W		0.248	0.772	0.384	0.149
p_J			0.884	0.674	0.111
week: 7 N	4	4	4	4	4
Mean	0.050	0.058	0.054	0.060	0.068
Median	0.049	0.057	0.054	0.061	0.074
Min	0.046	0.044	0.047	0.045	0.040
Max	0.055	0.076	0.059	0.074	0.086
p_W		0.248	0.248	0.248	0.248
p_J			0.272	0.102	0.043

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	0.050	0.059	0.057	0.061	0.054
Median	0.047	0.065	0.052	0.061	0.052
Min	0.040	0.034	0.044	0.052	0.047
Max	0.068	0.071	0.081	0.069	0.066
p_W		0.564	0.245	0.149	0.468
p_J			0.464	0.283	0.642
Luc (1)					
week: -1 N	4	4	4	4	4
Mean	0.005	0.005	0.005	0.005	0.005
Median	0.004	0.005	0.005	0.006	0.005
Min	0.003	0.003	0.003	0.002	0.004
Max	0.007	0.007	0.008	0.007	0.006
p_W		0.765	0.655	0.661	0.372
p_J			0.714	0.674	0.618
week: 7 N	4	4	4	4	4
Mean	0.003	0.004	0.004	0.005	0.004
Median	0.003	0.004	0.004	0.005	0.004
Min	0.002	0.002	0.001	0.003	0.003
Max	0.004	0.006	0.006	0.006	0.005
p_W		0.559	0.770	0.144	0.372
p_J			0.770	0.304	0.388
week: 13 N	4	4	4	4	4
Mean	0.009	0.007	0.008	0.008	0.008
Median	0.009	0.008	0.009	0.008	0.008
Min	0.006	0.005	0.003	0.007	0.006
Max	0.011	0.008	0.011	0.009	0.008
p_W		0.237	0.883	0.655	0.353
p_J			0.826	0.926	0.666
Neut (G/l)					
week: -1 N	4	4	4	4	4
Mean	6.093	5.803	5.223	5.135	5.005
Median	6.105	5.945	5.335	5.130	4.885
Min	4.780	4.360	4.610	4.040	3.780
Max	7.380	6.960	5.610	6.240	6.470
p_W		0.773	0.248	0.248	0.248
p_J			0.380	0.207	0.090

Hematology (statistics) : males

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	7 N	4	4	4	4	4
	Mean	6.183	5.783	6.928	6.983	5.725
	Median	6.315	6.180	6.810	5.885	5.690
	Min	5.200	4.200	6.350	5.290	4.710
	Max	6.900	6.570	7.740	10.87	6.810
	p_W		0.564	0.149	1.000	0.386
	p_J			0.188	0.641	0.690
week:	13 N	4	4	4	4	4
	Mean	5.605	5.908	6.468	5.588	4.963
	Median	5.310	5.855	6.065	5.580	5.130
	Min	3.670	4.300	5.450	4.570	4.190
	Max	8.130	7.620	8.290	6.620	5.400
	p_W		0.773	0.386	0.773	0.773
	p_J			0.464	0.779	0.370
Eos (G/l)						
week:	-1 N	4	4	4	4	4
	Mean	0.290	0.243	0.353	0.268	0.265
	Median	0.295	0.215	0.345	0.250	0.275
	Min	0.190	0.150	0.210	0.150	0.120
	Max	0.380	0.390	0.510	0.420	0.390
	p_W		0.564	0.386	0.770	1.000
	p_J			0.510	1.000	0.894
week:	7 N	4	4	4	4	4
	Mean	0.280	0.273	0.340	0.343	0.253
	Median	0.295	0.270	0.345	0.195	0.245
	Min	0.190	0.240	0.190	0.170	0.190
	Max	0.340	0.310	0.480	0.810	0.330
	p_W		0.465	0.309	0.384	0.663
	p_J			0.464	0.641	0.550
week:	13 N	4	4	4	4	4
	Mean	0.208	0.218	0.238	0.180	0.148
	Median	0.210	0.215	0.265	0.175	0.140
	Min	0.140	0.190	0.100	0.110	0.100
	Max	0.270	0.250	0.320	0.260	0.210
	p_W		0.885	0.564	0.386	0.191
	p_J			0.464	0.852	0.163

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Baso (G/l)					
week: -1 N	4	4	4	4	4
Mean	0.053	0.058	0.065	0.050	0.048
Median	0.050	0.050	0.050	0.055	0.040
Min	0.040	0.040	0.030	0.030	0.040
Max	0.070	0.090	0.130	0.060	0.070
p_W		0.877	0.883	1.000	0.350
p_J			0.884	0.852	0.550
week: 7 N	4	4	4	4	4
Mean	0.036	0.048	0.058	0.038	0.035
Median	0.033	0.045	0.050	0.035	0.025
Min	0.030	0.030	0.040	0.020	0.020
Max	0.050	0.070	0.090	0.060	0.070
p_W		0.297	0.080	1.000	0.372
p_J			0.092	0.709	0.528
week: 13 N	4	4	4	4	4
Mean	0.038	0.038	0.043	0.035	0.028
Median	0.035	0.040	0.040	0.030	0.025
Min	0.030	0.030	0.030	0.020	0.020
Max	0.050	0.040	0.060	0.060	0.040
p_W		0.874	0.544	0.659	0.178
p_J			0.558	0.889	0.232
Lympho (G/l)					
week: -1 N	4	4	4	4	4
Mean	3.585	4.033	4.470	3.925	3.883
Median	3.500	4.220	4.510	4.115	3.940
Min	3.240	2.930	3.850	3.030	3.300
Max	4.100	4.760	5.010	4.440	4.350
p_W		0.386	0.043 *	0.386	0.386
p_J			0.057	0.262	0.550
week: 7 N	4	4	4	4	4
Mean	3.780	4.023	4.370	4.005	3.865
Median	3.835	3.945	4.240	4.190	3.840
Min	2.730	3.570	3.760	3.140	3.330
Max	4.720	4.630	5.240	4.500	4.450
p_W		0.663	0.386	0.773	1.000
p_J			0.272	0.544	0.921

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	3.263	3.608	3.695	3.550	3.465
Median	3.260	3.650	3.410	3.775	3.410
Min	2.940	3.210	2.920	2.530	2.960
Max	3.590	3.920	5.040	4.120	4.080
p_W		0.149	0.773	0.386	0.564
p_J			0.558	0.350	0.550
Mono (G/l)					
week: -1 N	4	4	4	4	4
Mean	0.523	0.610	0.480	0.543	0.638
Median	0.465	0.605	0.515	0.525	0.585
Min	0.350	0.390	0.270	0.410	0.470
Max	0.810	0.840	0.620	0.710	0.910
p_W		0.386	0.885	0.773	0.248
p_J			0.942	0.963	0.528
week: 7 N	4	4	4	4	4
Mean	0.544	0.623	0.665	0.735	0.720
Median	0.538	0.615	0.680	0.740	0.780
Min	0.490	0.500	0.530	0.430	0.430
Max	0.610	0.760	0.770	1.030	0.890
p_W		0.110	0.083	0.248	0.248
p_J			0.034	0.028	0.034
week: 13 N	4	4	4	4	4
Mean	0.478	0.605	0.628	0.600	0.500
Median	0.515	0.660	0.625	0.625	0.460
Min	0.340	0.360	0.480	0.450	0.420
Max	0.540	0.740	0.780	0.700	0.660
p_W		0.149	0.149	0.149	0.773
p_J			0.143	0.262	0.947
Luc (G/l)					
week: -1 N	4	4	4	4	4
Mean	0.045	0.055	0.053	0.048	0.050
Median	0.035	0.060	0.045	0.055	0.055
Min	0.030	0.020	0.030	0.020	0.030
Max	0.080	0.080	0.090	0.060	0.060
p_W		0.661	0.457	0.770	0.552
p_J			0.608	0.779	0.740

Hematology (statistics) : males

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	0.031	0.043	0.040	0.053	0.043
	Median	0.033	0.045	0.040	0.055	0.040
	Min	0.020	0.020	0.010	0.040	0.030
	Max	0.040	0.060	0.070	0.060	0.060
	p_W		0.557	0.375	0.028 *	0.375
	p_J			0.464	0.102	0.259
week: 13	N	4	4	4	4	4
	Mean	0.080	0.073	0.090	0.083	0.068
	Median	0.075	0.075	0.105	0.085	0.065
	Min	0.060	0.050	0.040	0.050	0.060
	Max	0.110	0.090	0.110	0.110	0.080
	p_W		0.661	0.552	1.000	0.538
	p_J			0.510	0.641	0.666
Plt (G/l)						
week: -1	N	4	4	4	4	4
	Mean	287.0	270.5	303.3	263.5	294.8
	Median	273.0	280.5	307.5	273.0	312.0
	Min	241.0	194.0	248.0	216.0	225.0
	Max	361.0	327.0	350.0	292.0	330.0
	p_W		0.564	0.773	0.564	0.773
	p_J			0.770	0.674	0.921
week: 7	N	4	4	4	4	4
	Mean	313.5	293.5	313.5	303.8	331.0
	Median	331.0	292.5	324.5	322.0	342.5
	Min	214.0	200.0	242.0	172.0	249.0
	Max	378.0	389.0	363.0	399.0	390.0
	p_W		0.564	1.000	0.773	0.663
	p_J			1.000	0.926	0.572
week: 13	N	4	4	4	4	4
	Mean	287.8	293.3	286.5	289.0	326.0
	Median	267.5	303.0	289.5	284.0	338.0
	Min	226.0	204.0	268.0	231.0	257.0
	Max	390.0	363.0	299.0	357.0	371.0
	p_W		1.000	0.564	1.000	0.386
	p_J			0.770	0.852	0.288

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
PT(CS) (sec)					
week: -1 N	4	4	4	4	4
Mean	30.52	31.11	33.34	34.53	33.99
Median	30.56	30.79	33.12	34.62	34.39
Min	26.72	27.61	28.96	30.67	32.09
Max	34.23	35.27	38.17	38.21	35.10
p_W		0.564	0.386	0.149	0.149
p_J			0.242	0.062	0.054
week: 7 N	4	4	4	4	4
Mean	31.39	32.92	35.36	35.07	34.54
Median	32.11	31.73	37.04	33.93	34.64
Min	27.46	29.94	28.54	33.29	32.18
Max	33.90	38.29	38.83	39.11	36.69
p_W		0.773	0.149	0.248	0.149
p_J			0.188	0.112	0.111
week: 13 N	4	4	4	4	4
Mean	29.34	32.10	33.15	34.17	33.38
Median	29.51	31.16	33.45	33.76	33.47
Min	27.17	29.20	27.94	30.43	32.48
Max	31.20	36.89	37.76	38.75	34.12
p_W		0.149	0.248	0.043 *	0.021 *
p_J			0.143	0.050	0.028

Statistical tests and flags used:
* if p_W < 0.05
+- if p_J < 0.01

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
RBC (T/l)					
week: -1 N	4	4	4	4	4
Mean	6.683	6.755	6.614	6.745	6.785
Median	6.625	6.690	6.678	6.800	6.810
Min	6.260	6.080	6.290	6.370	6.520
Max	7.220	7.560	6.810	7.010	7.000
p_W		0.885	0.773	0.773	0.663
p_J			0.826	0.744	0.595
week: 7 N	4	4	4	4	4
Mean	7.058	7.100	6.708	7.035	6.785
Median	7.105	7.070	6.710	7.080	6.790
Min	6.610	6.460	6.480	6.580	6.470
Max	7.410	7.800	6.930	7.400	7.090
p_W		1.000	0.083	0.663	0.149
p_J			0.242	0.744	0.425
week: 13 N	4	4	4	4	4
Mean	6.665	6.893	6.570	6.830	6.610
Median	6.650	6.760	6.560	6.825	6.560
Min	6.260	6.250	6.470	6.710	6.240
Max	7.100	7.800	6.690	6.960	7.080
p_W		0.885	0.772	0.564	0.564
p_J			0.510	0.484	0.868
Hb (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	9.400	9.538	9.400	9.550	9.375
Median	9.350	9.350	9.600	9.550	9.300
Min	8.400	8.800	8.600	9.000	9.000
Max	10.50	10.65	9.800	10.10	9.900
p_W		0.773	1.000	0.663	0.884
p_J			0.942	0.709	0.842
week: 7 N	4	4	4	4	4
Mean	9.825	9.975	9.475	9.825	9.325
Median	9.650	9.900	9.550	9.850	9.200
Min	9.300	9.200	8.800	9.500	9.100
Max	10.70	10.90	10.00	10.10	9.800
p_W		0.773	0.663	0.663	0.108
p_J			0.608	0.889	0.245

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	9.425	9.775	9.400	9.700	9.325
Median	9.250	9.550	9.400	9.800	9.100
Min	8.700	9.000	9.000	9.300	8.900
Max	10.50	11.00	9.800	9.900	10.20
p_W		0.468	0.770	0.384	0.885
p_J			0.770	0.304	0.974
Hct (1)					
week: -1 N	4	4	4	4	4
Mean	0.448	0.459	0.448	0.453	0.452
Median	0.445	0.450	0.458	0.457	0.448
Min	0.407	0.420	0.408	0.425	0.438
Max	0.495	0.516	0.467	0.474	0.474
p_W		0.773	1.000	0.773	0.773
p_J			0.884	0.852	0.842
week: 7 N	4	4	4	4	4
Mean	0.472	0.477	0.449	0.472	0.448
Median	0.464	0.476	0.454	0.474	0.446
Min	0.452	0.438	0.420	0.457	0.434
Max	0.510	0.517	0.470	0.484	0.468
p_W		0.773	0.248	0.468	0.083
p_J			0.306	0.963	0.245
week: 13 N	4	4	4	4	4
Mean	0.443	0.455	0.435	0.453	0.436
Median	0.439	0.446	0.438	0.455	0.426
Min	0.408	0.416	0.413	0.437	0.419
Max	0.486	0.513	0.450	0.463	0.474
p_W		0.564	1.000	0.386	0.564
p_J			0.884	0.455	0.947
MCV (fl)					
week: -1 N	4	4	4	4	4
Mean	66.98	67.95	67.64	67.24	66.50
Median	67.15	67.75	68.15	68.05	67.60
Min	65.10	67.20	64.80	62.95	63.10
Max	68.50	69.10	69.45	69.90	67.70
p_W		0.386	0.564	0.773	0.772
p_J			0.421	0.544	0.868

Hematology (statistics) : females

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	66.93	67.20	66.93	67.23	66.13
	Median	67.05	67.35	67.20	67.75	66.40
	Min	64.70	66.30	64.40	63.90	63.50
	Max	68.90	67.80	68.90	69.50	68.20
	p_W		1.000	0.885	0.561	0.564
	p_J			0.942	0.815	0.642
week: 13	N	4	4	4	4	4
	Mean	66.48	66.10	66.18	66.25	66.05
	Median	67.00	66.10	66.35	66.35	66.65
	Min	63.10	65.60	63.80	63.60	63.70
	Max	68.80	66.60	68.20	68.70	67.20
	p_W		1.000	0.564	0.773	0.773
	p_J			0.770	0.852	0.816
RDW (1)						
week: -1	N	4	4	4	4	4
	Mean	0.140	0.147	0.142	0.143	0.147
	Median	0.138	0.145	0.142	0.143	0.144
	Min	0.135	0.140	0.140	0.137	0.139
	Max	0.150	0.157	0.145	0.148	0.161
	p_W		0.149	0.245	0.386	0.191
	p_J			0.421	0.513	0.370
week: 7	N	4	4	4	4	4
	Mean	0.135	0.136	0.133	0.136	0.138
	Median	0.135	0.135	0.135	0.135	0.136
	Min	0.131	0.133	0.122	0.130	0.130
	Max	0.140	0.141	0.140	0.142	0.149
	p_W		0.770	0.884	1.000	1.000
	p_J			0.826	0.963	0.842
week: 13	N	4	4	4	4	4
	Mean	0.130	0.135	0.133	0.134	0.136
	Median	0.129	0.135	0.132	0.133	0.137
	Min	0.127	0.133	0.130	0.130	0.127
	Max	0.136	0.137	0.137	0.138	0.142
	p_W		0.146	0.237	0.191	0.309
	p_J			0.421	0.427	0.232

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
MCH (fmol)					
week: -1 N	4	4	4	4	4
Mean	1.405	1.411	1.423	1.418	1.383
Median	1.410	1.398	1.430	1.425	1.400
Min	1.350	1.390	1.370	1.330	1.310
Max	1.450	1.460	1.460	1.490	1.420
p_W		1.000	0.468	0.773	0.468
p_J			0.558	0.544	0.790
week: 7 N	4	4	4	4	4
Mean	1.393	1.403	1.410	1.400	1.373
Median	1.395	1.410	1.420	1.410	1.390
Min	1.330	1.370	1.350	1.330	1.310
Max	1.450	1.420	1.450	1.450	1.400
p_W		0.882	0.663	0.770	0.561
p_J			0.608	0.674	0.595
week: 13 N	4	4	4	4	4
Mean	1.413	1.420	1.433	1.420	1.408
Median	1.415	1.420	1.440	1.420	1.405
Min	1.340	1.390	1.390	1.360	1.380
Max	1.480	1.450	1.460	1.480	1.440
p_W		0.885	0.772	0.885	0.773
p_J			0.558	0.779	0.690
MCHC (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	20.97	20.83	21.01	21.07	20.76
Median	20.99	20.72	21.01	21.17	20.76
Min	20.68	20.66	20.89	20.71	20.55
Max	21.20	21.21	21.11	21.24	20.97
p_W		0.564	1.000	0.386	0.191
p_J			0.770	0.243	0.690
week: 7 N	4	4	4	4	4
Mean	20.79	20.89	21.08	20.82	20.72
Median	20.84	21.02	21.03	20.82	20.73
Min	20.50	20.44	20.95	20.76	20.52
Max	20.98	21.08	21.33	20.86	20.90
p_W		0.248	0.043 *	0.773	0.564
p_J			0.079	0.926	0.319

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	21.26	21.47	21.65	21.46	21.33
Median	21.27	21.50	21.74	21.47	21.34
Min	20.84	21.18	21.35	21.28	20.98
Max	21.66	21.70	21.76	21.63	21.66
p_W		0.386	0.043 *	0.386	0.885
p_J			0.028	0.262	0.921
HDW (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	1.103	1.104	1.064	1.069	1.098
Median	1.105	1.103	1.053	1.073	1.065
Min	1.020	1.020	1.010	1.010	1.000
Max	1.180	1.190	1.140	1.120	1.260
p_W		0.885	0.564	0.564	0.564
p_J			0.510	0.401	0.406
week: 7 N	4	4	4	4	4
Mean	1.165	1.185	1.128	1.143	1.118
Median	1.170	1.190	1.125	1.145	1.080
Min	1.100	1.140	1.040	1.080	1.060
Max	1.220	1.220	1.220	1.200	1.250
p_W		0.663	0.661	0.559	0.248
p_J			0.770	0.455	0.259
week: 13 N	4	4	4	4	4
Mean	1.090	1.110	1.090	1.090	1.100
Median	1.080	1.115	1.090	1.095	1.100
Min	1.060	1.060	1.060	1.050	0.950
Max	1.140	1.150	1.120	1.120	1.250
p_W		0.465	0.659	1.000	1.000
p_J			0.942	0.779	0.842
Reti (1)					
week: -1 N	4	4	4	4	4
Mean	0.021	0.023	0.023	0.019	0.022
Median	0.022	0.025	0.025	0.019	0.023
Min	0.015	0.013	0.015	0.015	0.017
Max	0.026	0.028	0.027	0.024	0.025
p_W		0.561	0.559	0.381	0.885
p_J			0.558	0.544	0.618

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Hematology (statistics) : females

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	0.021	0.020	0.017	0.016	0.020
	Median	0.020	0.019	0.014	0.017	0.018
	Min	0.018	0.013	0.013	0.011	0.016
	Max	0.024	0.028	0.028	0.018	0.027
	p_W		0.772	0.243	0.028 *	0.552
	p_J			0.272	0.123	0.445
week: 13	N	4	4	4	4	4
	Mean	0.017	0.016	0.016	0.015	0.015
	Median	0.017	0.014	0.016	0.017	0.016
	Min	0.013	0.011	0.010	0.009	0.011
	Max	0.019	0.024	0.020	0.018	0.018
	p_W		0.559	0.884	0.462	0.384
	p_J			0.826	0.744	0.618
WBC (G/l)						
week: -1	N	4	4	4	4	4
	Mean	9.613	13.06	9.445	9.834	10.51
	Median	9.630	11.72	9.010	10.05	10.40
	Min	8.780	8.490	8.600	8.030	9.250
	Max	10.41	20.33	11.16	11.21	11.98
	p_W		0.248	0.564	0.773	0.564
	p_J			0.770	0.709	0.790
week: 7	N	4	4	4	4	4
	Mean	12.26	11.24	9.238	9.283	11.07
	Median	11.45	12.14	8.960	8.915	11.14
	Min	9.110	7.410	7.700	7.050	10.14
	Max	17.05	13.28	11.33	12.25	11.86
	p_W		0.773	0.059	0.191	0.564
	p_J			0.164	0.093	0.319
week: 13	N	4	4	4	4	4
	Mean	10.86	10.56	9.308	9.230	10.70
	Median	10.08	11.15	8.055	7.550	11.16
	Min	9.000	7.310	7.810	7.240	8.750
	Max	14.28	12.63	13.31	14.58	11.73
	p_W		0.773	0.149	0.248	0.773
	p_J			0.464	0.161	0.690

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Neut (1)					
week: -1 N	4	4	4	4	4
Mean	0.524	0.616	0.544	0.524	0.569
Median	0.527	0.580	0.535	0.543	0.560
Min	0.471	0.550	0.521	0.421	0.524
Max	0.571	0.756	0.583	0.589	0.632
p_W		0.083	0.468	1.000	0.248
p_J			0.714	0.815	0.690
week: 7 N	4	4	4	4	4
Mean	0.565	0.611	0.569	0.521	0.607
Median	0.526	0.626	0.570	0.509	0.614
Min	0.504	0.548	0.538	0.483	0.536
Max	0.702	0.643	0.598	0.585	0.665
p_W		0.248	0.248	0.386	0.386
p_J			0.661	0.262	0.947
week: 13 N	4	4	4	4	4
Mean	0.599	0.625	0.589	0.580	0.612
Median	0.587	0.634	0.591	0.599	0.620
Min	0.552	0.566	0.517	0.491	0.563
Max	0.669	0.666	0.655	0.633	0.645
p_W		0.386	0.773	0.885	0.663
p_J			0.884	0.544	0.790
Eos (1)					
week: -1 N	4	4	4	4	4
Mean	0.030	0.019	0.025	0.033	0.031
Median	0.030	0.020	0.021	0.036	0.027
Min	0.025	0.007	0.013	0.018	0.018
Max	0.037	0.030	0.044	0.043	0.051
p_W		0.245	0.561	0.561	0.770
p_J			0.608	0.513	0.388
week: 7 N	4	4	4	4	4
Mean	0.027	0.021	0.024	0.052	0.027
Median	0.027	0.018	0.027	0.049	0.026
Min	0.017	0.013	0.010	0.022	0.011
Max	0.037	0.035	0.033	0.086	0.045
p_W		0.248	0.663	0.149	1.000
p_J			0.510	0.243	0.528

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	0.022	0.018	0.020	0.030	0.029
Median	0.022	0.018	0.016	0.029	0.024
Min	0.011	0.010	0.010	0.012	0.017
Max	0.032	0.024	0.040	0.050	0.051
p_W		0.468	0.564	0.386	0.773
p_J			0.464	0.709	0.406
Baso (1)					
week: -1 N	4	4	4	4	4
Mean	0.006	0.005	0.005	0.005	0.006
Median	0.005	0.004	0.005	0.005	0.007
Min	0.005	0.002	0.004	0.004	0.003
Max	0.008	0.008	0.006	0.006	0.008
p_W		0.353	0.508	0.278	0.655
p_J			0.661	0.575	0.690
week: 7 N	4	4	4	4	4
Mean	0.005	0.006	0.004	0.005	0.004
Median	0.005	0.005	0.004	0.005	0.004
Min	0.004	0.003	0.003	0.004	0.002
Max	0.007	0.012	0.004	0.006	0.006
p_W		0.655	0.036 *	0.877	0.234
p_J			0.067	0.674	0.425
week: 13 N	4	4	4	4	4
Mean	0.005	0.005	0.004	0.004	0.004
Median	0.004	0.004	0.004	0.004	0.004
Min	0.003	0.003	0.003	0.003	0.003
Max	0.007	0.009	0.005	0.004	0.005
p_W		0.762	0.544	0.617	0.877
p_J			0.608	0.709	0.974
Lympho (1)					
week: -1 N	4	4	4	4	4
Mean	0.395	0.302	0.377	0.391	0.345
Median	0.384	0.340	0.378	0.358	0.358
Min	0.352	0.149	0.364	0.325	0.272
Max	0.459	0.381	0.390	0.524	0.391
p_W		0.149	1.000	0.564	0.386
p_J			0.884	0.926	0.595

Hematology (statistics) : females

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	0.353	0.323	0.356	0.366	0.316
	Median	0.395	0.317	0.343	0.362	0.298
	Min	0.207	0.291	0.335	0.294	0.259
	Max	0.414	0.366	0.402	0.448	0.407
	p_W		0.248	0.384	1.000	0.386
	p_J			0.770	0.926	0.445
week: 13	N	4	4	4	4	4
	Mean	0.325	0.305	0.336	0.335	0.307
	Median	0.338	0.293	0.338	0.323	0.293
	Min	0.246	0.266	0.285	0.284	0.266
	Max	0.379	0.369	0.384	0.411	0.375
	p_W		0.564	0.773	1.000	0.564
	p_J			0.661	0.513	0.947
Mono (1)						
week: -1	N	4	4	4	4	4
	Mean	0.042	0.054	0.046	0.043	0.045
	Median	0.041	0.050	0.046	0.043	0.042
	Min	0.037	0.033	0.033	0.028	0.034
	Max	0.051	0.084	0.057	0.056	0.061
	p_W		0.561	0.773	0.885	0.773
	p_J			0.826	0.709	0.642
week: 7	N	4	4	4	4	4
	Mean	0.046	0.036	0.046	0.054	0.044
	Median	0.044	0.037	0.045	0.058	0.043
	Min	0.038	0.031	0.030	0.040	0.029
	Max	0.060	0.039	0.062	0.059	0.061
	p_W		0.059	0.773	0.561	0.773
	p_J			0.826	0.327	0.690
week: 13	N	4	4	4	4	4
	Mean	0.043	0.040	0.044	0.046	0.043
	Median	0.040	0.040	0.043	0.048	0.044
	Min	0.037	0.036	0.039	0.035	0.031
	Max	0.055	0.045	0.052	0.053	0.055
	p_W		0.772	0.561	0.772	0.661
	p_J			0.510	0.375	0.618

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Luc (1)					
week: -1 N	4	4	4	4	4
Mean	0.004	0.004	0.004	0.005	0.005
Median	0.004	0.005	0.004	0.005	0.005
Min	0.003	0.002	0.004	0.003	0.003
Max	0.005	0.006	0.005	0.006	0.006
p_W		0.557	0.765	0.544	0.343
p_J			0.714	0.575	0.388
week: 7 N	4	4	4	4	4
Mean	0.004	0.004	0.003	0.003	0.003
Median	0.004	0.004	0.003	0.003	0.003
Min	0.003	0.002	0.002	0.002	0.002
Max	0.006	0.007	0.004	0.003	0.004
p_W		0.882	0.137	0.098	0.137
p_J			0.188	0.123	0.090
week: 13 N	4	4	4	4	4
Mean	0.007	0.007	0.007	0.005	0.006
Median	0.008	0.008	0.007	0.006	0.006
Min	0.006	0.005	0.005	0.004	0.004
Max	0.008	0.008	0.010	0.006	0.008
p_W		0.877	0.766	0.037 *	0.225
p_J			0.826	0.112	0.127
Neut (G/l)					
week: -1 N	4	4	4	4	4
Mean	5.043	8.399	5.154	5.103	5.945
Median	5.275	6.780	4.715	5.055	5.945
Min	4.130	4.680	4.680	4.490	5.110
Max	5.490	15.36	6.505	5.810	6.780
p_W		0.149	0.773	0.564	0.149
p_J			0.942	0.544	0.666
week: 7 N	4	4	4	4	4
Mean	7.143	6.948	5.280	4.773	6.708
Median	5.960	7.600	5.105	4.530	6.725
Min	4.690	4.060	4.140	4.120	5.920
Max	11.96	8.530	6.770	5.910	7.460
p_W		0.773	0.386	0.083	0.386
p_J			0.380	0.076	0.690

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	6.588	6.653	5.563	5.400	6.520
Median	5.860	7.335	4.650	4.455	6.765
Min	5.070	4.140	4.230	3.780	5.520
Max	9.560	7.800	8.720	8.910	7.030
p_W		0.773	0.149	0.149	0.564
p_J			0.464	0.225	0.642
Eos (G/l)					
week: -1 N	4	4	4	4	4
Mean	0.293	0.226	0.228	0.315	0.318
Median	0.280	0.233	0.200	0.340	0.315
Min	0.220	0.080	0.110	0.190	0.170
Max	0.390	0.360	0.400	0.390	0.470
p_W		0.564	0.564	0.663	1.000
p_J			0.661	0.674	0.370
week: 7 N	4	4	4	4	4
Mean	0.335	0.215	0.213	0.450	0.295
Median	0.380	0.220	0.220	0.390	0.295
Min	0.160	0.160	0.120	0.270	0.130
Max	0.420	0.260	0.290	0.750	0.460
p_W		0.189	0.149	0.772	0.773
p_J			0.188	0.513	0.642
week: 13 N	4	4	4	4	4
Mean	0.245	0.193	0.178	0.243	0.313
Median	0.210	0.200	0.140	0.225	0.270
Min	0.100	0.070	0.100	0.150	0.160
Max	0.460	0.300	0.330	0.370	0.550
p_W		0.663	0.465	1.000	0.564
p_J			0.464	0.852	0.303
Baso (G/l)					
week: -1 N	4	4	4	4	4
Mean	0.058	0.053	0.045	0.048	0.065
Median	0.050	0.055	0.040	0.045	0.065
Min	0.050	0.040	0.040	0.040	0.040
Max	0.080	0.060	0.060	0.060	0.090
p_W		0.877	0.129	0.278	0.554
p_J			0.188	0.207	0.921

Hematology (statistics) : females

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	0.063	0.058	0.030	0.045	0.043
	Median	0.060	0.050	0.030	0.045	0.040
	Min	0.050	0.040	0.020	0.030	0.020
	Max	0.080	0.090	0.040	0.060	0.070
	p_W		0.538	0.019 *	0.139	0.106
	p_J			0.010	0.069	0.078
week: 13	N	4	4	4	4	4
	Mean	0.045	0.053	0.038	0.035	0.043
	Median	0.045	0.050	0.040	0.030	0.045
	Min	0.020	0.040	0.030	0.020	0.030
	Max	0.070	0.070	0.040	0.060	0.050
	p_W		0.655	0.442	0.465	0.882
	p_J			0.380	0.112	0.335
Lympho (G/l)						
week: -1	N	4	4	4	4	4
	Mean	3.778	3.558	3.559	3.908	3.663
	Median	3.845	3.340	3.455	3.700	3.805
	Min	3.390	3.030	3.250	2.640	2.520
	Max	4.030	4.520	4.075	5.590	4.520
	p_W		0.386	0.386	1.000	1.000
	p_J			0.558	0.709	0.816
week: 7	N	4	4	4	4	4
	Mean	4.085	3.565	3.263	3.503	3.498
	Median	4.030	3.830	3.105	3.225	3.330
	Min	3.520	2.720	2.960	2.070	2.830
	Max	4.760	3.880	3.880	5.490	4.500
	p_W		0.564	0.083	0.386	0.248
	p_J			0.164	0.148	0.173
week: 13	N	4	4	4	4	4
	Mean	3.435	3.160	3.063	3.095	3.300
	Median	3.460	3.045	3.035	2.745	3.145
	Min	3.200	2.700	2.380	2.060	2.510
	Max	3.620	3.850	3.800	4.830	4.400
	p_W		0.386	0.248	0.248	0.564
	p_J			0.242	0.161	0.388

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Mono (G/l)					
week: -1 N	4	4	4	4	4
Mean	0.413	0.770	0.424	0.418	0.470
Median	0.395	0.495	0.413	0.375	0.490
Min	0.330	0.390	0.360	0.300	0.320
Max	0.530	1.700	0.510	0.620	0.580
p_W		0.191	1.000	0.773	0.564
p_J			0.942	0.544	0.894
week: 7 N	4	4	4	4	4
Mean	0.593	0.408	0.425	0.485	0.490
Median	0.475	0.450	0.455	0.495	0.495
Min	0.390	0.230	0.230	0.420	0.290
Max	1.030	0.500	0.560	0.530	0.680
p_W		0.468	0.564	1.000	0.564
p_J			0.608	0.889	0.816
week: 13 N	4	4	4	4	4
Mean	0.465	0.430	0.408	0.405	0.458
Median	0.465	0.455	0.390	0.390	0.440
Min	0.330	0.280	0.300	0.320	0.330
Max	0.600	0.530	0.550	0.520	0.620
p_W		0.564	0.468	0.561	0.885
p_J			0.510	0.455	0.921
Luc (G/l)					
week: -1 N	4	4	4	4	4
Mean	0.040	0.055	0.041	0.046	0.050
Median	0.035	0.060	0.040	0.048	0.050
Min	0.030	0.030	0.035	0.030	0.040
Max	0.060	0.070	0.050	0.060	0.060
p_W		0.234	0.552	0.457	0.237
p_J			0.714	0.674	0.388
week: 7 N	4	4	4	4	4
Mean	0.048	0.043	0.025	0.030	0.033
Median	0.050	0.045	0.020	0.030	0.030
Min	0.030	0.020	0.020	0.020	0.020
Max	0.060	0.060	0.040	0.040	0.050
p_W		0.655	0.037 *	0.074	0.137
p_J			0.048	0.056	0.090

Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	0.078	0.078	0.065	0.053	0.063
Median	0.080	0.075	0.070	0.045	0.060
Min	0.050	0.050	0.040	0.030	0.040
Max	0.100	0.110	0.080	0.090	0.090
p_W		0.884	0.234	0.189	0.306
p_J			0.421	0.102	0.144
Plt (G/l)					
week: -1 N	4	4	4	4	4
Mean	285.8	296.3	223.6	257.0	278.3
Median	270.0	285.5	221.8	243.0	283.5
Min	240.0	244.0	213.0	222.0	248.0
Max	363.0	370.0	238.0	320.0	298.0
p_W		0.564	0.021 *	0.248	0.564
p_J			0.040	0.112	0.740
week: 7 N	4	4	4	4	4
Mean	305.5	328.0	244.0	305.3	321.0
Median	306.5	297.0	235.5	293.5	332.5
Min	288.0	248.0	222.0	264.0	264.0
Max	321.0	470.0	283.0	370.0	355.0
p_W		0.773	0.021 *	0.564	0.564
p_J			0.023	0.283	1.000
week: 13 N	4	4	4	4	4
Mean	299.5	295.8	245.0	303.5	318.3
Median	292.5	283.5	246.5	298.0	320.5
Min	261.0	241.0	209.0	197.0	279.0
Max	352.0	375.0	278.0	421.0	353.0
p_W		0.564	0.043 *	1.000	0.386
p_J			0.028	0.262	0.842
PT(CS) (sec)					
week: -1 N	4	4	4	4	4
Mean	32.83	32.69	32.59	31.45	31.75
Median	32.90	32.25	32.59	31.91	32.52
Min	31.68	27.41	27.09	29.61	28.70
Max	33.84	38.84	38.10	32.37	33.27
p_W		1.000	1.000	0.083	0.564
p_J			0.884	0.401	0.507

Hematology (statistics) : females

dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	7 N	4	4	4	4	4
	Mean	31.09	32.61	31.45	30.13	29.06
	Median	31.26	32.60	30.87	30.19	29.80
	Min	29.04	27.74	27.97	28.74	25.55
	Max	32.79	37.52	36.11	31.39	31.10
	p_W		1.000	1.000	0.386	0.248
	p_J			0.770	0.641	0.319
week:	13 N	4	4	4	4	4
	Mean	31.20	32.15	32.39	30.74	30.96
	Median	31.35	31.90	32.33	30.90	31.24
	Min	28.88	28.31	28.67	29.16	27.08
	Max	33.21	36.51	36.22	31.98	34.30
	p_W		0.773	0.564	0.773	1.000
	p_J			0.661	0.926	0.790

5.4. Blood chemistry (statistics)

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Gluc (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	5.673	5.955	6.075	5.713	5.865
Median	5.720	5.890	6.125	5.680	5.815
Min	5.230	5.430	5.880	5.530	5.610
Max	6.020	6.610	6.170	5.960	6.220
p_W		0.386	0.043 *	1.000	0.564
p_J			0.057	0.779	0.790
week: 7 N	4	4	4	4	4
Mean	5.700	5.710	6.293	5.528	5.933
Median	5.610	5.725	6.280	5.525	5.845
Min	5.540	5.350	6.180	5.370	5.580
Max	6.040	6.040	6.430	5.690	6.460
p_W		0.885	0.021 *	0.386	0.248
p_J			0.016	0.744	0.528
week: 13 N	4	4	4	4	4
Mean	5.820	5.655	5.888	5.570	5.525
Median	5.895	5.575	5.935	5.570	5.555
Min	5.130	5.350	5.520	5.310	5.290
Max	6.360	6.120	6.160	5.830	5.700
p_W		0.564	1.000	0.248	0.248
p_J			0.770	0.455	0.144
Urea (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	3.270	3.093	3.328	3.388	4.060
Median	3.405	3.055	3.495	3.220	4.060
Min	1.980	3.010	2.550	2.640	2.830
Max	4.290	3.250	3.770	4.470	5.290
p_W		0.248	0.773	0.773	0.386
p_J			0.884	0.852	0.259

Blood chemistry (statistics) : males

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	3.483	3.213	3.323	3.648	3.480
	Median	3.465	3.235	3.225	3.530	3.510
	Min	2.770	2.580	2.680	3.370	2.460
	Max	4.230	3.800	4.160	4.160	4.440
	p_W		0.564	0.564	0.772	1.000
	p_J			0.661	0.674	0.715
week: 13	N	4	4	4	4	4
	Mean	3.945	3.625	3.710	4.120	3.968
	Median	3.875	3.590	3.510	4.105	4.060
	Min	2.770	3.340	2.830	3.890	2.980
	Max	5.260	3.980	4.990	4.380	4.770
	p_W		0.468	0.663	0.564	0.773
	p_J			0.464	0.513	0.425
Creat-e (umol/l)						
week: -1	N	4	4	4	4	4
	Mean	66.05	69.60	73.83	67.53	75.33
	Median	65.60	69.75	73.05	67.15	74.40
	Min	64.30	65.60	67.70	60.60	69.60
	Max	68.70	73.30	81.50	75.20	82.90
	p_W		0.083	0.083	0.564	0.021 *
	p_J			0.040	0.455	0.054
week: 7	N	4	4	4	4	4
	Mean	64.18	71.88	76.03	67.93	73.50
	Median	65.30	72.20	75.70	67.25	74.30
	Min	58.50	68.80	65.70	63.80	65.00
	Max	67.60	74.30	87.00	73.40	80.40
	p_W		0.020 *	0.083	0.309	0.083
	p_J			0.008 +	0.327	0.184
week: 13	N	4	4	4	4	4
	Mean	73.90	77.90	74.90	72.60	77.25
	Median	74.30	78.25	74.30	72.25	74.60
	Min	65.70	73.50	65.90	69.70	72.90
	Max	81.30	81.60	85.10	76.20	86.90
	p_W		0.386	0.773	0.773	0.564
	p_J			0.770	0.575	0.947

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Bili-tot (umol/l)					
week: -1 N	4	4	4	4	4
Mean	1.858	2.380	2.500	2.380	2.020
Median	1.905	2.260	2.380	2.260	2.020
Min	1.480	2.140	2.380	2.140	1.900
Max	2.140	2.860	2.860	2.860	2.140
p_W		0.065	0.017 *	0.065	0.536
p_J			0.013	0.062	0.894
week: 7 N	4	4	4	4	4
Mean	2.385	2.753	2.935	2.875	2.508
Median	2.325	2.570	2.935	3.060	2.570
Min	2.200	2.200	2.690	2.200	1.710
Max	2.690	3.670	3.180	3.180	3.180
p_W		0.369	0.036 *	0.137	0.767
p_J			0.057	0.069	0.388
week: 13 N	4	4	4	4	4
Mean	2.693	2.938	2.938	2.998	2.878
Median	2.695	2.690	2.940	2.935	2.695
Min	2.200	2.450	2.690	2.690	2.450
Max	3.180	3.920	3.180	3.430	3.670
p_W		0.661	0.457	0.306	0.655
p_J			0.306	0.225	0.528
Prot (g/l)					
week: -1 N	4	4	4	4	4
Mean	54.24	55.35	54.59	52.75	54.47
Median	54.64	55.80	55.26	53.50	54.82
Min	52.58	51.65	51.40	49.97	51.46
Max	55.11	58.15	56.46	54.04	56.77
p_W		0.773	0.386	0.149	0.773
p_J			0.770	0.225	0.550
week: 7 N	4	4	4	4	4
Mean	55.49	57.03	57.29	54.80	54.33
Median	54.88	56.33	57.03	54.76	54.19
Min	53.19	55.61	55.26	52.62	53.41
Max	59.01	59.83	59.85	57.08	55.53
p_W		0.386	0.248	0.564	0.773
p_J			0.242	0.779	0.184

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	57.72	59.73	58.78	57.27	56.76
Median	57.35	60.76	58.46	56.88	56.78
Min	53.94	56.12	57.72	55.03	54.74
Max	62.26	61.29	60.49	60.29	58.75
p_W		0.564	0.468	0.773	0.773
p_J			0.826	0.427	0.153
Alb (g/l)					
week: -1 N	4	4	4	4	4
Mean	31.18	30.93	31.82	29.85	30.68
Median	31.16	31.23	31.61	29.89	30.83
Min	30.68	29.38	30.86	27.53	29.51
Max	31.71	31.89	33.20	32.10	31.56
p_W		0.885	0.386	0.386	0.386
p_J			0.272	0.744	0.486
week: 7 N	4	4	4	4	4
Mean	31.48	32.21	33.17	31.78	30.83
Median	31.31	31.89	33.16	31.27	30.64
Min	30.25	31.12	32.59	30.80	30.25
Max	33.04	33.92	33.77	33.77	31.78
p_W		0.309	0.083	0.885	0.468
p_J			0.048	0.608	0.288
week: 13 N	4	4	4	4	4
Mean	32.88	32.98	34.28	32.55	32.27
Median	32.62	32.90	34.25	32.88	32.38
Min	31.43	32.24	33.86	30.27	31.71
Max	34.84	33.87	34.77	34.15	32.62
p_W		1.000	0.248	0.773	0.386
p_J			0.107	0.779	0.465
Glob (g/l)					
week: -1 N	4	4	4	4	4
Mean	23.07	24.42	22.78	22.90	23.78
Median	23.71	25.26	23.02	22.39	23.88
Min	20.87	20.91	20.54	21.94	21.95
Max	23.98	26.26	24.53	24.88	25.43
p_W		0.149	0.564	0.773	0.386
p_J			0.770	0.513	0.947

Blood chemistry (statistics) : males

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	24.01	24.82	24.12	23.03	23.50
	Median	23.84	24.85	24.26	23.08	23.13
	Min	22.40	23.68	21.90	21.82	22.47
	Max	25.97	25.91	26.08	24.14	25.28
	p_W		0.564	0.773	0.386	0.773
	p_J			0.826	0.283	0.195
week: 13	N	4	4	4	4	4
	Mean	24.85	26.76	24.50	24.72	24.49
	Median	25.26	27.05	24.13	24.73	24.72
	Min	21.45	23.87	23.12	23.30	22.39
	Max	27.42	29.05	26.63	26.14	26.13
	p_W		0.386	0.564	0.564	0.564
	p_J			0.464	0.350	0.259
A/G (1)						
week: -1	N	4	4	4	4	4
	Mean	1.358	1.275	1.403	1.310	1.290
	Median	1.315	1.220	1.420	1.305	1.295
	Min	1.280	1.190	1.270	1.170	1.230
	Max	1.520	1.470	1.500	1.460	1.340
	p_W		0.149	0.773	0.564	0.386
	p_J			0.884	0.674	0.507
week: 7	N	4	4	4	4	4
	Mean	1.315	1.298	1.380	1.380	1.315
	Median	1.295	1.320	1.355	1.385	1.325
	Min	1.260	1.200	1.290	1.300	1.200
	Max	1.410	1.350	1.520	1.450	1.410
	p_W		1.000	0.248	0.191	0.885
	p_J			0.272	0.093	0.352
week: 13	N	4	4	4	4	4
	Mean	1.330	1.240	1.403	1.320	1.320
	Median	1.285	1.250	1.420	1.305	1.295
	Min	1.240	1.110	1.270	1.220	1.250
	Max	1.510	1.350	1.500	1.450	1.440
	p_W		0.309	0.468	0.885	0.885
	p_J			0.380	0.544	0.666

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Chol (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	4.390	4.088	3.688	3.455	3.390
Median	4.465	3.965	3.590	3.420	3.390
Min	3.780	3.620	3.210	3.000	3.160
Max	4.850	4.800	4.360	3.980	3.620
p_W		0.386	0.149	0.043 *	0.021 *
p_J			0.079	0.013	0.003 -
week: 7 N	4	4	4	4	4
Mean	4.578	3.880	3.866	3.475	3.285
Median	4.500	3.630	3.515	3.460	3.265
Min	3.810	3.440	3.300	3.190	3.140
Max	5.500	4.820	5.135	3.790	3.470
p_W		0.083	0.149	0.021 *	0.021 *
p_J			0.107	0.020	0.001 -
week: 13 N	4	4	4	4	4
Mean	4.293	4.023	3.743	3.575	3.513
Median	4.190	3.730	3.630	3.615	3.455
Min	3.620	3.600	3.220	3.150	3.380
Max	5.170	5.030	4.490	3.920	3.760
p_W		0.386	0.149	0.248	0.043 *
p_J			0.107	0.093	0.028
Trigly (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	0.430	0.423	0.494	0.343	0.363
Median	0.460	0.450	0.490	0.335	0.340
Min	0.310	0.280	0.360	0.320	0.280
Max	0.490	0.510	0.635	0.380	0.490
p_W		0.885	0.564	0.248	0.468
p_J			0.464	0.350	0.163
week: 7 N	4	4	4	4	4
Mean	0.408	0.320	0.303	0.315	0.308
Median	0.405	0.315	0.300	0.330	0.330
Min	0.310	0.240	0.200	0.270	0.220
Max	0.510	0.410	0.410	0.330	0.350
p_W		0.149	0.149	0.139	0.149
p_J			0.092	0.135	0.163

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	0.293	0.261	0.298	0.273	0.275
Median	0.325	0.275	0.285	0.260	0.290
Min	0.180	0.195	0.200	0.240	0.190
Max	0.340	0.300	0.420	0.330	0.330
p_W		0.248	0.564	0.468	0.468
p_J			1.000	0.815	0.790
Phos-Lip (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	5.116	4.888	4.508	4.203	4.048
Median	5.165	4.765	4.465	4.195	4.050
Min	4.460	4.330	3.910	3.600	3.840
Max	5.675	5.690	5.190	4.820	4.250
p_W		0.773	0.149	0.043 *	0.021 *
p_J			0.188	0.025	0.003 -
week: 7 N	4	4	4	4	4
Mean	5.090	4.535	4.571	4.168	4.110
Median	4.990	4.390	4.190	4.225	4.110
Min	4.600	4.100	4.100	3.890	3.920
Max	5.780	5.260	5.805	4.330	4.300
p_W		0.083	0.248	0.021 *	0.021 *
p_J			0.092	0.020	0.003 -
week: 13 N	4	4	4	4	4
Mean	4.923	4.841	4.623	4.343	4.383
Median	4.755	4.695	4.515	4.380	4.370
Min	4.450	4.190	4.110	3.940	4.280
Max	5.730	5.785	5.350	4.670	4.510
p_W		1.000	0.773	0.248	0.110
p_J			0.558	0.191	0.078
Na+ (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	147.6	145.9	147.2	147.2	146.7
Median	147.1	145.8	146.9	147.5	147.1
Min	146.5	144.5	145.8	146.0	144.2
Max	149.7	147.6	149.3	147.8	148.2
p_W		0.080	0.384	0.772	0.772
p_J			0.464	0.963	0.974

Blood chemistry (statistics) : males

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	147.1	146.4	147.6	146.2	146.5
	Median	147.1	146.4	146.8	146.1	146.7
	Min	145.9	145.3	146.3	145.2	145.0
	Max	148.4	147.6	150.7	147.2	147.6
	p_W		0.468	1.000	0.248	0.559
	p_J			0.942	0.327	0.352
week: 13	N	4	4	4	4	4
	Mean	147.5	148.0	147.8	147.1	146.1
	Median	146.6	147.6	148.0	146.9	146.3
	Min	145.3	146.7	145.6	146.0	144.5
	Max	151.5	150.0	149.7	148.7	147.3
	p_W		0.386	0.564	0.773	0.564
	p_J			0.558	0.963	0.245
K+ (mmol/l)						
week: -1	N	4	4	4	4	4
	Mean	4.595	4.880	4.815	4.485	4.720
	Median	4.505	4.905	4.725	4.510	4.735
	Min	4.180	4.480	4.500	4.390	4.610
	Max	5.190	5.230	5.310	4.530	4.800
	p_W		0.149	0.248	0.772	0.248
	p_J			0.143	0.926	0.465
week: 7	N	4	4	4	4	4
	Mean	4.580	4.445	4.655	4.578	4.653
	Median	4.605	4.490	4.650	4.550	4.665
	Min	4.400	4.110	4.120	4.510	4.530
	Max	4.710	4.690	5.200	4.700	4.750
	p_W		0.384	0.561	1.000	0.375
	p_J			0.770	0.674	0.232
week: 13	N	4	4	4	4	4
	Mean	4.735	4.835	4.720	4.560	4.580
	Median	4.655	4.765	4.615	4.545	4.660
	Min	4.220	4.510	4.440	4.340	4.240
	Max	5.410	5.300	5.210	4.810	4.760
	p_W		0.564	1.000	0.773	0.773
	p_J			0.942	0.641	0.642

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Ca++ (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	2.825	2.795	2.830	2.745	2.743
Median	2.825	2.800	2.835	2.755	2.730
Min	2.790	2.690	2.730	2.670	2.700
Max	2.860	2.890	2.920	2.800	2.810
p_W		0.564	1.000	0.043 *	0.059
p_J			0.942	0.207	0.058
week: 7 N	4	4	4	4	4
Mean	2.933	2.940	2.955	2.833	2.845
Median	2.950	2.935	2.950	2.845	2.850
Min	2.840	2.860	2.870	2.740	2.790
Max	2.990	3.030	3.050	2.900	2.890
p_W		1.000	0.564	0.083	0.110
p_J			0.661	0.148	0.028
week: 13 N	4	4	4	4	4
Mean	2.783	2.753	2.773	2.665	2.633
Median	2.770	2.720	2.795	2.645	2.655
Min	2.730	2.690	2.630	2.630	2.540
Max	2.860	2.880	2.870	2.740	2.680
p_W		0.386	1.000	0.042 *	0.021 *
p_J			0.661	0.069	0.006 -
Cl- (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	109.7	109.9	108.8	110.8	109.6
Median	109.4	109.8	109.4	111.4	109.6
Min	108.2	108.9	106.1	108.4	109.0
Max	111.8	111.0	110.5	111.9	110.1
p_W		0.663	0.773	0.248	0.773
p_J			0.826	0.304	0.618
week: 7 N	4	4	4	4	4
Mean	108.1	107.7	107.7	109.7	110.2
Median	108.1	107.7	107.6	109.6	110.0
Min	107.0	106.6	106.3	107.5	108.5
Max	109.1	108.8	109.1	112.2	112.3
p_W		0.564	0.559	0.386	0.083
p_J			0.558	0.484	0.058

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	113.4	113.2	111.8	114.5	113.4
Median	113.9	113.3	111.5	114.4	113.6
Min	111.4	111.7	110.5	113.6	112.1
Max	114.6	114.6	113.9	115.4	114.4
p_W		0.884	0.149	0.248	0.564
p_J			0.213	0.484	0.666
PO4-in (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	2.215	2.225	2.220	2.310	2.090
Median	2.160	2.240	2.220	2.310	2.080
Min	2.100	2.150	2.150	2.140	2.030
Max	2.440	2.270	2.290	2.480	2.170
p_W		0.468	0.468	0.386	0.144
p_J			0.510	0.327	0.303
week: 7 N	4	4	4	4	4
Mean	1.983	1.885	2.006	1.973	1.803
Median	1.980	1.925	1.985	1.975	1.765
Min	1.860	1.750	1.880	1.920	1.740
Max	2.110	1.940	2.175	2.020	1.940
p_W		0.149	0.773	0.885	0.043 *
p_J			0.884	0.608	0.219
week: 13 N	4	4	4	4	4
Mean	1.668	1.625	1.725	1.830	1.583
Median	1.665	1.630	1.765	1.815	1.535
Min	1.640	1.520	1.510	1.750	1.440
Max	1.700	1.720	1.860	1.940	1.820
p_W		0.773	0.248	0.021 *	0.248
p_J			0.341	0.017	0.528
ASAT (GOT) (U/l)					
week: -1 N	4	4	4	4	4
Mean	18.79	24.06	21.13	19.73	21.13
Median	18.95	22.35	21.15	19.25	19.90
Min	13.65	20.50	18.00	17.40	18.60
Max	23.60	31.05	24.20	23.00	26.10
p_W		0.309	0.468	0.773	0.564
p_J			0.661	0.709	0.790

Blood chemistry (statistics) : males

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	23.03	24.70	25.30	24.98	21.13
	Median	23.65	26.10	24.20	23.90	20.50
	Min	19.90	16.80	22.40	21.70	18.60
	Max	24.90	29.80	30.40	30.40	24.90
	p_W		0.561	0.659	0.772	0.237
	p_J			0.510	0.674	0.425
week: 13	N	4	4	4	4	4
	Mean	20.95	20.98	23.00	21.45	19.88
	Median	21.10	20.20	23.60	21.45	20.50
	Min	19.90	18.00	19.30	17.40	17.40
	Max	21.70	25.50	25.50	25.50	21.10
	p_W		1.000	0.243	0.661	0.372
	p_J			0.272	0.544	0.690
ALAT (GPT) (U/l)						
week: -1	N	4	4	4	4	4
	Mean	50.01	49.63	42.75	39.43	41.48
	Median	45.95	50.40	42.90	41.10	40.75
	Min	30.40	37.00	40.00	25.90	34.80
	Max	77.75	60.70	45.20	49.60	49.60
	p_W		0.663	0.306	0.564	0.564
	p_J			0.380	0.225	0.163
week: 7	N	4	4	4	4	4
	Mean	66.90	47.75	44.98	41.09	41.30
	Median	51.45	48.10	46.65	41.45	41.10
	Min	35.50	37.80	38.50	28.85	36.30
	Max	129.2	57.00	48.10	52.60	46.70
	p_W		0.773	0.885	0.564	0.773
	p_J			0.714	0.401	0.259
week: 13	N	4	4	4	4	4
	Mean	73.40	49.08	49.05	47.20	42.93
	Median	50.35	47.80	46.65	43.70	41.45
	Min	36.30	43.70	43.70	40.70	31.80
	Max	156.6	57.00	59.20	60.70	57.00
	p_W		0.773	0.663	0.561	0.386
	p_J			0.770	0.350	0.078

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
AlP (U/l)					
week: -1 N	4	4	4	4	4
Mean	92.65	107.0	126.4	104.3	107.5
Median	95.05	103.3	125.4	97.35	114.1
Min	70.10	85.60	116.1	86.20	78.00
Max	110.4	135.8	138.9	136.3	123.7
p_W		0.248	0.021 *	0.564	0.248
p_J			0.013	0.191	0.352
week: 7 N	4	4	4	4	4
Mean	80.46	93.38	107.3	87.68	150.1
Median	81.85	96.20	105.9	83.95	147.3
Min	50.55	76.30	92.70	77.20	98.90
Max	107.6	104.8	124.5	105.6	206.8
p_W		0.564	0.083	0.773	0.043 *
p_J			0.079	0.575	0.039
week: 13 N	4	4	4	4	4
Mean	65.00	76.98	84.58	79.23	135.2
Median	66.75	78.85	81.70	76.60	129.3
Min	38.00	55.50	74.10	70.70	91.80
Max	88.50	94.70	100.8	93.00	190.3
p_W		0.386	0.149	0.386	0.021 *
p_J			0.143	0.304	0.008 +
GGT (U/l)					
week: -1 N	4	4	4	4	4
Mean	4.000	3.825	3.675	3.350	3.975
Median	3.850	3.800	3.500	3.200	3.800
Min	3.200	3.200	3.200	3.200	3.200
Max	5.100	4.500	4.500	3.800	5.100
p_W		0.881	0.642	0.321	0.881
p_J			0.608	0.207	0.690
week: 7 N	4	4	4	4	4
Mean	1.275	2.050	0.800	2.675	3.500
Median	0.000	2.500	0.000	2.500	3.500
Min	0.000	0.000	0.000	2.500	3.200
Max	5.100	3.200	3.200	3.200	3.800
p_W		0.439	0.850	0.225	0.234
p_J			0.884	0.401	0.018

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	4.125	3.650	3.175	3.675	4.325
Median	3.800	3.500	3.200	3.500	4.500
Min	3.200	2.500	2.500	3.200	3.800
Max	5.700	5.100	3.800	4.500	4.500
p_W		0.457	0.129	0.544	0.363
p_J			0.164	0.484	0.445
CK (U/l)					
week: -1 N	4	4	4	4	4
Mean	187.6	223.4	225.0	216.0	212.6
Median	192.4	222.6	226.3	215.2	216.3
Min	148.4	194.0	177.0	198.2	191.9
Max	217.3	254.4	270.3	235.3	225.8
p_W		0.149	0.083	0.191	0.248
p_J			0.107	0.243	0.486
week: 7 N	4	4	4	4	4
Mean	178.9	173.1	289.9	214.9	191.4
Median	162.7	174.9	180.2	200.9	195.1
Min	155.8	141.0	165.4	179.1	154.8
Max	234.3	201.4	633.9	278.8	220.5
p_W		1.000	0.384	0.149	0.773
p_J			0.380	0.112	0.232
week: 13 N	4	4	4	4	4
Mean	148.2	172.2	203.5	181.5	170.1
Median	141.6	171.7	212.0	191.9	162.7
Min	128.3	129.3	173.8	123.0	131.4
Max	181.3	216.2	216.2	219.4	223.7
p_W		0.245	0.042 *	0.245	0.245
p_J			0.034	0.084	0.273

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Gluc (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	5.743	5.370	6.003	5.875	5.500
Median	5.820	5.395	5.965	5.910	5.445
Min	5.390	5.100	5.590	5.730	5.130
Max	5.940	5.590	6.490	5.950	5.980
p_W		0.083	0.564	0.468	0.386
p_J			0.608	0.191	0.842
week: 7 N	4	4	4	4	4
Mean	5.875	5.660	6.268	5.728	5.788
Median	5.825	5.620	6.195	5.730	5.745
Min	5.490	5.410	5.960	5.490	5.520
Max	6.360	5.990	6.720	5.960	6.140
p_W		0.386	0.083	0.468	1.000
p_J			0.143	0.926	0.947
week: 13 N	4	4	4	4	4
Mean	5.505	5.463	5.858	5.570	5.310
Median	5.465	5.390	5.645	5.585	5.470
Min	5.190	5.190	5.550	5.500	4.600
Max	5.900	5.880	6.590	5.610	5.700
p_W		0.885	0.149	0.248	0.773
p_J			0.164	0.191	0.642
Urea (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	4.020	3.808	4.210	3.798	4.013
Median	4.075	3.830	4.135	3.920	3.935
Min	3.340	3.340	3.650	2.580	2.680
Max	4.590	4.230	4.920	4.770	5.500
p_W		0.468	0.773	1.000	1.000
p_J			0.770	0.926	0.894
week: 7 N	4	4	4	4	4
Mean	3.730	3.915	4.330	4.330	3.723
Median	3.570	4.000	4.040	4.345	3.720
Min	3.070	3.160	3.890	3.860	3.040
Max	4.710	4.500	5.350	4.770	4.410
p_W		0.773	0.248	0.248	1.000
p_J			0.306	0.135	0.618

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	4.075	4.220	4.258	4.185	4.158
Median	4.045	3.970	4.380	4.420	4.240
Min	3.830	3.680	3.680	3.010	2.950
Max	4.380	5.260	4.590	4.890	5.200
p_W		0.663	0.386	0.564	1.000
p_J			0.661	0.575	0.740
Creat-e (umol/l)					
week: -1 N	4	4	4	4	4
Mean	79.10	75.75	79.90	79.03	76.70
Median	79.50	74.40	79.90	77.80	77.00
Min	73.30	68.40	75.20	71.60	64.80
Max	84.10	85.80	84.60	88.90	88.00
p_W		0.564	0.773	1.000	0.564
p_J			0.884	0.852	0.894
week: 7 N	4	4	4	4	4
Mean	79.23	73.73	80.65	77.05	75.40
Median	76.45	74.45	80.10	78.00	76.55
Min	71.90	66.20	74.30	69.70	61.90
Max	92.10	79.80	88.10	82.50	86.60
p_W		0.248	0.663	1.000	0.773
p_J			0.714	0.674	0.921
week: 13 N	4	4	4	4	4
Mean	78.38	74.43	82.95	80.90	77.88
Median	77.60	74.85	84.15	83.75	77.95
Min	71.20	69.20	75.30	71.70	72.30
Max	87.10	78.80	88.20	84.40	83.30
p_W		0.386	0.149	0.564	1.000
p_J			0.242	0.225	0.550
Bili-tot (umol/l)					
week: -1 N	4	4	4	4	4
Mean	2.440	2.618	2.260	2.345	2.530
Median	2.380	2.620	2.300	2.345	2.470
Min	2.140	1.900	1.970	2.220	2.470
Max	2.860	3.330	2.470	2.470	2.710
p_W		0.661	0.561	1.000	0.766
p_J			0.661	0.779	0.528

Blood chemistry (statistics) : females

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 7	N	4	4	4	4	4
	Mean	2.755	2.755	2.693	2.755	2.570
	Median	2.815	2.695	2.695	2.815	2.450
	Min	2.450	2.450	2.200	2.450	2.200
	Max	2.940	3.180	3.180	2.940	3.180
	p_W		1.000	0.882	1.000	0.372
	p_J			0.826	0.926	0.486
week: 13	N	4	4	4	4	4
	Mean	2.755	3.490	3.245	3.120	2.570
	Median	2.695	3.675	3.185	3.180	2.570
	Min	2.450	2.690	2.940	2.200	2.200
	Max	3.180	3.920	3.670	3.920	2.940
	p_W		0.080	0.137	0.372	0.457
	p_J			0.213	0.427	0.425
Prot (g/l)						
week: -1	N	4	4	4	4	4
	Mean	55.08	54.97	53.98	54.59	55.73
	Median	54.93	55.28	53.50	54.55	55.01
	Min	52.55	52.50	51.32	52.95	53.82
	Max	57.90	56.83	57.59	56.32	59.08
	p_W		0.885	0.386	0.773	0.773
	p_J			0.510	0.608	0.974
week: 7	N	4	4	4	4	4
	Mean	55.45	54.74	53.32	54.38	54.95
	Median	55.08	54.08	53.51	54.30	54.58
	Min	53.98	51.56	51.56	53.87	52.57
	Max	57.65	59.23	54.72	55.07	58.06
	p_W		0.564	0.149	0.309	1.000
	p_J			0.164	0.401	0.790
week: 13	N	4	4	4	4	4
	Mean	57.43	57.97	58.48	56.75	57.58
	Median	56.78	57.46	56.92	57.19	56.93
	Min	55.52	57.09	56.55	54.86	56.72
	Max	60.66	59.86	63.52	57.77	59.72
	p_W		0.248	0.384	0.885	0.564
	p_J			0.661	0.963	0.921

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Alb (g/l)					
week: -1 N	4	4	4	4	4
Mean	32.27	33.31	32.69	32.71	33.30
Median	32.27	33.30	32.45	32.29	32.88
Min	31.85	33.09	31.14	30.99	32.65
Max	32.69	33.54	34.70	35.26	34.78
p_W		0.021 *	0.564	1.000	0.043 *
p_J			0.380	0.852	0.425
week: 7 N	4	4	4	4	4
Mean	32.43	33.20	32.91	33.02	32.81
Median	32.59	32.97	33.02	32.98	32.65
Min	31.55	32.35	31.83	32.48	31.49
Max	32.97	34.52	33.78	33.62	34.47
p_W		0.248	0.248	0.248	1.000
p_J			0.242	0.262	0.690
week: 13 N	4	4	4	4	4
Mean	33.24	34.25	34.52	33.96	33.43
Median	33.67	34.52	34.08	34.04	33.35
Min	31.48	33.04	33.07	32.38	32.90
Max	34.16	34.91	36.84	35.38	34.11
p_W		0.149	0.386	0.386	0.773
p_J			0.272	0.427	0.765
Glob (g/l)					
week: -1 N	4	4	4	4	4
Mean	22.81	21.67	21.29	21.89	22.43
Median	22.67	22.14	21.05	21.70	22.23
Min	20.70	18.96	20.18	21.06	20.97
Max	25.21	23.44	22.89	23.08	24.30
p_W		0.386	0.386	0.564	0.564
p_J			0.242	0.513	0.842
week: 7 N	4	4	4	4	4
Mean	23.02	21.54	20.41	21.37	22.14
Median	22.86	20.65	20.34	21.32	22.63
Min	21.69	18.71	19.71	20.70	19.69
Max	24.68	26.15	21.26	22.13	23.59
p_W		0.386	0.021 *	0.043 *	0.564
p_J			0.107	0.225	0.740

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	24.19	23.72	23.96	22.80	24.15
Median	23.69	23.76	23.31	22.83	23.71
Min	22.73	22.41	22.56	21.24	22.95
Max	26.65	24.95	26.68	24.28	26.23
p_W		0.773	0.773	0.248	1.000
p_J			0.770	0.225	0.690
A/G (1)					
week: -1 N	4	4	4	4	4
Mean	1.420	1.545	1.535	1.498	1.488
Median	1.420	1.495	1.540	1.490	1.475
Min	1.300	1.420	1.520	1.340	1.430
Max	1.540	1.770	1.540	1.670	1.570
p_W		0.248	0.091	0.386	0.191
p_J			0.048	0.304	0.486
week: 7 N	4	4	4	4	4
Mean	1.413	1.575	1.613	1.548	1.490
Median	1.410	1.600	1.610	1.555	1.455
Min	1.340	1.270	1.550	1.470	1.380
Max	1.490	1.830	1.680	1.610	1.670
p_W		0.468	0.020 *	0.043 *	0.309
p_J			0.124	0.243	0.690
week: 13 N	4	4	4	4	4
Mean	1.380	1.448	1.443	1.493	1.390
Median	1.370	1.445	1.435	1.530	1.395
Min	1.280	1.350	1.380	1.330	1.280
Max	1.500	1.550	1.520	1.580	1.490
p_W		0.386	0.386	0.146	0.885
p_J			0.464	0.176	0.740
Chol (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	3.918	3.734	3.963	4.140	4.035
Median	3.965	3.835	3.945	4.120	4.125
Min	2.730	2.575	3.000	3.750	3.720
Max	5.010	4.690	4.960	4.570	4.170
p_W		0.564	1.000	0.564	1.000
p_J			1.000	0.575	0.690

Blood chemistry (statistics) : females

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	7 N	4	4	4	4	4
	Mean	4.078	3.678	3.848	4.363	3.745
	Median	4.110	3.990	3.825	4.535	3.795
	Min	2.740	2.690	3.050	3.490	3.190
	Max	5.350	4.040	4.690	4.890	4.200
	p_W		0.561	0.773	0.773	0.773
	p_J			0.770	0.513	1.000
week:	13 N	4	4	4	4	4
	Mean	4.056	3.633	3.923	4.433	3.690
	Median	3.880	3.800	3.815	4.610	3.860
	Min	3.030	2.810	3.310	3.540	2.860
	Max	5.435	4.120	4.750	4.970	4.180
	p_W		0.384	1.000	0.564	0.773
	p_J			0.884	0.304	0.790
Trigly (mmol/l)						
week:	-1 N	4	4	4	4	4
	Mean	0.430	0.470	0.373	0.465	0.380
	Median	0.435	0.475	0.390	0.460	0.365
	Min	0.360	0.450	0.290	0.390	0.320
	Max	0.490	0.480	0.420	0.550	0.470
	p_W		0.384	0.248	0.564	0.248
	p_J			0.188	0.815	0.259
week:	7 N	4	4	4	4	4
	Mean	0.330	0.390	0.284	0.360	0.375
	Median	0.340	0.375	0.295	0.360	0.375
	Min	0.280	0.280	0.195	0.260	0.300
	Max	0.360	0.530	0.350	0.460	0.450
	p_W		0.381	0.309	0.564	0.564
	p_J			0.464	0.926	0.666
week:	13 N	4	4	4	4	4
	Mean	0.265	0.280	0.220	0.285	0.273
	Median	0.260	0.280	0.205	0.265	0.275
	Min	0.220	0.210	0.180	0.220	0.210
	Max	0.320	0.350	0.290	0.390	0.330
	p_W		0.773	0.149	0.770	0.885
	p_J			0.164	0.744	0.947

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Phos-Lip (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	4.563	4.616	4.508	4.698	4.843
Median	4.695	4.735	4.615	4.705	4.915
Min	3.390	3.140	3.530	4.410	4.510
Max	5.470	5.855	5.270	4.970	5.030
p_W		1.000	1.000	1.000	1.000
p_J			0.884	0.926	0.666
week: 7 N	4	4	4	4	4
Mean	4.688	4.438	4.430	5.003	4.635
Median	4.770	4.720	4.420	5.055	4.745
Min	3.560	3.500	3.790	4.550	4.010
Max	5.650	4.810	5.090	5.350	5.040
p_W		0.564	0.564	0.773	0.773
p_J			0.510	0.544	0.765
week: 13 N	4	4	4	4	4
Mean	4.699	4.480	4.608	5.023	4.633
Median	4.550	4.680	4.505	5.150	4.725
Min	3.850	3.470	4.110	4.320	3.980
Max	5.845	5.090	5.310	5.470	5.100
p_W		0.773	1.000	0.564	0.773
p_J			0.770	0.262	0.507
Na+ (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	147.6	148.5	148.8	148.0	149.2
Median	147.5	148.8	148.5	148.0	149.3
Min	146.4	146.9	147.8	146.4	148.2
Max	149.0	149.4	150.3	149.6	150.1
p_W		0.309	0.149	0.468	0.083
p_J			0.213	0.575	0.135
week: 7 N	4	4	4	4	4
Mean	145.3	145.5	147.5	148.0	148.0
Median	145.3	145.4	147.4	148.4	148.1
Min	144.7	143.8	146.4	146.3	147.2
Max	146.0	147.6	148.7	149.0	148.6
p_W		1.000	0.021 *	0.021 *	0.021 *
p_J			0.048	0.003 +	0.001 +

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	147.7	147.6	148.6	149.1	148.4
Median	147.3	147.6	147.7	149.1	148.3
Min	147.0	147.0	145.9	147.7	147.8
Max	149.1	148.1	153.2	150.7	149.2
p_W		0.885	0.885	0.081	0.149
p_J			0.770	0.191	0.063
K+ (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	4.304	4.368	4.318	4.388	4.415
Median	4.315	4.395	4.335	4.420	4.390
Min	3.905	4.200	4.110	4.020	4.070
Max	4.680	4.480	4.490	4.690	4.810
p_W		0.564	0.773	0.564	0.773
p_J			0.826	0.575	0.507
week: 7 N	4	4	4	4	4
Mean	4.178	4.329	4.098	4.223	4.055
Median	4.250	4.285	4.090	4.250	4.105
Min	3.950	3.660	4.030	3.880	3.730
Max	4.260	5.085	4.180	4.510	4.280
p_W		0.772	0.245	0.772	0.772
p_J			0.306	0.641	0.465
week: 13 N	4	4	4	4	4
Mean	4.045	4.228	4.078	4.075	3.998
Median	4.060	4.175	4.035	4.150	4.025
Min	3.860	3.980	3.880	3.660	3.770
Max	4.200	4.580	4.360	4.340	4.170
p_W		0.386	0.885	0.564	0.564
p_J			0.826	0.744	0.690
Ca++ (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	2.720	2.755	2.773	2.780	2.843
Median	2.735	2.750	2.770	2.780	2.840
Min	2.670	2.650	2.750	2.750	2.820
Max	2.740	2.870	2.800	2.810	2.870
p_W		0.772	0.019 *	0.020 *	0.019 *
p_J			0.124	0.045	0.001 +

Blood chemistry (statistics) : females

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	7 N	4	4	4	4	4
	Mean	2.865	2.905	2.845	2.923	2.878
	Median	2.850	2.915	2.845	2.940	2.875
	Min	2.760	2.840	2.800	2.870	2.860
	Max	3.000	2.950	2.890	2.940	2.900
	p_W		0.386	1.000	0.297	0.468
	p_J			0.714	0.484	0.790
week:	13 N	4	4	4	4	4
	Mean	2.645	2.675	2.673	2.645	2.678
	Median	2.645	2.670	2.660	2.650	2.665
	Min	2.590	2.620	2.650	2.620	2.650
	Max	2.700	2.740	2.720	2.660	2.730
	p_W		0.468	0.384	1.000	0.309
	p_J			0.341	0.963	0.445
Cl- (mmol/l)						
week:	-1 N	4	4	4	4	4
	Mean	110.8	110.3	110.1	111.0	110.9
	Median	111.1	109.5	110.5	111.5	110.9
	Min	109.2	108.7	108.7	108.6	110.0
	Max	111.6	113.3	110.7	112.3	111.8
	p_W		0.564	0.149	0.564	0.885
	p_J			0.421	0.889	0.666
week:	7 N	4	4	4	4	4
	Mean	111.1	109.2	108.4	108.1	109.2
	Median	111.4	109.5	108.5	108.1	109.1
	Min	108.1	105.9	106.1	105.9	107.7
	Max	113.3	111.9	110.7	110.2	111.0
	p_W		0.248	0.110	0.083	0.191
	p_J			0.092	0.062	0.195
week:	13 N	4	4	4	4	4
	Mean	114.7	113.4	114.5	115.2	114.1
	Median	114.6	113.4	113.4	114.4	114.0
	Min	114.2	112.7	112.6	114.1	112.7
	Max	115.3	114.1	118.7	118.0	115.6
	p_W		0.021 *	0.248	0.564	0.663
	p_J			0.079	0.815	0.868

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
PO4-in (mmol/l)					
week: -1 N	4	4	4	4	4
Mean	1.918	1.990	2.048	2.083	1.940
Median	1.925	2.010	2.005	1.995	1.935
Min	1.850	1.800	1.900	1.980	1.900
Max	1.970	2.140	2.280	2.360	1.990
p_W		0.773	0.248	0.021 *	0.773
p_J			0.306	0.076	0.486
week: 7 N	4	4	4	4	4
Mean	1.830	1.994	1.763	1.978	1.598
Median	1.790	1.960	1.750	1.985	1.585
Min	1.640	1.810	1.630	1.850	1.560
Max	2.100	2.245	1.920	2.090	1.660
p_W		0.149	0.386	0.248	0.043 *
p_J			0.558	0.513	0.127
week: 13 N	4	4	4	4	4
Mean	1.425	1.600	1.505	1.525	1.533
Median	1.400	1.550	1.530	1.520	1.515
Min	1.330	1.520	1.370	1.510	1.370
Max	1.570	1.780	1.590	1.550	1.730
p_W		0.080	0.146	0.243	0.245
p_J			0.213	0.427	0.550
ASAT (GOT) (U/l)					
week: -1 N	4	4	4	4	4
Mean	18.05	21.90	20.80	23.45	24.23
Median	17.75	21.40	20.80	24.55	23.30
Min	16.20	16.20	18.60	18.60	20.50
Max	20.50	28.60	23.00	26.10	29.80
p_W		0.139	0.146	0.080	0.028 *
p_J			0.164	0.045	0.017
week: 7 N	4	4	4	4	4
Mean	17.80	24.70	19.73	23.15	21.63
Median	17.10	23.95	19.25	23.30	21.15
Min	14.60	20.50	18.00	16.20	19.30
Max	22.40	30.40	22.40	29.80	24.90
p_W		0.059	0.191	0.248	0.110
p_J			0.510	0.375	0.388

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	4	4	4
Mean	17.54	24.55	18.25	18.65	20.50
Median	16.75	23.90	18.65	18.65	20.50
Min	13.65	19.30	14.60	14.90	18.00
Max	23.00	31.10	21.10	22.40	23.00
p_W		0.083	0.772	0.663	0.309
p_J			0.884	0.852	0.790
ALAT (GPT) (U/l)					
week: -1 N	4	4	4	4	4
Mean	43.65	46.64	45.73	50.90	52.05
Median	45.50	48.50	44.80	48.85	50.75
Min	31.80	25.15	40.00	43.70	45.20
Max	51.80	64.40	53.30	62.20	61.50
p_W		0.663	0.773	0.309	0.248
p_J			0.826	0.427	0.184
week: 7 N	4	4	4	4	4
Mean	44.63	44.25	48.50	49.05	42.55
Median	47.40	44.80	48.50	45.55	42.90
Min	32.60	37.00	47.40	38.50	39.20
Max	51.10	50.40	49.60	66.60	45.20
p_W		0.663	1.000	0.773	0.384
p_J			0.714	0.926	0.273
week: 13 N	4	4	4	4	4
Mean	47.38	47.40	48.15	48.50	45.93
Median	43.70	45.55	49.25	50.35	44.45
Min	31.80	32.60	40.00	40.70	41.50
Max	70.30	65.90	54.10	52.60	53.30
p_W		0.885	0.564	0.561	0.885
p_J			0.510	0.401	0.740
AlP (U/l)					
week: -1 N	4	4	4	4	4
Mean	82.55	106.8	76.51	91.70	93.95
Median	80.45	99.00	73.80	96.75	95.65
Min	76.30	93.80	52.55	63.40	87.00
Max	93.00	135.5	105.9	109.9	97.50
p_W		0.021 *	0.248	0.248	0.043 *
p_J			0.884	0.744	0.618

Blood chemistry (statistics) : females

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	7 N	4	4	4	4	4
	Mean	78.33	89.38	64.80	90.65	173.0
	Median	78.45	89.45	61.70	100.0	174.8
	Min	72.70	78.30	45.90	59.20	157.1
	Max	83.70	100.3	89.90	103.4	185.3
	p_W		0.083	0.248	0.245	0.021 *
	p_J			0.558	0.513	0.010 +
week:	13 N	4	4	4	4	4
	Mean	64.10	70.83	59.43	76.90	165.9
	Median	65.35	70.25	55.60	84.35	172.0
	Min	54.10	64.50	46.80	45.90	140.6
	Max	71.60	78.30	79.70	93.00	179.2
	p_W		0.149	0.386	0.248	0.021 *
	p_J			0.770	0.350	0.005 +
GGT (U/l)						
week:	-1 N	4	4	4	4	4
	Mean	3.025	3.525	2.838	1.900	3.650
	Median	3.200	3.200	3.150	1.250	3.800
	Min	2.500	3.200	1.250	0.000	3.200
	Max	3.200	4.500	3.800	5.100	3.800
	p_W		0.186	0.881	0.294	0.040 *
	p_J			0.770	0.455	0.595
week:	7 N	4	4	4	4	4
	Mean	1.425	0.625	1.875	1.600	3.425
	Median	1.250	0.000	2.500	1.600	3.200
	Min	0.000	0.000	0.000	0.000	3.150
	Max	3.200	2.500	2.500	3.200	4.150
	p_W		0.405	0.874	0.752	0.074
	p_J			0.770	0.513	0.028
week:	13 N	4	4	4	4	4
	Mean	2.700	2.850	2.225	3.475	2.700
	Median	3.150	3.150	2.850	3.150	2.850
	Min	0.000	0.000	0.000	2.500	0.000
	Max	4.500	5.100	3.200	5.100	5.100
	p_W		0.883	0.557	0.655	1.000
	p_J			0.608	0.852	0.947

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Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
CK (U/l)					
week: -1 N	4	4	4	4	4
Mean	189.0	208.6	215.2	242.0	264.7
Median	189.8	203.5	224.7	242.2	231.6
Min	163.2	159.0	163.2	197.2	182.3
Max	213.1	268.2	248.0	286.2	413.4
p_W		0.885	0.309	0.083	0.248
p_J			0.421	0.102	0.078
week: 7 N	4	4	4	4	4
Mean	125.4	194.5	140.2	250.0	171.7
Median	126.2	190.8	138.9	188.7	183.4
Min	113.4	156.9	115.5	106.0	129.3
Max	135.7	239.6	167.5	516.8	190.8
p_W		0.021 *	0.386	0.248	0.083
p_J			0.510	0.262	0.207
week: 13 N	4	4	4	4	4
Mean	114.3	170.9	124.8	136.7	130.6
Median	110.8	166.4	116.6	132.0	130.4
Min	107.1	153.7	107.1	114.5	114.5
Max	128.3	197.2	159.0	168.5	147.3
p_W		0.021 *	0.559	0.083	0.043 *
p_J			0.661	0.513	0.572

5.5. Urine analysis (statistics)

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Urine analysis (statistics) : males

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Rel dens (1)					
week: -1 N	4	4	4	4	4
Mean	1.034	1.026	1.040	1.021	1.031
Median	1.030	1.023	1.042	1.021	1.028
Min	1.026	1.016	1.027	1.013	1.019
Max	1.049	1.041	1.049	1.032	1.047
p_W		0.384	0.468	0.243	0.468
p_J			0.510	0.427	0.572
week: 7 N	4	4	4	4	4
Mean	1.018	1.025	1.031	1.013	1.017
Median	1.016	1.028	1.029	1.013	1.020
Min	1.013	1.012	1.020	1.011	1.005
Max	1.028	1.032	1.045	1.017	1.023
p_W		0.386	0.083	0.240	0.885
p_J			0.107	0.513	0.352
week: 13 N	4	4	4	4	4
Mean	1.029	1.030	1.031	1.022	1.021
Median	1.031	1.029	1.029	1.022	1.020
Min	1.018	1.025	1.022	1.014	1.011
Max	1.034	1.036	1.042	1.029	1.032
p_W		0.770	1.000	0.080	0.245
p_J			0.884	0.225	0.073
pH (1)					
week: -1 N	4	4	4	4	4
Mean	6.250	6.000	7.375	5.875	5.875
Median	6.000	6.000	7.250	5.750	6.000
Min	5.500	5.500	6.000	5.500	5.500
Max	7.500	6.500	9.000	6.500	6.000
p_W		0.752	0.189	0.642	0.762
p_J			0.164	0.963	0.618

Urine analysis (statistics) : males

Dose (ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week:	7 N	4	4	4	4	4
	Mean	5.750	5.625	6.250	5.750	5.125
	Median	5.500	5.500	6.250	5.500	5.000
	Min	5.000	5.000	5.000	5.000	5.000
	Max	7.000	6.500	7.500	7.000	5.500
	p_W		1.000	0.457	1.000	0.321
	p_J			0.464	0.815	0.388
week:	13 N	4	4	4	4	4
	Mean	6.188	6.250	6.375	6.125	6.000
	Median	6.250	6.250	6.250	6.250	6.000
	Min	5.750	6.000	6.000	5.500	6.000
	Max	6.500	6.500	7.000	6.500	6.000
	p_W		0.752	0.544	0.877	0.505
	p_J			0.558	0.963	0.445

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Urine analysis (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Rel dens (1)					
week: -1 N	4	4	4	4	4
Mean	1.039	1.024	1.021	1.027	1.023
Median	1.042	1.024	1.016	1.027	1.020
Min	1.021	1.016	1.010	1.013	1.014
Max	1.052	1.032	1.042	1.041	1.037
p_W		0.191	0.083	0.248	0.149
p_J			0.048	0.161	0.153
week: 7 N	4	4	4	4	4
Mean	1.020	1.022	1.025	1.016	1.016
Median	1.017	1.022	1.024	1.015	1.017
Min	1.015	1.019	1.019	1.010	1.008
Max	1.030	1.025	1.031	1.026	1.022
p_W		0.248	0.149	0.386	0.564
p_J			0.124	0.815	0.370
week: 13 N	4	4	3	4	4
Mean	1.035	1.029	1.024	1.019	1.029
Median	1.034	1.026	1.016	1.019	1.032
Min	1.032	1.023	1.015	1.011	1.016
Max	1.039	1.039	1.041	1.027	1.036
p_W		0.191	0.480	0.021 *	0.468
p_J			0.157	0.021	0.237
pH (1)					
week: -1 N	4	4	4	4	4
Mean	6.375	6.250	6.125	6.938	7.000
Median	6.500	6.250	6.000	6.500	7.000
Min	5.500	5.000	5.000	6.000	5.500
Max	7.000	7.500	7.500	8.750	8.500
p_W		0.767	0.559	0.659	0.457
p_J			0.558	0.815	0.445
week: 7 N	4	4	4	4	4
Mean	5.875	6.375	6.500	6.250	6.750
Median	5.750	6.500	6.750	6.250	6.750
Min	5.500	5.000	5.000	5.000	5.500
Max	6.500	7.500	7.500	7.500	8.000
p_W		0.766	0.306	0.557	0.180
p_J			0.558	0.709	0.370

Urine analysis (statistics) : females

Dose (ppm)	group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
week: 13 N	4	4	3	4	4
Mean	6.500	6.625	7.667	7.750	6.750
Median	6.500	6.750	8.500	7.750	6.500
Min.	6.500	6.000	6.000	6.500	6.000
Max	6.500	7.000	8.500	9.000	8.000
p_W		0.505	0.430	0.047 *	1.000
p_J			0.279	0.064	0.452

5.6. Organ weights and ratios (statistics)

5.6.1. Organ weights (statistics)

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Organ weights (statistics): males week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Body (kg)	N	4	4	4	4	4
	Mean	10.31	10.44	10.89	10.78	10.36
	Median	10.31	10.30	10.83	10.81	9.880
	Min	9.960	10.18	10.30	10.26	9.660
	Max	10.64	10.96	11.60	11.24	12.00
	p_W		0.564	0.248	0.149	0.248
	p_J			0.107	0.076	0.842
Brain (g)	N	4	4	4	4	4
	Mean	83.93	83.99	80.93	90.15	80.87
	Median	84.07	83.69	79.95	90.70	81.34
	Min	80.11	78.72	74.94	84.47	74.60
	Max	87.46	89.85	88.87	94.73	86.20
	p_W		0.773	0.386	0.043 *	0.386
	p_J			0.306	0.191	0.947
Heart (g)	N	4	4	4	4	4
	Mean	99.50	98.21	95.05	93.10	97.61
	Median	97.94	98.26	96.51	92.34	99.83
	Min	93.66	91.47	88.80	89.31	86.28
	Max	108.5	104.9	98.38	98.40	104.5
	p_W		0.773	0.386	0.083	0.773
	p_J			0.380	0.112	0.388
Liver (g)	N	4	4	4	4	4
	Mean	325.4	343.6	349.4	336.5	407.1
	Median	318.2	334.7	354.6	339.7	397.2
	Min	304.8	317.6	308.3	321.9	380.3
	Max	360.5	387.3	379.8	344.8	453.7
	p_W		0.248	0.248	0.248	0.021 *
	p_J			0.242	0.304	0.006 +

Organ weights (statistics): males week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Kidney (both)						
(g)	N	4	4	4	4	4
	Mean	52.36	51.80	52.18	54.02	52.42
	Median	51.09	51.57	52.44	56.10	50.19
	Min	45.50	45.93	43.39	46.80	48.76
	Max	61.78	58.14	60.44	57.07	60.52
	p_W		0.773	1.000	0.564	1.000
	p_J			0.884	0.513	0.690
Adrenal (both)						
(g)	N	4	4	4	4	4
	Mean	1.074	1.057	1.153	1.119	1.160
	Median	1.079	1.057	1.153	1.120	1.170
	Min	0.991	0.772	0.990	1.074	0.866
	Max	1.149	1.343	1.315	1.160	1.433
	p_W		1.000	0.564	0.564	0.564
	p_J			0.558	0.513	0.388
Thymus						
(g)	N	4	4	4	4	4
	Mean	6.612	7.122	7.675	7.481	7.705
	Median	6.156	6.767	8.192	7.158	8.114
	Min	4.170	4.687	5.282	5.348	4.648
	Max	9.965	10.27	9.035	10.26	9.945
	p_W		0.773	0.386	0.386	0.773
	p_J			0.380	0.350	0.465
Testis (both)						
(g)	N	4	4	4	4	4
	Mean	18.25	16.45	17.90	17.08	16.48
	Median	17.31	17.48	17.92	17.13	16.37
	Min	16.65	12.63	15.74	16.68	14.57
	Max	21.73	18.21	20.01	17.39	18.64
	p_W		0.773	0.773	0.773	0.564
	p_J			1.000	0.779	0.595
Spleen						
(g)	N	4	4	4	4	4
	Mean	22.92	35.39	31.07	38.36	32.89
	Median	21.98	37.96	28.47	34.32	29.72
	Min	20.24	22.27	21.30	23.30	23.02
	Max	27.48	43.35	46.06	61.50	49.09
	p_W		0.043 *	0.248	0.043 *	0.083
	p_J			0.188	0.093	0.127

Organ weights (statistics): males week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Thyroid gland (g)	N	4	4	4	4	4
	Mean	0.778	0.866	0.956	0.901	0.947
	Median	0.795	0.855	0.950	0.859	0.965
	Min	0.708	0.650	0.803	0.790	0.751
	Max	0.816	1.106	1.121	1.094	1.107
	p_W		0.773	0.043 *	0.110	0.149
	p_J			0.107	0.176	0.135

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Organ weights (statistics): females week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Body (kg)	N	4	4	4	4	4
	Mean	10.18	10.10	9.825	9.625	9.775
	Median	10.08	10.08	9.920	9.570	9.650
	Min	9.900	9.480	8.660	8.760	9.200
	Max	10.66	10.74	10.80	10.60	10.60
	p_W		0.773	0.773	0.386	0.386
	p_J			0.558	0.304	0.273
Brain (g)	N	4	4	4	4	4
	Mean	83.32	83.40	81.74	81.36	82.54
	Median	84.43	81.94	79.15	81.24	80.15
	Min	77.15	76.02	75.21	75.09	76.71
	Max	87.29	93.68	93.44	87.86	93.14
	p_W		1.000	0.386	0.773	0.564
	p_J			0.380	0.455	0.595
Heart (g)	N	4	4	4	4	4
	Mean	103.0	87.44	91.16	95.25	92.72
	Median	104.5	86.79	89.83	99.93	90.39
	Min	96.01	80.58	78.54	74.97	86.97
	Max	106.9	95.59	106.4	106.2	103.2
	p_W		0.021 *	0.149	0.386	0.043 *
	p_J			0.079	0.304	0.288
Liver (g)	N	4	4	4	4	4
	Mean	302.9	288.8	297.5	293.7	387.3
	Median	301.6	282.2	293.5	297.6	392.6
	Min	277.7	251.7	278.6	250.3	338.9
	Max	330.6	339.2	324.4	329.4	425.2
	p_W		0.564	0.773	0.386	0.021 *
	p_J			0.884	0.641	0.084

Organ weights (statistics): females week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Kidney (both) (g)	N	4	4	4	4	4
	Mean	48.86	48.18	40.67	43.15	47.01
	Median	47.55	49.15	40.57	41.10	49.01
	Min	44.12	42.78	37.60	40.51	38.00
	Max	56.20	51.65	43.94	49.90	52.02
	p_W		0.773	0.021 *	0.149	0.773
	p_J			0.019	0.025	0.288
Adrenal (both) (g)	N	4	4	4	4	4
	Mean	1.228	1.051	1.255	1.181	1.217
	Median	1.201	1.072	1.276	1.195	1.165
	Min	1.170	0.904	1.094	1.020	1.004
	Max	1.341	1.156	1.375	1.315	1.536
	p_W		0.021 *	0.564	0.564	0.386
	p_J			0.884	1.000	0.894
Thymus (g)	N	4	4	4	4	4
	Mean	9.680	7.465	9.256	8.584	7.168
	Median	9.532	7.020	9.109	6.391	7.413
	Min	6.947	6.145	7.585	4.222	5.004
	Max	12.71	9.676	11.22	17.33	8.844
	p_W		0.149	0.773	0.386	0.386
	p_J			0.884	0.350	0.259
Ovary (both) (g)	N	4	4	4	4	4
	Mean	0.880	0.717	1.409	1.290	1.172
	Median	0.818	0.748	0.932	0.846	0.901
	Min	0.675	0.525	0.824	0.794	0.541
	Max	1.211	0.846	2.949	2.672	2.346
	p_W		0.386	0.248	0.386	0.564
	p_J			0.242	0.225	0.232
Spleen (g)	N	4	4	4	4	4
	Mean	46.68	29.93	43.22	29.77	34.10
	Median	46.24	26.96	43.36	29.73	30.27
	Min	28.20	18.70	23.53	24.59	22.24
	Max	66.05	47.11	62.62	35.03	53.63
	p_W		0.083	0.773	0.083	0.248
	p_J			0.558	0.191	0.232

Organ weights (statistics): females week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Thyroid gland (g)	N	4	4	4	4	4
	Mean	0.770	0.897	0.741	0.757	0.766
	Median	0.699	0.847	0.711	0.713	0.793
	Min	0.565	0.704	0.595	0.581	0.609
	Max	1.117	1.191	0.946	1.020	0.870
	p_W		0.386	0.773	1.000	0.663
	p_J			1.000	0.779	0.974

5.6.2. Organ to body weight ratios (statistics)

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Organ to body weight ratios (statistics): males week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Brain						
(o/oo)	N	4	4	4	4	4
	Mean	8.146	8.055	7.440	8.364	7.843
	Median	8.163	7.962	7.625	8.411	7.893
	Min	7.917	7.589	6.691	8.022	7.183
	Max	8.340	8.706	7.818	8.612	8.403
	p_W		0.564	0.021 *	0.386	0.564
	p_J			0.028	0.926	0.690
Heart						
(o/oo)	N	4	4	4	4	4
	Mean	9.653	9.416	8.742	8.637	9.465
	Median	9.544	9.233	8.488	8.721	9.355
	Min	9.253	8.898	8.481	8.354	8.636
	Max	10.27	10.30	9.511	8.754	10.52
	p_W		0.386	0.083	0.021 *	0.773
	p_J			0.040	0.007 -	0.207
Liver						
(o/oo)	N	4	4	4	4	4
	Mean	31.57	32.99	32.12	31.25	39.41
	Median	31.20	32.65	31.92	30.57	38.50
	Min	29.98	28.98	29.09	30.27	37.81
	Max	33.88	37.68	35.55	33.61	42.85
	p_W		0.773	1.000	1.000	0.021 *
	p_J			0.884	0.852	0.046
Kidney (both)						
(o/oo)	N	4	4	4	4	4
	Mean	5.080	4.979	4.793	5.014	5.062
	Median	5.102	5.006	4.782	5.083	5.045
	Min	4.309	4.191	4.213	4.407	4.990
	Max	5.806	5.711	5.396	5.483	5.169
	p_W		0.564	0.564	1.000	1.000
	p_J			0.558	0.852	0.894

Organ to body weight ratios (statistics): males week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Adrenal (both)						
(o/oo)	N	4	4	4	4	4
	Mean	0.104	0.101	0.106	0.104	0.112
	Median	0.104	0.099	0.107	0.104	0.115
	Min	0.094	0.076	0.096	0.098	0.087
	Max	0.115	0.131	0.113	0.111	0.129
	p_W		0.773	1.000	1.000	0.386
	p_J			0.884	0.926	0.425
Thymus						
(o/oo)	N	4	4	4	4	4
	Mean	0.645	0.678	0.704	0.690	0.754
	Median	0.593	0.657	0.733	0.663	0.766
	Min	0.395	0.460	0.505	0.521	0.481
	Max	1.001	0.937	0.843	0.913	1.001
	p_W		1.000	0.564	0.564	0.564
	p_J			0.661	0.575	0.352
Testis (both)						
(o/oo)	N	4	4	4	4	4
	Mean	1.769	1.576	1.646	1.587	1.597
	Median	1.722	1.649	1.657	1.604	1.508
	Min	1.590	1.240	1.435	1.484	1.472
	Max	2.042	1.765	1.834	1.655	1.898
	p_W		0.248	0.386	0.149	0.149
	p_J			0.464	0.262	0.163
Spleen						
(o/oo)	N	4	4	4	4	4
	Mean	2.221	3.380	2.840	3.591	3.121
	Median	2.144	3.558	2.744	3.228	3.024
	Min	2.012	2.188	1.902	2.118	2.344
	Max	2.583	4.217	3.971	5.791	4.091
	p_W		0.083	0.386	0.149	0.083
	p_J			0.380	0.225	0.232
Thyroid gland						
(o/oo)	N	4	4	4	4	4
	Mean	0.076	0.083	0.088	0.084	0.091
	Median	0.075	0.084	0.087	0.080	0.090
	Min	0.071	0.063	0.072	0.072	0.078
	Max	0.081	0.101	0.109	0.103	0.106
	p_W		0.773	0.248	0.248	0.043 *
	p_J			0.306	0.304	0.111

Statistical tests and flags used:
WILCOXON: * if p_W < 0.05
JONCKHEERE: +- if p_J < 0.01

Organ to body weight ratios (statistics): females week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Brain						
(o/oo)	N	4	4	4	4	4
	Mean	8.184	8.255	8.327	8.474	8.443
	Median	8.270	8.114	8.301	8.503	8.540
	Min	7.777	7.886	7.931	7.892	7.907
	Max	8.417	8.905	8.774	8.999	8.787
	p_W		1.000	0.564	0.386	0.386
	p_J			0.770	0.401	0.288
Heart						
(o/oo)	N	4	4	4	4	4
	Mean	10.12	8.680	9.273	9.939	9.496
	Median	10.10	8.898	9.115	9.660	9.702
	Min	9.698	7.660	8.611	8.312	8.645
	Max	10.58	9.265	10.25	12.12	9.933
	p_W		0.021 *	0.083	0.564	0.149
	p_J			0.107	0.455	0.642
Liver						
(o/oo)	N	4	4	4	4	4
	Mean	29.77	28.55	30.36	30.45	39.72
	Median	29.07	27.93	30.35	30.92	38.01
	Min	27.59	26.11	28.44	28.57	36.83
	Max	33.33	32.24	32.32	31.41	46.02
	p_W		0.564	0.564	0.386	0.021 *
	p_J			0.464	0.262	0.003 +
Kidney (both)						
(o/oo)	N	4	4	4	4	4
	Mean	4.813	4.782	4.151	4.496	4.815
	Median	4.724	4.622	4.154	4.572	4.747
	Min	4.139	4.438	3.953	3.908	4.113
	Max	5.665	5.448	4.342	4.931	5.654
	p_W		0.773	0.083	0.564	1.000
	p_J			0.028	0.191	0.790

Organ to body weight ratios (statistics): females week 14

Dose(ppm)		group 1 0	group 2 50	group 3 125	group 4 250	group 5 1250
Adrenal (both)						
(o/oo)	N	4	4	4	4	4
	Mean	0.121	0.104	0.128	0.123	0.124
	Median	0.119	0.101	0.124	0.123	0.118
	Min	0.114	0.095	0.119	0.113	0.109
	Max	0.131	0.120	0.145	0.133	0.153
	p_W		0.083	0.248	1.000	0.773
	p_J			0.464	0.401	0.507
Thymus						
(o/oo)	N	4	4	4	4	4
	Mean	0.946	0.737	0.941	0.873	0.729
	Median	0.921	0.714	0.942	0.720	0.768
	Min	0.702	0.619	0.802	0.417	0.544
	Max	1.241	0.901	1.081	1.635	0.834
	p_W		0.248	0.773	0.564	0.248
	p_J			0.661	0.852	0.352
Ovary (both)						
(o/oo)	N	4	4	4	4	4
	Mean	0.087	0.072	0.141	0.130	0.119
	Median	0.081	0.075	0.099	0.095	0.092
	Min	0.063	0.049	0.084	0.079	0.059
	Max	0.122	0.088	0.284	0.252	0.233
	p_W		0.564	0.248	0.248	0.773
	p_J			0.242	0.112	0.259
Spleen						
(o/oo)	N	4	4	4	4	4
	Mean	4.547	2.942	4.352	3.071	3.445
	Median	4.571	2.658	4.561	3.056	3.156
	Min	2.848	1.973	2.487	2.733	2.407
	Max	6.196	4.478	5.798	3.439	5.059
	p_W		0.149	0.773	0.083	0.248
	p_J			1.000	0.455	0.465
Thyroid gland						
(o/oo)	N	4	4	4	4	4
	Mean	0.076	0.088	0.075	0.078	0.078
	Median	0.069	0.084	0.075	0.076	0.082
	Min	0.053	0.073	0.063	0.064	0.066
	Max	0.113	0.111	0.088	0.096	0.083
	p_W		0.386	0.564	0.773	0.386
	p_J			0.884	1.000	0.894

6. APPENDIX B: INDIVIDUAL DATA

6.1. Identification of the animals, age and body weight at week -1

GROUP DOSE	MALES				FEMALES			
	DOG NO.	TATTOO NO.	AGE WEEKS	BODYWEIGHT kg	DOG NO.	TATTOO NO.	AGE WEEKS	BODYWEIGHT kg
GROUP 1	1	1995	28	10.0	21	5802	30	10.1
	2	1005	28	9.9	22	6572	30	10.5
0 ppm	3	2131	25	10.8	23	2858	31	9.2
	4	3069	24	8.7	24	1022	30	10.2
GROUP 2	5	1991	28	9.9	25	2876	28	9.7
	6	3065	26	9.2	26	6576	29	10.5
50 ppm	7	2129	26	9.9	27	1034	29	9.8
	8	1011	24	9.1	28	1020	30	9.8
GROUP 3	9	3061	26	10.2	29	5798	30	9.0
	10	1003	28	9.8	30	6568	30	11.1
125 ppm	11	5679	26	10.6	31	1012	33	10.3
	12	1007	24	9.1	32	1001	28	8.8
GROUP 4	13	1985	28	10.1	33	5800	30	9.1
	14	1999	28	10.3	34	6570	30	9.8
250 ppm	15	1019	24	10.4	35	1036	29	10.5
	16	6325	24	9.5	36	3978	30	8.7
GROUP 5	17	3067	25	8.9	37	1032	30	9.6
	18	2880	28	9.4	38	6574	30	10.6
1250 ppm	19	5677	26	11.1	39	1038	29	9.8
	20	1009	24	8.9	40	3982	30	8.9

MEAN AGE MALES = 26 WEEKS
MEAN AGE FEMALES = 30 WEEKS

MEAN WEIGHT MALES = 9.8 kg
MEAN WEIGHT FEMALES = 9.8 kg

6.2. Mortality (individuals)

Mortality (individuals) : males group 1 : 0 ppm

Animal number	date of death	study week	study day	necropsy	type of death
1	23 Feb 95	14	95	yes	Sacrifice 1
2	23 Feb 95	14	95	yes	Sacrifice 1
3	21 Feb 95	14	93	yes	Sacrifice 1
4	21 Feb 95	14	93	yes	Sacrifice 1

Mortality (individuals) : males group 2 : 50 ppm

Animal number	date of death	study week	study day	necropsy	type of death
5	21 Feb 95	14	93	yes	Sacrifice 1
6	21 Feb 95	14	93	yes	Sacrifice 1
7	23 Feb 95	14	95	yes	Sacrifice 1
8	23 Feb 95	14	95	yes	Sacrifice 1

Mortality (individuals) : males group 3 : 125 ppm

Animal number	date of death	study week	study day	necropsy	type of death
9	23 Feb 95	14	95	yes	Sacrifice 1
10	23 Feb 95	14	95	yes	Sacrifice 1
11	21 Feb 95	14	93	yes	Sacrifice 1
12	21 Feb 95	14	93	yes	Sacrifice 1

Mortality (individuals) : males group 4 : 250 ppm

Animal number	date of death	study week	study day	necropsy	type of death
13	20 Feb 95	14	92	yes	Sacrifice 1
14	20 Feb 95	14	92	yes	Sacrifice 1
15	22 Feb 95	14	94	yes	Sacrifice 1
16	22 Feb 95	14	94	yes	Sacrifice 1

Mortality (individuals) : males group 5 : 1250 ppm

Animal number	date of death	study week	study day	necropsy	type of death
17	22 Feb 95	14	94	yes	Sacrifice 1
18	22 Feb 95	14	94	yes	Sacrifice 1
19	20 Feb 95	14	92	yes	Sacrifice 1
20	20 Feb 95	14	92	yes	Sacrifice 1

Mortality (individuals) : females group 1 : 0 ppm

Animal number	date of death	study week	study day	necropsy	type of death
21	21 Feb 95	14	93	yes	Sacrifice 1
22	21 Feb 95	14	93	yes	Sacrifice 1
23	20 Feb 95	14	92	yes	Sacrifice 1
24	20 Feb 95	14	92	yes	Sacrifice 1

Mortality (individuals) : females group 2 : 50 ppm

Animal number	date of death	study week	study day	necropsy	type of death
25	22 Feb 95	14	94	yes	Sacrifice 1
26	22 Feb 95	14	94	yes	Sacrifice 1
27	21 Feb 95	14	93	yes	Sacrifice 1
28	21 Feb 95	14	93	yes	Sacrifice 1

Mortality (individuals) : females group 3 : 125 ppm

Animal number	date of death	study week	study day	necropsy	type of death
29	20 Feb 95	14	92	yes	Sacrifice 1
30	20 Feb 95	14	92	yes	Sacrifice 1
31	22 Feb 95	14	94	yes	Sacrifice 1
32	22 Feb 95	14	94	yes	Sacrifice 1

Mortality (individuals) : females group 4 : 250 ppm

Animal number	date of death	study week	study day	necropsy	type of death
33	20 Feb 95	14	92	yes	Sacrifice 1
34	20 Feb 95	14	92	yes	Sacrifice 1
35	22 Feb 95	14	94	yes	Sacrifice 1
36	22 Feb 95	14	94	yes	Sacrifice 1

Mortality (individuals) : females group 5 : 1250 ppm

Animal number	date of death	study week	study day	necropsy	type of death
37	21 Feb 95	14	93	yes	Sacrifice 1
38	21 Feb 95	14	93	yes	Sacrifice 1
39	21 Feb 95	14	93	yes	Sacrifice 1
40	22 Feb 95	14	94	yes	Sacrifice 1

6.3. In-life observations (individuals)

6.3.1. Vomiting and diarrhea

Explanation of signs

0	normal feces
1	slight diarrhea
2	moderate diarrhea
*	vomiting

Vomiting and diarrhea, males

WEEK	-1	1	2	3	4	5	6	7
DAYS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS
GROUP1								
1+2	0000001	1000100	1100100	1011111	1111111	1111000	1111111	1001111
3+4	0000000	0000000	0000000	0000011	0100000	0010000	0000000	0000000
GROUP2								
5+6	1111111	1111111	1110111	1111111	1111101	1111111	1111111	2111111
7+8	1111111	1100100	1000100	1010111	1110100	0111110	0010110	1101001
GROUP3								
9+10	1000000	0000000	0000000	0000000	0000000	0101000	0000011	1100000
11+12	0000100	0100100	0100000	0011110	1100100	0000100	0002110	1000000
GROUP4								
13+14	1100111	1111100	0010000	0010011	1110101	1111111	1212111	1112221
15+16	0010011	0000000	0000000	0000000	0000000	0011000	0000000	0100000
GROUP5								
17+18	1101111	1011110	1101110	1011111	1111211	1111111	0111111	1101000
19+20	0000100	1011111	2210111	0000100	0100100	1000000	0102011	2111111

Vomiting and diarrhea, males (continued)

WEEK	8	9	10	11	12	13	14
DAYS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS
GROUP1							
1+2	1111111	1111111	1111111	1111111	1111110	1110011	1111
3+4	0000000	0000000	0000000	0001011	0000110	0100000	0
GROUP2							
5+6	1111111	1111111	1111111	1111111	1110100	0111111	11
7+8	0000100	0110001	0011110	1111111	1111111	0100011	0111
GROUP3							
9+10	0000000	0110000	0000000	0001111	0010000	0000000	0000
11+12	0000000	0011000	0000000	0000000	0110000	0001101	10
GROUP4							
13+14	1111111	0000000	0000000	1110110	0011111	0001001	01
15+16	0000000	0000000	0000000	0000011	0110000	0100000	011
GROUP5							
17+18	0111111	1111111	1121111	1111111	1111111	1111111	111
19+20	1100001	0000100	1011000	0010110	1011100	1101100	0

For explanation of signs see page 200

Vomiting and diarrhea, females

WEEK	-1	1	2	3	4	5	6	7
DAYS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS
GROUP1								
21+22	1111111	1111211	1111111	0111111	1111111	1111111	1111111	1111111
23+24	1010000	0000000	1000110	0000000	0101000	1110000	0001000	0000111
GROUP2								
25+26	0101100	2110100	1000000	1000000	0100000	0011000	1111110	1001011
27+28	0001011	0010000	0000000	1000000	0000000	0000000	2110000	0000000
GROUP3								
29+30	0000000	1010100	0101000	1100000	1000111	1000111	0000101	0111111
31+32	0111111	1110100	0000000	0111011	1111111	1111001	1111111	1111111
GROUP4								
33+34	1111111	0010100	1011010	1100001	1010000	1101011	0000111	1100011
35+36	0000011	0100000	0010011	1111111	1111111	1111111	1111111	1211111
GROUP5								
37+38	1010000	0010100	0000111 *	1111111	1111111	1101000	1102111	1111111
39+40	1110111	0111110	1111111	1011111	1110111	1101001	1212211	2111111

For explanation of signs see page 200

Vomiting and diarrhea, females (continued)

WEEK	8	9	10	11	12	13	14
DAYS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS	MTWTFSS
GROUP1							
21+22	1111111	1111111	1111111	1111111	1111111	1111111	11
23+24	1111111	0010000	0000111	1110011	1000100	1011111	1
GROUP2							
25+26	0000000	0000000	1010001	1000011	0001100	1011010	011
27+28	0000000	0100000	0010000	0000101	1110000	0000000	00
GROUP3							
29+30	1100000	0110000	0100100	0000000	0000000	0011000	0
31+32	1121111	1111111	1111110	0111111	1111100	0100101	111
31						@	
GROUP4							
33+34	1111111	0111111	1211111	1111111	0011110	1110010	1
34						@	
35+36	0111011	1011111	1110000	0110011	1111000	1111111	011
GROUP5							
37+38	1000000	0000000	0111001	1101001	0111100	1110111	11
37					@		
39+40	1111111 *	1111110	1111011	1110111	0111000	1111111	11
40							1

For explanation of signs see page 200

6.3.2. Clinical signs

Clinical observations, males

Group	Animal nos.	Week	Observation
1	1	2- 7	Hair loss on the back
	2	1-13	nrcso
	3, 4	1-13	nrcso
2	5, 6	1-13	nrcso
	7, 8	1-13	nrcso
3	9,10	1-13	nrcso
	11,12	1-13	nrcso
4	13,14	1-13	nrcso
	15,16	1-13	nrcso
5	17,18	1-13	nrcso
	19,20	1-13	nrcso

nrcso = no relevant clinical signs observed

Clinical observations, females

Group	Animal nos.	Week	Observation
1	21,22	1-13	nrcso
	23,24	1-13	nrcso
2	25,26	1-13	nrcso
	27	7	Wounds on the neck and back of the neck visible, induced by the the neckchain
		8-13	Scab formation
	28	1-13	nrcso
3	29,30	1-13	nrcso
	31,32	1-13	nrcso
4	33,34	1-13	nrcso
	35,36	1-13	nrcso
5	37,38	1-13	nrcso
	39,40	1-13	nrcso

nrcso = no relevant clinical signs observed

6.4. Body weight (individuals)

Body weight (individuals) : males group 1 : 0 ppm
(kg/animal)

	Animal no			
	1	2	3	4
week:				
-1	10.00	9.900	10.80	8.700
1	10.20	10.00	10.80	8.800
2	10.20	10.10	10.70	9.000
3	10.40	10.30	10.80	9.200
4	10.70	10.40	11.00	9.400
5	10.70	10.60	11.10	9.600
6	10.80	10.70	11.10	9.700
7	10.90	10.70	11.30	9.900
8	10.90	11.00	11.30	10.00
9	11.00	11.10	11.20	10.20
10	11.10	11.10	11.30	10.20
11	11.20	11.10	11.40	10.30
12	11.00	11.00	11.30	10.50
13	10.90	11.10	11.50	10.60

Body weight (individuals) : males group 2 : 50 ppm
(kg/animal)

	Animal no			
	5	6	7	8
week:				
-1	9.900	9.200	9.900	9.100
1	9.900	9.400	10.10	9.300
2	9.900	9.400	10.10	9.400
3	10.10	9.500	10.30	9.600
4	10.20	9.800	10.40	9.800
5	10.50	10.20	10.60	10.10
6	10.60	10.20	10.70	10.20
7	10.60	10.40	10.90	10.30
8	10.60	10.60	11.00	10.50
9	10.80	10.70	11.20	10.60
10	10.90	10.70	11.30	10.70
11	10.90	10.90	11.40	10.70
12	11.00	10.90	11.50	10.80
13	10.80	10.90	11.50	10.90

Body weight (individuals) : males group 3 : 125 ppm
(kg/animal)

	Animal no			
	9	10	11	12
week:				
-1	10.20	9.800	10.60	9.100
1	10.40	10.20	10.80	9.400
2	10.50	9.900	10.90	9.400
3	10.70	10.20	11.10	9.600
4	10.80	10.40	11.30	9.700
5	11.10	10.40	11.70	10.10
6	11.20	10.50	11.70	10.20
7	11.40	10.50	11.70	10.30
8	11.50	10.70	11.90	10.40
9	11.60	10.70	12.10	10.60
10	11.80	10.80	12.10	10.70
11	11.90	10.90	12.20	10.80
12	11.90	10.90	12.30	10.90
13	11.90	10.90	12.20	10.80

Body weight (individuals) : males group 4 : 250 ppm
(kg/animal)

	Animal no			
	13	14	15	16
week:				
-1	10.10	10.30	10.40	9.500
1	10.30	10.50	10.50	9.900
2	10.30	10.60	10.70	9.900
3	10.30	10.70	10.90	10.30
4	10.40	10.80	11.20	10.50
5	10.70	11.00	11.30	10.80
6	10.70	11.10	11.50	11.10
7	10.90	11.00	11.70	11.00
8	11.00	11.30	11.70	11.30
9	11.10	11.20	11.90	11.70
10	11.00	11.30	11.90	11.60
11	10.90	11.40	12.00	11.60
12	10.90	11.20	11.80	11.70
13	10.90	11.30	12.10	11.70

Body weight (individuals) : males group 5 : 1250 ppm
(kg/animal)

	Animal no			
	17	18	19	20
week:				
-1	8.900	9.400	11.10	8.900
1	9.100	9.400	11.20	8.900
2	9.300	9.600	11.30	8.900
3	9.400	9.800	11.50	9.200
4	9.600	10.00	11.60	9.400
5	9.800	10.10	11.90	9.700
6	10.00	10.20	11.90	9.900
7	10.10	10.30	12.00	9.900
8	10.30	10.40	12.10	10.10
9	10.40	10.40	12.20	10.30
10	10.60	10.40	12.40	10.20
11	10.60	10.40	12.50	10.40
12	10.40	10.30	12.50	10.40
13	10.50	10.30	12.40	10.50

Body weight (individuals) : females group 1 : 0 ppm
(kg/animal)

	Animal no			
	21	22	23	24
week:				
-1	10.10	10.50	9.200	10.20
1	10.20	10.70	9.400	10.40
2	10.20	10.50	9.300	10.40
3	10.40	10.60	9.500	10.50
4	10.50	10.80	9.500	10.50
5	10.60	11.00	9.700	10.70
6	10.70	11.10	9.900	10.80
7	10.70	11.10	9.900	11.00
8	10.70	11.10	10.00	11.10
9	10.70	11.20	10.20	11.20
10	10.70	11.20	10.20	11.10
11	10.80	11.20	10.20	11.20
12	10.80	11.10	10.20	11.30
13	10.80	11.10	10.20	11.40

Body weight (individuals) : females group 2 : 50 ppm
(kg/animal)

	Animal no			
	25	26	27	28
week:				
-1	9.700	10.50	9.800	9.800
1	9.500	10.70	10.00	10.20
2	9.700	10.70	9.900	10.10
3	9.800	10.80	10.10	10.20
4	9.900	10.90	10.10	10.40
5	10.20	10.90	10.20	10.70
6	10.10	11.10	10.30	10.40
7	10.30	11.20	10.20	10.80
8	10.30	11.40	10.30	11.00
9	10.30	11.30	10.30	11.20
10	10.40	11.40	10.20	11.10
11	10.40	11.40	10.20	11.10
12	10.40	11.40	10.30	11.20
13	10.40	11.30	10.20	11.20

Body weight (individuals) : females group 3 : 125 ppm
(kg/animal)

	Animal no			
	29	30	31	32
week:				
-1	9.000	11.10	10.30	8.800
1	9.200	11.20	10.40	9.000
2	9.100	11.00	10.40	9.100
3	9.100	11.20	10.40	9.300
4	9.300	11.40	10.60	9.400
5	9.300	11.50	10.60	9.600
6	9.300	11.50	10.60	9.700
7	9.300	11.50	10.70	9.800
8	9.300	11.50	10.70	9.900
9	9.300	11.50	10.90	10.00
10	9.100	11.40	10.80	10.00
11	9.100	11.50	10.90	10.00
12	9.200	11.60	11.10	10.20
13	9.300	11.50	11.10	10.20

Body weight (individuals) : females group 4 : 250 ppm
(kg/animal)

	Animal no			
	33	34	35	36
week:				
-1	9.100	9.800	10.50	8.700
1	8.900	10.00	10.60	8.800
2	9.000	10.20	10.60	8.800
3	9.200	10.40	10.70	8.900
4	9.400	10.20	10.90	9.100
5	9.600	10.70	10.90	9.200
6	9.600	10.80	11.00	9.200
7	9.600	10.90	11.10	9.300
8	9.800	11.00	11.10	9.400
9	9.800	11.20	11.20	9.400
10	9.800	11.10	11.10	9.400
11	9.800	11.10	11.20	9.500
12	9.800	11.20	11.10	9.500
13	9.800	11.40	11.00	9.400

Body weight (individuals) : females group 5 : 1250 ppm
(kg/animal)

	Animal no			
	37	38	39	40
week:				
-1	9.600	10.60	9.800	8.900
1	9.700	10.70	9.900	9.000
2	9.800	10.70	9.800	9.000
3	9.900	10.70	10.00	9.200
4	10.00	10.70	10.00	9.300
5	10.30	11.10	10.20	9.400
6	10.30	11.00	10.30	9.600
7	10.40	11.10	10.10	9.600
8	10.40	11.00	10.20	9.600
9	10.40	11.20	10.40	9.600
10	10.30	11.20	10.20	9.600
11	10.50	11.20	10.20	9.700
12	10.60	11.10	10.20	9.600
13	10.60	11.00	10.20	9.600

6.5. Food consumption (individuals)

Food consumption (individuals) : males
(g/animal/day) group 1 : 0 ppm

	Animal no.			
	1	2	3	4
week:				
-1	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : males
(g/animal/day) group 2 : 50 ppm

	Animal no.			
	5	6	7	8
week:				
-1	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : males
(g/animal/day) group 3 : 125 ppm

	Animal no.			
	9	10	11	12
week:				
-1	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : males
(g/animal/day) group 4 : 250 ppm

	Animal no.			
	13	14	15	16
week:				
-1	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : males
(g/animal/day) group 5 : 1250 ppm

	Animal no.			
	17	18	19	20
week:				
-1	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : females
(g/animal/day) group 1 : 0 ppm

	Animal no.			
	21	22	23	24
week:				
-1	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : females
(g/animal/day) group 2 : 50 ppm

	Animal no.			
	25	26	27	28
week:				
-1	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : females
(g/animal/day) group 3 : 125 ppm

	Animal no.			
	29	30	31	32
week:				
-1	345.7	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	347.1	350.0	350.0	350.0
4	337.1	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	317.1	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : females
(g/animal/day) group 4 : 250 ppm

	Animal no.			
	33	34	35	36
week:				
-1	341.4	350.0	350.0	344.3
1	321.4	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	345.7	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

Food consumption (individuals) : females
(g/animal/day) group 5 : 1250 ppm

	Animal no.			
	37	38	39	40
week:				
-1	350.0	350.0	350.0	350.0
1	350.0	350.0	350.0	350.0
2	350.0	350.0	350.0	350.0
3	350.0	350.0	350.0	350.0
4	350.0	350.0	350.0	350.0
5	350.0	350.0	350.0	350.0
6	350.0	350.0	350.0	350.0
7	350.0	350.0	350.0	350.0
8	350.0	350.0	350.0	350.0
9	350.0	350.0	350.0	350.0
10	350.0	350.0	350.0	350.0
11	350.0	350.0	350.0	350.0
12	350.0	350.0	350.0	350.0
13	350.0	350.0	350.0	350.0

6.6. Eye examinations (individuals)

A detailed examination of both sides of the third eyelid under local anesthesia revealed conjunctivitis follicularis of variable degree for all male and female dogs of the control and treated groups at pretest and week 13.

All the other findings for individual dogs are listed in the following tables.

Individual findings, male

Group	Dog no.	Week	Findings
1	1	-4	Lens: one opaque spot visible, both eyes
	1	13	Lens: one opaque spot visible, both eyes
	2	-4	Lens: persistent hyaloid vessel visible, both eyes
	2	13	Lens: persistent hyaloid vessel visible, both eyes
	3	-4	noao
	3	13	noao
	4	-4	Lens: persistent hyaloid vessel visible, both eyes
	4	13	Lens: persistent hyaloid vessel visible, both eyes
2	5	-4	noao
	5	13	noao
	6	-4	noao
	6	13	noao
	7	-4	noao
	7	13	noao
	8	-4	noao
	8	13	noao
3	9	-4	noao
	9	13	noao
	10	-4	noao
	10	13	noao
	11	-4	noao
	11	13	noao
	12	-4	noao
	12	13	noao
4	13	-4	Fundus: Tap. lucidum, hyperreflective spot nasal the disc, right eye
	13	13	Fundus: Tap. lucidum, hyperreflective spot nasal the disc, right eye
	14	-4	noao
	14	13	noao
	15	-4	noao
	15	13	noao
	16	-4	noao
	16	13	noao
5	17	-4	noao
	17	13	noao
	18	-4	noao
	18	13	noao
	19	-4	noao
	19	13	noao
	20	-4	noao
	20	13	noao

noao = no ocular abnormality observed

Individual findings, females

Group	Dog No.	Week	Findings
1	21	-4	noao
	21	13	noao
	22	-4	noao
	22	13	noao
	23	-4	noao
	23	13	noao
	24	-4	Fundus: Tap. lucidum, multiple retinal folds visible, both eyes
	24	13	Fundus: Tap. lucidum, multiple retinal folds visible, both eyes
2	25	-4	noao
	25	13	noao
	26	-4	noao
	26	13	noao
	27	-4	noao
	27	13	noao
	28	-4	Fundus: Tap. lucidum, one hyperreflective spot visible, left eye
	28	13	Fundus: Tap. lucidum, one hyperreflective spot visible, left eye
3	29	-4	noao
	29	13	noao
	30	-4	noao
	30	13	noao
	31	-4	noao
	31	13	noao
	32	-4	noao
	32	13	noao
4	33	-4	noao
	33	13	noao
	34	-4	noao
	34	13	noao
	35	-4	Lens: multiple opaque dots visible, both eyes
	35	13	Lens: multiple opaque dots visible, both eyes
	36	-4	noao
	36	13	noao
5	37	-4	noao
	37	13	noao
	38	-4	noao
	38	13	noao
	39	-4	noao
	39	13	noao
	40	-4	noao
	40	13	noao

6.7. Hematology (individuals)

Hematology (individuals): males group 1
0 ppm

		Animal no 1	2	3	4
RBC (T/l)					
week:	-1	5.960	6.280	6.600	5.930
	7	6.285	6.500	6.340	6.160
	13	6.910	6.610	6.180	5.990
Hb (mmol/l)					
week:	-1	8.400	8.700	9.200	8.800
	7	8.700	8.900	8.700	9.100
	13	9.300	9.100	8.700	8.900
Hct (1)					
week:	-1	0.392	0.412	0.431	0.405
	7	0.421	0.426	0.417	0.432
	13	0.447	0.425	0.406	0.411
MCV (fl)					
week:	-1	65.70	65.60	65.30	68.20
	7	67.00	65.60	65.80	70.20
	13	64.70	64.30	65.60	68.70
RDW (1)					
week:	-1	0.153	0.144	0.140	0.139
	7	0.136	0.138	0.142	0.129
	13	0.137	0.138	0.132	0.129
MCH (fmol)					
week:	-1	1.410	1.390	1.400	1.490
	7	1.380	1.370	1.380	1.480
	13	1.350	1.380	1.410	1.480

Hematology (individuals): males

group 1
0 ppm

		Animal no 1	2	3	4
MCHC (mmol/l)					
week:	-1	21.48	21.21	21.37	21.86
	7	20.60	20.83	20.95	21.06
	13	20.90	21.45	21.48	21.58
HDW (mmol/l)					
week:	-1	1.250	1.140	1.010	1.030
	7	1.215	1.220	1.190	1.110
	13	1.140	1.200	1.120	1.060
Reti (1)					
week:	-1	0.024	0.025	0.015	0.025
	7	0.016	0.021	0.015	0.021
	13	0.019	0.019	0.016	0.023
WBC (G/l)					
week:	-1	11.21	8.870	10.42	11.86
	7	10.07	10.55	11.83	10.95
	13	12.21	8.480	10.12	7.870
Neut (1)					
week:	-1	0.594	0.539	0.532	0.622
	7	0.646	0.581	0.583	0.475
	13	0.666	0.573	0.569	0.467
Eos (1)					
week:	-1	0.034	0.031	0.018	0.026
	7	0.028	0.030	0.016	0.031
	13	0.022	0.029	0.017	0.018
Baso (1)					
week:	-1	0.006	0.006	0.004	0.004
	7	0.004	0.003	0.002	0.004
	13	0.004	0.003	0.003	0.005

Hematology (individuals): males

group 1
0 ppm

		Animal no 1	2	3	4
Lympho (1)					
week:	-1	0.324	0.380	0.393	0.273
	7	0.271	0.338	0.347	0.431
	13	0.256	0.347	0.354	0.431
Mono (1)					
week:	-1	0.038	0.040	0.049	0.068
	7	0.050	0.046	0.049	0.055
	13	0.043	0.040	0.050	0.068
Luc (1)					
week:	-1	0.004	0.004	0.003	0.007
	7	0.004	0.002	0.003	0.004
	13	0.009	0.008	0.006	0.011
Neut (G/l)					
week:	-1	6.660	4.780	5.550	7.380
	7	6.500	6.130	6.900	5.200
	13	8.130	4.860	5.760	3.670
Eos (G/l)					
week:	-1	0.380	0.280	0.190	0.310
	7	0.280	0.310	0.190	0.340
	13	0.270	0.250	0.170	0.140
Baso (G/l)					
week:	-1	0.070	0.050	0.040	0.050
	7	0.035	0.030	0.030	0.050
	13	0.050	0.030	0.030	0.040
Lympho (G/l)					
week:	-1	3.630	3.370	4.100	3.240
	7	2.730	3.570	4.100	4.720
	13	3.130	2.940	3.590	3.390

Hematology (individuals): males

group 1
0 ppm

		Animal no 1	2	3	4
Mono (G/l) week:	-1	0.420	0.350	0.510	0.810
	7	0.495	0.490	0.580	0.610
	13	0.520	0.340	0.510	0.540
Luc (G/l) week:	-1	0.040	0.030	0.030	0.080
	7	0.035	0.020	0.030	0.040
	13	0.110	0.060	0.060	0.090
Plt (G/l) week:	-1	361.0	293.0	241.0	253.0
	7	378.0	324.0	214.0	338.0
	13	390.0	292.0	243.0	226.0
PT(CS) (sec) week:	-1	33.14	34.23	27.97	26.72
	7	33.90	33.53	30.68	27.46
	13	30.13	31.20	28.89	27.17

Hematology (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
RBC (T/l) week:	-1	6.090	6.120	6.210	6.290
	7	6.740	6.430	6.470	6.140
	13	6.530	6.160	6.910	6.330
Hb (mmol/l) week:	-1	8.800	8.700	8.800	8.700
	7	9.800	9.000	9.000	8.500
	13	9.600	8.700	9.600	8.900

Hematology (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
Hct (l)					
week:	-1	0.411	0.416	0.413	0.421
	7	0.464	0.439	0.436	0.410
	13	0.441	0.407	0.450	0.417
MCV (fl)					
week:	-1	67.40	68.00	66.40	66.80
	7	68.80	68.30	67.40	66.80
	13	67.50	66.10	65.20	65.90
RDW (l)					
week:	-1	0.147	0.132	0.140	0.135
	7	0.137	0.129	0.132	0.129
	13	0.132	0.125	0.129	0.130
MCH (fmol)					
week:	-1	1.450	1.420	1.410	1.390
	7	1.450	1.400	1.400	1.390
	13	1.470	1.410	1.380	1.410
MCHC (mmol/l)					
week:	-1	21.45	20.93	21.24	20.75
	7	21.05	20.51	20.71	20.76
	13	21.75	21.39	21.24	21.39
HDW (mmol/l)					
week:	-1	1.090	0.970	1.120	1.010
	7	1.210	1.100	1.210	1.110
	13	1.130	1.040	1.120	1.080
Reti (l)					
week:	-1	0.027	0.019	0.026	0.028
	7	0.021	0.018	0.021	0.016
	13	0.021	0.014	0.017	0.021

Hematology (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
WBC (G/l)					
week:	-1	8.570	9.840	12.01	12.79
	7	11.13	9.980	10.61	11.45
	13	11.89	9.110	10.03	10.78
Neut (1)					
week:	-1	0.588	0.443	0.580	0.536
	7	0.590	0.421	0.569	0.552
	13	0.641	0.472	0.556	0.570
Eos (1)					
week:	-1	0.017	0.023	0.017	0.030
	7	0.022	0.027	0.025	0.027
	13	0.018	0.028	0.019	0.021
Baso (1)					
week:	-1	0.005	0.009	0.004	0.004
	7	0.007	0.005	0.003	0.003
	13	0.004	0.004	0.003	0.004
Lympho (1)					
week:	-1	0.342	0.461	0.325	0.373
	7	0.321	0.464	0.342	0.372
	13	0.270	0.417	0.349	0.364
Mono (1)					
week:	-1	0.046	0.058	0.070	0.050
	7	0.056	0.076	0.057	0.044
	13	0.062	0.071	0.067	0.034
Luc (1)					
week:	-1	0.003	0.007	0.004	0.006
	7	0.005	0.006	0.003	0.002
	13	0.007	0.008	0.005	0.008

Hematology (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
Neut (G/l) week:	-1	5.030	4.360	6.960	6.860
	7	6.570	4.200	6.040	6.320
	13	7.620	4.300	5.570	6.140
Eos (G/l) week:	-1	0.150	0.220	0.210	0.390
	7	0.240	0.270	0.270	0.310
	13	0.210	0.250	0.190	0.220
Baso (G/l) week:	-1	0.040	0.090	0.050	0.050
	7	0.070	0.050	0.040	0.030
	13	0.040	0.040	0.030	0.040
Lympho (G/l) week:	-1	2.930	4.540	3.900	4.760
	7	3.570	4.630	3.630	4.260
	13	3.210	3.800	3.500	3.920
Mono (G/l) week:	-1	0.390	0.570	0.840	0.640
	7	0.620	0.760	0.610	0.500
	13	0.740	0.650	0.670	0.360
Luc (G/l) week:	-1	0.020	0.070	0.050	0.080
	7	0.060	0.060	0.030	0.020
	13	0.080	0.070	0.050	0.090
Plt (G/l) week:	-1	194.0	327.0	237.0	324.0
	7	200.0	389.0	299.0	286.0
	13	204.0	363.0	267.0	339.0

Hematology (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
PT(CS) (sec) week:	-1	33.37	27.61	28.20	35.27
	7	31.97	31.49	29.94	38.29
	13	30.69	31.62	29.20	36.89

Hematology (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
RBC (T/l) week:	-1	5.860	6.380	6.660	6.190
	7	6.800	6.400	6.470	6.170
	13	6.660	6.210	6.600	6.160
Hb (mmol/l) week:	-1	8.400	9.200	9.500	9.000
	7	9.600	9.000	9.100	9.000
	13	9.400	8.800	9.300	9.000
Hct (1) week:	-1	0.398	0.429	0.451	0.442
	7	0.465	0.429	0.439	0.431
	13	0.447	0.404	0.432	0.419
MCV (fl) week:	-1	67.80	67.30	67.60	71.30
	7	68.30	67.10	67.90	69.90
	13	67.10	65.00	65.50	68.00
RDW (1) week:	-1	0.145	0.143	0.147	0.145
	7	0.135	0.134	0.134	0.129
	13	0.133	0.132	0.133	0.127

Hematology (individuals): males

group 3
125 ppm

		Animal no			
		9	10	11	12
MCH (fmol)					
week:	-1	1.430	1.440	1.430	1.450
	7	1.410	1.410	1.410	1.460
	13	1.410	1.410	1.410	1.460
MCHC (mmol/l)					
week:	-1	21.14	21.39	21.12	20.28
	7	20.67	21.00	20.78	20.89
	13	21.09	21.66	21.56	21.46
HDW (mmol/l)					
week:	-1	1.030	1.160	1.150	0.990
	7	1.140	1.260	1.130	1.050
	13	1.100	1.170	1.120	1.170
Reti (1)					
week:	-1	0.027	0.020	0.029	0.034
	7	0.027	0.016	0.017	0.014
	13	0.027	0.013	0.020	0.016
WBC (G/l)					
week:	-1	10.56	10.69	10.15	11.16
	7	13.46	11.31	12.46	12.39
	13	12.80	10.90	11.33	9.610
Neut (1)					
week:	-1	0.531	0.511	0.454	0.467
	7	0.575	0.580	0.510	0.569
	13	0.647	0.606	0.488	0.567
Eos (1)					
week:	-1	0.048	0.032	0.020	0.030
	7	0.024	0.033	0.015	0.039
	13	0.018	0.028	0.009	0.033

Hematology (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
Baso (1)					
week:	-1	0.003	0.007	0.003	0.012
	7	0.004	0.004	0.003	0.007
	13	0.005	0.004	0.003	0.004
Lympho (1)					
week:	-1	0.365	0.398	0.493	0.427
	7	0.336	0.333	0.420	0.319
	13	0.270	0.309	0.445	0.304
Mono (1)					
week:	-1	0.048	0.048	0.026	0.055
	7	0.057	0.047	0.051	0.059
	13	0.052	0.044	0.052	0.081
Luc (1)					
week:	-1	0.005	0.004	0.003	0.008
	7	0.003	0.004	0.001	0.006
	13	0.008	0.009	0.003	0.011
Neut (G/l)					
week:	-1	5.610	5.460	4.610	5.210
	7	7.740	6.560	6.350	7.060
	13	8.290	6.600	5.530	5.450
Eos (G/l)					
week:	-1	0.510	0.350	0.210	0.340
	7	0.320	0.370	0.190	0.480
	13	0.220	0.310	0.100	0.320
Baso (G/l)					
week:	-1	0.030	0.070	0.030	0.130
	7	0.060	0.040	0.040	0.090
	13	0.060	0.040	0.030	0.040

Hematology (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
Lympho (G/l) week:	-1	3.850	4.250	5.010	4.770
	7	4.520	3.760	5.240	3.960
	13	3.450	3.370	5.040	2.920
Mono (G/l) week:	-1	0.510	0.520	0.270	0.620
	7	0.770	0.530	0.630	0.730
	13	0.660	0.480	0.590	0.780
Luc (G/l) week:	-1	0.050	0.040	0.030	0.090
	7	0.040	0.040	0.010	0.070
	13	0.110	0.100	0.040	0.110
Plt (G/l) week:	-1	290.0	325.0	248.0	350.0
	7	349.0	363.0	242.0	300.0
	13	299.0	282.0	268.0	297.0
PT(CS) (sec) week:	-1	28.96	32.21	38.17	34.03
	7	28.54	35.38	38.70	38.83
	13	27.94	30.82	36.08	37.76

Hematology (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
RBC (T/l) week:	-1	5.610	5.940	5.320	5.660
	7	5.980	6.370	5.760	5.910
	13	6.040	6.400	6.080	5.920

Hematology (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
Hb (mmol/l)					
week:	-1	8.200	8.400	7.500	7.600
	7	8.700	8.900	8.300	7.800
	13	8.600	8.900	8.700	7.800
Hct (1)					
week:	-1	0.389	0.391	0.357	0.360
	7	0.415	0.423	0.395	0.380
	13	0.405	0.408	0.412	0.369
MCV (fl)					
week:	-1	69.40	65.70	67.10	63.60
	7	69.40	66.30	68.50	64.40
	13	67.00	63.80	67.80	62.30
RDW (1)					
week:	-1	0.141	0.146	0.154	0.143
	7	0.131	0.141	0.148	0.131
	13	0.130	0.135	0.140	0.129
MCH (fmol)					
week:	-1	1.460	1.420	1.420	1.350
	7	1.450	1.400	1.440	1.320
	13	1.420	1.390	1.430	1.320
MCHC (mmol/l)					
week:	-1	21.09	21.56	21.13	21.22
	7	20.87	21.16	21.02	20.55
	13	21.24	21.79	21.06	21.13
HDW (mmol/l)					
week:	-1	1.050	1.110	0.990	1.070
	7	1.160	1.260	1.300	1.170
	13	1.180	1.110	1.080	1.030

Hematology (individuals): males

group 4
250 ppm

		Animal no			
		13	14	15	16
Reti (1)					
week:	-1	0.023	0.017	0.014	0.024
	7	0.024	0.016	0.019	0.021
	13	0.025	0.011	0.012	0.016
WBC (G/l)					
week:	-1	10.50	8.830	9.110	11.42
	7	16.72	9.740	10.60	11.55
	13	11.78	7.730	9.370	11.26
Neut (1)					
week:	-1	0.498	0.569	0.444	0.546
	7	0.650	0.543	0.517	0.545
	13	0.562	0.591	0.525	0.554
Eos (1)					
week:	-1	0.014	0.036	0.021	0.036
	7	0.013	0.083	0.016	0.015
	13	0.022	0.014	0.014	0.019
Baso (1)					
week:	-1	0.006	0.003	0.006	0.004
	7	0.003	0.002	0.004	0.003
	13	0.005	0.003	0.005	0.002
Lympho (1)					
week:	-1	0.422	0.343	0.468	0.346
	7	0.269	0.322	0.383	0.374
	13	0.350	0.327	0.380	0.354
Mono (1)					
week:	-1	0.054	0.046	0.054	0.062
	7	0.062	0.045	0.074	0.060
	13	0.052	0.059	0.069	0.062

Hematology (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
Luc (1)					
week:	-1	0.006	0.002	0.007	0.005
	7	0.003	0.005	0.006	0.004
	13	0.009	0.007	0.008	0.008
Neut (G/l)					
week:	-1	5.230	5.030	4.040	6.240
	7	10.87	5.290	5.480	6.290
	13	6.620	4.570	4.920	6.240
Eos (G/l)					
week:	-1	0.150	0.310	0.190	0.420
	7	0.220	0.810	0.170	0.170
	13	0.260	0.110	0.130	0.220
Baso (G/l)					
week:	-1	0.060	0.030	0.060	0.050
	7	0.060	0.020	0.040	0.030
	13	0.060	0.020	0.040	0.020
Lympho (G/l)					
week:	-1	4.440	3.030	4.270	3.960
	7	4.500	3.140	4.060	4.320
	13	4.120	2.530	3.560	3.990
Mono (G/l)					
week:	-1	0.560	0.410	0.490	0.710
	7	1.030	0.430	0.790	0.690
	13	0.610	0.450	0.640	0.700
Luc (G/l)					
week:	-1	0.060	0.020	0.060	0.050
	7	0.060	0.050	0.060	0.040
	13	0.110	0.050	0.080	0.090

Hematology (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
Plt (G/l)					
week:	-1	292.0	216.0	256.0	290.0
	7	399.0	172.0	312.0	332.0
	13	357.0	231.0	285.0	283.0
PT(CS) (sec)					
week:	-1	30.67	35.36	33.87	38.21
	7	33.29	33.44	34.42	39.11
	13	30.43	35.31	32.20	38.75

Hematology (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
RBC (T/l)					
week:	-1	5.430	5.690	5.880	5.970
	7	5.530	6.080	6.610	5.670
	13	5.700	5.970	6.450	6.130
Hb (mmol/l)					
week:	-1	7.800	8.100	8.200	8.400
	7	7.800	8.400	9.300	8.000
	13	8.200	8.400	9.100	8.500
Hct (1)					
week:	-1	0.371	0.385	0.392	0.400
	7	0.381	0.415	0.447	0.382
	13	0.383	0.396	0.424	0.404
MCV (fl)					
week:	-1	68.30	67.70	66.70	66.90
	7	68.90	68.30	67.60	67.40
	13	67.20	66.20	65.70	66.00

Hematology (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
RDW (1)					
week:	-1	0.137	0.142	0.155	0.148
	7	0.133	0.139	0.141	0.135
	13	0.134	0.138	0.140	0.134
MCH (fmol)					
week:	-1	1.430	1.430	1.400	1.410
	7	1.420	1.380	1.400	1.410
	13	1.430	1.410	1.410	1.390
MCHC (mmol/l)					
week:	-1	20.92	21.12	21.00	21.07
	7	20.55	20.14	20.70	20.90
	13	21.29	21.36	21.45	21.14
HDW (mmol/l)					
week:	-1	1.090	1.080	1.130	1.400
	7	1.160	1.200	1.120	1.080
	13	1.110	1.080	1.100	0.990
Reti (1)					
week:	-1	0.020	0.016	0.026	0.026
	7	0.014	0.023	0.020	0.017
	13	0.013	0.018	0.018	0.018
WBC (G/l)					
week:	-1	10.24	7.730	10.15	11.41
	7	12.27	9.120	10.87	10.30
	13	9.990	7.770	9.670	9.260
Neut (1)					
week:	-1	0.470	0.488	0.487	0.567
	7	0.555	0.516	0.523	0.554
	13	0.534	0.539	0.508	0.583

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Hematology (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
Eos (1)					
week:	-1	0.038	0.015	0.022	0.029
	7	0.023	0.022	0.017	0.032
	13	0.017	0.014	0.011	0.023
Baso (1)					
week:	-1	0.004	0.005	0.004	0.006
	7	0.003	0.003	0.006	0.002
	13	0.002	0.003	0.004	0.003
Lympho (1)					
week:	-1	0.420	0.427	0.429	0.313
	7	0.342	0.382	0.409	0.323
	13	0.372	0.381	0.422	0.334
Mono (1)					
week:	-1	0.062	0.061	0.053	0.079
	7	0.072	0.075	0.040	0.086
	13	0.066	0.054	0.047	0.050
Luc (1)					
week:	-1	0.006	0.004	0.005	0.005
	7	0.005	0.003	0.005	0.003
	13	0.008	0.008	0.008	0.006
Neut (G/l)					
week:	-1	4.820	3.780	4.950	6.470
	7	6.810	4.710	5.680	5.700
	13	5.340	4.190	4.920	5.400
Eos (G/l)					
week:	-1	0.390	0.120	0.220	0.330
	7	0.290	0.200	0.190	0.330
	13	0.170	0.110	0.100	0.210

Hematology (individuals): males

group 5
1250 ppm

		Animal no			
		17	18	19	20
Baso (G/l) week:	-1	0.040	0.040	0.040	0.070
	7	0.030	0.020	0.070	0.020
	13	0.020	0.020	0.040	0.030
Lympho (G/l) week:	-1	4.300	3.300	4.350	3.580
	7	4.200	3.480	4.450	3.330
	13	3.720	2.960	4.080	3.100
Mono (G/l) week:	-1	0.630	0.470	0.540	0.910
	7	0.880	0.680	0.430	0.890
	13	0.660	0.420	0.450	0.470
Luc (G/l) week:	-1	0.060	0.030	0.050	0.060
	7	0.060	0.030	0.050	0.030
	13	0.080	0.060	0.070	0.060
Plt (G/l) week:	-1	309.0	315.0	330.0	225.0
	7	361.0	390.0	324.0	249.0
	13	371.0	370.0	306.0	257.0
PT(CS) (sec) week:	-1	34.10	34.67	32.09	35.10
	7	36.69	33.80	32.18	35.48
	13	32.48	33.13	33.80	34.12

Hematology (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
RBC (T/l)					
week:	-1	6.320	7.220	6.930	6.260
	7	6.610	7.410	7.200	7.010
	13	6.260	7.100	6.820	6.480
Hb (mmol/l)					
week:	-1	9.000	10.50	9.700	8.400
	7	9.400	10.70	9.900	9.300
	13	9.000	10.50	9.500	8.700
Hct (1)					
week:	-1	0.427	0.495	0.462	0.407
	7	0.452	0.510	0.473	0.454
	13	0.431	0.486	0.446	0.408
MCV (fl)					
week:	-1	67.50	68.50	66.80	65.10
	7	68.40	68.90	65.70	64.70
	13	68.80	68.50	65.50	63.10
RDW (1)					
week:	-1	0.135	0.139	0.136	0.150
	7	0.135	0.131	0.135	0.140
	13	0.127	0.128	0.130	0.136
MCH (fmol)					
week:	-1	1.420	1.450	1.400	1.350
	7	1.420	1.450	1.370	1.330
	13	1.430	1.480	1.400	1.340
MCHC (mmol/l)					
week:	-1	21.06	21.20	20.92	20.68
	7	20.77	20.98	20.91	20.50
	13	20.84	21.66	21.33	21.21

Hematology (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
HDW (mmol/l)					
week:	-1	1.020	1.040	1.180	1.170
	7	1.100	1.150	1.220	1.190
	13	1.080	1.060	1.080	1.140
Reti (1)					
week:	-1	0.024	0.020	0.015	0.026
	7	0.024	0.018	0.020	0.020
	13	0.019	0.013	0.015	0.019
WBC (G/l)					
week:	-1	9.610	8.780	10.41	9.650
	7	17.05	9.110	11.56	11.33
	13	14.28	9.000	10.23	9.920
Neut (1)					
week:	-1	0.571	0.471	0.521	0.532
	7	0.702	0.515	0.504	0.537
	13	0.669	0.563	0.552	0.611
Eos (1)					
week:	-1	0.025	0.025	0.037	0.034
	7	0.024	0.017	0.030	0.037
	13	0.032	0.011	0.024	0.019
Baso (1)					
week:	-1	0.005	0.005	0.008	0.005
	7	0.004	0.005	0.007	0.005
	13	0.004	0.004	0.007	0.003
Lympho (1)					
week:	-1	0.352	0.459	0.378	0.389
	7	0.207	0.414	0.412	0.378
	13	0.246	0.379	0.354	0.322

Hematology (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
Mono (1)					
week:	-1	0.043	0.037	0.051	0.038
	7	0.060	0.042	0.045	0.038
	13	0.042	0.037	0.055	0.037
Luc (1)					
week:	-1	0.005	0.003	0.005	0.003
	7	0.003	0.006	0.003	0.005
	13	0.007	0.006	0.008	0.008
Neut (G/l)					
week:	-1	5.490	4.130	5.420	5.130
	7	11.96	4.690	5.830	6.090
	13	9.560	5.070	5.650	6.070
Eos (G/l)					
week:	-1	0.240	0.220	0.390	0.320
	7	0.410	0.160	0.350	0.420
	13	0.460	0.100	0.240	0.180
Baso (G/l)					
week:	-1	0.050	0.050	0.080	0.050
	7	0.070	0.050	0.080	0.050
	13	0.050	0.040	0.070	0.020
Lympho (G/l)					
week:	-1	3.390	4.030	3.940	3.750
	7	3.520	3.770	4.760	4.290
	13	3.510	3.410	3.620	3.200
Mono (G/l)					
week:	-1	0.420	0.330	0.530	0.370
	7	1.030	0.390	0.520	0.430
	13	0.600	0.330	0.560	0.370

Hematology (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
Luc (G/l) week:	-1	0.040	0.030	0.060	0.030
	7	0.050	0.050	0.030	0.060
	13	0.100	0.050	0.080	0.080
Plt (G/l) week:	-1	240.0	272.0	363.0	268.0
	7	288.0	293.0	320.0	321.0
	13	261.0	292.0	352.0	293.0
PT(CS) (sec) week:	-1	31.68	33.84	33.26	32.54
	7	30.19	32.79	32.33	29.04
	13	33.21	33.15	28.88	29.54

Hematology (individuals): females

group 2
50 ppm

		Animal no 25	26	27	28
RBC (T/l) week:	-1	7.060	7.560	6.080	6.320
	7	7.800	7.250	6.460	6.890
	13	7.800	6.820	6.250	6.700
Hb (mmol/l) week:	-1	9.800	10.65	8.900	8.800
	7	10.90	10.30	9.200	9.500
	13	11.00	9.800	9.000	9.300
Hct (l) week:	-1	0.474	0.516	0.420	0.425
	7	0.517	0.489	0.438	0.463
	13	0.513	0.452	0.416	0.440

Hematology (individuals): females

group 2
50 ppm

		Animal no 25	26	27	28
MCV (fl)					
week:	-1	67.20	68.20	69.10	67.30
	7	66.30	67.50	67.80	67.20
	13	65.90	66.30	66.60	65.60
RDW (1)					
week:	-1	0.157	0.147	0.143	0.140
	7	0.141	0.137	0.133	0.133
	13	0.133	0.135	0.137	0.135
MCH (fmol)					
week:	-1	1.390	1.405	1.460	1.390
	7	1.400	1.420	1.420	1.370
	13	1.410	1.430	1.450	1.390
MCHC (mmol/l)					
week:	-1	20.71	20.66	21.21	20.72
	7	21.08	21.05	20.99	20.44
	13	21.41	21.58	21.70	21.18
HDW (mmol/l)					
week:	-1	1.020	1.105	1.190	1.100
	7	1.140	1.170	1.210	1.220
	13	1.060	1.100	1.150	1.130
Reti (1)					
week:	-1	0.013	0.025	0.025	0.028
	7	0.013	0.016	0.022	0.028
	13	0.011	0.014	0.014	0.024
WBC (G/l)					
week:	-1	8.490	20.33	11.88	11.55
	7	7.410	12.02	12.26	13.28
	13	7.310	11.71	10.58	12.63

Hematology (individuals): females

group 2
50 ppm

		Animal no 25	26	27	28
Neut (1)					
week:	-1	0.551	0.756	0.550	0.608
	7	0.548	0.622	0.630	0.643
	13	0.566	0.650	0.666	0.618
Eos (1)					
week:	-1	0.010	0.007	0.030	0.029
	7	0.035	0.015	0.013	0.020
	13	0.010	0.014	0.022	0.024
Baso (1)					
week:	-1	0.008	0.002	0.003	0.005
	7	0.012	0.005	0.003	0.004
	13	0.009	0.003	0.003	0.004
Lympho (1)					
week:	-1	0.376	0.149	0.381	0.303
	7	0.366	0.316	0.317	0.291
	13	0.369	0.280	0.266	0.305
Mono (1)					
week:	-1	0.050	0.084	0.033	0.050
	7	0.031	0.039	0.035	0.038
	13	0.039	0.045	0.036	0.041
Luc (1)					
week:	-1	0.006	0.004	0.002	0.006
	7	0.007	0.003	0.002	0.005
	13	0.007	0.008	0.005	0.008
Neut (G/l)					
week:	-1	4.680	15.36	6.540	7.020
	7	4.060	7.480	7.720	8.530
	13	4.140	7.620	7.050	7.800

Hematology (individuals): females

group 2
50 ppm

		Animal no			
		25	26	27	28
Eos (G/l)					
week:	-1	0.080	0.125	0.360	0.340
	7	0.260	0.180	0.160	0.260
	13	0.070	0.160	0.240	0.300
Baso (G/l)					
week:	-1	0.060	0.050	0.040	0.060
	7	0.090	0.050	0.040	0.050
	13	0.070	0.040	0.040	0.060
Lympho (G/l)					
week:	-1	3.190	3.030	4.520	3.490
	7	2.720	3.790	3.880	3.870
	13	2.700	3.270	2.820	3.850
Mono (G/l)					
week:	-1	0.420	1.700	0.390	0.570
	7	0.230	0.470	0.430	0.500
	13	0.280	0.530	0.390	0.520
Luc (G/l)					
week:	-1	0.050	0.070	0.030	0.070
	7	0.050	0.040	0.020	0.060
	13	0.050	0.090	0.060	0.110
Plt (G/l)					
week:	-1	244.0	300.0	370.0	271.0
	7	248.0	289.0	470.0	305.0
	13	241.0	284.0	375.0	283.0
PT(CS) (sec)					
week:	-1	38.84	34.56	27.41	29.93
	7	37.52	36.59	28.60	27.74
	13	36.51	34.46	28.31	29.33

Hematology (individuals): females

group 3
125 ppm

		Animal no			
		29	30	31	32
RBC (T/l)					
week:	-1	6.770	6.810	6.585	6.290
	7	6.930	6.910	6.480	6.510
	13	6.690	6.560	6.560	6.470
Hb (mmol/l)					
week:	-1	9.800	9.600	9.600	8.600
	7	10.00	9.700	9.400	8.800
	13	9.800	9.300	9.500	9.000
Hct (1)					
week:	-1	0.467	0.459	0.458	0.408
	7	0.470	0.461	0.446	0.420
	13	0.450	0.429	0.447	0.413
MCV (fl)					
week:	-1	69.00	67.30	69.45	64.80
	7	67.70	66.70	68.90	64.40
	13	67.30	65.40	68.20	63.80
RDW (1)					
week:	-1	0.140	0.143	0.145	0.140
	7	0.122	0.140	0.133	0.136
	13	0.130	0.130	0.137	0.134
MCH (fmol)					
week:	-1	1.450	1.410	1.460	1.370
	7	1.440	1.400	1.450	1.350
	13	1.460	1.420	1.460	1.390
MCHC (mmol/l)					
week:	-1	21.04	20.89	20.98	21.11
	7	21.33	20.95	21.02	21.03
	13	21.72	21.75	21.35	21.76

Hematology (individuals): females

group 3
125 ppm

		Animal no			
		29	30	31	32
HDW (mmol/l)					
week:	-1	1.060	1.140	1.045	1.010
	7	1.040	1.210	1.040	1.220
	13	1.060	1.120	1.090	1.090
Reti (1)					
week:	-1	0.023	0.027	0.026	0.015
	7	0.014	0.028	0.013	0.013
	13	0.017	0.020	0.015	0.010
WBC (G/l)					
week:	-1	9.090	8.600	11.16	8.930
	7	8.850	7.700	11.33	9.070
	13	8.190	7.810	13.31	7.920
Neut (1)					
week:	-1	0.521	0.546	0.583	0.524
	7	0.581	0.538	0.598	0.558
	13	0.517	0.561	0.655	0.621
Eos (1)					
week:	-1	0.029	0.013	0.013	0.044
	7	0.033	0.024	0.010	0.029
	13	0.040	0.018	0.010	0.013
Baso (1)					
week:	-1	0.005	0.005	0.004	0.006
	7	0.004	0.003	0.003	0.004
	13	0.004	0.003	0.003	0.005
Lympho (1)					
week:	-1	0.390	0.390	0.365	0.364
	7	0.335	0.402	0.343	0.343
	13	0.384	0.375	0.285	0.300

Hematology (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
Mono (1)					
week:	-1	0.050	0.042	0.033	0.057
	7	0.046	0.030	0.044	0.062
	13	0.045	0.039	0.041	0.052
Luc (1)					
week:	-1	0.005	0.004	0.004	0.004
	7	0.002	0.003	0.002	0.004
	13	0.010	0.005	0.005	0.008
Neut (G/l)					
week:	-1	4.730	4.700	6.505	4.680
	7	5.150	4.140	6.770	5.060
	13	4.230	4.380	8.720	4.920
Eos (G/l)					
week:	-1	0.260	0.110	0.140	0.400
	7	0.290	0.180	0.120	0.260
	13	0.330	0.140	0.140	0.100
Baso (G/l)					
week:	-1	0.040	0.040	0.040	0.060
	7	0.030	0.020	0.030	0.040
	13	0.040	0.030	0.040	0.040
Lympho (G/l)					
week:	-1	3.550	3.360	4.075	3.250
	7	2.960	3.100	3.880	3.110
	13	3.140	2.930	3.800	2.380
Mono (G/l)					
week:	-1	0.460	0.360	0.365	0.510
	7	0.410	0.230	0.500	0.560
	13	0.370	0.300	0.550	0.410

Hematology (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
Luc (G/l)					
week:	-1	0.050	0.040	0.035	0.040
	7	0.020	0.020	0.020	0.040
	13	0.080	0.040	0.070	0.070
Plt (G/l)					
week:	-1	213.0	228.0	215.5	238.0
	7	248.0	223.0	222.0	283.0
	13	234.0	209.0	278.0	259.0
PT(CS) (sec)					
week:	-1	34.24	30.94	27.09	38.10
	7	33.33	27.97	28.40	36.11
	13	36.22	30.40	28.67	34.26

Hematology (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
RBC (T/l)					
week:	-1	6.780	7.010	6.370	6.820
	7	6.960	7.400	7.200	6.580
	13	6.710	6.870	6.960	6.780
Hb (mmol/l)					
week:	-1	10.10	9.300	9.000	9.800
	7	10.10	9.800	9.900	9.500
	13	9.900	9.300	9.700	9.900
Hct (1)					
week:	-1	0.474	0.441	0.425	0.473
	7	0.484	0.473	0.475	0.457
	13	0.461	0.437	0.449	0.463

Hematology (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
MCV (fl)					
week:	-1	69.90	62.95	66.70	69.40
	7	69.50	63.90	66.00	69.50
	13	68.70	63.60	64.40	68.30
RDW (1)					
week:	-1	0.137	0.148	0.140	0.146
	7	0.130	0.142	0.133	0.137
	13	0.130	0.138	0.132	0.134
MCH (fmol)					
week:	-1	1.490	1.330	1.410	1.440
	7	1.440	1.330	1.380	1.450
	13	1.480	1.360	1.390	1.450
MCHC (mmol/l)					
week:	-1	21.24	21.15	21.19	20.71
	7	20.76	20.79	20.85	20.86
	13	21.58	21.35	21.63	21.28
HDW (mmol/l)					
week:	-1	1.010	1.095	1.050	1.120
	7	1.100	1.200	1.080	1.190
	13	1.050	1.080	1.110	1.120
Reti (1)					
week:	-1	0.024	0.018	0.015	0.019
	7	0.017	0.016	0.011	0.018
	13	0.018	0.018	0.009	0.015
WBC (G/l)					
week:	-1	11.21	10.68	8.030	9.420
	7	9.110	12.25	7.050	8.720
	13	7.710	14.58	7.240	7.390

Hematology (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
Neut (1)					
week:	-1	0.518	0.421	0.568	0.589
	7	0.501	0.483	0.585	0.516
	13	0.491	0.611	0.633	0.586
Eos (1)					
week:	-1	0.030	0.018	0.043	0.042
	7	0.043	0.022	0.055	0.086
	13	0.036	0.012	0.021	0.050
Baso (1)					
week:	-1	0.004	0.006	0.005	0.004
	7	0.004	0.005	0.005	0.006
	13	0.004	0.004	0.004	0.003
Lympho (1)					
week:	-1	0.387	0.524	0.329	0.325
	7	0.391	0.448	0.294	0.332
	13	0.411	0.332	0.284	0.313
Mono (1)					
week:	-1	0.056	0.028	0.049	0.037
	7	0.059	0.040	0.059	0.057
	13	0.051	0.035	0.053	0.044
Luc (1)					
week:	-1	0.005	0.004	0.006	0.003
	7	0.003	0.003	0.002	0.003
	13	0.006	0.006	0.005	0.004
Neut (G/l)					
week:	-1	5.810	4.490	4.560	5.550
	7	4.560	5.910	4.120	4.500
	13	3.780	8.910	4.580	4.330

Hematology (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
Eos (G/l) week:	-1	0.330	0.190	0.350	0.390
	7	0.390	0.270	0.390	0.750
	13	0.280	0.170	0.150	0.370
Baso (G/l) week:	-1	0.050	0.060	0.040	0.040
	7	0.040	0.060	0.030	0.050
	13	0.030	0.060	0.030	0.020
Lympho (G/l) week:	-1	4.340	5.590	2.640	3.060
	7	3.560	5.490	2.070	2.890
	13	3.170	4.830	2.060	2.320
Mono (G/l) week:	-1	0.620	0.300	0.400	0.350
	7	0.530	0.490	0.420	0.500
	13	0.390	0.520	0.390	0.320
Luc (G/l) week:	-1	0.060	0.045	0.050	0.030
	7	0.030	0.040	0.020	0.030
	13	0.050	0.090	0.040	0.030
Plt (G/l) week:	-1	252.0	320.0	222.0	234.0
	7	318.0	370.0	269.0	264.0
	13	329.0	421.0	197.0	267.0
PT(CS) (sec) week:	-1	29.61	31.66	32.16	32.37
	7	30.14	31.39	28.74	30.23
	13	31.98	31.78	29.16	30.02

Hematology (individuals): females

group 5
1250 ppm

		Animal no 37	38	39	40
RBC (T/l)					
week:	-1	7.000	6.930	6.520	6.690
	7	7.000	7.090	6.580	6.470
	13	7.080	6.670	6.450	6.240
Hb (mmol/l)					
week:	-1	9.900	9.000	9.300	9.300
	7	9.800	9.300	9.100	9.100
	13	10.20	9.200	9.000	8.900
Hct (1)					
week:	-1	0.474	0.438	0.442	0.453
	7	0.468	0.450	0.434	0.441
	13	0.474	0.424	0.427	0.419
MCV (fl)					
week:	-1	67.60	63.10	67.70	67.60
	7	66.80	63.50	66.00	68.20
	13	67.00	63.70	66.30	67.20
RDW (1)					
week:	-1	0.145	0.161	0.139	0.142
	7	0.137	0.149	0.134	0.130
	13	0.139	0.142	0.134	0.127
MCH (fmol)					
week:	-1	1.410	1.310	1.420	1.390
	7	1.400	1.310	1.380	1.400
	13	1.440	1.380	1.390	1.420
MCHC (mmol/l)					
week:	-1	20.83	20.68	20.97	20.55
	7	20.90	20.58	20.87	20.52
	13	21.51	21.66	20.98	21.17

Hematology (individuals): females

group 5
1250 ppm

		Animal no 37	38	39	40
HDW (mmol/l)					
week:	-1	1.120	1.260	1.010	1.000
	7	1.090	1.250	1.060	1.070
	13	1.150	1.250	1.050	0.950
Reti (1)					
week:	-1	0.025	0.024	0.017	0.022
	7	0.016	0.016	0.027	0.020
	13	0.017	0.018	0.011	0.014
WBC (G/l)					
week:	-1	9.260	11.98	9.250	11.54
	7	10.14	11.05	11.23	11.86
	13	10.74	11.73	8.750	11.58
Neut (1)					
week:	-1	0.632	0.566	0.553	0.524
	7	0.641	0.536	0.665	0.586
	13	0.645	0.563	0.631	0.608
Eos (1)					
week:	-1	0.051	0.018	0.018	0.036
	7	0.045	0.019	0.011	0.032
	13	0.051	0.017	0.018	0.029
Baso (1)					
week:	-1	0.006	0.003	0.008	0.007
	7	0.004	0.004	0.002	0.006
	13	0.004	0.004	0.003	0.005
Lympho (1)					
week:	-1	0.272	0.361	0.355	0.391
	7	0.279	0.407	0.259	0.317
	13	0.266	0.375	0.287	0.298

Hematology (individuals): females

group 5
1250 ppm

		Animal no			
		37	38	39	40
Mono (1)					
week:	-1	0.034	0.048	0.061	0.036
	7	0.029	0.031	0.061	0.055
	13	0.031	0.034	0.055	0.053
Luc (1)					
week:	-1	0.005	0.003	0.005	0.006
	7	0.002	0.003	0.002	0.004
	13	0.004	0.006	0.006	0.008
Neut (G/l)					
week:	-1	5.850	6.780	5.110	6.040
	7	6.500	5.920	7.460	6.950
	13	6.920	6.610	5.520	7.030
Eos (G/l)					
week:	-1	0.470	0.210	0.170	0.420
	7	0.460	0.210	0.130	0.380
	13	0.550	0.200	0.160	0.340
Baso (G/l)					
week:	-1	0.060	0.040	0.070	0.090
	7	0.040	0.040	0.020	0.070
	13	0.040	0.050	0.030	0.050
Lympho (G/l)					
week:	-1	2.520	4.330	3.280	4.520
	7	2.830	4.500	2.900	3.760
	13	2.850	4.400	2.510	3.440
Mono (G/l)					
week:	-1	0.320	0.580	0.570	0.410
	7	0.290	0.340	0.680	0.650
	13	0.330	0.400	0.480	0.620

Hematology (individuals): females

group 5
1250 ppm

		Animal no 37	38	39	40
Luc (G/l)					
week:	-1	0.050	0.040	0.050	0.060
	7	0.020	0.040	0.020	0.050
	13	0.040	0.070	0.050	0.090
Plt (G/l)					
week:	-1	248.0	298.0	284.0	283.0
	7	264.0	355.0	316.0	349.0
	13	279.0	330.0	311.0	353.0
PT(CS) (sec)					
week:	-1	33.27	32.83	28.70	32.21
	7	28.64	30.95	25.55	31.10
	13	30.76	31.71	27.08	34.30

6.8. Blood chemistry (individuals)

Blood chemistry (individuals): males group 1
0 ppm

		Animal no 1	2	3	4
Gluc (mmol/l)					
week:	-1	5.630	5.810	5.230	6.020
	7	5.550	6.040	5.540	5.670
	13	5.890	6.360	5.130	5.900
Urea (mmol/l)					
week:	-1	3.470	4.290	3.340	1.980
	7	3.220	4.230	3.710	2.770
	13	3.770	5.260	3.980	2.770
Creat-e (umol/l)					
week:	-1	65.90	68.70	65.30	64.30
	7	58.50	66.80	67.60	63.80
	13	65.70	81.30	71.20	77.40
Bili-tot (umol/l)					
week:	-1	1.480	1.670	2.140	2.140
	7	2.200	2.690	2.450	2.200
	13	2.200	3.180	2.940	2.450
Prot (g/l)					
week:	-1	54.61	52.58	54.66	55.11
	7	59.01	53.90	53.19	55.86
	13	62.26	53.94	56.80	57.89
Alb (g/l)					
week:	-1	30.90	31.71	30.68	31.41
	7	33.04	31.50	30.25	31.12
	13	34.84	32.49	31.43	32.75

Blood chemistry (individuals): males

group 1
0 ppm

		Animal no 1	2	3	4
Glob (g/l)					
week:	-1	23.71	20.87	23.98	23.70
	7	25.97	22.40	22.94	24.74
	13	27.42	21.45	25.37	25.14
A/G (1)					
week:	-1	1.300	1.520	1.280	1.330
	7	1.270	1.410	1.320	1.260
	13	1.270	1.510	1.240	1.300
Chol (mmol/l)					
week:	-1	3.780	4.190	4.740	4.850
	7	3.810	4.080	4.920	5.500
	13	3.620	3.850	4.530	5.170
Trigly (mmol/l)					
week:	-1	0.490	0.310	0.480	0.440
	7	0.380	0.310	0.510	0.430
	13	0.340	0.180	0.320	0.330
Phos-Lip (mmol/l)					
week:	-1	4.460	4.850	5.480	5.675
	7	4.600	4.660	5.320	5.780
	13	4.450	4.470	5.040	5.730
Na+ (mmol/l)					
week:	-1	149.7	147.7	146.5	146.5
	7	148.4	147.5	145.9	146.7
	13	151.5	146.8	146.3	145.3
K+ (mmol/l)					
week:	-1	5.190	4.580	4.180	4.430
	7	4.710	4.710	4.500	4.400
	13	5.410	4.830	4.220	4.480

Blood chemistry (individuals): males

group 1
0 ppm

		Animal no 1	2	3	4
Ca++ (mmol/l)					
week:	-1	2.840	2.810	2.790	2.860
	7	2.990	2.970	2.840	2.930
	13	2.860	2.730	2.790	2.750
Cl- (mmol/l)					
week:	-1	111.8	109.8	108.9	108.2
	7	107.7	109.1	108.4	107.0
	13	114.5	114.6	113.2	111.4
PO4-in (mmol/l)					
week:	-1	2.440	2.100	2.150	2.170
	7	2.110	1.960	1.860	2.000
	13	1.660	1.640	1.700	1.670
ASAT (GOT) (U/l)					
week:	-1	22.40	23.60	15.50	13.65
	7	24.90	24.90	22.40	19.90
	13	21.70	21.70	19.90	20.50
ALAT (GPT) (U/l)					
week:	-1	45.20	46.70	77.75	30.40
	7	35.50	64.40	129.2	38.50
	13	47.40	53.30	156.6	36.30
AlP (U/l)					
week:	-1	70.10	105.9	84.20	110.4
	7	50.55	80.00	83.70	107.6
	13	38.00	60.30	73.20	88.50
GGT (U/l)					
week:	-1	3.200	3.200	4.500	5.100
	7	0.000	0.000	5.100	0.000
	13	3.800	3.200	5.700	3.800

Blood chemistry (individuals): males group 1
0 ppm

		Animal no 1	2	3	4
CK (U/l)					
week:	-1	212.0	217.3	172.8	148.4
	7	234.3	156.9	155.8	168.5
	13	154.8	128.3	128.3	181.3

Blood chemistry (individuals): males group 2
50 ppm

		Animal no 5	6	7	8
Gluc (mmol/l)					
week:	-1	5.740	6.610	5.430	6.040
	7	5.630	6.040	5.350	5.820
	13	5.410	5.740	5.350	6.120
Urea (mmol/l)					
week:	-1	3.070	3.040	3.010	3.250
	7	3.400	3.800	3.070	2.580
	13	3.620	3.980	3.560	3.340
Creat-e (umol/l)					
week:	-1	69.30	73.30	70.20	65.60
	7	74.30	74.30	70.10	68.80
	13	76.50	81.60	80.00	73.50
Bili-tot (umol/l)					
week:	-1	2.140	2.860	2.380	2.140
	7	2.690	3.670	2.200	2.450
	13	2.690	3.920	2.450	2.690
Prot (g/l)					
week:	-1	51.65	58.15	54.10	57.50
	7	55.61	59.83	56.97	55.69
	13	56.12	60.26	61.29	61.26

Blood chemistry (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
Alb (g/l)					
week:	-1	30.74	31.89	29.38	31.71
	7	31.77	33.92	31.12	32.01
	13	32.25	33.55	32.24	33.87
Glob (g/l)					
week:	-1	20.91	26.26	24.72	25.79
	7	23.84	25.91	25.85	23.68
	13	23.87	26.71	29.05	27.39
A/G (1)					
week:	-1	1.470	1.210	1.190	1.230
	7	1.330	1.310	1.200	1.350
	13	1.350	1.260	1.110	1.240
Chol (mmol/l)					
week:	-1	3.620	3.850	4.800	4.080
	7	3.790	3.470	4.820	3.440
	13	3.800	3.660	5.030	3.600
Trigly (mmol/l)					
week:	-1	0.410	0.490	0.280	0.510
	7	0.300	0.410	0.240	0.330
	13	0.290	0.260	0.195	0.300
Phos-Lip (mmol/l)					
week:	-1	4.330	4.630	5.690	4.900
	7	4.440	4.100	5.260	4.340
	13	4.730	4.190	5.785	4.660
Na+ (mmol/l)					
week:	-1	145.8	144.5	145.8	147.6
	7	147.6	145.3	146.7	146.1
	13	147.5	147.6	146.7	150.0

Blood chemistry (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
K+ (mmol/l)					
week:	-1	4.480	5.230	4.600	5.210
	7	4.110	4.690	4.530	4.450
	13	4.540	4.990	4.510	5.300
Ca++ (mmol/l)					
week:	-1	2.690	2.830	2.770	2.890
	7	2.960	2.910	2.860	3.030
	13	2.690	2.740	2.700	2.880
Cl- (mmol/l)					
week:	-1	111.0	109.4	110.1	108.9
	7	106.9	108.8	108.5	106.6
	13	114.6	113.3	113.3	111.7
PO4-in (mmol/l)					
week:	-1	2.150	2.270	2.260	2.220
	7	1.940	1.750	1.920	1.930
	13	1.690	1.570	1.520	1.720
ASAT (GOT) (U/l)					
week:	-1	23.60	20.50	31.05	21.10
	7	28.60	23.60	29.80	16.80
	13	22.40	18.00	25.50	18.00
ALAT (GPT) (U/l)					
week:	-1	37.00	54.10	46.70	60.70
	7	40.70	55.50	37.80	57.00
	13	45.20	50.40	43.70	57.00
AlP (U/l)					
week:	-1	85.60	94.40	112.1	135.8
	7	76.30	88.20	104.2	104.8
	13	55.50	67.30	90.40	94.70

Blood chemistry (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
GGT (U/l)					
week:	-1	3.800	4.500	3.800	3.200
	7	2.500	3.200	0.000	2.500
	13	5.100	3.200	2.500	3.800
CK (U/l)					
week:	-1	213.1	194.0	254.4	232.1
	7	162.2	187.6	201.4	141.0
	13	129.3	177.0	216.2	166.4

Blood chemistry (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
Gluc (mmol/l)					
week:	-1	6.090	5.880	6.160	6.170
	7	6.180	6.260	6.300	6.430
	13	6.150	5.520	6.160	5.720
Urea (mmol/l)					
week:	-1	2.550	3.400	3.590	3.770
	7	2.680	2.920	3.530	4.160
	13	2.830	3.250	3.770	4.990
Creat-e (umol/l)					
week:	-1	67.70	68.00	78.10	81.50
	7	74.60	65.70	76.80	87.00
	13	65.90	69.40	79.20	85.10
Bili-tot (umol/l)					
week:	-1	2.380	2.860	2.380	2.380
	7	3.180	2.690	2.690	3.180
	13	2.940	3.180	2.690	2.940

Blood chemistry (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
Prot (g/l)					
week:	-1	51.40	54.92	56.46	55.59
	7	59.85	57.79	55.26	56.27
	13	57.89	57.72	59.03	60.49
Alb (g/l)					
week:	-1	30.86	32.15	33.20	31.06
	7	33.77	32.96	33.36	32.59
	13	34.77	33.94	34.55	33.86
Glob (g/l)					
week:	-1	20.54	22.77	23.26	24.53
	7	26.08	24.83	21.90	23.68
	13	23.12	23.78	24.48	26.63
A/G (1)					
week:	-1	1.500	1.410	1.430	1.270
	7	1.290	1.330	1.520	1.380
	13	1.500	1.430	1.410	1.270
Chol (mmol/l)					
week:	-1	4.360	3.210	3.390	3.790
	7	5.135	3.300	3.540	3.490
	13	4.490	3.220	3.580	3.680
Trigly (mmol/l)					
week:	-1	0.570	0.360	0.410	0.635
	7	0.370	0.200	0.230	0.410
	13	0.360	0.210	0.200	0.420
Phos-Lip (mmol/l)					
week:	-1	5.190	3.910	4.210	4.720
	7	5.805	4.100	4.220	4.160
	13	5.350	4.110	4.500	4.530

Blood chemistry (individuals): males

group 3
125 ppm

	Animal no 9	10	11	12
Na+ (mmol/l)				
week: -1	146.4	145.8	147.4	149.3
7	150.7	146.6	146.3	146.9
13	149.7	145.6	147.3	148.6
K+ (mmol/l)				
week: -1	4.500	4.730	4.720	5.310
7	4.120	4.510	4.790	5.200
13	4.440	4.510	5.210	4.720
Ca++ (mmol/l)				
week: -1	2.730	2.770	2.920	2.900
7	3.050	2.880	3.020	2.870
13	2.870	2.630	2.860	2.730
Cl- (mmol/l)				
week: -1	108.5	110.2	106.1	110.5
7	106.3	109.1	107.5	107.7
13	110.5	112.3	110.6	113.9
PO4-in (mmol/l)				
week: -1	2.150	2.290	2.250	2.190
7	2.175	1.980	1.990	1.880
13	1.810	1.720	1.860	1.510
ASAT (GOT) (U/l)				
week: -1	18.00	22.40	24.20	19.90
7	22.40	24.20	24.20	30.40
13	23.60	25.50	23.60	19.30
ALAT (GPT) (U/l)				
week: -1	42.90	42.90	45.20	40.00
7	48.10	45.90	38.50	47.40
13	59.20	45.90	47.40	43.70

Blood chemistry (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
AlP (U/l) week:	-1	121.7	116.1	138.9	129.0
	7	109.0	92.70	124.5	102.8
	13	80.30	74.10	100.8	83.10
GGT (U/l) week:	-1	3.200	3.200	4.500	3.800
	7	0.000	0.000	3.200	0.000
	13	3.200	2.500	3.800	3.200
CK (U/l) week:	-1	177.0	221.5	270.3	231.1
	7	165.4	165.4	195.0	633.9
	13	173.8	215.2	208.8	216.2

Blood chemistry (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
Gluc (mmol/l) week:	-1	5.960	5.680	5.530	5.680
	7	5.640	5.370	5.410	5.690
	13	5.830	5.460	5.310	5.680
Urea (mmol/l) week:	-1	3.280	4.470	3.160	2.640
	7	3.530	3.370	4.160	3.530
	13	3.950	3.890	4.380	4.260
Creat-e (umol/l) week:	-1	67.30	75.20	60.60	67.00
	7	73.40	69.70	64.80	63.80
	13	76.20	72.40	69.70	72.10

Blood chemistry (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
Bili-tot (umol/l)					
week:	-1	2.140	2.860	2.140	2.380
	7	2.200	3.180	2.940	3.180
	13	2.690	3.430	2.690	3.180
Prot (g/l)					
week:	-1	53.12	54.04	49.97	53.88
	7	52.62	57.08	55.64	53.87
	13	56.72	57.03	60.29	55.03
Alb (g/l)					
week:	-1	30.78	32.10	27.53	29.00
	7	30.80	33.77	31.50	31.03
	13	32.03	33.73	34.15	30.27
Glob (g/l)					
week:	-1	22.34	21.94	22.44	24.88
	7	21.82	23.31	24.14	22.84
	13	24.69	23.30	26.14	24.76
A/G (1)					
week:	-1	1.380	1.460	1.230	1.170
	7	1.410	1.450	1.300	1.360
	13	1.300	1.450	1.310	1.220
Chol (mmol/l)					
week:	-1	3.980	3.000	3.390	3.450
	7	3.490	3.430	3.790	3.190
	13	3.920	3.350	3.880	3.150
Trigly (mmol/l)					
week:	-1	0.380	0.320	0.330	0.340
	7	0.330	0.330	0.270	0.330
	13	0.330	0.240	0.270	0.250

Blood chemistry (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
Phos-Lip (mmol/l)					
week:	-1	4.820	3.600	4.160	4.230
	7	4.290	4.160	4.330	3.890
	13	4.670	4.120	4.640	3.940
Na+ (mmol/l)					
week:	-1	146.0	147.5	147.8	147.4
	7	147.2	146.2	146.0	145.2
	13	147.3	146.0	148.7	146.5
K+ (mmol/l)					
week:	-1	4.390	4.510	4.510	4.530
	7	4.510	4.520	4.700	4.580
	13	4.340	4.550	4.540	4.810
Ca++ (mmol/l)					
week:	-1	2.670	2.740	2.770	2.800
	7	2.740	2.830	2.900	2.860
	13	2.660	2.630	2.740	2.630
Cl- (mmol/l)					
week:	-1	111.9	111.0	111.8	108.4
	7	112.2	111.0	108.2	107.5
	13	113.8	113.6	115.0	115.4
PO4-in (mmol/l)					
week:	-1	2.140	2.210	2.410	2.480
	7	2.020	1.920	1.990	1.960
	13	1.940	1.750	1.850	1.780
ASAT (GOT) (U/l)					
week:	-1	17.40	18.00	23.00	20.50
	7	30.40	21.70	24.20	23.60
	13	20.50	17.40	25.50	22.40

Blood chemistry (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
ALAT (GPT) (U/l)					
week:	-1	36.30	45.90	49.60	25.90
	7	40.70	42.20	52.60	28.85
	13	40.70	43.70	60.70	43.70
AlP (U/l)					
week:	-1	86.20	100.6	94.10	136.3
	7	82.50	85.40	77.20	105.6
	13	80.80	72.40	70.70	93.00
GGT (U/l)					
week:	-1	3.800	3.200	3.200	3.200
	7	3.200	2.500	2.500	2.500
	13	4.500	3.200	3.800	3.200
CK (U/l)					
week:	-1	198.2	218.4	235.3	212.0
	7	185.5	179.1	216.2	278.8
	13	183.4	123.0	200.3	219.4

Blood chemistry (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
Gluc (mmol/l)					
week:	-1	5.760	5.610	6.220	5.870
	7	5.610	5.580	6.080	6.460
	13	5.290	5.670	5.700	5.440
Urea (mmol/l)					
week:	-1	4.230	5.290	3.890	2.830
	7	4.010	4.440	3.010	2.460
	13	4.770	4.290	3.830	2.980

Blood chemistry (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
Creat-e (umol/l)					
week:	-1	77.80	69.60	82.90	71.00
	7	80.40	68.80	79.80	65.00
	13	75.30	73.90	86.90	72.90
Bili-tot (umol/l)					
week:	-1	2.140	2.140	1.900	1.900
	7	2.940	3.180	2.200	1.710
	13	2.940	3.670	2.450	2.450
Prot (g/l)					
week:	-1	54.24	55.39	51.46	56.77
	7	53.41	55.53	54.12	54.25
	13	57.29	56.26	54.74	58.75
Alb (g/l)					
week:	-1	30.32	31.56	29.51	31.34
	7	30.61	30.25	30.66	31.78
	13	32.41	31.71	32.35	32.62
Glob (g/l)					
week:	-1	23.92	23.83	21.95	25.43
	7	22.80	25.28	23.46	22.47
	13	24.88	24.55	22.39	26.13
A/G (1)					
week:	-1	1.270	1.320	1.340	1.230
	7	1.340	1.200	1.310	1.410
	13	1.300	1.290	1.440	1.250
Chol (mmol/l)					
week:	-1	3.160	3.520	3.620	3.260
	7	3.140	3.300	3.470	3.230
	13	3.450	3.380	3.760	3.460

Blood chemistry (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
Trigly (mmol/l)					
week:	-1	0.280	0.330	0.490	0.350
	7	0.220	0.350	0.340	0.320
	13	0.300	0.190	0.280	0.330
Phos-Lip (mmol/l)					
week:	-1	3.840	4.250	4.170	3.930
	7	3.920	4.300	4.100	4.120
	13	4.280	4.290	4.450	4.510
Na+ (mmol/l)					
week:	-1	144.2	147.4	146.8	148.2
	7	145.0	147.5	147.6	145.9
	13	146.5	146.0	144.5	147.3
K+ (mmol/l)					
week:	-1	4.800	4.760	4.710	4.610
	7	4.710	4.750	4.620	4.530
	13	4.760	4.730	4.590	4.240
Ca++ (mmol/l)					
week:	-1	2.700	2.720	2.740	2.810
	7	2.840	2.790	2.860	2.890
	13	2.660	2.650	2.540	2.680
Cl- (mmol/l)					
week:	-1	109.0	110.1	109.5	109.6
	7	108.5	111.0	109.0	112.3
	13	113.1	114.4	112.1	114.1
PO4-in (mmol/l)					
week:	-1	2.170	2.030	2.100	2.060
	7	1.780	1.940	1.750	1.740
	13	1.610	1.820	1.460	1.440

Blood chemistry (individuals): males

group 5
1250 ppm

		Animal no			
		17	18	19	20
ASAT (GOT) (U/l)					
week:	-1	20.50	26.10	19.30	18.60
	7	21.70	24.90	19.30	18.60
	13	20.50	20.50	21.10	17.40
ALAT (GPT) (U/l)					
week:	-1	34.80	41.50	49.60	40.00
	7	41.50	36.30	46.70	40.70
	13	40.00	31.80	57.00	42.90
AlP (U/l)					
week:	-1	108.5	119.7	123.7	78.00
	7	147.2	147.5	206.8	98.90
	13	137.5	121.1	190.3	91.80
GGT (U/l)					
week:	-1	5.100	3.800	3.800	3.200
	7	3.200	3.800	3.500	3.500
	13	3.800	4.500	4.500	4.500
CK (U/l)					
week:	-1	191.9	225.8	222.6	209.9
	7	174.9	220.5	215.2	154.8
	13	164.3	131.4	223.7	161.1

Blood chemistry (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
Gluc (mmol/l)					
week:	-1	5.940	5.730	5.910	5.390
	7	6.360	5.800	5.850	5.490
	13	5.480	5.900	5.450	5.190
Urea (mmol/l)					
week:	-1	3.340	3.770	4.590	4.380
	7	3.220	4.710	3.920	3.070
	13	3.830	4.200	4.380	3.890
Creat-e (umol/l)					
week:	-1	75.50	83.50	73.30	84.10
	7	71.90	92.10	72.20	80.70
	13	74.80	87.10	71.20	80.40
Bili-tot (umol/l)					
week:	-1	2.860	2.620	2.140	2.140
	7	2.690	2.450	2.940	2.940
	13	2.450	3.180	2.450	2.940
Prot (g/l)					
week:	-1	52.55	55.25	57.90	54.61
	7	54.36	55.80	57.65	53.98
	13	55.52	56.89	60.66	56.66
Alb (g/l)					
week:	-1	31.85	32.54	32.69	31.99
	7	31.55	32.89	32.97	32.29
	13	31.48	34.16	34.01	33.32
Glob (g/l)					
week:	-1	20.70	22.71	25.21	22.62
	7	22.81	22.91	24.68	21.69
	13	24.04	22.73	26.65	23.34

Blood chemistry (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
A/G (1)					
week:	-1	1.540	1.430	1.300	1.410
	7	1.380	1.440	1.340	1.490
	13	1.310	1.500	1.280	1.430
Chol (mmol/l)					
week:	-1	4.370	5.010	2.730	3.560
	7	4.500	5.350	2.740	3.720
	13	3.920	5.435	3.030	3.840
Trigly (mmol/l)					
week:	-1	0.410	0.460	0.360	0.490
	7	0.360	0.280	0.330	0.350
	13	0.250	0.270	0.220	0.320
Phos-Lip (mmol/l)					
week:	-1	5.090	5.470	3.390	4.300
	7	5.130	5.650	3.560	4.410
	13	4.530	5.845	3.850	4.570
Na+ (mmol/l)					
week:	-1	147.5	147.4	149.0	146.4
	7	145.2	146.0	145.3	144.7
	13	147.5	147.0	149.1	147.1
K+ (mmol/l)					
week:	-1	4.270	3.905	4.680	4.360
	7	4.260	3.950	4.260	4.240
	13	4.120	3.860	4.200	4.000
Ca++ (mmol/l)					
week:	-1	2.670	2.740	2.740	2.730
	7	2.760	2.870	3.000	2.830
	13	2.590	2.660	2.700	2.630

Blood chemistry (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
Cl- (mmol/l)					
week:	-1	111.4	109.2	110.8	111.6
	7	112.1	110.7	108.1	113.3
	13	114.5	114.7	115.3	114.2
PO4-in (mmol/l)					
week:	-1	1.920	1.970	1.850	1.930
	7	1.800	1.780	2.100	1.640
	13	1.570	1.330	1.470	1.330
ASAT (GOT) (U/l)					
week:	-1	16.20	16.20	19.30	20.50
	7	14.60	16.80	17.40	22.40
	13	13.65	14.90	18.60	23.00
ALAT (GPT) (U/l)					
week:	-1	48.10	51.80	42.90	31.80
	7	50.40	51.10	44.40	32.60
	13	45.90	70.30	41.50	31.80
AlP (U/l)					
week:	-1	77.50	76.30	83.40	93.00
	7	79.70	77.20	72.70	83.70
	13	67.60	71.60	54.10	63.10
GGT (U/l)					
week:	-1	3.200	3.200	3.200	2.500
	7	0.000	0.000	2.500	3.200
	13	2.500	4.500	3.800	0.000
CK (U/l)					
week:	-1	213.1	201.4	178.1	163.2
	7	113.4	118.7	135.7	133.6
	13	107.1	109.2	128.3	112.4

Blood chemistry (individuals): females group 2
50 ppm

		Animal no 25	26	27	28
Gluc (mmol/l)					
week:	-1	5.100	5.590	5.460	5.330
	7	5.810	5.430	5.410	5.990
	13	5.190	5.510	5.270	5.880
Urea (mmol/l)					
week:	-1	4.230	3.340	3.590	4.070
	7	4.320	4.500	3.680	3.160
	13	5.260	4.200	3.740	3.680
Creat-e (umol/l)					
week:	-1	80.30	85.80	68.50	68.40
	7	78.30	79.80	66.20	70.60
	13	77.60	78.80	72.10	69.20
Bili-tot (umol/l)					
week:	-1	1.900	3.330	2.380	2.860
	7	2.940	3.180	2.450	2.450
	13	3.920	3.920	2.690	3.430
Prot (g/l)					
week:	-1	52.50	56.83	55.31	55.25
	7	53.36	51.56	59.23	54.80
	13	57.09	57.40	59.86	57.52
Alb (g/l)					
week:	-1	33.54	33.39	33.20	33.09
	7	34.52	32.85	33.08	32.35
	13	34.68	34.36	34.91	33.04
Glob (g/l)					
week:	-1	18.96	23.44	22.11	22.16
	7	18.84	18.71	26.15	22.45
	13	22.41	23.04	24.95	24.48

Blood chemistry (individuals): females

group 2
50 ppm

		Animal no 25	26	27	28
A/G (1)					
week:	-1	1.770	1.420	1.500	1.490
	7	1.830	1.760	1.270	1.440
	13	1.550	1.490	1.400	1.350
Chol (mmol/l)					
week:	-1	2.575	4.690	4.120	3.550
	7	2.690	4.040	4.040	3.940
	13	2.810	4.120	3.800	3.800
Trigly (mmol/l)					
week:	-1	0.450	0.480	0.470	0.480
	7	0.400	0.280	0.350	0.530
	13	0.300	0.210	0.260	0.350
Phos-Lip (mmol/l)					
week:	-1	3.140	5.855	4.980	4.490
	7	3.500	4.770	4.670	4.810
	13	3.470	5.090	4.740	4.620
Na+ (mmol/l)					
week:	-1	149.4	148.5	149.0	146.9
	7	145.0	143.8	145.7	147.6
	13	148.1	147.0	147.8	147.3
K+ (mmol/l)					
week:	-1	4.390	4.400	4.200	4.480
	7	4.230	4.340	3.660	5.085
	13	3.980	4.020	4.330	4.580
Ca++ (mmol/l)					
week:	-1	2.650	2.870	2.790	2.710
	7	2.950	2.840	2.890	2.940
	13	2.620	2.700	2.740	2.640

Blood chemistry (individuals): females

group 2
50 ppm

		Animal no 25	26	27	28
Cl- (mmol/l)					
week:	-1	113.3	109.6	109.4	108.7
	7	111.9	111.6	107.4	105.9
	13	114.1	113.1	112.7	113.6
PO4-in (mmol/l)					
week:	-1	2.130	1.890	2.140	1.800
	7	2.245	1.830	2.090	1.810
	13	1.520	1.580	1.780	1.520
ASAT (GOT) (U/l)					
week:	-1	21.70	16.20	28.60	21.10
	7	22.40	20.50	30.40	25.50
	13	19.30	21.70	26.10	31.10
ALAT (GPT) (U/l)					
week:	-1	51.80	25.15	64.40	45.20
	7	45.90	37.00	50.40	43.70
	13	45.90	32.60	65.90	45.20
AlP (U/l)					
week:	-1	93.80	135.5	98.00	100.0
	7	78.30	100.3	87.90	91.00
	13	64.50	78.30	68.70	71.80
GGT (U/l)					
week:	-1	4.500	3.200	3.200	3.200
	7	2.500	0.000	0.000	0.000
	13	5.100	2.500	3.800	0.000
CK (U/l)					
week:	-1	268.2	159.0	243.8	163.2
	7	198.2	156.9	183.4	239.6
	13	169.6	153.7	163.2	197.2

Blood chemistry (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
Gluc (mmol/l)					
week:	-1	6.490	6.240	5.690	5.590
	7	6.720	6.020	6.370	5.960
	13	5.550	5.570	6.590	5.720
Urea (mmol/l)					
week:	-1	4.200	4.070	3.650	4.920
	7	4.100	3.980	3.890	5.350
	13	4.590	4.470	4.290	3.680
Creat-e (umol/l)					
week:	-1	75.20	84.60	81.70	78.10
	7	74.30	88.10	79.50	80.70
	13	75.30	88.20	87.40	80.90
Bili-tot (umol/l)					
week:	-1	2.380	2.220	1.970	2.470
	7	2.940	2.200	2.450	3.180
	13	2.940	2.940	3.670	3.430
Prot (g/l)					
week:	-1	53.00	53.99	57.59	51.32
	7	52.84	54.17	54.72	51.56
	13	56.92	56.92	63.52	56.55
Alb (g/l)					
week:	-1	32.15	32.75	34.70	31.14
	7	33.13	32.91	33.78	31.83
	13	34.36	33.07	36.84	33.79
Glob (g/l)					
week:	-1	20.85	21.24	22.89	20.18
	7	19.71	21.26	20.94	19.73
	13	22.56	23.85	26.68	22.76

Blood chemistry (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
A/G (1)					
week:	-1	1.540	1.540	1.520	1.540
	7	1.680	1.550	1.610	1.610
	13	1.520	1.390	1.380	1.480
Chol (mmol/l)					
week:	-1	3.710	4.960	4.180	3.000
	7	3.610	4.690	4.040	3.050
	13	3.400	4.230	4.750	3.310
Trigly (mmol/l)					
week:	-1	0.420	0.400	0.380	0.290
	7	0.290	0.300	0.350	0.195
	13	0.210	0.200	0.290	0.180
Phos-Lip (mmol/l)					
week:	-1	4.390	5.270	4.840	3.530
	7	4.170	5.090	4.670	3.790
	13	4.110	4.880	5.310	4.130
Na+ (mmol/l)					
week:	-1	148.6	148.3	150.3	147.8
	7	146.4	147.1	147.6	148.7
	13	147.1	145.9	153.2	148.2
K+ (mmol/l)					
week:	-1	4.390	4.280	4.110	4.490
	7	4.030	4.110	4.180	4.070
	13	3.880	4.070	4.000	4.360
Ca++ (mmol/l)					
week:	-1	2.750	2.790	2.800	2.750
	7	2.890	2.800	2.810	2.880
	13	2.650	2.650	2.670	2.720

Blood chemistry (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
Cl- (mmol/l)					
week:	-1	110.7	110.6	110.3	108.7
	7	106.1	109.8	110.7	107.1
	13	112.6	113.9	118.7	112.9
PO4-in (mmol/l)					
week:	-1	1.960	1.900	2.280	2.050
	7	1.770	1.630	1.730	1.920
	13	1.480	1.370	1.590	1.580
ASAT (GOT) (U/l)					
week:	-1	19.90	18.60	21.70	23.00
	7	18.60	18.00	19.90	22.40
	13	16.20	14.60	21.10	21.10
ALAT (GPT) (U/l)					
week:	-1	45.90	53.30	43.70	40.00
	7	48.10	48.90	47.40	49.60
	13	48.10	54.10	50.40	40.00
AlP (U/l)					
week:	-1	71.80	75.80	52.55	105.9
	7	60.30	63.10	45.90	89.90
	13	58.00	53.20	46.80	79.70
GGT (U/l)					
week:	-1	3.800	2.500	1.250	3.800
	7	2.500	2.500	2.500	0.000
	13	0.000	3.200	2.500	3.200
CK (U/l)					
week:	-1	203.5	248.0	163.2	245.9
	7	120.8	167.5	115.5	156.9
	13	107.1	120.8	112.4	159.0

Blood chemistry (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
Gluc (mmol/l)					
week:	-1	5.730	5.920	5.950	5.900
	7	5.750	5.710	5.490	5.960
	13	5.600	5.500	5.570	5.610
Urea (mmol/l)					
week:	-1	3.950	4.770	2.580	3.890
	7	4.530	4.770	3.860	4.160
	13	4.740	4.100	3.010	4.890
Creat-e (umol/l)					
week:	-1	78.60	88.90	71.60	77.00
	7	80.80	82.50	69.70	75.20
	13	84.40	83.90	71.70	83.60
Bili-tot (umol/l)					
week:	-1	2.470	2.470	2.220	2.220
	7	2.940	2.450	2.690	2.940
	13	3.180	2.200	3.920	3.180
Prot (g/l)					
week:	-1	55.03	54.07	52.95	56.32
	7	53.87	54.61	53.98	55.07
	13	54.86	56.66	57.77	57.72
Alb (g/l)					
week:	-1	32.84	30.99	31.74	35.26
	7	32.68	32.48	33.28	33.62
	13	33.62	32.38	34.45	35.38
Glob (g/l)					
week:	-1	22.19	23.08	21.21	21.06
	7	21.19	22.13	20.70	21.45
	13	21.24	24.28	23.32	22.34

Blood chemistry (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
A/G (1)					
week:	-1	1.480	1.340	1.500	1.670
	7	1.540	1.470	1.610	1.570
	13	1.580	1.330	1.480	1.580
Chol (mmol/l)					
week:	-1	3.750	4.410	4.570	3.830
	7	3.490	4.580	4.890	4.490
	13	3.540	4.970	4.860	4.360
Trigly (mmol/l)					
week:	-1	0.400	0.390	0.550	0.520
	7	0.340	0.260	0.380	0.460
	13	0.250	0.220	0.390	0.280
Phos-Lip (mmol/l)					
week:	-1	4.770	4.640	4.970	4.410
	7	4.550	5.120	5.350	4.990
	13	4.320	5.470	5.220	5.080
Na+ (mmol/l)					
week:	-1	146.4	148.0	147.9	149.6
	7	146.3	147.8	148.9	149.0
	13	147.7	150.7	147.7	150.4
K+ (mmol/l)					
week:	-1	4.690	4.490	4.350	4.020
	7	4.440	4.510	3.880	4.060
	13	4.340	4.170	4.130	3.660
Ca++ (mmol/l)					
week:	-1	2.770	2.790	2.750	2.810
	7	2.940	2.940	2.940	2.870
	13	2.640	2.620	2.660	2.660

Blood chemistry (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
Cl- (mmol/l)					
week:	-1	108.6	111.9	112.3	111.1
	7	105.9	110.2	108.3	107.9
	13	114.3	118.0	114.4	114.1
PO4-in (mmol/l)					
week:	-1	1.980	2.360	1.990	2.000
	7	1.920	2.050	2.090	1.850
	13	1.510	1.550	1.520	1.520
ASAT (GOT) (U/l)					
week:	-1	23.00	18.60	26.10	26.10
	7	29.80	21.70	24.90	16.20
	13	22.40	14.90	19.30	18.00
ALAT (GPT) (U/l)					
week:	-1	45.90	51.80	43.70	62.20
	7	38.50	66.60	45.90	45.20
	13	40.70	52.60	52.60	48.10
AlP (U/l)					
week:	-1	109.9	63.40	95.50	98.00
	7	100.0	59.20	100.0	103.4
	13	82.80	45.90	93.00	85.90
GGT (U/l)					
week:	-1	0.000	5.100	2.500	0.000
	7	0.000	3.200	3.200	0.000
	13	2.500	3.800	5.100	2.500
CK (U/l)					
week:	-1	197.2	219.4	265.0	286.2
	7	516.8	183.4	194.0	106.0
	13	168.5	114.5	142.0	121.9

Blood chemistry (individuals): females group 5
1250 ppm

		Animal no 37	38	39	40
Gluc (mmol/l) week:	-1	5.980	5.520	5.370	5.130
	7	6.140	5.630	5.860	5.520
	13	5.700	5.590	5.350	4.600
Urea (mmol/l) week:	-1	3.830	4.040	2.680	5.500
	7	3.280	4.160	3.040	4.410
	13	3.400	5.080	2.950	5.200
Creat-e (umol/l) week:	-1	73.10	80.90	64.80	88.00
	7	72.70	80.40	61.90	86.60
	13	75.60	80.30	72.30	83.30
Bili-tot (umol/l) week:	-1	2.470	2.470	2.710	2.470
	7	2.200	2.450	3.180	2.450
	13	2.450	2.690	2.940	2.200
Prot (g/l) week:	-1	53.82	55.09	54.92	59.08
	7	52.57	54.39	54.77	58.06
	13	57.06	56.80	56.72	59.72
Alb (g/l) week:	-1	32.85	32.65	32.91	34.78
	7	32.88	31.49	32.41	34.47
	13	34.11	32.90	33.20	33.49
Glob (g/l) week:	-1	20.97	22.44	22.01	24.30
	7	19.69	22.90	22.36	23.59
	13	22.95	23.90	23.52	26.23

Blood chemistry (individuals): females

group 5
1250 ppm

		Animal no 37	38	39	40
A/G (1)					
week:	-1	1.570	1.450	1.500	1.430
	7	1.670	1.380	1.450	1.460
	13	1.490	1.380	1.410	1.280
Chol (mmol/l)					
week:	-1	4.170	4.150	4.100	3.720
	7	3.730	3.860	4.200	3.190
	13	4.180	3.950	3.770	2.860
Trigly (mmol/l)					
week:	-1	0.320	0.330	0.470	0.400
	7	0.310	0.300	0.440	0.450
	13	0.330	0.230	0.210	0.320
Phos-Lip (mmol/l)					
week:	-1	5.030	4.860	4.970	4.510
	7	4.730	4.760	5.040	4.010
	13	5.100	4.890	4.560	3.980
Na+ (mmol/l)					
week:	-1	148.9	149.6	148.2	150.1
	7	147.2	148.6	148.1	148.0
	13	147.8	149.2	148.2	148.4
K+ (mmol/l)					
week:	-1	4.230	4.550	4.070	4.810
	7	3.960	4.250	3.730	4.280
	13	3.770	3.970	4.080	4.170
Ca++ (mmol/l)					
week:	-1	2.820	2.860	2.820	2.870
	7	2.860	2.870	2.880	2.900
	13	2.670	2.730	2.650	2.660

Blood chemistry (individuals): females

group 5
1250 ppm

		Animal no 37	38	39	40
Cl- (mmol/l)					
week:	-1	110.3	111.8	110.0	111.4
	7	108.1	110.0	107.7	111.0
	13	112.7	114.7	115.6	113.3
PO4-in (mmol/l)					
week:	-1	1.960	1.910	1.990	1.900
	7	1.600	1.570	1.660	1.560
	13	1.500	1.730	1.530	1.370
ASAT (GOT) (U/l)					
week:	-1	21.70	29.80	20.50	24.90
	7	19.90	24.90	19.30	22.40
	13	18.00	23.00	19.90	21.10
ALAT (GPT) (U/l)					
week:	-1	47.40	61.50	54.10	45.20
	7	39.20	42.90	42.90	45.20
	13	45.20	43.70	53.30	41.50
AlP (U/l)					
week:	-1	97.50	94.40	96.90	87.00
	7	157.1	171.2	178.5	185.3
	13	140.6	169.3	174.7	179.2
GGT (U/l)					
week:	-1	3.800	3.200	3.800	3.800
	7	4.150	3.200	3.150	3.200
	13	5.100	0.000	2.500	3.200
CK (U/l)					
week:	-1	194.0	413.4	182.3	269.2
	7	190.8	180.2	129.3	186.6
	13	129.3	147.3	114.5	131.4

6.9. Urine analysis (individuals)

Urine analysis (individuals): males group 1, 0 ppm

		Animal no 1	2	3	4
Rel dens (1)					
week:	-1	1.028	1.049	1.032	1.026
	7	1.017	1.013	1.028	1.014
	13	1.034	1.031	1.031	1.018
pH (1)					
week:	-1	7.500	6.500	5.500	5.500
	7	6.000	5.000	7.000	5.000
	13	5.750	6.000	6.500	6.500

Urine analysis (individuals): males group 2, 50 ppm

		Animal no 5	6	7	8
Rel dens (1)					
week:	-1	1.016	1.041	1.016	1.030
	7	1.029	1.026	1.012	1.032
	13	1.033	1.036	1.025	1.025
pH (1)					
week:	-1	5.500	6.500	5.500	6.500
	7	5.500	5.500	5.000	6.500
	13	6.000	6.000	6.500	6.500

Urine analysis (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
Rel dens (1)					
week:	-1	1.038	1.046	1.027	1.049
	7	1.045	1.032	1.026	1.020
	13	1.022	1.031	1.027	1.042
pH (1)					
week:	-1	7.000	6.000	7.500	9.000
	7	7.000	5.000	7.500	5.500
	13	7.000	6.000	6.000	6.500

Urine analysis (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
Rel dens (1)					
week:	-1	1.032	1.013	1.028	1.013
	7	1.017	1.011	1.014	1.011
	13	1.029	1.029	1.014	1.015
pH (1)					
week:	-1	5.500	5.500	6.500	6.000
	7	5.000	5.000	7.000	6.000
	13	6.500	6.000	6.500	5.500

Urine analysis (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
Rel dens (1)					
week:	-1	1.019	1.032	1.024	1.047
	7	1.005	1.023	1.022	1.017
	13	1.011	1.016	1.032	1.023
pH (1)					
week:	-1	6.000	6.000	6.000	5.500
	7	5.000	5.000	5.500	5.000
	13	6.000	6.000	6.000	6.000

Urine analysis (individuals): females group 1
0 ppm

		Animal no			
		21	22	23	24
Rel dens (1)					
week:	-1	1.021	1.032	1.052	1.052
	7	1.015	1.018	1.030	1.016
	13	1.035	1.039	1.032	1.033
pH (1)					
week:	-1	7.000	5.500	6.500	6.500
	7	5.500	5.500	6.500	6.000
	13	6.500	6.500	6.500	6.500

Urine analysis (individuals): females group 2
50 ppm

		Animal no			
		25	26	27	28
Rel dens (1)					
week:	-1	1.016	1.024	1.023	1.032
	7	1.019	1.022	1.025	1.021
	13	1.023	1.028	1.024	1.039
pH (1)					
week:	-1	6.500	5.000	7.500	6.000
	7	7.500	5.000	7.500	5.500
	13	6.500	7.000	7.000	6.000

Urine analysis (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
Rel dens (1)					
week:	-1	1.042	1.010	1.012	1.020
	7	1.028	1.019	1.031	1.020
	13	1.016	1.041	n.d.	1.015
pH (1)					
week:	-1	7.500	6.000	5.000	6.000
	7	7.500	7.000	6.500	5.000
	13	8.500	8.500	n.d.	6.000

Urine analysis (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
Rel dens (1)					
week:	-1	1.013	1.016	1.041	1.038
	7	1.010	1.026	1.017	1.012
	13	1.025	1.012	1.011	1.027
pH (1)					
week:	-1	7.000	6.000	6.000	8.750
	7	6.500	6.000	5.000	7.500
	13	8.500	6.500	7.000	9.000

Urine analysis (individuals): females

group 5
1250 ppm

		Animal no 37	38	39	40
Rel dens (1)					
week:	-1	1.024	1.015	1.014	1.037
	7	1.020	1.008	1.014	1.022
	13	1.029	1.035	1.016	1.036
pH (1)					
week:	-1	7.500	5.500	8.500	6.500
	7	6.500	5.500	8.000	7.000
	13	7.000	6.000	6.000	8.000

Urine analysis (individuals): males

group 1
0 ppm

		Animal no 1	2	3	4
Color (choice)					
week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N
Prot (score)					
week:	-1	+	+	0	0
	7	0	0	+	0
	13	0	0	0	0
Gluc (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score)					
week:	-1	0	+	+	0
	7	0	0	0	0
	13	0	+	0	+
Bili (score)					
week:	-1	0	0	+	0
	7	0	0	+	0
	13	+	+	+	0
Blood (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0

Urine analysis (individuals): males

group 1
0 ppm

		Animal no 1	2	3	4
RBC (score) week:	13	0	0	0	+
WBC (score) week:	7	+	0	0	0
	13	0	0	0	0
Epi-squa (score) week:	-1	+	0	++	++
	13	+	0	0	0
Epi-tr (score) week:	-1	0	+	0	++
	7	+	0	0	0
	13	+	+	0	+
Cst-Gran (score) week:	13	0	0	0	0
Cry-PO4 (score) week:	-1	+	0	0	0
	7	+	0	++	0
	13	0	0	+++	0
Cry-Caox (score) week:	13	0	0	+	0

Urine analysis (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
Color (choice)					
week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N
Prot (score)					
week:	-1	0	+	0	0
	7	0	0	0	0
	13	0	0	0	0
Gluc (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	+	0	+
Bili (score)					
week:	-1	0	0	0	0
	7	+	0	0	+
	13	++	0	+	+
Blood (score)					
week:	-1	+	0	0	0
	7	0	0	0	0
	13	0	0	0	0
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0

Urine analysis (individuals): males

group 2
50 ppm

		Animal no 5	6	7	8
RBC (score) week:	13	0	0	0	0
WBC (score) week:	7	0	0	0	0
	13	0	0	0	+
Epi-squa (score) week:	-1	++	0	+	+
	13	0	0	0	0
Epi-tr (score) week:	-1	+	0	0	0
	7	0	+	+	0
	13	+++	+	+	+
Cst-Gran (score) week:	13	+	0	0	0
Cry-PO4 (score) week:	-1	0	+	0	0
	7	0	0	0	+
	13	0	0	+	+
Cry-Caox (score) week:	13	0	0	0	0

Urine analysis (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
Color (choice)					
week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N
Prot (score)					
week:	-1	+	+	0	+++
	7	+	0	0	0
	13	0	+	0	0
Gluc (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score)					
week:	-1	0	0	+	0
	7	+	+	0	0
	13	+	+	+	+
Bili (score)					
week:	-1	0	0	0	0
	7	+	0	0	0
	13	0	+	0	+
Blood (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0

Urine analysis (individuals): males

group 3
125 ppm

		Animal no 9	10	11	12
RBC (score) week:	13	0	0	0	0
WBC (score) week:	7	0	0	0	0
	13	+	0	0	0
Epi-squa (score) week:	-1	0	0	+	0
	13	0	0	0	0
Epi-tr (score) week:	-1	0	0	0	++
	7	+	+	+	++
	13	+	+	+	+
Cst-Gran (score) week:	13	0	0	0	0
Cry-PO4 (score) week:	-1	++	0	++	+++
	7	++	0	++	0
	13	+	0	0	++
Cry-Caox (score) week:	13	0	0	0	0

Urine analysis (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
Color (choice)					
week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N
Prot (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	+	0	0	0
Gluc (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score)					
week:	-1	0	0	+	0
	7	0	0	0	0
	13	+	+	0	0
Bili (score)					
week:	-1	+	0	0	0
	7	0	0	0	0
	13	+	0	0	0
Blood (score)					
week:	-1	0	0	0	0
	7	0	0	+	0
	13	+	0	0	0
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0

Urine analysis (individuals): males

group 4
250 ppm

		Animal no 13	14	15	16
RBC (score) week:	13	0	0	0	0
WBC (score) week:	7	+	0	0	0
	13	++	0	0	0
Epi-squa (score) week:	-1	++	+	+	0
	13	0	0	0	0
Epi-tr (score) week:	-1	++	+	+	0
	7	+	+	++	++
	13	+	+	+	0
Cst-Gran (score) week:	13	0	0	0	0
Cry-PO4 (score) week:	-1	0	0	0	0
	7	0	0	+	0
	13	+	0	0	0
Cry-Caox (score) week:	13	0	0	0	0

Urine analysis (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
Color (choice)					
week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N
Prot (score)					
week:	-1	0	0	0	+
	7	0	0	+	0
	13	0	0	0	0
Gluc (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score)					
week:	-1	0	0	0	+
	7	0	+	+	0
	13	0	+	+	+
Bili (score)					
week:	-1	0	0	0	0
	7	0	0	+	0
	13	0	0	+	0
Blood (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0

Urine analysis (individuals): males

group 5
1250 ppm

		Animal no 17	18	19	20
RBC (score) week:	13	0	0	0	0
WBC (score) week:	7	0	0	0	0
	13	0	0	0	0
Epi-squa (score) week:	-1	0	0	0	0
	13	0	0	0	0
Epi-tr (score) week:	-1	+	0	+	+
	7	+	0	0	0
	13	++	+	+	0
Cst-Gran (score) week:	13	0	0	0	0
Cry-PO4 (score) week:	-1	0	++	0	0
	7	0	0	0	0
	13	0	0	0	0
Cry-Caox (score) week:	13	0	0	0	0

Urine analysis (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
Color (choice)					
week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N
Prot (score)					
week:	-1	0	0	+	+
	7	0	0	+	0
	13	+	0	+	++
Gluc (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score)					
week:	-1	+	+	+	0
	7	+	+	+	+
	13	+	+	+	+
Bili (score)					
week:	-1	0	0	+	0
	7	0	0	+	0
	13	0	0	+	0
Blood (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	+++	+
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0

Urine analysis (individuals): females

group 1
0 ppm

		Animal no 21	22	23	24
RBC (score)					
week:	7	0	0	0	0
	13	0	0	0	0
WBC (score)					
week:	7	+	0	0	0
	13	0	0	++	+
Epi-squa (score)					
week:	7	0	0	0	0
Epi-tr (score)					
week:	-1	+	0	0	+
	7	++	0	0	0
	13	+	0	+	+
Cry-PO4 (score)					
week:	-1	+	0	++	+
	7	0	0	+	0
	13	0	0	0	0

Urine analysis (individuals): females

group 2
50 ppm

		Animal no 25	26	27	28
Color (choice)					
week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N

Urine analysis (individuals): females

group 2
50 ppm

		Animal no 25	26	27	28
Prot (score) week:	-1	0	0	0	0
	7	0	0	+	0
	13	+	0	0	+
Gluc (score) week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score) week:	-1	0	0	0	+
	7	+	+	+	+
	13	+	+	+	+
Bili (score) week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Blood (score) week:	-1	0	0	0	0
	7	0	0	0	0
	13	+++	0	+	+
UBG (score) week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
RBC (score) week:	7	0	0	0	0
	13	0	+	0	0
WBC (score) week:	7	0	0	0	0
	13	++	0	+	+

Urine analysis (individuals): females

group 2
50 ppm

		Animal no 25	26	27	28
Epi-squa (score) week:	7	0	0	0	0
Epi-tr (score) week:	-1	++	0	0	0
	7	+	+	0	0
	13	++	+	0	+
Cry-PO4 (score) week:	-1	0	0	0	0
	7	+	++	0	+
	13	0	0	+	0

Urine analysis (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
Color (choice) week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	n.d.	N
Prot (score) week:	-1	+	0	0	0
	7	0	0	+	0
	13	0	+	n.d.	0
Gluc (score) week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	n.d.	0

Urine analysis (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
Keto (score)					
week:	-1	+	0	0	+
	7	+	0	0	+
	13	0	+	n.d.	0
Bili (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	n.d.	0
Blood (score)					
week:	-1	0	0	0	0
	7	0	0	0	++
	13	0	0	n.d.	+
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	n.d.	0
RBC (score)					
week:	7	0	0	0	++
	13	0	+	n.d.	+
WBC (score)					
week:	7	0	0	0	+
	13	0	0	n.d.	0
Epi-squa (score)					
week:	7	0	0	0	+
Epi-tr (score)					
week:	-1	++	0	0	+
	7	0	0	+	+++
	13	+	+	n.d.	+

Urine analysis (individuals): females

group 3
125 ppm

		Animal no 29	30	31	32
Cry-PO4 (score) week:	-1	+++	0	0	0
	7	0	+	+	0
	13	+	+	n.d.	0

Urine analysis (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
Color (choice) week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N
Prot (score) week:	-1	0	0	+	+++
	7	0	0	0	0
	13	+	0	0	+
Gluc (score) week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score) week:	-1	+	+	0	0
	7	+	0	+	0
	13	0	0	0	0
Bili (score) week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0

Urine analysis (individuals): females

group 4
250 ppm

		Animal no 33	34	35	36
Blood (score)					
week:	-1	0	0	0	0
	7	++	0	0	0
	13	0	+++	0	0
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
RBC (score)					
week:	7	+	0	0	0
	13	0	+	0	0
WBC (score)					
week:	7	0	0	0	0
	13	0	0	0	0
Epi-squa (score)					
week:	7	0	0	+	0
Epi-tr (score)					
week:	-1	0	++	0	0
	7	+	0	+	0
	13	0	0	+	+
Cry-PO4 (score)					
week:	-1	0	0	0	+++
	7	0	0	0	0
	13	0	0	+	0

Urine analysis (individuals): females

group 5
1250 ppm

		Animal no 37	38	39	40
Color (choice)					
week:	-1	N	N	N	N
	7	N	N	N	N
	13	N	N	N	N
Prot (score)					
week:	-1	+	0	0	0
	7	0	0	0	0
	13	0	0	0	+
Gluc (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Keto (score)					
week:	-1	0	0	+	+
	7	+	0	+	+
	13	+	0	+	+
Bili (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0
Blood (score)					
week:	-1	+	0	0	0
	7	0	0	0	0
	13	+	0	0	0
UBG (score)					
week:	-1	0	0	0	0
	7	0	0	0	0
	13	0	0	0	0

Urine analysis (individuals): females

group 5
1250 ppm

		Animal no 37	38	39	40
RBC (score)					
week:	7	0	0	0	0
	13	0	0	0	0
WBC (score)					
week:	7	0	0	0	0
	13	+	0	0	0
Epi-squa (score)					
week:	7	0	0	0	0
Epi-tr (score)					
week:	-1	++	0	++	0
	7	+	0	0	0
	13	+	+	+	+
Cry-PO4 (score)					
week:	-1	0	0	++	+
	7	+	0	0	+
	13	+	0	0	+

6.10. Organ weights and ratios (individuals)

6.10.1. Organ weights (individuals)

Organ weights (individuals) : males

group 1 : 0 ppm week 14

	Animal no 1	2	3	4
Body (kg)	10.06	10.56	10.64	9.960
Brain (g)	83.90	87.46	84.24	80.11
Heart (g)	97.43	108.5	98.45	93.66
Liver (g)	304.8	316.6	360.5	319.9
Kidney (both) (g)	53.38	45.50	61.78	48.79
Adrenal (both) (g)	1.016	0.991	1.149	1.141
Thymus (g)	5.207	4.170	7.104	9.965
Testis (both) (g)	16.65	16.79	21.73	17.83
Spleen (g)	20.24	21.92	27.48	22.03
Thyroid gland (g)	0.816	0.790	0.799	0.708

Organ weights (individuals) : males

group 2 : 50 ppm week 14

	Animal no 5	6	7	8
Body (kg)	10.32	10.28	10.96	10.18
Brain (g)	89.85	84.20	83.18	78.72
Heart (g)	94.86	91.47	101.7	104.9
Liver (g)	348.7	387.3	317.6	320.7
Kidney (both) (g)	53.85	49.29	45.93	58.14
Adrenal (both) (g)	1.079	1.343	1.035	0.772
Thymus (g)	4.887	8.646	10.27	4.687
Testis (both) (g)	18.21	17.78	17.18	12.63
Spleen (g)	33.45	43.35	42.47	22.27
Thyroid gland (g)	0.650	0.766	1.106	0.943

Organ weights (individuals) : males

group 3 : 125 ppm week 14

	Animal no 9	10	11	12
Body (kg)	11.20	10.46	11.60	10.30
Brain (g)	74.94	79.37	88.87	80.53

Organ weights (individuals) : males

group 3 : 125 ppm week 14

	Animal no 9	10	11	12
Heart (g)	95.06	88.80	98.38	97.96
Liver (g)	379.8	371.8	337.5	308.3
Kidney (both) (g)	60.44	55.67	49.21	43.39
Adrenal (both) (g)	1.120	1.185	1.315	0.990
Thymus (g)	7.702	5.282	9.035	8.682
Testis (both) (g)	20.01	19.19	16.65	15.74
Spleen (g)	21.30	26.06	46.06	30.87
Thyroid gland (g)	0.803	0.990	0.909	1.121

Organ weights (individuals) : males

group 4 : 250 ppm week 14

	Animal no 13	14	15	16
Body (kg)	10.26	10.62	11.24	11.00
Brain (g)	84.47	91.22	90.17	94.73
Heart (g)	89.31	92.78	98.40	91.89
Liver (g)	344.8	321.9	340.2	339.2

Organ weights (individuals) : males

group 4 : 250 ppm week 14

	Animal no 13	14	15	16
Kidney (both) (g)	56.26	46.80	55.94	57.07
Adrenal (both) (g)	1.137	1.160	1.103	1.074
Thymus (g)	5.348	7.723	10.26	6.592
Testis (both) (g)	16.98	17.39	16.68	17.28
Spleen (g)	41.12	61.50	27.51	23.30
Thyroid gland (g)	0.866	1.094	0.852	0.790

Organ weights (individuals) : males

group 5 : 1250 ppm week 14

	Animal no 17	18	19	20
Body (kg)	9.660	9.820	12.00	9.940
Brain (g)	74.60	82.52	86.20	80.16
Heart (g)	86.28	96.02	103.6	104.5
Liver (g)	414.0	380.4	453.7	380.3
Kidney (both) (g)	48.76	49.00	60.52	51.38
Adrenal (both) (g)	1.247	1.092	1.433	0.866

Organ weights (individuals) : males

group 5 : 1250 ppm week 14

	Animal no 17	18	19	20
Thymus (g)	4.648	9.740	6.488	9.945
Testis (both) (g)	14.57	18.64	18.10	14.63
Spleen (g)	23.53	23.02	49.09	35.90
Thyroid gland (g)	0.751	0.871	1.107	1.058

Organ weights (individuals) : females

group 1 : 0 ppm week 14

	Animal no 21	22	23	24
Body (kg)	9.900	10.24	9.920	10.66
Brain (g)	83.33	85.52	77.15	87.29
Heart (g)	96.01	106.9	104.9	104.1
Liver (g)	277.7	282.6	330.6	320.7
Kidney (both) (g)	47.82	47.28	56.20	44.12
Adrenal (both) (g)	1.170	1.341	1.191	1.210
Thymus (g)	6.947	12.71	7.662	11.40
Ovary (both) (g)	1.211	0.792	0.843	0.675
Spleen (g)	28.20	57.28	35.20	66.05
Thyroid gland (g)	0.642	0.756	1.117	0.565

Organ weights (individuals) : females

group 2 : 50 ppm week 14

	Animal no 25	26	27	28
Body (kg)	9.640	10.74	9.480	10.52
Brain (g)	76.02	85.55	78.33	93.68

Organ weights (individuals) : females

group 2 : 50 ppm week 14

	Animal no 25	26	27	28
Heart (g)	85.75	95.59	87.83	80.58
Liver (g)	251.7	297.7	266.7	339.2
Kidney (both) (g)	42.78	51.23	51.65	47.06
Adrenal (both) (g)	1.156	1.060	0.904	1.084
Thymus (g)	7.523	9.676	6.145	6.517
Ovary (both) (g)	0.846	0.525	0.782	0.713
Spleen (g)	27.93	25.98	18.70	47.11
Thyroid gland (g)	0.704	1.191	0.721	0.973

Organ weights (individuals) : females

group 3 : 125 ppm week 14

	Animal no 29	30	31	32
Body (kg)	8.660	10.80	10.38	9.460
Brain (g)	75.98	93.44	82.32	75.21
Heart (g)	78.54	93.00	106.4	86.66
Liver (g)	279.9	307.1	324.4	278.6

Organ weights (individuals) : females

group 3 : 125 ppm week 14

	Animal no 29	30	31	32
Kidney (both) (g)	37.60	43.94	41.03	40.11
Adrenal (both) (g)	1.094	1.318	1.234	1.375
Thymus (g)	8.576	9.642	11.22	7.585
Ovary (both) (g)	0.957	0.906	2.949	0.824
Spleen (g)	40.15	62.62	46.56	23.53
Thyroid gland (g)	0.648	0.946	0.773	0.595

Organ weights (individuals) : females

group 4 : 250 ppm week 14

	Animal no 33	34	35	36
Body (kg)	9.020	10.60	10.12	8.760
Brain (g)	75.09	83.65	87.86	78.83
Heart (g)	74.97	95.49	104.4	106.2
Liver (g)	277.5	329.4	317.8	250.3
Kidney (both) (g)	40.77	41.43	49.90	40.51
Adrenal (both) (g)	1.020	1.223	1.315	1.167

Organ weights (individuals) : females

group 4 : 250 ppm week 14

	Animal no 33	34	35	36
Thymus (g)	5.652	17.33	4.222	7.130
Ovary (both) (g)	0.889	2.672	0.803	0.794
Spleen (g)	24.65	35.03	34.80	24.59
Thyroid gland (g)	0.581	1.020	0.693	0.733

Organ weights (individuals) : females

group 5 : 1250 ppm week 14

	Animal no 37	38	39	40
Body (kg)	10.06	10.60	9.200	9.240
Brain (g)	79.54	93.14	80.75	76.71
Heart (g)	86.97	103.2	88.99	91.78
Liver (g)	382.6	402.6	338.9	425.2
Kidney (both) (g)	48.89	49.12	52.02	38.00
Adrenal (both) (g)	1.536	1.183	1.004	1.146
Thymus (g)	7.705	8.844	5.004	7.120
Ovary (both) (g)	2.346	0.855	0.946	0.541

Organ weights (individuals) : females

group 5 : 1250 ppm week 14

	Animal no 37	38	39	40
Spleen (g)	28.79	53.63	31.74	22.24
Thyroid gland (g)	0.830	0.870	0.756	0.609

6.10.2. Organ to body weight ratios (individuals)

Organ to body weight ratios (individuals) : males

group 1 : 0 ppm week 14

	Animal no 1	2	3	4
Brain (o/oo)	8.340	8.282	7.917	8.043
Heart (o/oo)	9.685	10.27	9.253	9.404
Liver (o/oo)	30.30	29.98	33.88	32.11
Kidney (both) (o/oo)	5.306	4.309	5.806	4.899
Adrenal (both) (o/oo)	0.101	0.094	0.108	0.115
Thymus (o/oo)	0.518	0.395	0.668	1.001
Testis (both) (o/oo)	1.655	1.590	2.042	1.790
Spleen (o/oo)	2.012	2.076	2.583	2.212
Thyroid gland (o/oo)	0.081	0.075	0.075	0.071

Organ to body weight ratios (individuals) : males

group 2 : 50 ppm week 14

	Animal no 5	6	7	8
Brain (o/oo)	8.706	8.191	7.589	7.733
Heart (o/oo)	9.192	8.898	9.275	10.30
Liver (o/oo)	33.79	37.68	28.98	31.50
Kidney (both) (o/oo)	5.218	4.795	4.191	5.711
Adrenal (both) (o/oo)	0.105	0.131	0.094	0.076
Thymus (o/oo)	0.474	0.841	0.937	0.460
Testis (both) (o/oo)	1.765	1.730	1.568	1.240
Spleen (o/oo)	3.241	4.217	3.875	2.188
Thyroid gland (o/oo)	0.063	0.075	0.101	0.093

Organ to body weight ratios (individuals) : males

group 3 : 125 ppm week 14

	Animal no 9	10	11	12
Brain (o/oo)	6.691	7.588	7.661	7.818
Heart (o/oo)	8.488	8.489	8.481	9.511
Liver (o/oo)	33.91	35.55	29.09	29.94

Organ to body weight ratios (individuals) : males

group 3 : 125 ppm week 14

	Animal no 9	10	11	12
Kidney (both) (o/oo)	5.396	5.322	4.242	4.213
Adrenal (both) (o/oo)	0.100	0.113	0.113	0.096
Thymus (o/oo)	0.688	0.505	0.779	0.843
Testis (both) (o/oo)	1.787	1.834	1.435	1.528
Spleen (o/oo)	1.902	2.491	3.971	2.997
Thyroid gland (o/oo)	0.072	0.095	0.078	0.109

Organ to body weight ratios (individuals) : males

group 4 : 250 ppm week 14

	Animal no 13	14	15	16
Brain (o/oo)	8.233	8.589	8.022	8.612
Heart (o/oo)	8.705	8.736	8.754	8.354
Liver (o/oo)	33.61	30.31	30.27	30.83
Kidney (both) (o/oo)	5.483	4.407	4.977	5.188
Adrenal (both) (o/oo)	0.111	0.109	0.098	0.098
Thymus (o/oo)	0.521	0.727	0.913	0.599

Organ to body weight ratios (individuals) : males

group 4 : 250 ppm week 14

	Animal no 13	14	15	16
Testis (both) (o/oo)	1.655	1.637	1.484	1.571
Spleen (o/oo)	4.008	5.791	2.448	2.118
Thyroid gland (o/oo)	0.084	0.103	0.076	0.072

Organ to body weight ratios (individuals) : males

group 5 : 1250 ppm week 14

	Animal no 17	18	19	20
Brain (o/oo)	7.723	8.403	7.183	8.064
Heart (o/oo)	8.932	9.778	8.636	10.52
Liver (o/oo)	42.85	38.74	37.81	38.26
Kidney (both) (o/oo)	5.048	4.990	5.043	5.169
Adrenal (both) (o/oo)	0.129	0.111	0.119	0.087
Thymus (o/oo)	0.481	0.992	0.541	1.001
Testis (both) (o/oo)	1.508	1.898	1.508	1.472
Spleen (o/oo)	2.436	2.344	4.091	3.612
Thyroid gland (o/oo)	0.078	0.089	0.092	0.106

Organ to body weight ratios (individuals) : females

group 1 : 0 ppm week 14

	Animal no 21	22	23	24
Brain (o/oo)	8.417	8.352	7.777	8.189
Heart (o/oo)	9.698	10.44	10.58	9.763
Liver (o/oo)	28.05	27.59	33.33	30.08
Kidney (both) (o/oo)	4.830	4.617	5.665	4.139
Adrenal (both) (o/oo)	0.118	0.131	0.120	0.114
Thymus (o/oo)	0.702	1.241	0.772	1.070
Ovary (both) (o/oo)	0.122	0.077	0.085	0.063
Spleen (o/oo)	2.848	5.594	3.548	6.196
Thyroid gland (o/oo)	0.065	0.074	0.113	0.053

Organ to body weight ratios (individuals) : females

group 2 : 50 ppm week 14

	Animal no 25	26	27	28
Brain (o/oo)	7.886	7.966	8.263	8.905
Heart (o/oo)	8.895	8.900	9.265	7.660
Liver (o/oo)	26.11	27.72	28.13	32.24

Organ to body weight ratios (individuals) : females

group 2 : 50 ppm week 14

	Animal no 25	26	27	28
Kidney (both) (o/oo)	4.438	4.770	5.448	4.473
Adrenal (both) (o/oo)	0.120	0.099	0.095	0.103
Thymus (o/oo)	0.780	0.901	0.648	0.619
Ovary (both) (o/oo)	0.088	0.049	0.082	0.068
Spleen (o/oo)	2.897	2.419	1.973	4.478
Thyroid gland (o/oo)	0.073	0.111	0.076	0.092

Organ to body weight ratios (individuals) : females

group 3 : 125 ppm week 14

	Animal no 29	30	31	32
Brain (o/oo)	8.774	8.652	7.931	7.950
Heart (o/oo)	9.069	8.611	10.25	9.161
Liver (o/oo)	32.32	28.44	31.26	29.45
Kidney (both) (o/oo)	4.342	4.069	3.953	4.240
Adrenal (both) (o/oo)	0.126	0.122	0.119	0.145
Thymus (o/oo)	0.990	0.893	1.081	0.802

Organ to body weight ratios (individuals) : females

group 3 : 125 ppm week 14

	Animal no 29	30	31	32
Ovary (both) (o/oo)	0.111	0.084	0.284	0.087
Spleen (o/oo)	4.636	5.798	4.486	2.487
Thyroid gland (o/oo)	0.075	0.088	0.074	0.063

Organ to body weight ratios (individuals) : females

group 4 : 250 ppm week 14

	Animal no 33	34	35	36
Brain (o/oo)	8.325	7.892	8.682	8.999
Heart (o/oo)	8.312	9.008	10.31	12.12
Liver (o/oo)	30.76	31.08	31.41	28.57
Kidney (both) (o/oo)	4.520	3.908	4.931	4.624
Adrenal (both) (o/oo)	0.113	0.115	0.130	0.133
Thymus (o/oo)	0.627	1.635	0.417	0.814
Ovary (both) (o/oo)	0.099	0.252	0.079	0.091
Spleen (o/oo)	2.733	3.305	3.439	2.807
Thyroid gland (o/oo)	0.064	0.096	0.068	0.084

Organ to body weight ratios (individuals) : females

group 5 : 1250 ppm week 14

	Animal no 37	38	39	40
Brain (o/oo)	7.907	8.787	8.777	8.302
Heart (o/oo)	8.645	9.731	9.673	9.933
Liver (o/oo)	38.03	37.98	36.83	46.02
Kidney (both) (o/oo)	4.860	4.634	5.654	4.113
Adrenal (both) (o/oo)	0.153	0.112	0.109	0.124
Thymus (o/oo)	0.766	0.834	0.544	0.771
Ovary (both) (o/oo)	0.233	0.081	0.103	0.059
Spleen (o/oo)	2.862	5.059	3.450	2.407
Thyroid gland (o/oo)	0.083	0.082	0.082	0.066

6.11. Macroscopical and microscopical findings (individuals):

6.11.1. List of findings in individual males

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Removal code : all Observation period : all

Selected experimental group(s): all

Selected animals: all

Selected findings : all

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Treatment ended in observation period, selected	4	4	4	4	4
Examined macroscopically					
S1	4	4	4	4	4
Total	4	4	4	4	4
Examined microscopically	4	4	4	4	4

Abbreviations used in pathology tables

S1, S2....	scheduled sacrifice(s)
MS	moribund sacrifice
FD	found dead
AD	accidental death

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 0 ppm

Male Nr. 1 / Days on study: 95 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin : Inflammatory cell infiltration +
Bone marrow : Fatty atrophy ++
Splenic white pulp lymphatic follicle : Hyperplasia +
Liver : Inflammatory cell infiltration +
Renal papilla : Calcification ++ bilateral
Choroid plexus : Lymphocytic infiltration +

Male Nr. 2 / Days on study: 95 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +
Spleen : Haemosiderosis +
Liver : Inflammatory cell infiltration +
Liver : Fatty change +
Renal papilla : Calcification + bilateral

Male Nr. 3 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis ++
Liver : Inflammatory cell infiltration +
Renal papilla : Calcification + bilateral
Parathyroid gland : Developmental cyst
Choroid plexus : Inflammatory cell infiltration +

Male Nr. 4 / Days on study: 93 / Scheduled sacrifice 1
Macro
A Lung : Mottled
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +
Spleen : Haemosiderosis +
A Lung blood vessel : Dilatation ++
Liver : Inflammatory cell infiltration +
Renal papilla : Calcification + bilateral
Prostatic glandular tissue : Atrophy +
Thymus : Lymphoid hyperplasia +

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 50 ppm

Male Nr. 5 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +
Spleen : Haemosiderosis ++
Liver : Inflammatory cell infiltration +
Liver : Fatty change ++
Renal papilla : Calcification ++ bilateral
C-cell of thyroid : Hyperplasia + focal

Male Nr. 6 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin hair follicle : Lymphocytic infiltration +
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Renal papilla : Calcification + bilateral
Prostate : Chronic inflammation ++
Adenohypophysis : Developmental cyst
Parathyroid gland : Developmental cyst

Male Nr. 7 / Days on study: 95 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Liver : Organizing necrosis +
Renal papilla : Calcification + bilateral
C-cell of thyroid : Hyperplasia ++ focal
Thymic medulla : Hyperplasia + focal

Male Nr. 8 / Days on study: 95 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Liver : Inflammatory cell infiltration +
Renal papilla : Calcification ++ bilateral
Prostate : Lymphocytic infiltration ++
Parathyroid gland : Developmental cyst

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 125 ppm

Male Nr. 9 / Days on study: 95 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Renal papilla : Calcification + bilateral

Male Nr. **10** / Days on study: 95 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Liver : Fatty change +
Renal papilla : Calcification + bilateral
Adrenal cortex : Fatty change + bilateral

Male Nr. **11** / Days on study: 93 / Scheduled sacrifice 1
Macro
A Lung : Mottled
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Bronchus : Foreign body ++
A Lung : Acute bronchopneumonia ++
Renal papilla : Calcification + bilateral
Prostate : Chronic inflammation ++
Adenohypophysis : Developmental cyst
Adrenal gland : Developmental malformation unilateral
Thyroid gland : Developmental cyst

Male Nr. **12** / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin hair follicle : Inflammatory cell infiltration +
Bone marrow : Fatty atrophy ++
Spleen : Congestion +
Spleen : Haemosiderosis +
Lung : Haemosiderosis +
Liver : Inflammatory cell infiltration +
Renal papilla : Calcification + bilateral
Urinary bladder : Inflammatory oedema +

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 250 ppm

Male Nr. 13 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Liver : Organizing necrosis ++
Duodenal mucosa : Cystic dilatation +
Renal papilla : Calcification + bilateral
Testis spermatogenic epithelium : Spermatic giant cell + unilateral

Male Nr. 14 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Renal papilla : Calcification ++ bilateral
Adenohypophysis : Developmental cyst

Male Nr. 15 / Days on study: 94 / Scheduled sacrifice 1
Macro
A Lung : Nodule (<.5 cm) several
Micro
Skin hair follicle : Parasitic granuloma ++
Bone marrow : Fatty atrophy ++
A Lung : Fibrosis ++ focal
Renal papilla : Calcification + bilateral
Prostatic glandular tissue : Atrophy +
Epididymis artery : Polyarteritis ++ unilateral
Thymic medulla : Hyperplasia + focal
Choroid plexus : Inflammatory cell infiltration +

Male Nr. 16 / Days on study: 94 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin hair follicle : Lymphocytic infiltration +
Bone marrow : Fatty atrophy ++
Renal papilla : Calcification ++ bilateral

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 1250 ppm

Male Nr. 17 / Days on study: 94 / Scheduled sacrifice 1
Macro
A Lung : Mottled
Micro
Skin hair follicle : Parasitic granuloma +++
Bone marrow : Fatty atrophy ++
A Lung : Acute bronchopneumonia ++ focal
Renal papilla : Calcification + bilateral
Epididymis : Spermatic granuloma ++ unilateral
Thyroid gland : Developmental cyst

Male Nr. 18 / Days on study: 94 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +
Renal papilla : Calcification ++ bilateral

Male Nr. 19 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Liver : Fatty change ++
Renal papilla : Calcification ++ bilateral

Male Nr. 20 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion ++
Spleen : Haemosiderosis +
Liver : Inflammatory cell infiltration +
Renal papilla : Calcification ++ bilateral
Pituitary gland : No examination for technical reasons
Adrenal cortex : Fatty change + bilateral

6.11.2. List of findings in individual females

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Removal code : all Observation period : all

Selected experimental group(s): all

Selected animals: all

Selected findings : all

Group	1	2	3	4	5
Exposure : ppm	0	50	125	250	1250
Animals initially in study	4	4	4	4	4
Treatment ended in observation period, selected	4	4	4	4	4
Examined macroscopically					
S1	4	4	4	4	4
Total	4	4	4	4	4
Examined microscopically	4	4	4	4	4

Abbreviations used in pathology tables

S1, S2....	scheduled sacrifice(s)
MS	moribund sacrifice
FD	found dead
AD	accidental death

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 0 ppm

Female Nr. 21 / Days on study: 93 / Scheduled sacrifice 1
Macro
A Lung : Mottled
Micro
Bone marrow : Fatty atrophy ++
Bronchus : Foreign body ++
A Lung : Chronic bronchopneumonia +++
Renal papilla : Calcification + bilateral

Female Nr. 22 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Spleen : Haemosiderosis +
Heart artery : Chronic necrotizing inflammation ++
Renal papilla : Calcification + bilateral
Ovarian follicle : Hypercellularity ++ bilateral
Adenohypophysis : Developmental cyst

Female Nr. 23 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin : Inflammatory cell infiltration +
Epidermis : Acanthosis +
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Spleen : Haemosiderosis +
Liver : Fatty change +
Renal papilla : Calcification ++ bilateral
Ovarian follicle : Hypercellularity ++ bilateral

Female Nr. 24 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Bronchus : Foreign body granuloma +
Renal papilla : Calcification ++ bilateral
Thyroid gland : Developmental cyst

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 50 ppm

Female Nr. 25 / Days on study: 94 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis ++
Renal papilla : Calcification ++ bilateral
Adenohypophysis : Developmental cyst

Female Nr. 26 / Days on study: 94 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin hair follicle : Parasitic granuloma +++
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Renal papilla : Inflammatory cell infiltration + focal unilateral
Renal papilla : Calcification + bilateral
Adenohypophysis : Developmental cyst
Parathyroid gland : Developmental cyst

Female Nr. 27 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Renal papilla : Calcification + bilateral
Ovarian follicle : Hypercellularity + unilateral
Adenohypophysis : Developmental cyst
Lacrimal gland : One organ, no examination for technical reasons

Female Nr. 28 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin hair follicle : Chronic inflammation ++
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Spleen : Haemosiderosis +
Liver : Fatty change +
Renal papilla : Calcification + bilateral
Adenohypophysis : Developmental cyst
Parathyroid gland : Developmental cyst

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 125 ppm

Female Nr. 29 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Liver : Inflammatory cell infiltration +
Renal papilla : Calcification ++ bilateral

Female Nr. 30 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Liver : Fatty change +
Renal papilla : Calcification + bilateral
Parathyroid gland : Developmental cyst

Female Nr. 31 / Days on study: 94 / Scheduled sacrifice 1
Macro
A Ovary : Cyst one right
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +
Spleen : Haemosiderosis +
Liver : Fatty change +
Renal papilla : Calcification + bilateral
A Ovary : Corpus luteum cyst +++ unilateral

Female Nr. 32 / Days on study: 94 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin hair follicle : Chronic inflammation +
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Renal papilla : Calcification + bilateral
Lacrimal gland : One organ, no examination for technical reasons

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 250 ppm

Female Nr. 33 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Renal papilla : Calcification ++ bilateral
Vagina : Lymphocytic infiltration ++
Adrenal cortex : Fatty change + bilateral

Female Nr. 34 / Days on study: 92 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Congestion +
Spleen : Haemosiderosis +
Liver : Inflammatory cell infiltration +
Liver : Fatty change ++
Renal papilla : Calcification + bilateral

Female Nr. 35 / Days on study: 94 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Liver : Inflammatory cell infiltration +
Liver : Fatty change +
Renal papilla : Calcification + bilateral
Vagina : Lymphocytic infiltration +
C-cell of thyroid : Hyperplasia + diffuse

Female Nr. 36 / Days on study: 94 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin : Inflammatory cell infiltration +
Bone marrow : Fatty atrophy ++
Liver : Inflammatory cell infiltration +
Renal papilla : Calcification ++ bilateral
Adenohypophysis : Developmental cyst

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 1250 ppm

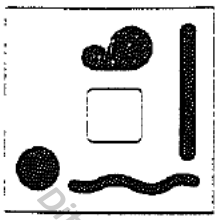
Female Nr. 37 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Liver : Fatty change +
Renal papilla : Calcification + bilateral

Female Nr. 38 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin hair follicle : Inflammatory cell infiltration ++
Bone marrow : Fatty atrophy ++
Spleen : Congestion +++
Spleen : Haemosiderosis +
Renal papilla : Calcification ++ bilateral

Female Nr. 39 / Days on study: 93 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis ++
Renal papilla : Calcification ++ bilateral
Ovarian follicle : Hypercellularity + bilateral
C-cell of thyroid : Hyperplasia + diffuse

Female Nr. 40 / Days on study: 94 / Scheduled sacrifice 1
Macro
Body as a whole : No changes observed
Micro
Skin : Inflammatory cell infiltration ++
Epidermis : Acanthosis ++
Bone marrow : Fatty atrophy ++
Spleen : Haemosiderosis +
Liver : Fatty change +
Renal papilla : Calcification + bilateral
Adenohypophysis : Developmental cyst
Adrenal cortex : Fatty change + bilateral

7. APPENDIX C: ANALYTICAL RESULTS



Study Title:

DETERMINATION OF CONTENT, HOMOGENEITY AND STABILITY OF CGA 329351 TECH. IN DOG FEED

ANALYTICAL REPORT TO:

3-MONTH SUBCHRONIC DIETARY TOXICITY STUDY IN BEAGLE DOGS

Author:

[redacted]

Study Completion Date:

May 18, 1995

Performing Laboratory:

R C C UMWELTCHEMIE AG
P.O. Box
CH-4452 Itingen/BL
Switzerland

Study Project No.:

RCC PROJECT 386234
CIBA-GEIGY PROJECT 943128

RCC
Group

SIGNATURE PAGE

RESPONSIBLE FOR ANALYTICS:

5.1.2.e Woo

Date: May 18, 1995

MANAGING DIRECTOR:

Dr. 5.1.2.e Woo

.....

Date: May 18, 1995

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GENERAL INFORMATION

GENERAL

RCC Project:	386234
CIBA-GEIGY Project:	943128
Sponsor:	CIBA-GEIGY Limited Crop Protection Division 4002 Basle / Switzerland
Study Director:	Dr. med. vet. 5.1.2.e Woo
Test Article:	CGA 329351 tech.
Testing Facility:	R C C UMWELTCHEMIE AG Department of Chemistry CH-4452 Itingen / Switzerland

PROJECT STAFF

Responsible for Analytics:	5.1.2.e Woo

SCHEDULE

Dates of Analysis:	see section 2.2
Study Completion Date:	May 18, 1995/mma

ARCHIVING

Raw data, copy of protocol, analytical report and test article reference sample for at least ten years at:

R C C AG
CH-4452 Itingen / Switzerland

GOOD LABORATORY PRACTICE

STATEMENT OF COMPLIANCE

PROJECT NUMBER: 386234

CIBA-GEIGY PROJECT NUMBER: 943128

TEST ARTICLE: CGA 329351 tech.

RESPONSIBLE FOR ANALYTICS: Mr. 5.1.2.e Woo

TITLE: Determination of Content, Homogeneity and Stability of CGA 329351 tech. in dog feed.

This study was conducted in compliance with Good Laboratory Practice Regulations (see page 9).

Responsible for Analytics: Mr. 5.1.2.e Woo

5.1.2.e Woo

Date: [illegible]

QUALITY ASSURANCE UNIT

R C C UMWELTCHEMIE AG, CH-4452 ITINGEN / SWITZERLAND

STATEMENT

PROJECT NUMBER: 386234

TEST ARTICLE: CGA 329351 tech.

RESPONSIBLE FOR ANALYTICS: Mr. [redacted]

TITLE: Determination of Content, Homogeneity and Stability of CGA 329351 tech. in dog feed.

Study procedures were periodically inspected and this report was audited by the Quality Assurance Unit. The dates are given below.

Dates of QAU Inspections/ Audits	Dates of Reports to the Responsible for Analytics and to the Management
11-JAN-95	11-JAN-95
16-MAY-95	16-MAY-95

Manager, Quality Assurance Unit: Mrs. [redacted]

[redacted]

Date: May 19, 1995

GOOD LABORATORY PRACTICE

The study was performed in compliance with:

"Good Laboratory Practice (GLP) in Switzerland, Procedures and Principles, March 1986."

- OECD Principles of Good Laboratory Practice (Council Decision 81/30, adopted on May 12, 1981, and the OECD Recommendation 89/87 concerning 'Mutual Recognition of Compliance with Good Laboratory Practice', adopted on October 2, 1989).

ABSTRACT

This chemical analysis determined content, homogeneity and stability of CGA 329351 tech. in dog feed.

Prepared on 15-NOV-94 and on 12-JAN-95:

The test article overall mean concentrations in pelleted diet samples were found to be 93.9 %, 101.2 %, 91.4 % and 91.7 % of the nominal concentrations for dose groups 2 (50 ppm), 3 (125 ppm), 4 (250 ppm) and 5 (1250 ppm), respectively. The homogeneity varied in the range from -2 % to +1 % of the mean concentrations.

CGA 329351 tech. was found to be stable in dog feed at room temperature over a period of 42 days.

1. INTRODUCTION

This report describes the analytical method used and the results obtained for content, homogeneity and stability of CGA 329351 tech. in dog feed. The analyses were performed by a HPLC method.

Analysis of homogeneity was performed by analyzing samples of each dose group from three different segments (beginning, middle, end) of pelleting process.

2. MATERIALS AND METHODS

2.1. DESCRIPTION OF TEST ARTICLE

(according to the information provided by the sponsor)

Code No:	CGA 329351 tech.
Batch No:	OP.4
Content of active ingredient:	97.1 %
Description:	viscous liquid
Date of receipt:	October 10, 1994
Storage conditions:	room temperature
Stability:	guaranteed by the sponsor until reanalysis date April 1998
Safety precautions:	All personnel which was exposed to the test material during weighing or mixing the test article wore dust masks, protective glasses and disposable plastic gloves.

2.2. SAMPLES

Shipment:	1
- Prepared by sponsor on:	15-NOV-94
- Received at RCC on:	22-NOV-94
- Dates of analysis:	20/21-DEC-94
Shipment:	2
- Prepared by sponsor on:	15-NOV-94
- Received at RCC on:	30-DEC-94
- Date of analysis:	09-JAN-95*
Shipment:	3
- Prepared by sponsor on:	12-JAN-95
- Received at RCC on:	17-JAN-95
- Dates of analysis:	17/20-MAR-95

* Samples of 42-day stability test at room temperature

2.3. STORAGE

Diet samples were prepared, samples were collected and immediately deepfrozen by the sponsor until shipment to RCC Umweltchemie AG. The samples of the stability test were kept at room temperature at the sponsor's facility for 42 days prior to deepfreezing. All samples were shipped to the analytical laboratories of RCC Umweltchemie AG, Itingen/Switzerland under deepfrozen conditions in a cool box and were, upon arrival, stored deepfrozen until sample work-up and analysis by HPLC. If necessary, worked-up sample solutions were stored in the refrigator prior to analysis by HPLC.

2.4. ANALYTICAL PROCEDURE

2.4.1. Standard Solutions

First, stock solutions of the test article (see section 2.1) in methanol with a concentration of 1.000 mg/ml were prepared as follows: 50 mg of the test article were each weighed into a 50 ml volumetric flask. Next, about 30 ml of methanol was added and these mixtures were treated in an ultrasonic bath for dissolution. Then, the volumetric flasks were filled to volume with methanol. Next, various standard solutions were prepared by respective dilution of these stock solutions with HPLC-eluent A (see section 2.4.4) to yield concentrations in the range from 0.2 µg/ml to 2 µg/ml. These standard solutions were used to calibrate the HPLC.

2.4.2. Analysis of Samples

Ten (10) grams of ground diet pellets were weighed into a 250 ml screw-top bottle and slurried with 10 ml of bidistilled water. Then, 90 ml of methanol was added and this suspension was extracted for one hour using a mechanical lab shaker. After 15 minutes of sedimentation, a sample was withdrawn from the supernatant and was further analyzed as discribed in sections 2.4.2.1. Finally, a 50 µl aliquot was quantified by HPLC.

2.4.2.1. Dilution (0 ppm-1250 ppm Dose Group)

Calculated aliquots of the supernatants derived from section 2.4.2 were diluted with HPLC-eluent A (see section 2.4.4) to yield concentrations within the calibration range before quantification by HPLC.

2.4.3. Preparation of Fortified Samples

To assess the recovery of CGA 329351 tech. from rodent feed by this method of analysis, ten (10) gram portions of control feed were fortified with calculated volumes (V_c) of freshly prepared solutions of CGA 329351 tech. in methanol with concentrations ranging from 100 µg/ml to 1000 µg/ml. As a result, recovery samples with concentrations equal or similar to the feed samples were prepared. These fortified samples were slurried with 10 ml of bidistilled water and (90-V_c) ml of methanol and were further analyzed exactly as described in sections 2.4.2 and 2.4.2.1.

2.4.4. HPLC-Determination

(Typical Operating Conditions)

Apparatus:

Merck L-6200	pump
Merck L-4000	photometer
Merck D-2500	integrator
Merck AS-4000	sampling unit

Column: Lichrospher RP-18; 5 µm; 125 x 4.6 mm

Eluent A:

Bidistilled water	60 % v/v
Acetonitrile	40 % v/v

Eluent B: Acetonitrile 100 % v/v

Gradient:

Run time (minutes)	Flow rate (ml/min)	% A	% B
0	1.0	100	0
8	1.0	100	0
8.1	1.0	0	100
14	1.0	0	100
14.1	1.0	100	0
30	1.0	100	0

Temperature: Room temperature

Flow rate: 1.0 ml/min

Detection: UV, 210 nm

Injection volume: 50 µl

2.4.5. Evaluation of Results

Injected samples were quantified by peak area or peak height with reference to the calibration curves. The latter were obtained by correlation of the peak area or peak height (in counts) of the analytical standards with their corresponding concentration in µg/ml.

An example of a calibration curve is listed in Table 1 and typical chromatograms of standard solutions are shown in Figure 1. From these or similar curves, the concentrations Y of CGA 329351 tech. in µg/ml of an injected sample were calculated from equation 1.

$$Y = a + b \cdot X \qquad (1)$$

where

Y = µg/ml CGA 329351 tech. of injected sample

a = y-axis intercept

b = slope

X = peak area or peak height of injected sample in counts

The concentrations of CGA 329351 tech. in dog feed were calculated according to equation 2.

$$C = \frac{Y \cdot V \cdot D \cdot 100\ \%}{W \cdot R} \qquad (2)$$

where

C = Concentration of CGA 329351 tech. in dog feed in ppm (mg/kg)

Y = µg/ml test article of injected sample calculated by equation 1

V = Volume of solvent used for dissolution (100 ml)

D = Dilution factor

W = Weight of diet sample (10 g)

R = Recovery (%)

3. RESULTS

The results obtained for content, homogeneity and stability of CGA 329351 tech. in dog feed are summarized in the attached tables on page 18.

The tabulated values represent rounded-off results obtained by calculations based on the exact raw data.

Prepared on 15-NOV-94 and on 12-JAN-95:

The test article overall mean concentrations in pelleted diet samples were found to be 93.9 %, 101.2 %, 91.4 % and 91.7 % of the nominal concentrations for dose groups 2 (50 ppm), 3 (125 ppm), 4 (250 ppm) and 5 (1250 ppm), respectively. The homogeneity varied in the range from -2 % to +1 % of the mean concentrations.

CGA 329351 tech. was found to be stable in dog feed at room temperature over a period of 42 days.

An example of a calibration curve of CGA 329351 tech. is listed in Table 1 and typical chromatograms of standard solutions and samples are shown in Figures 1 and 2, respectively.

Table 1: Example of a calibration curve

Standard (µg/ml)	Peak height (counts)	
	before samples	after samples
0.2	552	576
0.5	1413	1415
1	2835	2821
2	5719	5786

$Y = 9.94\ E\text{-}3 + 3.47\ E\text{-}4 \cdot X$ $(R^2 = 1.00)$

where

Y = µg/ml CGA 329351 tech. in injected sample

X = peak height of injected sample (in counts)

TEST ARTICLE IN FEED CONTENT, HOMOGENEITY AND STABILITY

Table 2:

DATE OF PREPARATION: 15-NOV-94

Dose Group Day	Nominal ppm	Date of analysis		Concentrat. found ppm	% of Nom.	Mean % of Nom.	± Dev. in % of Mean	Recovery ppm added	%
GROUP 1									
Day 0	0	21-DEC-94	B	0.000	---	---	---	---	---
Day 42			*	0.000	---	---			
GROUP 2									
Day 0	50	21-DEC-94	A	45.70	91.4	90.1	-2 / +1	50.0	96.4
Day 0			B	43.96	87.9				
Day 0			C	45.51	91.0				
Day 42			*	44.73	89.5	89.5		50.0	103.2
GROUP 3									
Day 0	125	21-DEC-94	A	115.8	92.7	93.1	0 / +1	100	99.6
Day 0			B	116.2	93.0				
Day 0			C	117.2	93.7				
Day 42			*	108.7	87.0	87.0		100	103.8
GROUP 4									
Day 0	250	20-DEC-94	A	231.2	92.5	92.8	0 / +0	250	96.8
Day 0			B	231.7	92.7				
Day 0			C	233.1	93.2				
Day 42			*	241.3	96.5	96.5		250	98.2
GROUP 5									
Day 0	1250	20-DEC-94	A	1141	91.2	91.3	0 / +0	1000	103.0
Day 0			B	1140	91.2				
Day 0			C	1142	91.4				
Day 42			*	1204	96.4	96.4		1000	105.2

A : Beginning)
B : Middle) of discharge from the pelleting machine
C : End)

* Stability test at room temperature over a period of 42-days

TEST ARTICLE IN FEED CONTENT

DATE OF PREPARATION: 12-JAN-95

Dose Group	Nominal ppm	Date of analysis	Concentrat. found ppm	% of Nom.	Mean % of Nom.	± Dev. in % of Mean	Recovery ppm added	%
Group 1	0	17-MAR-95	0.000	---	---	---	---	---
Group 2	50	20-MAR-95	48.82	97.6	---	---	50.0	82.5
Group 3	125	17-MAR-95	136.6	109.3	---	---	100	82.7
Group 4	250	17-MAR-95	225.1	90.0	---	---	250	93.6
Group 5	1250	17-MAR-95	1151	92.1	---	---	1000	113.4

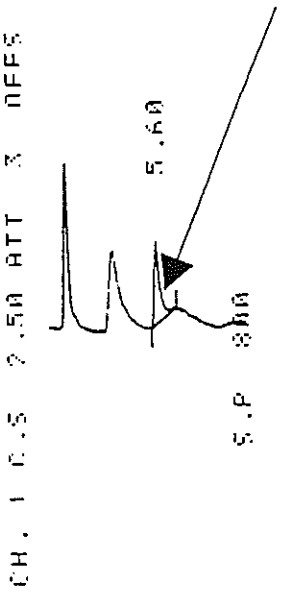
OVERALL MEAN CONCENTRATION

Dose Group	Nominal ppm	N	Mean % of Nom.
Group 2	50	2	93.9
Group 3	125	2	101.2
Group 4	250	2	91.4
Group 5	1250	2	91.7

Figure 1: Typical Chromatograms:

1. Standard solution 0.2 µg/ml, before samples
2. Standard solution 2 µg/ml, before samples

1.



2.

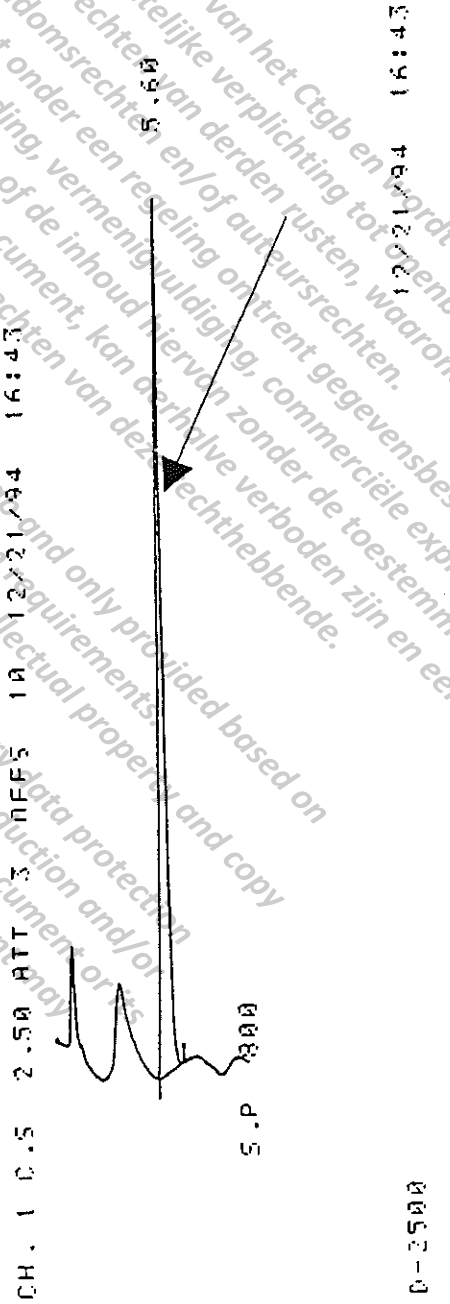
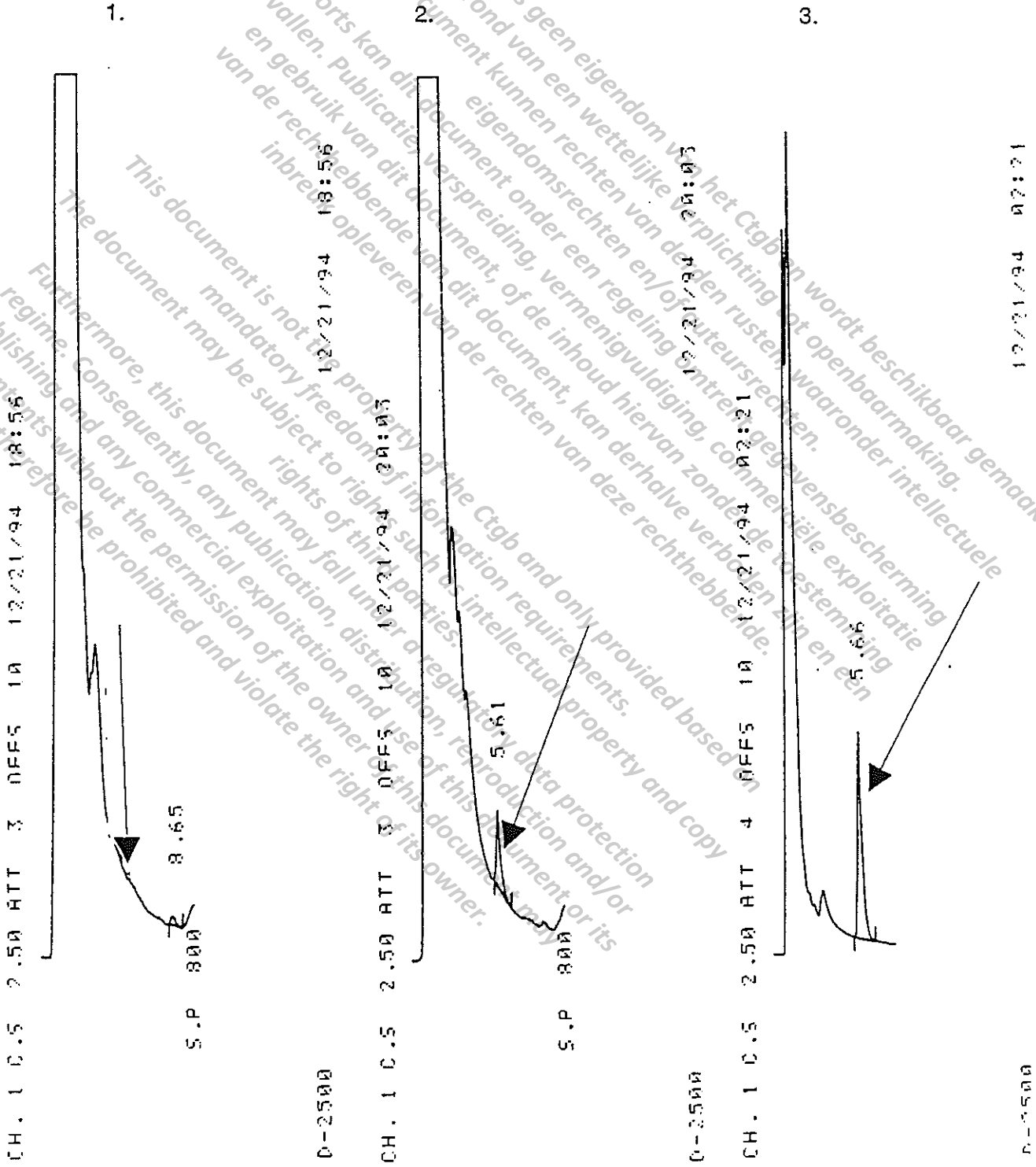


Figure 2: Typical Chromatograms:

1. Control sample
2. Sample, nominal 50 ppm; diluted 20x
3. Sample, nominal 1250 ppm; diluted 100x



8. APPENDIX D: REFERENCE VALUES

8.1. Units used in hematology

Parameter	SI Unit	Conventional Unit	Conversion Factor
Red Blood Cell Parameters			
Erythrocyte Count	$T/l = 10^{12}/l$	$10^6/\mu l$	1
Hemoglobin	mmol/l	g/100 ml	1.611
Hematocrit	1	%	100
Mean Corpuscular Volume	f l	μm^3	1
Red Cell Volume Distribution Width	1	%	100
Mean Corpuscular Hemoglobin	fmol	pg	16.11
Mean Corpuscular Hemoglobin Concentration	mmol/l	g/100 ml (%)	1.611
Hemoglobin Concentration Distribution Width	mmol/l	g/100 ml	1.611
White Blood Cell Parameters			
Leukocyte Count	$G/l = 10^9/l$	Number/ μl	1000
Differential Leukocyte Count	relative absolute	relative absolute	rel. abs.
Neutrophils	1 G/l	% Number/μl	100 1000
Eosinophils	1 G/l	% Number/μl	100 1000
Basophils	1 G/l	% Number/μl	100 1000
Lymphocytes	1 G/l	% Number/μl	100 1000
Monocytes	1 G/l	% Number/μl	100 1000
Large Unstained Cells	1 G/l	% Number/μl	100 1000
Blood Platelets			
Thrombocyte Count	$G/l = 10^9/l$	Number/ μl	1000

8.2. Reference values: Hematology

HEMATOLOGY REFERENCE VALUES
UNTREATED MALE DOGS (BEAGLE)

Age : 21 - 32 weeks Period : 12.09.91 - 31.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
RBC	M0002	T/l	146	5.210	5.890	6.560
Hb	M0002	mmol/l	146	7.300	8.200	9.000
Hct	M0002	1	146	0.348	0.399	0.437
MCV	M0002	fl	146	63.00	66.85	70.90
RDW	M0002	1	146	0.126	0.138	0.151
MCH	M0002	fmol	146	1.300	1.380	1.450
MCHC	M0002	mmol/l	146	19.80	20.57	21.17
HDW	M0002	mmol/l	146	0.930	1.080	1.360
Reti	M0002	1	4	0.025	0.034	0.042
	M0003	1	110	0.013	0.021	0.030
WBC	M0002	G/l	146	7.600	10.64	14.35
Neut	M0002	1	146	0.435	0.538	0.629
Eos	M0002	1	146	0.010	0.024	0.057
Baso	M0002	1	146	0.001	0.003	0.007
Lympho	M0002	1	146	0.284	0.372	0.464
Mono	M0002	1	146	0.036	0.059	0.084
Luc	M0002	1	146	0.002	0.006	0.016
Neut	M0002	G/l	106	3.630	5.485	8.090
Eos	M0002	G/l	106	0.090	0.250	0.670
Baso	M0002	G/l	106	0.010	0.030	0.080
Lympho	M0002	G/l	106	2.705	3.860	5.500
Mono	M0002	G/l	106	0.325	0.665	1.020
Luc	M0002	G/l	106	0.030	0.080	0.180
Plt	M0002	G/l	146	193.0	305.5	408.0
PT(CS)	M0001	sec	146	28.15	35.43	44.18
PTT	M0001	sec	8	45.82	68.17	89.71
MetHb	M0001	1	30	0.000	0.001	0.004
Osm-Res	M0001	NaCl g/l	6	4.690	4.955	5.110

HEMATOLOGY REFERENCE VALUES
UNTREATED MALE DOGS (BEAGLE)

Age : 33 - 45 weeks Period : 06.06.91 - 30.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
RBC	M0002	T/l	132	5.480	6.320	7.100
Hb	M0002	mmol/l	132	7.500	8.800	9.800
Hct	M0002	1	132	0.367	0.424	0.475
MCV	M0002	fl	132	63.10	66.60	70.80
RDW	M0002	1	132	0.129	0.137	0.150
MCH	M0002	fmol	132	1.320	1.390	1.450
MCHC	M0002	mmol/l	132	19.94	20.84	21.75
HDW	M0002	mmol/l	132	1.020	1.135	1.360
Reti	M0002	1	4	0.009	0.010	0.011
	M0003	1	80	0.010	0.018	0.039
WBC	M0002	G/l	132	7.530	9.860	13.91
Neut	M0002	1	132	0.450	0.555	0.671
Eos	M0002	1	132	0.011	0.025	0.051
Baso	M0002	1	132	0.001	0.003	0.008
Lympho	M0002	1	132	0.251	0.352	0.438
Mono	M0002	1	132	0.034	0.051	0.077
Luc	M0002	1	132	0.001	0.005	0.013
Neut	M0002	G/l	84	3.600	5.305	7.850
Eos	M0002	G/l	84	0.100	0.230	0.450
Baso	M0002	G/l	84	0.010	0.030	0.080
Lympho	M0002	G/l	84	2.540	3.480	4.480
Mono	M0002	G/l	84	0.320	0.525	0.830
Luc	M0002	G/l	84	0.020	0.050	0.120
Plt	M0002	G/l	132	210.0	291.5	397.0
PT(CS)	M0001	sec	132	28.96	33.92	43.41
PTT	M0001	sec	4	45.42	47.67	53.62
MetHb	M0001	1	20	0.000	0.000	0.004
Osm-Res	M0001	NaCl g/l	6	4.410	4.645	5.140

HEMATOLOGY REFERENCE VALUES
UNTREATED FEMALE DOGS (BEAGLE)

Age : 21 - 32 weeks Period : 12.09.91 - 31.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
RBC	M0002	T/l	140	5.460	6.115	7.010
Hb	M0002	mmol/l	140	7.600	8.650	9.800
Hct	M0002	1	140	0.375	0.422	0.472
MCV	M0002	fl	140	64.80	68.45	72.40
RDW	M0002	1	140	0.125	0.137	0.152
MCH	M0002	fmol	140	1.330	1.410	1.480
MCHC	M0002	mmol/l	140	19.83	20.60	21.37
HDW	M0002	mmol/l	140	0.940	1.070	1.390
Reti	M0002	1	4	0.022	0.030	0.042
	M0003	1	98	0.010	0.020	0.033
WBC	M0002	G/l	140	7.600	10.22	14.41
Neut	M0002	1	140	0.448	0.549	0.638
Eos	M0002	1	140	0.010	0.024	0.063
Baso	M0002	1	140	0.001	0.003	0.007
Lympho	M0002	1	140	0.264	0.354	0.476
Mono	M0002	1	140	0.032	0.050	0.074
Luc	M0002	1	140	0.001	0.005	0.012
Neut	M0002	G/l	100	3.970	5.440	8.500
Eos	M0002	G/l	100	0.090	0.250	0.710
Baso	M0002	G/l	100	0.010	0.030	0.070
Lympho	M0002	G/l	100	2.520	3.660	5.030
Mono	M0002	G/l	100	0.320	0.553	0.890
Luc	M0002	G/l	100	0.020	0.060	0.140
Plt	M0002	G/l	140	217.0	298.0	386.0
PT(CS)	M0001	sec	140	28.55	34.12	42.46
PTT	M0001	sec	8	54.26	63.86	88.33
MetHb	M0001	1	30	0.000	0.002	0.005
Osm-Res	M0001	NaCl g/l	6	4.470	4.905	5.070

HEMATOLOGY REFERENCE VALUES
UNTREATED FEMALE DOGS (BEAGLE)

Age : 33 - 45 weeks Period : 06.06.91 - 30.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
RBC	M0002	T/l	132	5.840	6.645	7.350
Hb	M0002	mmol/l	132	8.200	9.300	10.40
Hct	M0002	1	132	0.397	0.444	0.501
MCV	M0002	fl	132	63.60	67.80	71.60
RDW	M0002	1	132	0.125	0.137	0.148
MCH	M0002	fmol	132	1.330	1.420	1.480
MCHC	M0002	mmol/l	132	19.94	20.86	21.79
HDW	M0002	mmol/l	132	1.000	1.120	1.330
Reti	M0002	1	4	0.004	0.006	0.007
	M0003	1	80	0.010	0.017	0.030
WBC	M0002	G/l	132	7.310	10.18	13.98
Neut	M0002	1	132	0.489	0.568	0.678
Eos	M0002	1	132	0.011	0.027	0.054
Baso	M0002	1	132	0.002	0.004	0.007
Lympho	M0002	1	132	0.252	0.342	0.432
Mono	M0002	1	132	0.029	0.044	0.064
Luc	M0002	1	132	0.001	0.004	0.011
Neut	M0002	G/l	84	3.950	5.850	8.650
Eos	M0002	G/l	84	0.090	0.260	0.650
Baso	M0002	G/l	84	0.020	0.040	0.080
Lympho	M0002	G/l	84	2.530	3.490	4.550
Mono	M0002	G/l	84	0.300	0.460	0.780
Luc	M0002	G/l	84	0.020	0.040	0.100
Plt	M0002	G/l	132	220.0	292.5	382.0
PT(CS)	M0001	sec	132	27.49	33.36	41.45
PTT	M0001	sec	4	46.02	49.63	54.92
MetHb	M0001	1	20	0.000	0.000	0.004
Osm-Res	M0001	NaCl g/l	6	4.220	4.650	4.820

8.3. Reference values: Blood chemistry

BLOOD CHEMISTRY REFERENCE VALUES
UNTREATED MALE DOGS (BEAGLE)

Age : 21 - 32 weeks Period : 12.09.91 - 31.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Gluc	M0001	mmol/l	146	4.250	5.605	6.460
Urea	M0001	mmol/l	146	2.460	3.925	5.650
Creat-e	M0001	umol/l	146	56.30	71.70	84.80
Bili-tot	M0001	umol/l	146	1.490	2.560	4.460
Bili-dir	M0001	umol/l	6	0.000	0.000	0.000
Prot	M0001	g/l	146	50.46	54.81	60.00
Alb	M0001	g/l	146	28.59	31.46	34.00
Glob	M0001	g/l	146	19.55	23.13	28.07
A/G	M0001	1	146	1.090	1.350	1.620
PreAlb	M0001	1	26	0.000	0.000	0.000
Alb-el	M0001	1	26	0.524	0.565	0.616
Glob A1	M0001	1	26	0.063	0.077	0.095
Glob A2	M0001	1	26	0.043	0.082	0.117
Glob B	M0001	1	26	0.075	0.096	0.130
Glob G	M0001	1	26	0.137	0.183	0.211
PreAlb	M0001	g/l	26	0.000	0.000	0.000
Alb-el	M0001	g/l	26	27.50	31.60	34.50
Glob A1	M0001	g/l	26	3.500	4.050	5.200
Glob A2	M0001	g/l	26	2.400	4.550	6.200
Glob B	M0001	g/l	26	4.200	5.150	7.400
Glob G	M0001	g/l	26	7.800	9.600	12.10
Chol	M0001	mmol/l	146	2.900	3.700	4.990
Trigly	M0001	mmol/l	76	0.290	0.390	0.540
Phos-Lip	M0001	mmol/l	124	3.340	4.295	5.550
Na+	M0001	mmol/l	146	144.6	146.8	149.3
K+	M0001	mmol/l	146	4.140	4.495	5.100
Ca++	M0001	mmol/l	146	2.640	2.850	2.980
Mg++	M0001	mmol/l	8	0.580	0.655	0.740
Cl-	M0001	mmol/l	146	106.4	109.5	114.2
PO4-in	M0001	mmol/l	146	1.740	2.100	2.430
ASAT (GOT)	M0001	U/l	146	14.60	19.80	27.30
ALAT (GPT)	M0001	U/l	146	26.40	41.15	72.60
AlP	M0001	U/l	146	68.80	107.2	185.7
GGT	M0001	U/l	136	0.000	2.900	4.500
ChE-Pl	M0001	U/l	4	5065	5687	6009
ChE-RBC	M0002	U/l	4	2020	2180	3207
CK	M0001	U/l	136	124.0	173.3	379.5
T4	M0001	nmol/l	10	31.99	38.51	41.50
T3	M0001	nmol/l	10	0.880	1.315	2.230

BLOOD CHEMISTRY REFERENCE VALUES
UNTREATED MALE DOGS (BEAGLE)

Age : 33 - 45 weeks Period : 06.06.91 - 30.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Gluc	M0001	mmol/l	132	4.340	5.480	6.280
Urea	M0001	mmol/l	132	2.720	4.175	5.740
Creat-e	M0001	umol/l	132	67.30	78.30	92.40
Bili-tot	M0001	umol/l	132	1.660	2.580	4.760
Bili-dir	M0001	umol/l	6	0.000	0.000	0.000
Prot	M0001	g/l	132	53.70	57.64	63.94
Alb	M0001	g/l	132	30.41	33.39	36.52
Glob	M0001	g/l	132	21.25	24.42	28.22
A/G	M0001	1	132	1.150	1.360	1.590
PreAlb	M0001	1	22	0.000	0.000	0.000
Alb-el	M0001	1	22	0.534	0.570	0.601
Glob A1	M0001	1	22	0.047	0.059	0.082
Glob A2	M0001	1	22	0.072	0.086	0.106
Glob B	M0001	1	22	0.066	0.088	0.127
Glob G	M0001	1	22	0.156	0.194	0.224
PreAlb	M0001	g/l	22	0.000	0.000	0.000
Alb-el	M0001	g/l	22	29.90	34.15	36.70
Glob A1	M0001	g/l	22	3.000	3.600	4.900
Glob A2	M0001	g/l	22	4.300	5.200	6.200
Glob B	M0001	g/l	22	4.000	5.200	8.050
Glob G	M0001	g/l	22	9.400	11.35	13.50
Chol	M0001	mmol/l	132	2.810	3.485	4.600
Trigly	M0001	mmol/l	68	0.265	0.385	0.520
Phos-Lip	M0001	mmol/l	106	2.990	4.070	5.160
Na+	M0001	mmol/l	132	145.0	148.1	150.3
K+	M0001	mmol/l	132	3.990	4.435	4.810
Ca++	M0001	mmol/l	132	2.660	2.780	2.950
Mg++	M0001	mmol/l	8	0.740	0.790	0.910
Cl-	M0001	mmol/l	132	106.0	109.9	115.1
PO4-in	M0001	mmol/l	132	1.460	1.680	2.060
ASAT (GOT)	M0001	U/l	132	16.50	21.80	33.30
ALAT (GPT)	M0001	U/l	132	34.70	49.50	92.30
AlP	M0001	U/l	132	56.60	87.00	140.2
GGT	M0001	U/l	122	0.000	3.200	5.400
ChE-Pl	M0001	U/l	8	4598	5269	5942
ChE-RBC	M0002	U/l	8	2115	2347	3451
ChE-Br	M0002	U/g	4	2.365	2.449	2.945
CK	M0001	U/l	122	108.1	155.8	292.6
T4	M0001	nmol/l	10	29.18	42.92	52.12
T3	M0001	nmol/l	10	1.290	1.530	2.630

BLOOD CHEMISTRY REFERENCE VALUES
UNTREATED FEMALE DOGS (BEAGLE)

Age : 21 - 32 weeks Period : 12.09.91 - 31.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Gluc	M0001	mmol/l	134	4.310	5.585	6.370
Urea	M0001	mmol/l	134	2.710	4.235	6.140
Creat-e	M0001	umol/l	134	65.60	77.10	92.20
Bili-tot	M0001	umol/l	140	1.660	2.855	5.090
Bili-dir	M0001	umol/l	6	0.000	0.000	0.000
Prot	M0001	g/l	140	50.25	54.41	59.48
Alb	M0001	g/l	140	29.75	32.54	34.82
Glob	M0001	g/l	140	19.52	21.89	25.36
A/G	M0001	1	140	1.210	1.480	1.680
PreAlb	M0001	1	26	0.000	0.000	0.000
Alb-el	M0001	1	26	0.545	0.590	0.653
Glob A1	M0001	1	26	0.062	0.075	0.085
Glob A2	M0001	1	26	0.042	0.085	0.101
Glob B	M0001	1	26	0.057	0.083	0.107
Glob G	M0001	1	26	0.134	0.171	0.212
PreAlb	M0001	g/l	26	0.000	0.000	0.000
Alb-el	M0001	g/l	26	28.70	32.65	36.90
Glob A1	M0001	g/l	26	3.500	4.150	4.800
Glob A2	M0001	g/l	26	2.300	4.600	5.600
Glob B	M0001	g/l	26	3.200	4.650	5.900
Glob G	M0001	g/l	26	7.500	9.400	11.00
Chol	M0001	mmol/l	134	2.860	3.610	4.720
Trigly	M0001	mmol/l	76	0.280	0.410	0.550
Phos-Lip	M0001	mmol/l	112	3.100	4.135	5.140
Na+	M0001	mmol/l	134	144.8	147.2	150.0
K+	M0001	mmol/l	134	3.910	4.300	4.740
Ca++	M0001	mmol/l	134	2.580	2.800	2.960
Mg++	M0001	mmol/l	8	0.740	0.765	0.860
Cl-	M0001	mmol/l	134	106.8	110.0	115.5
PO4-in	M0001	mmol/l	134	1.440	1.855	2.330
ASAT (GOT)	M0001	U/l	140	15.75	21.65	31.50
ALAT (GPT)	M0001	U/l	140	28.80	42.70	86.60
AlP	M0001	U/l	140	60.00	94.25	154.2
GGT	M0001	U/l	130	0.000	2.600	4.800
ChE-Pl	M0001	U/l	4	4038	4670	7265
ChE-RBC	M0002	U/l	4	1729	2034	2628
CK	M0001	U/l	124	121.9	180.2	354.0
T4	M0001	nmol/l	10	29.61	35.89	52.63
T3	M0001	nmol/l	10	1.170	1.750	2.440

BLOOD CHEMISTRY REFERENCE VALUES
UNTREATED FEMALE DOGS (BEAGLE)

Age : 33 - 45 weeks Period : 06.06.91 - 30.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Gluc	M0001	mmol/l	132	4.530	5.515	6.380
Urea	M0001	mmol/l	132	3.130	4.545	6.320
Creat-e	M0001	umol/l	132	70.60	82.20	93.00
Bili-tot	M0001	umol/l	132	2.070	3.070	5.330
Bili-dir	M0001	umol/l	6	0.000	0.000	0.000
Prot	M0001	g/l	132	53.10	57.08	63.10
Alb	M0001	g/l	132	31.71	34.29	37.15
Glob	M0001	g/l	132	20.30	22.96	26.95
A/G	M0001	1	132	1.240	1.490	1.740
PreAlb	M0001	1	22	0.000	0.000	0.000
Alb-el	M0001	1	22	0.560	0.612	0.659
Glob A1	M0001	1	22	0.052	0.060	0.073
Glob A2	M0001	1	22	0.040	0.067	0.085
Glob B	M0001	1	22	0.058	0.087	0.118
Glob G	M0001	1	22	0.145	0.172	0.218
PreAlb	M0001	g/l	22	0.000	0.000	0.000
Alb-el	M0001	g/l	22	32.40	35.85	39.90
Glob A1	M0001	g/l	22	3.100	3.550	4.400
Glob A2	M0001	g/l	22	2.200	4.050	5.400
Glob B	M0001	g/l	22	3.600	5.125	6.900
Glob G	M0001	g/l	22	8.400	10.00	13.45
Chol	M0001	mmol/l	132	2.670	3.460	4.485
Trigly	M0001	mmol/l	68	0.270	0.410	0.590
Phos-Lip	M0001	mmol/l	106	3.020	3.970	5.130
Na+	M0001	mmol/l	132	144.2	148.3	151.0
K+	M0001	mmol/l	132	3.880	4.220	4.710
Ca++	M0001	mmol/l	132	2.620	2.750	2.920
Mg++	M0001	mmol/l	8	0.800	0.855	0.970
Cl-	M0001	mmol/l	132	106.3	110.3	115.7
PO4-in	M0001	mmol/l	132	1.170	1.523	1.980
ASAT (GOT)	M0001	U/l	132	16.40	24.80	37.60
ALAT (GPT)	M0001	U/l	132	30.60	50.30	88.70
AlP	M0001	U/l	132	46.80	80.80	125.3
GGT	M0001	U/l	122	0.000	3.200	5.100
ChE-Pl	M0001	U/l	8	4034	4579	6833
ChE-RBC	M0002	U/l	8	1839	2212	2805
ChE-Br	M0002	U/g	4	2.201	2.699	3.562
CK	M0001	U/l	122	106.0	160.6	290.4
T4	M0001	nmol/l	10	28.48	38.13	72.06
T3	M0001	nmol/l	10	0.980	1.835	2.360

8.4. Reference values: Urine analysis

URINE ANALYSIS REFERENCE VALUES
UNTREATED MALE DOGS (BEAGLE)

Age : 21 - 32 weeks Period : 11.09.91 - 31.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Rel dens	M0001	1	139	1.004	1.021	1.049
pH	M0001	1	139	5.000	6.500	8.500

URINE ANALYSIS REFERENCE VALUES
UNTREATED MALE DOGS (BEAGLE)

Age : 33 - 45 weeks Period : 03.06.91 - 30.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Rel dens	M0001	1	132	1.010	1.023	1.049
pH	M0001	1	132	5.000	6.750	8.500

URINE ANALYSIS REFERENCE VALUES
UNTREATED FEMALE DOGS (BEAGLE)

Age : 21 - 32 weeks Period : 11.09.91 - 31.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Rel dens	M0001	1	126	1.005	1.023	1.046
pH	M0001	1	126	5.000	6.500	8.500

URINE ANALYSIS REFERENCE VALUES
UNTREATED FEMALE DOGS (BEAGLE)

Age : 33 - 45 weeks Period : 03.06.91 - 30.03.95

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Rel dens	M0001	1	129	1.008	1.024	1.042
pH	M0001	1	129	5.000	7.000	9.000

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