

VOLUME 94 OF 103 OF SUBMISSION

CGA-329351 TECHNICAL

3-MONTH ORAL TOXICITY STUDY IN RATS

EPA GUIDELINES NO. 82-1

AUTHOR - DR. 5126 W69

STUDY COMPLETED ON AUGUST 9, 1995

CONDUCTED BY  
CIBA-GEIGY LIMITED  
BASLE, SWITZERLAND

LABORATORY STUDY NUMBER 943127

VOLUME 1 OF 1 OF STUDY

PAGE 1 OF 445

CIBA CROP PROTECTION  
CIBA-GEIGY CORPORATION  
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Date: 8/17/95

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Test No.: 943127

Test Article: CGA 329351 tech.

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 Grundsätze 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: *for* Dr. rer. nat. (absent!)

5.1.23 Woo  
date: August 9, 1995

Facility Management: \_\_\_\_\_, Ph.D.  
D.A.B.T., A.T.S.

5.1.23 Woo  
date: August 9, 1995

For the Sponsor:

5.1.23 Woo  
date: August 10, 1995

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**FLAGGING STATEMENT**

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

5.1.2.e WOO

Signature of Agent of Submitter/Sponsor

5.1.2.e WOO

August 17, 1995

Typed Name

Date

Submitter/Sponsor:

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Ciba-Geigy Corporation  
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**0.4. Signatures**

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

Study Director

for Dr. rer. nat. 5.1.2.e Woo (abunt)

5.1.2.e Woo

date: August 9, 1995

Laboratory

Dr. med. vet. 5.1.2.e Woo  
FVH Clinical Chemistry

Pathology

Dr. med. vet. 5.1.2.e Woo  
FVH Pathology

5.1.2.e Woo

MVDr, C.Sc.  
FVH Pathology

5.1.2.e Woo

Dr. rer. nat. 5.1.2.e Woo

5.1.2.e Woo

Statistics

5.1.2.e Woo dipl. stat.

5.1.2.e Woo

Facility Management

5.1.2.e Woo Ph.D.  
D.A.B.T. A.T.S.

5.1.2.e Woo

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0.5. Quality Assurance Statement

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

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Project 943127  
Test Substance CGA 329351 tech.  
Study Title 3-Month Oral Toxicity Study in Rats  
(Administration in Food)  
Study Director Dr. 5.1.2.e Woo  
QA-Inspector 5.1.2.e Woo

---

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

Activity	Performed	Reported
Facility Inspection	October 04, 1994	October 10, 1994
Protocol Audit	October 20, 1994	October 20, 1994
Study Related Inspection	October 24, 1994	October 24, 1994
Study Related Inspection	January 24, 1995	January 25, 1995
Study Related Inspection	February 22, 1995	February 23, 1995
Facility Inspection	March 16, 1995	March 22, 1995
Final Report Audit	July 06, 1995	July 07, 1995

August 9, 1995  
Date  
Form: QSS/AT12

5.1.2.e Woo

Inspector of Quality Assurance

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Test No.: 943127

Test Article: CGA 329351 tech.

## 1. SUMMARY AND CONCLUSION

The test article CGA 329351 tech. was administered in the diet for 3 months at dietary levels of 0, 25, 50, 250, 625, and 1250 ppm (= mg/kg food) to a total of 160 albino rats. In each dose group 10 animals per sex and group were sacrificed at the end of the treatment period; 10 animals per sex in the control and high dose groups, were kept on control diet for a 4-week recovery period before sacrifice.

The results of this study are summarized as follows:

### Dose levels

Corrected for the analytically determined test article concentrations in the diet, the mean daily intake of CGA 329351 tech. was 1.72, 3.50, 16.8, 44.8 and 90.5 mg/kg bodyweight in males, and 1.86, 3.71, 17.9, 49.2 and 95.0 mg/kg bodyweight in females.

### In-life observations

In life observations did not reveal treatment-related clinical signs or changed behaviour.

### Mortality

No deaths occurred in this study.

### Body weight

The body weight development was not disturbed by treatment.

### Food consumption

The mean food consumption was not influenced by treatment.

### Food consumption ratios

There was no effect of treatment on food consumption ratios.

### Water consumption

There was no effect of treatment on water consumption.

### Ophthalmological examination

There was no effect of treatment on investigated ophthalmologic parameters.

### Hematology

Treatment had no effect on the hematological profile.

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### Blood chemistry

Values recorded for blood chemistry parameters in treated rats were similar to those of controls, and were within the range of reference values reflecting the physiological variation of the parameters.

### Urine analysis

Treatment did not influence urine parameters investigated.

### Organ weights

Mean organ weights and organ to body weight ratios of the treated groups were comparable to those of the control group.

### Pathological findings

The macroscopical examination revealed no treatment-related changes.

The microscopical examination revealed a dose-related occurrence of hepatocellular inclusion bodies in male groups 5 and 6 (625 and 1250 ppm, respectively) and an increased incidence of hepatocellular hypertrophy in females of groups 5 and 6. Both findings were completely reversible within the 4-week recovery period.

### Conclusion

Under the conditions of this test, treatment with CGA 329351 tech. was well tolerated at all tested dose levels. Neither treatment-related overt signs of toxicity nor changes in body weight development, food/water consumption and laboratory parameters were noted. At the two upper dose levels histopathological investigations revealed reversible effects in the liver of both sexes.

It can be inferred from the observations made during the above study, that a "no-observable-effect level" for CGA 329351 tech. when offered to rats continuously in their food over a period of 3 months is 250 ppm, corresponding to a mean daily intake of 17.9 mg/kg body weight in males and 16.8 mg/kg body weight in females.

## 2. INTRODUCTION

### **Purpose**

The present study was designed to determine the oral toxicity of the test article in rats upon continuous administration for 3 months in their diet, to estimate a no-effect level of exposure, and to determine the reversibility of possible adverse effects after a 4-week recovery period.

### **Good laboratory practice**

This study was carried out in accordance with the Principles of Good Laboratory Practice as set forth in "Verfahren und Grundsätze der Guten Laborpraxis (GLP) in der Schweiz", Swiss Federal Department of the Interior and Intercantonal Office for the Control of Medicaments (IKS), March 1986.

The study was subjected to periodic internal quality assurance evaluation.

Analytical investigations, performed at RCC Umweltchemie AG, were inspected by the Quality Assurance Unit of RCC Umweltchemie AG, 4452 Itingen / Switzerland.

### **Basis for the study**

The study was carried out according to the following guidelines:

- FIFRA, Pesticide Assessment Guidelines, subdivision F: Hazard Evaluation, Human and Domestic Animals (November 1984); Section 82-1: Subchronic oral toxicity, 90-day study.
- OECD Guideline for testing of chemicals, No. 408, "Subchronic Oral Toxicity-Rodent: 90-day Study", adopted May 12, 1981.
- EEC Directive 87/302, Official Journal of the European Communities, May 30, 1988, L133, Page 8-11, Sub-chronic oral toxicity test: 90-day repeated oral dose using rodent species.

### **Sponsor**

CIBA-GEIGY Limited  
Crop Protection Division  
4002 Basle / Switzerland

**Personnel and responsible scientists**

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

Study director: Dr. rer. nat. [redacted]  
Longterm Toxicology

Technical assistant: [redacted]  
Longterm Toxicology

Supervisors: [redacted]  
Longterm Toxicology

Responsible for laboratory investigations: Dr. med. vet. [redacted]  
FVH Clinical Chemistry  
Clinical Laboratory

Assistant laboratory investigations: [redacted]  
Clinical Laboratory

Responsible for necropsy: Ms. [redacted], dipl. med. vet.  
Macropathology

Responsible for pathology services: PD Dr. med. vet. [redacted]  
FVH Fundamental Medicine

Assistant Logistics/Archives: Ms. [redacted]  
Pathology Services

Responsible for pathology: Dr. med. vet. [redacted]  
FVH Pathology  
Toxicological Pathology

Reviewing pathologist: [redacted], MVDr, C.Sc.  
FVH Pathology  
Experimental Pathology

Study pathologist: Dr. rer. nat. [redacted]  
Experimental Pathology

Responsible for statistics: [redacted], dipl.stat.  
Mathematical Applications

Responsible for analytics: [redacted], RCC

The job descriptions and the summaries of training and professional experience of personnel participating in this study are available at:

CIBA-GEIGY Limited, for Short/Long-term Toxicology  
4332 Stein / Switzerland Sisseln Facility

CIBA-GEIGY Limited, for Short/Long-term Toxicology  
4002 Basle / Switzerland (Pathology)  
and Mathematical Applications

RCC Umweltchemie AG for Analytical Laboratories  
4452 Itingen / Switzerland

#### Testing facility

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

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

Histopathological examination was performed at:

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

Analytical investigations were performed at:

RCC Umweltchemie AG  
4452 Itingen / Switzerland

#### Archivation and distribution

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 Research and Consulting Company Ltd., 4452 Itingen / Switzerland.

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

This report was distributed to:

Dr. 5.1.2.e Woo (Sponsor)

Archive

Test No.: 943127

Test Article: CGA 329351 tech.

### 3. MATERIALS AND METHODS

#### 3.1. Test article

Company code No.: CGA 329351 tech.

Batch No.: OP.4

Description: viscous liquid

Purity: 97.1 %

Date of receipt: October 10, 1994

Stability: April 1998

Storage conditions: room temperature

#### Pretest analytics

Analytical results of food samples (content, homogeneity and stability) containing the test article (Batch no. KGL-4634/5) at concentrations of 0, 1, 10, 100, 1000 and 12000 ppm were available from a previously conducted study (No. 933181). The results of the analyses (RCC project 365905) indicating stability and homogeneous distribution of the test article are filed in the archives of Short/Long-term Toxicology, CIBA-GEIGY Limited, 4332 Stein, Switzerland.

Analyses of homogeneity and stability were repeated with the first food batch used in this study.

The results of the analyses (RCC project no. 384254) are given in the results and appendix sections of this report.

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 Test Article: CGA 329351 tech.

### 3.2. Test system

#### 3.2.1. Experimental animals

Species: albino rats  
 Stock: Tif: RAIf (SPF),  
 hybrids of RII/1 x RII/2  
 (Sprague-Dawley derived)  
 Source: Animal Production  
 CIBA-GEIGY Limited  
 4332 Stein / Switzerland  
 Initial body weight:  
 (at week -1) 131.0 - 175.5 g in males  
 122.6 - 159.2 g in females  
 Initial age: approximately 5 weeks at delivery

#### 3.2.2. Husbandry

The study was carried out under specified pathogen free (SPF) standard laboratory conditions. The animals were housed in groups of 5 in macrolon cages type 4 with wire mesh tops and standardized granulated soft wood bedding (Societe Parisienne des Sciures Pantin).

The animal room was air conditioned:

Temperature:  $22 \pm 2^{\circ}\text{C}$   
 Relative humidity (%):  $55 \pm 10$   
 Ventilation: 16-20 air changes/hour  
 Light cycle: 12 hours light per day

Neither insecticides nor chemicals were applied in the animal room with the exception of disinfectant: BRADOPHEN<sup>TM</sup>.

#### 3.2.3. Identification

By tattoo of tail for cage number and by tattoo of right ear auricle with numbers 1 to 5 for individual identification of the animals in the cages.



### 3.3. Procedures

A written protocol, dated October 11, 1994, was prepared prior to the initiation of this study.

#### 3.3.1. Study schedule

Study initiation  
(protocol date): October 11, 1994  
Delivery of animals: October 17, 1994  
Start of acclimatization: October 18, 1994  
Treatment start: October 25, 1994  
Laboratory investigations: January 24/25, 1995  
Date of sacrifice 1: January 25-27, 1995  
Recovery start: January 24/25, 1995  
Laboratory investigations: February 21, 1995 (recovery group)  
Date of sacrifice 2  
(experimental end date): February 22, 1995 (recovery group)

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Test No.: 943127

Test Article: CGA 329351 tech.

## 3.3.2. Animal number and distribution

Number of animals: 160 (total)  
 10 males, 10 females per dose group, plus 10 males and 10 females in the control and high dose group for recovery evaluation.

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

Animal No. <sup>1</sup> (cage no.) <sup>2</sup>	Group 1 Control	Group 2 25 ppm	Group 3 50 ppm	Group 4 250 ppm	Group 5 625 ppm	Group 6 1250 ppm
MALES I	1-10 <sup>1</sup> (1-2) <sup>2</sup>	21-30 (5-6)	31-40 (7-8)	41-50 (9-10)	51-60 (11-12)	61-70 (13-14)
MALES II	11-20 (3-4)					71-80 (15-16)
FEMALES I	81-90 (17-18)	101-110 (21-22)	111-120 (23-24)	121-130 (25-26)	131-140 (27-28)	141-150 (29-30)
FEMALES II	91-100 (19-20)					151-160 (31-32)

- I EXPERIMENTAL GROUP I  
 10 animals per sex and group for evaluation of toxicity, including laboratory investigations
- II EXPERIMENTAL GROUP II  
 10 animals per sex and groups 1 and 6 for reversibility evaluation after 4 weeks of recovery, including laboratory investigations

### 3.3.3. Acclimatization

An acclimatization period of 7 days was allowed between delivery and start of the treatment. Immediately after delivery, the animals were distributed into groups. In order to set up a fully randomized experiment, they were assigned to these groups by means of computer-generated random numbers. Furthermore, they were weighed and the first eye examination was performed.

From the same batch of animals a small number was retained for possible replacement during the acclimatization period. These animals were subjected to identical conditions during this period, and those not used were removed at the start of the experiment.

### 3.3.4. Treatment

The treatment was performed over a period of 3 months on a main group (experimental group I) and a recovery group (experimental group II) of animals. The animals of experimental group I were sacrificed at the end of the treatment period.

### 3.3.5. Recovery

After the treatment period, animals of experimental group II were kept on control diet for a consecutive recovery phase of 4 weeks before sacrifice.

### 3.3.6. Dietary levels

0, 25, 50, 250, 625 and 1250 ppm (=mg/kg food).

### 3.3.7. Rationale for dose selection

The dose level selection was based on the following studies:  
5.1.2.e Woo 1977. 3 months dietary study in rats with compound CGA 48988, Geigy Pharmaceuticals, Stamford Lodge, England, Report no. 8/77/S.L..

5.1.2.e Woo and 5.1.2.e Woo, 1980. CGA 48988 Toxicity and oncogenicity in dietary administration to rats for two years, Life Science Research Inc., Stock, England, Report no. 80/CIA009/315.

CGA 48988 was tested at 50, 250, and 1250 ppm in both the 90-day and 2-year studies. For this study with CGA 329351 tech. the feeding levels of 25, 50, 250, 625 and 1250 ppm were selected.

### 3.4. Test article administration and diet

#### 3.4.1. Route of administration

The test article was administered orally (admixed to pelleted food).

#### 3.4.2. Diet

Pelleted, certified standard diet (Nafag No. 8900 FOR GLP) containing the appropriate concentrations of the test article was provided ad libitum (except as noted under Laboratory Investigations). 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).

#### 3.4.3. Preparation of the diet

The test article was dissolved in acetone. A premix was made for each group using aliquots of this solution added to fixed amounts of Bolus alba and diet with the addition of a further amount of acetone to equalize the quantity of acetone used for each group.

After removal of the acetone by vacuum at room temperature, the premix for each group was mixed with further fixed quantities of diet to yield diets containing the appropriate concentration of test article.

Diet was prepared at about monthly intervals and stored in stainless steel containers at room temperature in a separate area.

#### 3.4.4. Control analysis

Control analyses of the test article content were undertaken with diet used for treatment days 1-29 and 57-92. These analyses were carried out in the analytical laboratories of RCC Umweltchemie AG, 4452 Itingen / Switzerland. The results thereof (RCC project no. 384254) are given in the results and appendix sections of this report.

#### 3.4.5. Control animals

The animals in the control group (group 1) were fed with similarly prepared and pelleted food without the test article.

#### 3.4.6. Water

Tap water was given ad libitum. The drinking water quality fulfilled the critical parameters in the specifications of the "Schweizerisches Lebensmittelbuch" (Ed. 1972). The 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 inhouse chemical analysis by the analytical laboratories of the Pharmaceuticals Division, CIBA-GEIGY Limited.

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### 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 reaction to treatment, examination was carried out daily, and observations were recorded at least weekly.

#### **Ophthalmological examination**

Animals of the highest dose group and of the control group were examined prior to dosing (day -6), towards the end (day 87) of the treatment period, and towards the end of the recovery period (day 115). Examination included observation of eye appearance and of the periocular region, and detection of pupillary reflex using an ophthalmoscope.

#### **Body weight**

The weight of all animals was recorded individually at weekly (midweek) weighing sessions. The first weights were recorded during the acclimatization period.

#### **Food consumption**

The food consumption was recorded weekly (cagewise) and was calculated for periods of one week. The calculation was based on the weight of the offered diet at the beginning of a weighing period and its difference to the re-weighed amount after several days.

The individual food consumption values were calculated from the food consumption per cage and the number of animals present.

#### **Food consumption ratios**

The food consumption ratios were calculated as mean of individual ratios according to the following formula:

$$\frac{\text{weekly food consumption (g)}}{\text{midweek body weight (g)}} \times \frac{1000}{7}$$

Unit: g food/kg body weight per day

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### Water consumption

The water consumption was recorded weekly (cagewise) and was calculated for periods of one week. The calculation was based on the weight of the offered water at the beginning of a weighing period and its difference to the re-weighed amount after one day.

The individual water consumption was calculated from the water consumption per cage and the number of animals present.

### Test article intake

The test article intake was calculated according to the following formula (rounded to 3 meaningful digits):

$$\frac{\text{food consumption ratio} \times \text{nominal dose (ppm)}}{1000}$$

Unit: mg test article/kg body weight per day

An overall mean value (MEAN1) was calculated based on the nominal content of the test article in the food. Additionally, this mean value was corrected for the analytically determined test article content in the food (MEAN2).

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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 the end of the treatment period (January 24-25, 1995), and additionally at the end of the recovery period (February 21, 1995) on animals of the control and high dose group kept for reversibility evaluation.

To reduce the biological variability due to circadian rhythms, blood sampling was performed in the morning. Ether anesthesia was used to restrain the animals. Blood was withdrawn from the orbital sinus using glass capillary tubes. The following anti-coagulants 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 overnight prior to blood removal.

Urine for analysis was collected overnight. The individual animals were housed in special metabolism cages. Food and water was withheld during the time of urine collection.

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

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## 3.6.1. Parameters and methods used in hematology

Parameters determined by the Technicon H\*1 <1>, <2>  
(Method code: M0002)

Red blood cell parameters	Abbreviation	Unit
Erythrocyte count	RBC	T/l
Hemoglobin	Hb	mmol/l
Hematocrit	Hct	l
Mean corpuscular volume	MCV	fl
Red cell volume distribution width<3>	RDW	l
Mean corpuscular hemoglobin	MCH	fmol
Mean corpuscular hemoglobin concentration	MCHC	mmol/l
Hemoglobin concentration distribution width<3>	HDW	mmol/l
<b>White blood cell parameters</b>		
Leukocyte count	WBC	G/l
Differential leukocyte count		rel. abs.
Neutrophils	Neut	l G/l
Eosinophils	Eos	l G/l
Basophils	Baso	l G/l
Lymphocytes	Lympho	l G/l
Monocytes	Mono	l G/l
Large unstained cells	Luc	l G/l
<b>Blood platelets</b>		
Thrombocyte Count	Plt	G/l
<b><u>Prothrombin time</u></b>		
Photometric assay using chromogenic substrate on a Cobas Bio centrifugal analyser (Method code: M0001)	PT (CS)	sec

**References**

- <1> D.T. Davies, G.V. Fisher (1991): The Validation and Application of the Technicon H\*1 for the Complete Automated Evaluation of Laboratory Animal Haematology  
Comp Haematol Int 1, 91-105
- <2> W. Groner, J. Boyett, A. Johnson, M. Scantlebury (1986): Variability of Erythrocyte Size and Hemoglobin Content Observed in Man and Four Selected Mammals  
Blood Cells 12, 65-80
- <3> C. Fossat et al. (1987): New Parameters in Erythrocyte Counting  
Arch Pathol Lab Med 111, 1150-1154

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## 3.6.2. Parameters and methods used in blood chemistry

Parameter	Method of analysis (Method code) Instrument	Abbreviation	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
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

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Parameter	Method of analysis (Method code) Instrument	Abbreviation	Unit
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

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## 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

<u>Parameter</u>	<u>Abbreviation</u>	<u>Method of analysis</u> (Method code)
Urine volume	Volume	Gravimetric (M0001)
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

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### 3.7. Pathology

#### 3.7.1. Macroscopical examination

At the end of the 3-month treatment and the additional 4-week recovery period, all animals of experimental groups I and II, respectively, were bled under ether anesthesia and subjected to detailed necropsy.

At necropsy the following weights were recorded from all animals:

body (exsanguinated)  
heart  
liver  
kidneys  
adrenals  
thymus  
ovaries/testes  
spleen

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

skin  
mammary area  
spleen  
mesenteric lymph node  
axillary lymph node  
sternum with bone marrow  
femur with joint  
skeletal muscle  
trachea  
lung  
heart  
aorta  
submandibular salivary gland, both  
liver  
pancreas  
esophagus  
stomach  
small intestine (duodenum, jejunum, ileum)  
large intestine (cecum, colon, rectum)  
kidney, both  
urinary bladder  
prostate  
seminal vesicle  
testis, both  
epididymis, both  
uterus  
vagina  
ovary, both  
pituitary gland

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adrenal gland, both  
thyroid with parathyroid gland  
thymus  
peripheral nerve  
brain  
spinal cord  
eye with optic nerve, both  
orbital gland, both  
extraorbital lacrimal gland, both  
Zymbal gland, both  
muzzle  
tongue  
any tissue with gross lesions

### 3.7.2. Microscopical examination

After the fixation, organ samples listed below were taken from all animals of the 3-month control and all treated groups (experimental group I), embedded in paraplast, sectioned at 3-5 microns, and stained with hematoxylin and eosin.

spleen  
mesenteric lymph node  
axillary lymph node  
femur with joint  
trachea  
lung  
heart  
aorta  
submandibular salivary gland, both  
liver  
pancreas  
esophagus  
stomach  
small intestine (duodenum, ileum, jejunum)  
large intestine (cecum, colon, rectum)  
kidney, both  
urinary bladder  
testis, both  
epididymis, both  
uterus  
vagina  
ovary, both  
pituitary gland  
adrenal gland, both  
thyroid with parathyroid gland  
thymus  
peripheral nerve  
brain  
any organ with gross lesions

Based on microscopical findings in the high dose group at the end of treatment, the liver was additionally examined in the control and high dose recovery groups (experimental group II).

### 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.

The histopathological examination of the recovery groups (experimental group II) was restricted to the liver as described above. No other organs were examined in the recovery groups. Where no findings were noted, the diagnosis "organs and tissues as a whole" was used as a summary denominator of examined tissues for reporting "no changes observed".

The microscopical findings were assessed with respect to their severity (with exceptions specified by the Standard Operating Procedures), as well as their incidence (number of affected animals per group).

The degree of severity is defined according to the following criteria:

Grade "+", minimal: histopathological change that is a noticeable but not prominent feature of the tissue.

Grade "++", moderate: histopathological change that is a prominent but not dominant feature of the tissue.

Grade "+++", marked: histopathological change that is a dominant feature of the tissue.

In paired organs, the findings of different 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 lesion (with exceptions specified by the Standard Operating Procedures) is described with the individual findings.

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### 3.8. Statistical analysis

#### General

For each time point and parameter an univariate statistical analysis was performed. Nonparametric methods <1> were applied, to allow for non normal as well as normal data distribution.

Each treated group was compared to the control group by Lepage's two-sample test <2> and tested for increasing or decreasing trends from control up to the respective dose group by Jonckheere's test for ordered alternatives <3>. The Lepage test is a combination of Wilcoxon and Ansari-Bradley statistics, i.e. a combined test for location and dispersion. The Lepage test has a good power against the more general alternative that the distributions differ not only in location but also in dispersion. The Jonckheere test is sensitive to monotone dose-related effects.

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, 95, 232-238
- <2> Y. Lepage, Biometrika (1971) 58: pp. 213-217
- <3> A. R. Jonckheere, Biometrika (1954) 41: pp. 133-145



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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

IQ-Range the interquartile range, the difference between the 75th and the 25th percentile

Min, Max the smallest value, the largest value

p\_L p-value, the probability of an outcome being greater than or equal to Lepage's test statistic, if the null hypothesis is true. Not given, if sample sizes too small

\*, significant difference in location and/or dispersion between treated group and control at the level specified in the header of the table

a, indicative of a difference in location

b, indicative of a difference in dispersion

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). 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

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### 3.9. Deviations

#### 3.9.1. Amendments

Amendment no.1, dated May 12, 1995:

On request of the sponsor the study title was changed to:

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)  
Test No. 943127  
CGA 329351 tech.

#### 3.9.2. Deviations from the protocol

5.12.e Woo, Ph.D., D.A.B.T., A.T.S. was appointed facility manager as per April 1, 1995.

Dr. 5.12.e Woo was the study pathologist and Dr. 5.12.e Woo was the reviewing pathologist.

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.

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## 4. RESULTS

### 4.1. Dietary levels

#### 4.1.1. Analytical results

##### Stability

Prior to the beginning of a previous study (933181), food samples containing the test article (Batch no. KGL-4634/5) at concentrations of 0, 1, 10, 100, 1000 and 12000 ppm were dispatched to RCC Umweltchemie AG, 4452 Itingen / Switzerland for determination of content, homogeneity and stability. The results (Feed Analysis Report RCC project 365905) indicated stability of the test article in pelleted food for 5 weeks when stored at room temperature. Additionally, stability analysis was repeated with the diet used in this study, containing the test article (Batch no. OP.4) at concentrations of 0, 25, 50, 250, 625 and 1250 ppm. Stability over 5 weeks was confirmed (Feed Analysis Report RCC project 384254).

##### Homogeneity

Homogeneity of the test article distribution in pelleted food was analyzed in samples from the first food batch used in this study. The results showed a homogeneous distribution of the test article in the diet (Feed Analysis Report RCC project 384254).

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Concentrations

The contents of the test article in the diets were analyzed in the food batches used on days 1-29 and 57-92 of the study, respectively.

The results of these analyses (Feed Analysis Report RCC project 384254) showed that the contents of CGA 329351 tech. in the diet were in agreement with the nominal concentrations. The analyses revealed concentrations of 90,2-105,7 % of the nominal values, resulting in mean concentrations of 94.7-100.5 %.

TEST MATERIAL CONTENT

CONTENT	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 6
NOMINAL (ppm)	25	50	250	625	1250
ANALYTICAL (ppm)					
study weeks 1- 4 A	24.33	47.36	229.1	620.0	1221
B	25.05	47.01	225.6	626.8	1217
C	23.48	47.01	229.0	631.4	1206
9-13	24.95	52.85	245.5	619.5	1298
MEAN ( % )	98.5	100.0	94.7	99.6	100.5

A, B, C: Samples from beginning (A), middle (B), and end (C) of pelleting process for homogeneity determination.  
The mean of these 3 values is used for the overall mean calculation.

4.1.2. Test article intake

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

Mean test article intake values were calculated based on the food consumption ratios. They were corrected for actual amount of test article in the diet according to the results of chemical analysis (analytical concentration as % of nominal concentration).

The calculated mean daily intake of CGA 329351 tech., based on the nominal concentrations in the diet was 1.74, 3.50, 17.7, 45.0 and 90.0 mg/kg body weight in males, and 1.89, 3.71, 18.9, 49.4 and 94.5 mg/kg bodyweight in females.

Corrected for the analytically determined test article concentrations in the diet, the mean daily intake of CGA 329351 tech. was 1.72, 3.50, 16.8, 44.8 and 90.5 mg/kg bodyweight in males, and 1.86, 3.71, 17.9, 49.2 and 95.0 mg/kg bodyweight in females.

DAILY INTAKE: MALES

DAILY INTAKE (mg/kg bodyweight)	GROUP 2 (25 ppm)	GROUP 3 (50 ppm)	GROUP 4 (250 ppm)	Group 5 (625 ppm)	Group 6 (1250 ppm)
WEEK 1	2.573	5.435	25.75	66.88	137.1
2	2.408	5.015	24.76	63.50	130.5
3	2.012	4.105	20.30	50.81	104.2
4	1.997	3.931	20.04	50.19	104.2
5	1.783	3.472	18.14	45.39	89.0
6	1.743	3.357	17.41	44.26	86.8
7	1.746	3.454	17.34	43.94	87.1
8	1.512	3.078	15.79	39.89	80.2
9	1.351	2.773	14.67	37.88	71.0
10	1.404	2.811	14.56	36.27	73.1
11	1.464	2.832	14.55	36.32	72.7
12	1.307	2.545	13.30	33.85	64.8
13	1.375	2.736	13.89	35.41	69.6
MEAN 1	1.744	3.503	17.73	44.97	90.0
MEAN 2	1.718	3.503	16.79	44.79	90.5

MEAN 1 Based on the nominal value of the diet

MEAN 2 Based on the analytically determined value in the diet

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## DAILY INTAKE: FEMALES

DAILY INTAKE (mg/kg bodyweight)	GROUP 2 (25 ppm)	GROUP 3 (50 ppm)	GROUP 4 (250 ppm)	Group 5 (625 ppm)	Group 6 (1250 ppm)
WEEK 1	2.548	5.120	25.48	65.25	124.6
2	2.441	4.970	25.33	61.19	128.1
3	2.178	4.691	21.71	55.91	110.0
4	2.227	4.239	23.10	58.08	111.5
5	1.777	3.811	18.50	51.94	90.2
6	1.966	3.740	19.16	49.64	92.9
7	1.951	3.889	18.47	48.65	95.5
8	1.718	3.052	16.80	45.07	86.8
9	1.537	2.915	16.36	44.13	78.3
10	1.546	3.217	16.95	42.64	78.7
11	1.512	2.964	15.01	39.78	78.4
12	1.533	2.657	13.98	38.78	75.4
13	1.580	3.017	14.57	40.98	78.4
MEAN 1	1.886	3.714	18.88	49.39	94.5
MEAN 2	1.858	3.714	17.88	49.19	95.0

MEAN 1 Based on the nominal value of the diet

MEAN 2 Based on the analytically determined value in the diet

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Test Article: CGA 329351 tech.

**4.2. In-life observations**

The clinical signs observed during the course of the study are presented in the appendix section of this report and in the following summary table. Identical observations occurring repeatedly in the same animal are indicated only once in the summary table.

In life observations did not reveal treatment-related clinical signs or changed behaviour.

**INCIDENCE OF ANTEMORTEM OBSERVATIONS**

OBSERVATIONS	males						females					
	1	2	3	4	5	6	1	2	3	4	5	6
Group:	1	2	3	4	5	6	1	2	3	4	5	6
eye, exudate	1	-	-	-	-	-	-	-	-	-	-	-
hair loss	-	-	-	2	-	-	-	-	-	-	-	-
mass	-	-	-	-	-	-	1	-	-	-	-	-
skin lesion	1	1	-	-	-	-	-	-	-	-	-	-
no findings	18	9	10	8	10	20	19	10	10	10	10	20

Test No.: 943127

Test Article: CGA 329351 tech.

#### 4.3. Mortality

No deaths occurred in this study.

#### 4.4. Body weight

Mean body weight values are presented in the following tables and plots. The individual body weight values collected during the study and the results of the statistical analysis of these data are filed in the appendix sections of this report.

Body weight development was unaffected by treatment with CGA 329351 tech. at feeding levels up to 1250 ppm.

Animals of group 5 (625 ppm) gained more weight than the control and the other treated groups. However, since there was no dose dependency and no corroborative findings in organ weights analysis and histopathology, this effect was not attributed to the treatment but to reflect biological variability.

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Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

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

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	149.3	149.9	149.4	149.5	150.6	150.7
1	203.4	206.0	199.3	203.2	207.7	205.1
2	260.2	260.4	255.2	258.1	267.3	261.6
3	308.2	306.3	302.8	305.9	315.7	306.2
4	338.8	337.3	332.6	336.6	348.1	337.3
5	367.8	367.3	359.9	366.6	377.6	367.5
6	391.4	392.1	384.0	391.3	406.4	394.3
7	408.4	409.7	398.0	408.1	426.5	410.9
8	430.0	430.3	420.6	430.8	451.8	432.1
9	445.5	445.9	436.0	449.0	470.8	448.5
10	457.3	461.5	447.1	462.7	487.0	462.7
11	470.8	477.0	460.2	479.0	503.2	476.8
12	482.2	490.7	470.8	486.3	513.9	487.2
13	492.7	503.8	481.1	500.5	527.1	497.7
recovery						494.9
week: 14	510.4					505.1
15	524.2					523.3
16	537.2					535.3
17	547.3					

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Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$

JONCKHEERE: +- if  $p_J < 0.01$

**Body weight (means) : females**  
 (g/animal)

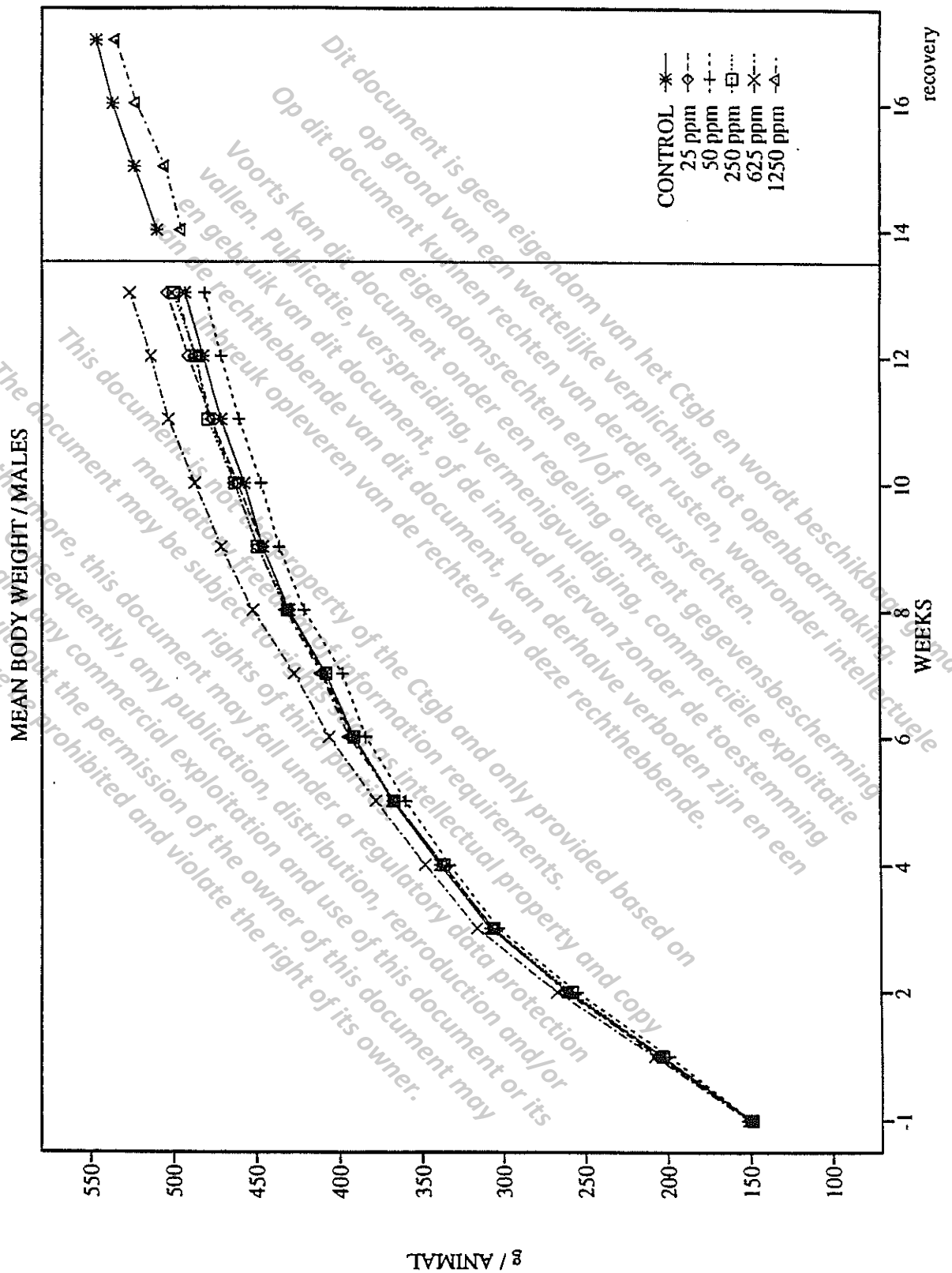
Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	135.0	135.0	135.2	135.1	135.7	135.0
1	160.2	163.9	159.2	166.5	167.2	162.6
2	189.9	195.0	191.0	199.0	197.0	190.7
3	213.2	216.3	219.3	220.7	225.4	216.8
4	228.8	237.6	241.3	241.8	245.2*	232.7
5	241.8	252.5	250.5	262.0	261.1	248.5
6	254.8	263.8	265.4	273.0	271.8	260.3
7	263.2	272.8	275.7	279.6	280.5	266.1
8	275.2	284.3	284.2	290.1	289.6	277.2
9	282.2	289.4	286.3	293.5	296.8	285.7
10	290.0	297.7	296.1	302.0	306.5	289.9
11	293.8	301.2	304.3	312.6	308.9	294.4
12	294.2	302.2	299.6	309.9	310.2	299.0
13	301.9	310.1	307.0	312.6	319.3	305.9
recovery						
week: 14	308.0					309.3
15	315.6					320.2
16	321.2					331.0
17	328.7					332.5

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3-MONTH ORAL TOXICITY STUDY IN RATS

Test No.: 943127  
 Test Article: CGA 329351 tech.



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Test Article: CGA 329351 tech.

#### 4.5. Food consumption

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

The values collected during the study and the results of the statistical analysis of these data are included in the appendix sections of this report.

Mean food consumption was not influenced by treatment.

The dose-independent slightly higher food consumption noted in group 5 (625 ppm) was regarded a reflection of biological variability.

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therefore be prohibited and violate the right of its owner.*

Statistical tests and flags used:  
 JONCKHEERE: +- if p<sub>J</sub> < 0.05

Food consumption (means, determined cagewise) : males  
 (g/animal/week)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	132.1	137.3	133.7	132.5	138.0	140.3
1	145.0	147.8	150.9	145.9	154.5	156.7 +
2	187.1	174.6	178.4	178.3	189.3	190.2
3	174.2	170.7	173.2	173.3	179.3	177.9
4	192.4	186.4	182.1	188.2	195.0	195.7
5	188.9	180.7	173.7	185.4	191.2	182.0
6	191.8	188.4	179.2	189.7	200.8	190.1
7	200.8	197.1	191.0	197.0	209.2	198.8
8	187.9	179.1	179.8	189.3	201.3	192.6
9	173.6	166.0	168.0	182.9	199.0	177.0
10	179.1	178.3	174.3	187.0	197.2	187.7
11	184.6	192.2	180.8	193.2	204.0	192.4
12	171.6	176.6	166.3	179.0	194.1	175.2
13	187.3	190.7	182.7	192.4	208.2	192.1
recovery						
week: 14	180.7					180.1
15	197.5					203.7
16	190.5					197.3
17	196.5					203.6

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)

Test No.: 943127  
 Test Article: CGA 329351 tech.

Statistical tests and flags used:  
 JONCKHEERE: +- if  $p_J < 0.05$

Food consumption (means, determined cagewise) : females  
 (g/animal/week)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	104.2	106.3	105.7	109.2 +	113.4 +	106.9
1	106.9	116.6	112.9	117.8 +	121.1 +	112.9
2	131.0	132.1	132.4	139.6	133.4	136.1
3	128.7	131.2	143.0	132.8	139.9	133.0
4	140.5	147.4	140.7	154.8	157.3 +	144.5
5	136.8	124.8	132.0	133.8	150.2	123.8
6	142.9	144.1	137.5	144.5	149.3	134.5
7	151.4	148.4	148.6	142.8	151.2	141.5
8	137.7	136.0	120.6	134.9	144.5	133.9
9	130.4	123.7	115.8 -	133.1	145.1	124.1
10	147.0	127.9	132.2	142.2	144.8	126.7
11	130.4	126.8	125.2	129.8	136.3	128.2
12	122.9	128.9	110.4	119.8	133.5	125.4
13	133.5	136.2	128.2	126.2	145.1	133.0
recovery						
week: 14	115.3					120.6
15	135.7					146.8
16	136.5					145.1
17	144.2					135.4

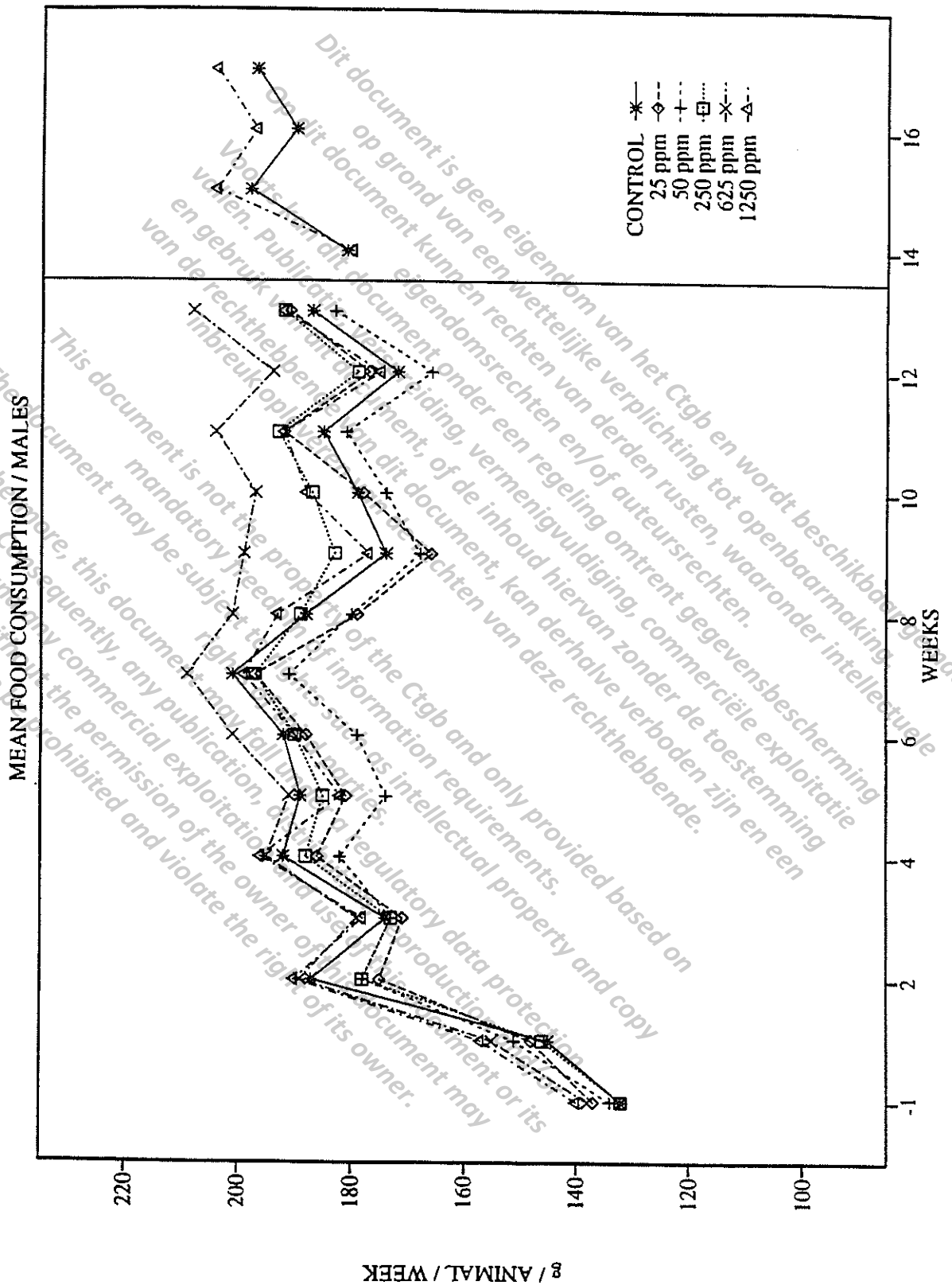
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Test No.: 943127

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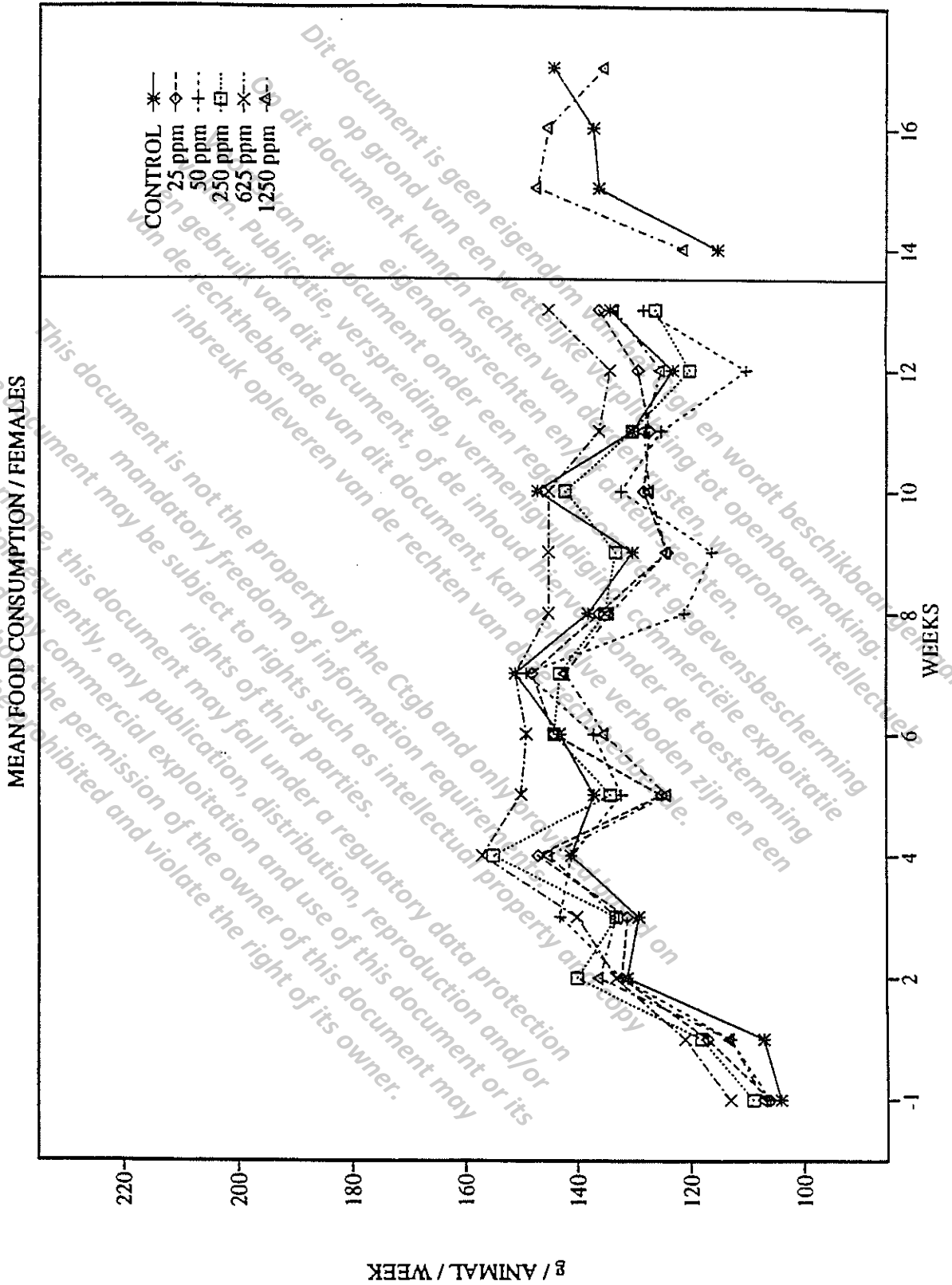


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#### 4.6. Food consumption ratios

Mean food consumption ratios are presented in the following tables and plots. Statistical analysis of these data was not performed.

Mean food consumption ratios of the treated groups were comparable to those of the control group and therefore considered uninfluenced by treatment.

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)

Test No.: 943127

Test Article: CGA 329351 tech.

No statistical tests performed

Food consumption ratios (means, determined cagewise) : males  
(g food/kg bodyweight/day)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	126.9	131.5	128.3	127.2	132.2	133.7
1	102.2	102.9	108.7	103.0	107.0	109.7
2	103.0	96.33	100.3	99.02	101.6	104.4
3	80.97	80.47	82.10	81.20	81.29	83.36
4	81.45	79.87	78.61	80.14	80.30	83.38
5	73.77	71.31	69.43	72.57	72.62	71.22
6	70.42	69.72	67.14	69.64	70.81	69.41
7	70.65	69.83	69.07	69.34	70.31	69.71
8	62.82	60.48	61.56	63.17	63.83	64.17
9	55.96	54.02	55.46	58.69	60.61	56.82
10	56.22	56.15	56.22	58.23	58.03	58.48
11	56.25	58.55	56.63	58.21	58.11	58.18
12	51.09	52.27	50.90	53.20	54.16	51.85
13	54.56	54.98	54.72	55.56	56.65	55.71
recovery						
week: 14	50.78					52.47
15	54.24					58.20
16	50.99					54.43
17	51.67					54.93

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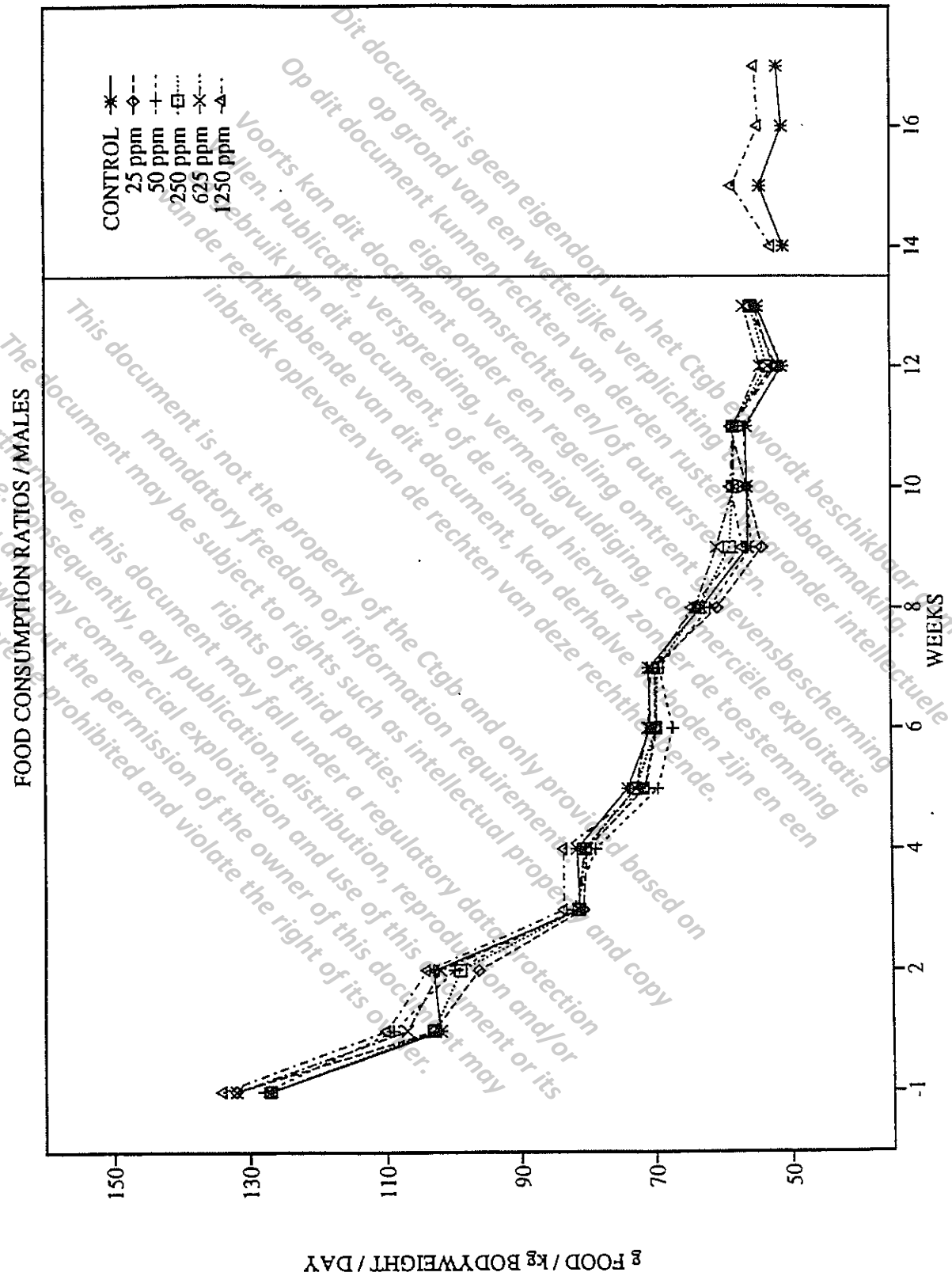
Test No.: 943127

Test Article: CGA 329351 tech.

No statistical tests performedFood consumption ratios (means, determined cagewise) : females  
(g food/kg bodyweight/day)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	110.6	112.9	112.5	115.7	120.0	113.6
1	95.73	101.9	102.4	101.9	104.4	99.67
2	99.23	97.62	99.40	101.3	97.91	102.5
3	87.00	87.12	93.82	86.82	89.46	87.97
4	88.28	89.09	84.77	92.38	92.92	89.22
5	81.39	71.08	76.22	73.99	83.11	72.13
6	80.62	78.62	74.80	76.65	79.43	74.34
7	82.80	78.04	77.77	73.88	77.84	76.39
8	72.09	68.70	61.04	67.21	72.11	69.41
9	66.67	61.46	58.29	65.42	70.60	62.65
10	72.43	61.82	64.33	67.81	68.22	62.99
11	63.81	60.48	59.27	60.03	63.64	62.74
12	60.04	61.31	53.14	55.91	62.04	60.33
13	63.65	63.19	60.34	58.29	65.56	62.72
recovery						
week: 14	53.72					56.02
15	61.57					65.95
16	60.87					63.18
17	62.88					58.54

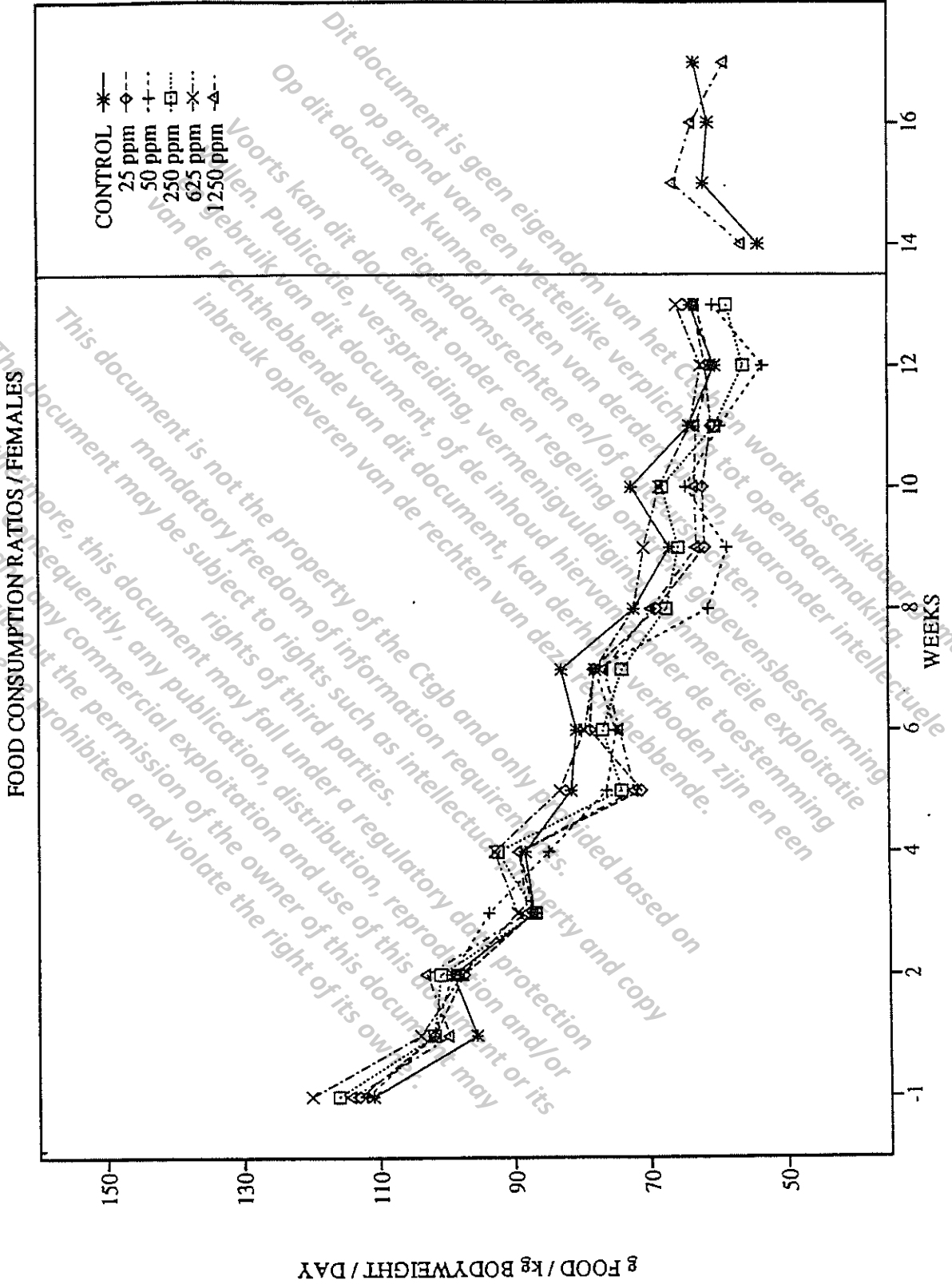
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#### 4.7. Water consumption

Mean water consumption values are presented in the following tables and plots. The individual water consumption was calculated from the water consumption per cage and the number of animals present. The values collected during the study and the results of the statistical analysis of these data are included in the appendix sections of this report.

Mean water consumption was uninfluenced by treatment.

Minor deviations are considered to reflect biological variability.

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 56

Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:

JONCKHEERE: +- if  $p_J < 0.05$

Water consumption (means, determined cagewise) : males  
(g/animal/week)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	172.5	176.1	168.6	168.4	177.8	181.3
1	208.0	207.6	197.2	215.7	205.2	208.5
2	241.5	235.0	213.6	244.9	246.5	233.2
3	264.4	270.1	238.5	290.0	276.4	235.3
4	267.9	277.6	244.7	285.7	284.9	248.2
5	267.6	274.5	246.6	310.9	291.7	262.3
6	277.0	295.3	268.4	297.9	302.5	262.7
7	273.7	271.0	255.4	294.8	335.3	265.0
8	279.3	292.2	274.4	325.0	310.7	278.2
9	270.6	282.2	263.6	321.3	301.0	255.9
10	278.6	307.7	273.1	314.7	331.2	273.2
11	234.9	292.7	250.2	291.8	288.3 +	260.7
12	267.4	288.3	245.1	256.0	300.4	250.6
13	236.4	284.1	230.5	277.0	277.8	249.3
recovery						
week: 14	194.5					210.4
15	250.5					238.1
16	244.3					243.5
17	229.6					238.6

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)

Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:

JONCKHEERE: +- if  $p_J < 0.05$

Water consumption (means, determined cagewise) : females  
(g/animal/week)

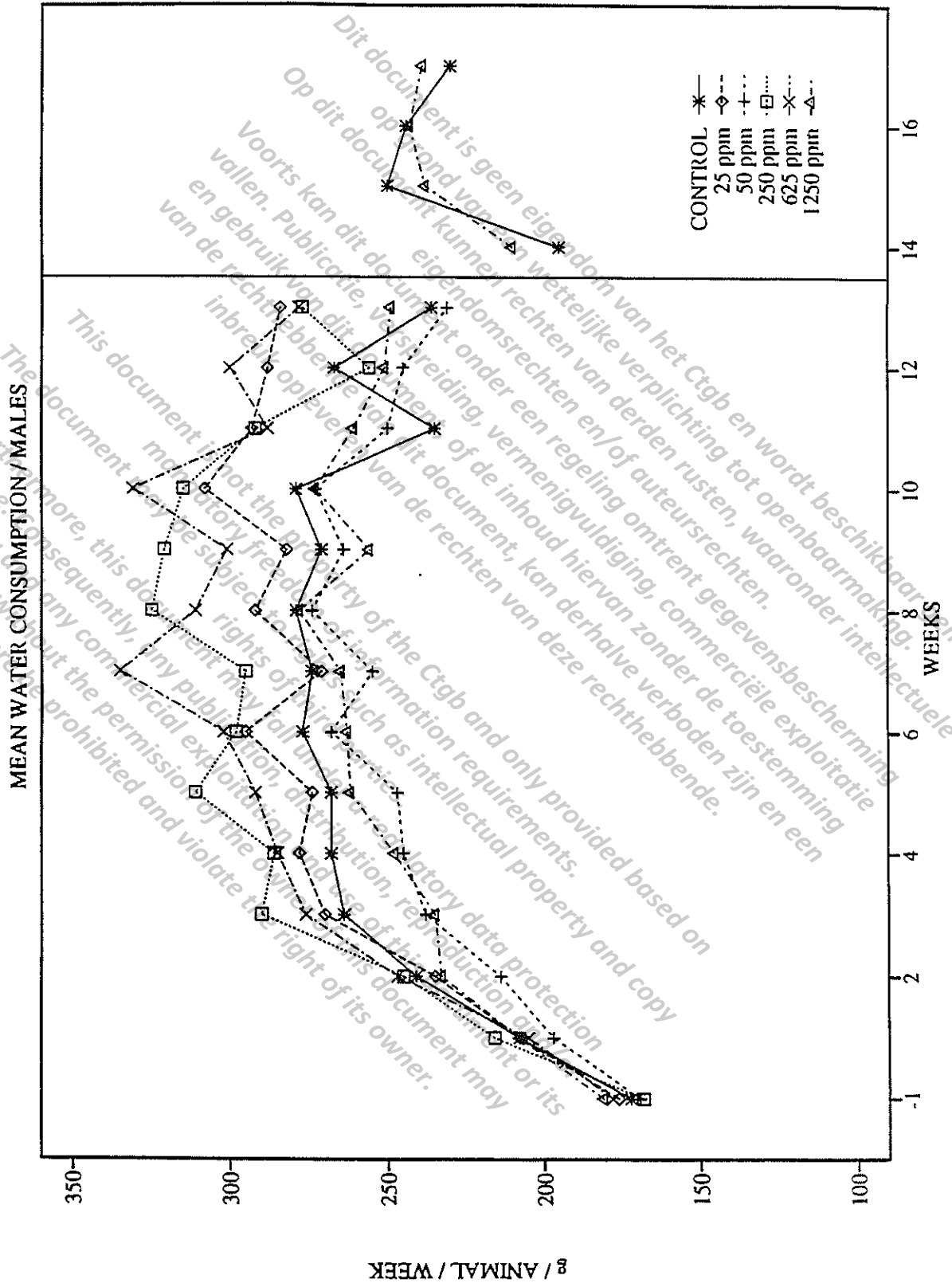
Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	155.5	161.8	156.3	158.9	163.4	145.8
1	174.7	184.2	163.7	196.1	187.5	175.4
2	191.8	190.6	206.6	195.4	180.5	180.0
3	204.1	200.7	218.9	203.1	216.4	201.0
4	222.6	216.4	232.3	245.6	231.7	210.8
5	207.3	200.1	213.9	210.1	218.4	209.8
6	223.3	196.8	232.3	229.5	218.0	212.8
7	219.1	195.6	243.1	192.7	212.4	196.0
8	212.6	205.7	240.5	212.6	229.5	217.1
9	213.3	177.5	198.9	206.2	218.0	192.2
10	225.3	213.5	216.3	241.5	237.1	198.0
11	205.4	188.6	200.6	207.6	222.1	203.9
12	193.0	181.9	225.3	181.9	215.4	204.1
13	205.0	216.7	206.0	199.6	226.1	205.1
recovery						
week: 14	192.4					186.1
15	226.1					223.1
16	231.6					245.4
17	234.2					190.8

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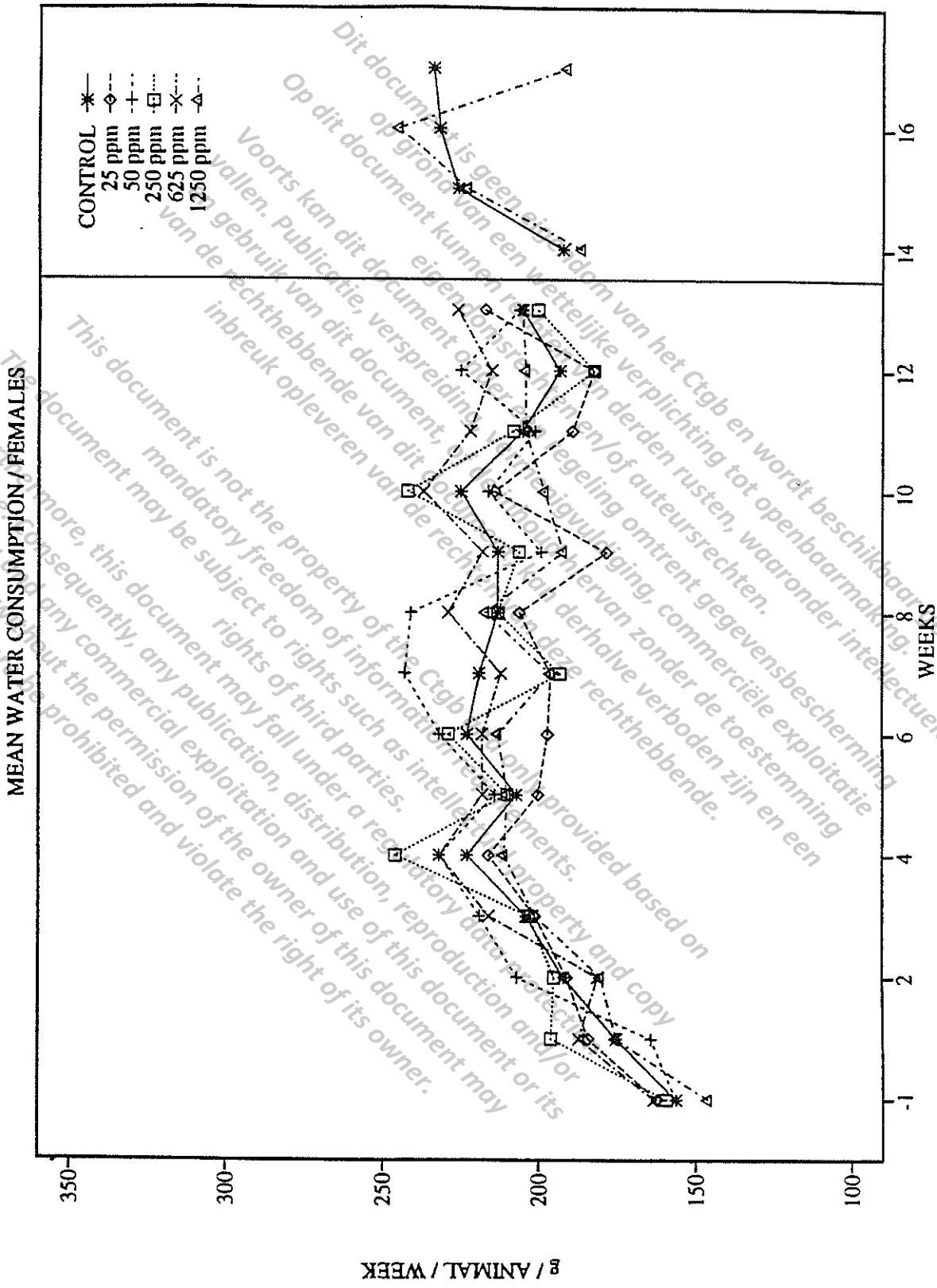


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#### 4.8. Ophthalmological examination

Examinations included inspection of the surroundings of the eyes, of sclera, cornea, iris and adaptation of the pupil to the ophthalmoscopic light beam. Animals of the control and highest treatment level groups were examined at day -6 (acclimatation period), towards

The opthalmological examinations performed did not reveal evidence of effects on the eye.

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#### 4.9. 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.

The treatment had no effect on the hematological profile.

Slightly increased neutrophil counts were noted in group 5 males (625 ppm), and the statistical analysis indicated weak positive trends in several other white blood cell parameters. However, the deviations did not show a dose-effect relationship or did not delineate a biologically important drift from concomitant control values and reference values. The findings were therefore attributed to normal biological variation. In addition, a slightly prolonged prothrombin time was noted in males of group 6 (1250 ppm), while a minimal acceleration was recorded in females treated at the same dose level. As both values were within the range of reference values these findings were attributed to chance.

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)

Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$

JONCKHEERE: +- if  $p_J < 0.01$

Hematology (means) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
RBC (T/l)						
week: 14	8.533	8.649	8.327	8.428	8.515	8.500
18	8.726					8.635
Hb (mmol/l)						
week: 14	9.615	9.760	9.560	9.710	9.580	9.545
18	9.620					9.520
Hct (l)						
week: 14	0.433	0.445 +	0.432	0.438	0.432	0.434
18	0.444					0.443
MCV (fl)						
week: 14	50.82	51.43	51.87	52.06	50.69	51.17
18	50.93					51.29
RDW (l)						
week: 14	0.137	0.127	0.131	0.129	0.126	0.130
18	0.129					0.130
MCH (fmol)						
week: 14	1.128	1.128	1.147	1.152	1.126	1.123
18	1.103					1.104
MCHC (mmol/l)						
week: 14	22.18	21.94	22.12	22.14	22.22	21.97
18	21.66					21.52
HDW (mmol/l)						
week: 14	1.654	1.637	1.891	1.734	1.722	1.778
18	1.503					1.696

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (means) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
WBC (G/l)						
week: 14	10.76	11.14	11.48	12.12	12.92	12.87 +
18	10.39					10.31
Neut (1)						
week: 14	0.166	0.180	0.185	0.179	0.259**	0.189
18	0.183					0.164
Eos (1)						
week: 14	0.016	0.014	0.012	0.019	0.014	0.012
18	0.016					0.013
Baso (1)						
week: 14	0.004	0.004	0.004	0.004	0.004	0.004
18	0.004					0.004
Lympho (1)						
week: 14	0.707	0.702	0.692	0.700	0.618	0.685
18	0.688					0.699
Mono (1)						
week: 14	0.062	0.060	0.069	0.061	0.065	0.067
18	0.060					0.066
Luc (1)						
week: 14	0.046	0.040	0.039	0.038	0.040	0.043
18	0.049					0.054
Neut (G/l)						
week: 14	1.788	1.989	2.172	2.189	3.367**	2.447
18	1.900					1.732
Eos (G/l)						
week: 14	0.173	0.163	0.122	0.237	0.178	0.145
18	0.169					0.130*

Hematology (means) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Baso (G/l)						
week: 14	0.038	0.044	0.042	0.050	0.051	0.052 +
18	0.037					0.043
Lympho (G/l)						
week: 14	7.607	7.832	7.907	8.435	7.942	8.797
18	7.159					7.157
Mono (G/l)						
week: 14	0.660	0.663	0.798	0.744	0.853	0.890 +
18	0.620					0.681
Luc (G/l)						
week: 14	0.492	0.442	0.440	0.464	0.526	0.542
18	0.500					0.560
Plt (G/l)						
week: 14	971.1	916.4	935.1	976.7	931.0	991.7
18	998.7					1037
PT(CS) (sec)						
week: 14	32.58	32.54	36.49	34.43	34.23	36.65**
18	35.01					36.71

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)

Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$

JONCKHEERE: +- if  $p_J < 0.01$

Hematology (means) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
RBC (T/l)						
week: 14	7.812	7.601	7.713	7.836	7.721	7.579
18	7.898					7.870
Hb (mmol/l)						
week: 14	9.380	9.230	9.310	9.260	9.280	9.185
18	9.575					9.600
Hct (l)						
week: 14	0.426	0.418	0.418	0.418	0.420	0.418
18	0.446					0.443
MCV (fl)						
week: 14	54.57	55.05	54.22	53.48	54.39	55.14
18	56.57					56.32
RDW (l)						
week: 14	0.128	0.121	0.131	0.134	0.126	0.130
18	0.129					0.118
MCH (fmol)						
week: 14	1.200	1.217	1.208	1.183	1.205	1.213
18	1.214					1.219
MCHC (mmol/l)						
week: 14	22.01	22.10	22.26	22.13	22.14	21.99
18	21.45					21.67
HDW (mmol/l)						
week: 14	1.525	1.508	1.582	1.568	1.428	1.586
18	1.532					1.497

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)

66

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (means) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
WBC (G/l)						
week: 14	7.180	7.023	7.524	5.897	6.762	6.971
18	7.064					6.539
Neut (1)						
week: 14	0.132	0.126	0.143	0.162	0.131	0.128
18	0.190					0.122
Eos (1)						
week: 14	0.016	0.016	0.018	0.019	0.017	0.015
18	0.015					0.015
Baso (1)						
week: 14	0.003	0.003	0.003	0.003	0.003	0.003
18	0.003					0.003
Lympho (1)						
week: 14	0.736	0.752	0.738	0.717	0.746	0.754
18	0.684					0.760
Mono (1)						
week: 14	0.069	0.063	0.059	0.058	0.062	0.064
18	0.067					0.063
Luc (1)						
week: 14	0.043	0.040	0.040	0.042	0.041	0.037
18	0.041					0.039
Neut (G/l)						
week: 14	1.081	0.884	1.102	1.003	0.869	0.877
18	1.714					0.777
Eos (G/l)						
week: 14	0.112	0.107	0.127	0.112	0.119	0.105
18	0.099					0.099

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (means) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Baso (G/l)						
week: 14	0.026	0.023	0.027	0.015	0.021	0.019
18	0.019					0.019
Lympho (G/l)						
week: 14	5.157	5.284	5.535	4.188	5.069	5.264
18	4.515					4.991
Mono (G/l)						
week: 14	0.498	0.446	0.443	0.337	0.414	0.452
18	0.446					0.405
Luc (G/l)						
week: 14	0.307	0.283	0.292	0.243	0.272	0.256
18	0.275					0.246
Plt (G/l)						
week: 14	1004	1015	982.4	985.3	994.1	995.1
18	1028					964.9
PT(CS) (sec)						
week: 14	28.99	28.88	28.95	28.54	27.97	26.15*-
18	27.10					27.43

#### 4.10. 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.

The treatment had no effect on blood chemistry parameters investigated.

Values recorded in treated rats were similar to those of controls, and none of the statistically significant differences were considered to be related to the treatment. The following changes were judged as incidental because all individual values were within the range of reference values: minimally higher creatinine levels in males of groups 3, 4, 5 and 6 (see the graph on the next page); a trend to lower potassium concentrations in males of group 6; a small increase in phosphate levels in males of groups 5 and 6, and a trend to higher globulin levels in females of group 6. Minimally lower glucose concentrations were recorded for males of groups 3, 5 and 6. However, the magnitude of the changes was too small to be toxicologically relevant (see also the graph on the following page). The minimally higher cholesterol levels observed in females of group 6 were also considered to represent the normal physiological variation of this parameter because only 2 of 20 values were minimally above the upper limit of reference values. Some changes were in the opposite direction of those considered to be toxicologically relevant: decreased bilirubin in females of groups 4 and 6, and lower ALAT activities in females of group 6. Furthermore, a minimal deviation of chloride occurred in males of group 2, which was without any relation to the dose administered, and therefore considered not to be a treatment-related effect.

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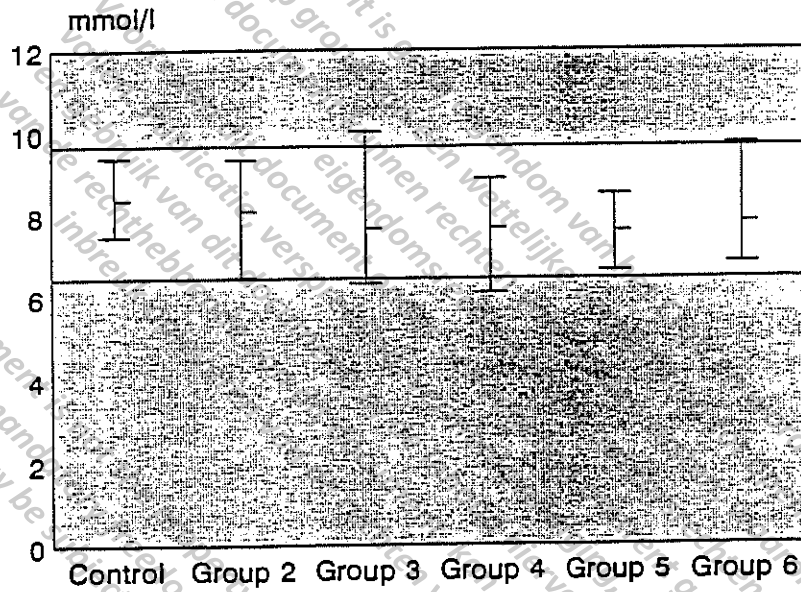
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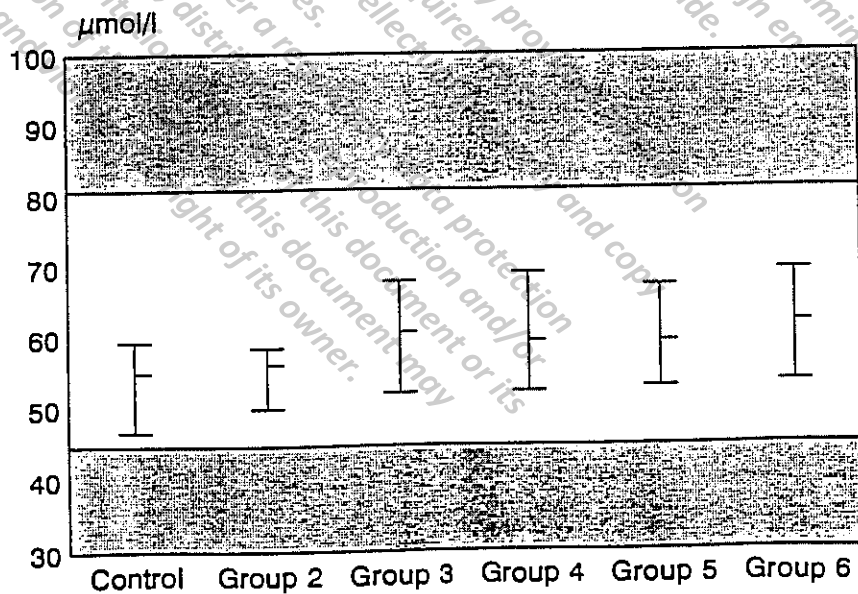
Test Article: CGA 329351 tech.

Test No. 943127. Glucose, Males, Week 14



Values of actual groups (minimum, maximum, mean) compared with reference range (5-95 percentiles)

Test No. 943127, Creatinine, Males, Week 14



Values of actual groups (minimum, maximum, mean) compared with reference range (5-95 percentiles)

Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$   
 JONCKHEERE: +- if  $p_J < 0.01$

Blood chemistry (means): males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Gluc (mmol/l)						
week: 14	8.365	8.098	7.678*	7.672	7.610 -	7.815*
18	8.734					9.575
Urea (mmol/l)						
week: 14	5.701	5.684	6.049	5.563	5.612	5.675
18	5.889					5.465
Creat-e (umol/l)						
week: 14	55.15	56.23	60.70*	59.42 +	59.30 +	61.91**
18	56.82					57.05
Bili-tot (umol/l)						
week: 14	2.093	1.995	2.190	2.189	1.947	2.103
18	2.016					2.264
Prot (g/l)						
week: 14	66.31	67.86	66.07	67.05	68.52	66.91
18	68.99					67.22
Alb (g/l)						
week: 14	35.31	35.77	35.19	35.31	35.49	35.35
18	36.11					36.20
Glob (g/l)						
week: 14	31.00	32.09	30.88	31.74	33.03	31.56
18	32.88					31.02 -
A/G (l)						
week: 14	1.144	1.117	1.142	1.115	1.078	1.122
18	1.101					1.168**
Chol (mmol/l)						
week: 14	1.916	2.005	1.883	2.010	1.993	1.914
18	2.250					2.086

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (means) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Na+ (mmol/l)						
week: 14	142.6	142.4	142.9	141.9	141.7	142.0
18	144.0					143.0
K+ (mmol/l)						
week: 14	3.664	3.595	3.594	3.673	3.435	3.446 -
18	3.586					3.477
Ca++ (mmol/l)						
week: 14	2.632	2.651	2.608	2.643	2.664	2.647
18	2.668					2.612
Cl- (mmol/l)						
week: 14	99.96	97.58*-	99.14	99.92	98.85	99.08
18	103.7					103.7
PO4-in (mmol/l)						
week: 14	1.645	1.691	1.715	1.780	1.818**	1.772 *
18	1.562					1.472
ASAT (GOT) (U/l)						
week: 14	59.66	66.06	61.09	70.35	75.41	59.62
18	60.95					62.75
ALAT (GPT) (U/l)						
week: 14	35.99	41.98	34.20	39.84	48.98	35.11
18	37.61					34.29
ALP (U/l)						
week: 14	80.82	87.55	83.16	77.06	71.83	73.58
18	76.21					79.88
GGT (U/l)						
week: 14	0.000	0.000	0.000	0.000	0.000	0.000
18	0.250					0.000

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

Blood chemistry (means) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Gluc (mmol/l)						
week: 14	7.731	7.883	7.404	7.643	7.699	7.604
18	7.709					8.014
Urea (mmol/l)						
week: 14	7.409	6.856	6.711	6.980	7.226	6.997
18	7.852					7.102
Creat-e (umol/l)						
week: 14	57.44	58.17	58.19	57.35	58.25	56.93
18	62.35					60.40
Bili-tot (umol/l)						
week: 14	3.286	3.037	2.718	2.577*-	2.979	2.600*-
18	2.679					2.360
Prot (g/l)						
week: 14	66.44	66.12	65.99	66.32	69.28	67.82
18	70.21					69.29
Alb (g/l)						
week: 14	36.72	36.65	36.77	36.59	38.03	37.20
18	37.50					37.43
Glob (g/l)						
week: 14	29.72	29.47	29.23	29.74	31.25	30.62 +
18	32.70					31.86
A/G (1)						
week: 14	1.239	1.244	1.260	1.232	1.219	1.216
18	1.157					1.179
Chol (mmol/l)						
week: 14	2.104	2.148	2.349	2.224	2.508	2.578**
18	2.254					2.338



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## Blood chemistry (means) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Na+ (mmol/l)						
week: 14	143.3	143.5	143.1	143.2	143.2	143.1
18	144.0					144.0
K+ (mmol/l)						
week: 14	2.810	2.857	2.911	2.853	2.739	2.806
18	3.123					2.952
Ca++ (mmol/l)						
week: 14	2.576	2.540	2.532	2.544	2.577	2.568
18	2.590					2.565
Cl- (mmol/l)						
week: 14	100.3	100.8	99.81	101.5	99.57	99.32
18	105.8					106.3
PO4-in (mmol/l)						
week: 14	1.411	1.436	1.461	1.382	1.436	1.392
18	1.312					1.205
ASAT (GOT) (U/l)						
week: 14	56.21	55.11	55.55	61.36	55.78	53.50
18	78.81					52.45
ALAT (GPT) (U/l)						
week: 14	32.43	30.37	28.51	34.05	27.62	26.00*-
18	36.73					22.38
AlP (U/l)						
week: 14	48.08	47.26	47.08	48.24	38.41	43.33
18	47.22					46.05
GGT (U/l)						
week: 14	0.208	0.000	0.000	0.000	0.000	0.000
18	1.193					0.000

#### 4.11. 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.

The treatment did not influence urine parameters investigated.

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD)

Test No.: 943127  
 Test Article: CGA 329351 tech.

Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$   
 JONCKHEERE: +- if  $p_J < 0.01$

Urine analysis (means) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Volume (ml)						
week: 14	5.925	6.960	5.860	6.990	7.210	6.710
18	6.610					7.000
Rel dens (1)						
week: 14	1.047	1.043	1.043	1.041	1.045	1.043
18	1.038					1.040
pH (1)						
week: 14	6.450	6.500	6.600	6.900	6.750	6.700
18	6.800					7.025

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Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$

JONCKHEERE: +- if  $p_J < 0.01$

Urine analysis (means) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Volume (ml)						
week: 14	5.265	3.630	5.790	5.130	4.160	5.700
18	5.690					5.040
Rel dens (1)						
week: 14	1.039	1.047	1.035	1.039	1.043	1.034
18	1.033					1.033
pH (1)						
week: 14	6.575	6.350	6.750	6.350	6.400	6.800
18	6.700					6.650

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No statistical tests performed

## Urine analysis (incidence): males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Color (choice)						
week: 14	0/20	0/10	0/10	0/10	0/10	0/20
18	0/10					0/10
Prot (score)						
week: 14	20/20	10/10	10/10	10/10	10/10	20/20
18	10/10					10/10
Gluc (score)						
week: 14	0/20	0/10	0/10	0/10	0/10	0/20
18	0/10					0/10
Keto (score)						
week: 14	20/20	10/10	10/10	10/10	10/10	20/20
18	10/10					10/10
Bili (score)						
week: 14	0/20	0/10	0/10	0/10	0/10	0/20
18	0/10					0/10
Blood (score)						
week: 14	0/20	0/10	0/10	0/10	1/10	0/20
18	0/10					0/10
UBG (score)						
week: 14	0/20	0/10	0/10	0/10	0/10	0/20
18	0/10					0/10

No statistical tests performed

**Urine analysis (incidence) : females**

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>Color (choice)</b>						
week: 14	0/20	0/10	0/10	0/10	0/10	0/20
18	1/10					0/10
<b>Prot (score)</b>						
week: 14	20/20	9/10	10/10	9/10	10/10	18/20
18	9/10					9/10
<b>Gluc (score)</b>						
week: 14	0/20	0/10	0/10	0/10	0/10	0/20
18	0/10					0/10
<b>Keto (score)</b>						
week: 14	11/20	10/10	9/10	7/10	6/10	19/20
18	10/10					10/10
<b>Bili (score)</b>						
week: 14	0/20	0/10	0/10	0/10	0/10	0/20
18	0/10					0/10
<b>Blood (score)</b>						
week: 14	2/20	0/10	0/10	0/10	0/10	0/20
18	1/10					0/10
<b>UBG (score)</b>						
week: 14	0/20	0/10	0/10	0/10	0/10	0/20
18	0/10					0/10

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Test Article: CGA 329351 tech.

#### 4.12. Organ weights and ratios

Mean organ weights and organ to body weight ratios are presented in the following summary tables. The individual organ weights and ratios and the results of the statistical analysis of these data are filed in the appendix sections of this report.

The mean organ weights and organ to body weight ratios of the treated groups were comparable to those of the control group.

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## 4.12.1. Organ weights (means): 1. sacrifice

## Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$ JONCKHEERE: +- if  $p_J < 0.01$ 

## Organ weights (means): males week 14

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Body (g)	454.5	485.1	458.8	479.7	501.7	473.9
Heart (g)	1.383	1.414	1.326	1.454	1.436	1.416
Liver (g)	18.35	19.44	16.50	19.54	20.33	18.69
Kidney (both) (g)	2.896	3.108	2.857	2.979	3.185	3.070
Adrenal (both) (mg)	70.38	77.81	70.71	74.49	74.98	72.21
Thymus (mg)	544.5	491.6	452.8	512.3	497.9	443.7
Testis (both) (g)	3.881	3.874	3.625	4.052	3.994	3.694
Spleen (g)	0.782	0.800	0.727	0.833	0.785	0.778



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Statistical tests and flags used:LEPAGE: \* if  $p_L < 0.01$ JONCKHEERE: +- if  $p_J < 0.01$ 

## Organ weights (means): females week 14

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Body (g)	277.3	287.3	285.5	291.7	290.3	268.0
Heart (g)	0.946	0.963	0.927	0.956	0.966	0.930
Liver (g)	10.22	10.30	10.26	11.16	11.37	10.41
Kidney (both) (g)	1.927	2.094	1.997	2.037	2.171	2.004
Adrenal (both) (mg)	86.36	92.81	84.91	90.73	93.58	83.99
Thymus (mg)	354.4	351.3	345.4	305.4	375.2	340.5
Ovary (both) (mg)	157.8	165.0	164.1	169.5	165.5	152.3
Spleen (g)	0.532	0.537	0.587	0.570	0.559	0.558

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## 4.12.2. Organ weights (means): 2. sacrifice

Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$ 

Organ weights (means): males week 18

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Body (g)	522.3					505.9
Heart (g)	1.531					1.460
Liver (g)	19.26					19.43
Kidney (both) (g)	3.174					3.137
Adrenal (both) (mg)	77.77					65.87
Thymus (mg)	530.7					464.0
Testis (both) (g)	3.792					4.047
Spleen (g)	0.772					0.817

Statistical tests and flags used:  
 LEPAGE: \* if p<sub>L</sub> < 0.01

Organ weights (means): females week 18

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Body (g)	305.2					309.0
Heart (g)	1.015					1.006
Liver (g)	10.27					10.89
Kidney (both) (g)	2.180					2.066
Adrenal (both) (mg)	94.03					87.84
Thymus (mg)	277.1					313.1
Ovary (both) (mg)	170.6					170.1
Spleen (g)	0.558					0.577

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## 4.12.3. Organ to body weight ratios (means): 1. sacrifice

Statistical tests and flags used:LEPAGE: \* if p<sub>L</sub> < 0.01JONCKHEERE: +- if p<sub>J</sub> < 0.01

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

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Heart (o/oo)	3.041	2.915	2.896	3.037	2.865	3.000
Liver (o/oo)	40.29	40.02	35.87	40.73	40.54	39.30
Kidney (both) (o/oo)	6.373	6.420	6.243	6.236	6.347	6.510
Adrenal (both) (o/oo)	0.155	0.162	0.154	0.155	0.150	0.153
Thymus (o/oo)	1.199	1.002	0.999	1.061	0.997	0.945
Testis (both) (o/oo)	8.552	8.014	8.009	8.515	8.001	7.826
Spleen (o/oo)	1.724	1.643	1.591	1.745	1.573	1.652

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## Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01JONCKHEERE: +- if p<sub>J</sub> < 0.01

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

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Heart (o/oo)	3.427	3.372	3.262	3.289	3.336	3.464
Liver (o/oo)	36.83	35.98	35.99	38.23	39.38	38.84 +
Kidney (both) (o/oo)	6.946	7.337	7.064	6.998	7.496	7.489
Adrenal (both) (o/oo)	0.314	0.324	0.301	0.311	0.325	0.314
Thymus (o/oo)	1.276	1.226	1.222	1.045	1.294	1.272
Ovary (both) (o/oo)	0.576	0.580	0.582	0.587	0.572	0.567
Spleen (o/oo)	1.922	1.879	2.089	1.972	1.934	2.094

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Test Article: CGA 329351 tech.

## 4.12.4. Organ to body weight ratios (means): 2. sacrifice

Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$ 

## Organ to body weight ratios (means): males

week 18

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Heart (o/oo)	2.945					2.881
Liver (o/oo)	36.80					38.29
Kidney (both) (o/oo)	6.105					6.209
Adrenal (both) (o/oo)	0.149					0.131
Thymus (o/oo)	1.034					0.919
Testis (both) (o/oo)	7.265					8.056
Spleen (o/oo)	1.478					1.616

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Statistical tests and flags used:

LEPAGE: \* if p\_L < 0.01

Organ to body weight ratios (means): females week 18

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Heart (o/oo)		3.336				3.275
Liver (o/oo)		33.72				35.18
Kidney (both) (o/oo)		7.228				6.714
Adrenal (both) (o/oo)		0.308				0.284
Thymus (o/oo)		0.907				1.031
Ovary (both) (o/oo)		0.561				0.550
Spleen (o/oo)		1.846				1.878

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#### 4.13. Pathology

Detailed findings for individual animals are presented in Appendix B.

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

##### **4.13.1. Macroscopical findings**

On macroscopical examination, no treatment-related changes were noted. A mass of the liver, reported in 1/10 males of group 4 (250 ppm), correlated microscopically with a developmental malformation of incidental origin. A mass of the urinary bladder, reported in 1/10 males of the recovery control group (experimental group II), correlated microscopically with a marked precipitate. A mass of the abdominal wall, reported in 1/10 females of the recovery control group (experimental group II), correlated microscopically with a carcinoma of the mammary gland. All other macroscopical findings were also considered incidental, as neither their features, nor their distribution among the groups indicated a relationship to treatment.

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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	6
Exposure : ppm	0	25	50	250	625	1250
-----	-----	-----	-----	-----	-----	-----
Animals initially in study	20	10	10	10	10	20
Treatment ended in observation period, <u>selected</u>	20	10	10	10	10	20
<u>Examined macroscopically</u>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<u>Examined microscopically</u>	20	10	10	10	10	20

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	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>SKIN</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>MAMMARY AREA</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>SPLEEN</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>MESENTERIC LYMPH NODE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>AXILLARY LYMPH NODE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>STERNUM WITH BONE MARROW</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

Test No.: 943127

Test Article: CGA 329351 tech.

## SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>FEMUR WITH JOINT</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>SKELLETAL MUSCLE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>TRACHEA</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>LUNG</b>						
<b>MOTTLED</b>						
S1	2	0	0	0	0	0
Total	2	0	0	0	0	0
<b>NO CHANGES OBSERVED</b>						
S1	8	10	10	10	10	10
S2	10	0	0	0	0	10
Total	18	10	10	10	10	20
<b>HEART</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>AORTA</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**SUMMARY OF MACROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20

**TONGUE**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**SUBMANDIBULAR SALIVARY GLAND**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**LIVER**

**MASS**

S1	0	0	0	1	0	0
Total	0	0	0	1	0	0

**NO CHANGES OBSERVED**

S1	10	10	10	9	10	10
S2	10	0	0	0	0	10
Total	20	10	10	9	10	20

**PANCREAS**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**OESOPHAGUS**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**STOMACH**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

Test No.: 943127

Test Article: CGA 329351 tech.

**SUMMARY OF MACROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>SMALL INTESTINE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>LARGE INTESTINE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>KIDNEY</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>RENAL PELVIS</b>						
<b>DILATATION</b>						
S1	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>URINARY BLADDER</b>						
<b>NODULE (&lt;.5 CM)</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	9	0	0	0	0	10
Total	19	10	10	10	10	20
<b>PROSTATE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**SUMMARY OF MACROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20

**SEMINAL VESICLE**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**TESTIS**

**SMALL**

S1	0	0	0	0	0	1
Total	0	0	0	0	0	1

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	9
S2	10	0	0	0	0	10
Total	20	10	10	10	10	19

**EPIDIDYMIS**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**PITUITARY GLAND**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**ADRENAL GLAND**

One organ, damaged at autopsy

(1)	(0)	(0)	(0)	(0)	(1)
-----	-----	-----	-----	-----	-----

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	9	0	0	0	0	9
Total	19	10	10	10	10	19

**THYROID WITH PARATHYROID GLAND**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

Test No.: 943127  
 Test Article: CGA 329351 tech.

## SUMMARY OF MACROSCOPICAL FINDINGS IN MALES

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>THYMUS</b>						
<b>MOTTLED</b>						
S1	0	0	1	0	0	0
Total	0	0	1	0	0	0
<b>NO CHANGES OBSERVED</b>						
S1	10	10	9	10	10	10
S2	10	0	0	0	0	10
Total	20	10	9	10	10	20
<b>PERIPHERAL NERVE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>BRAIN</b>						
Damaged during autopsy	(0)	(0)	(1)	(0)	(0)	(0)
<b>NO CHANGES OBSERVED</b>						
S1	10	10	9	10	10	10
S2	10	0	0	0	0	10
Total	20	10	9	10	10	20
<b>SPINAL CORD</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>EYE WITH OPTIC NERVE</b>						
One organ, not taken	(0)	(0)	(0)	(0)	(0)	(1)
One organ, damaged at autopsy	(1)	(0)	(0)	(0)	(0)	(0)
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	9	0	0	0	0	9
Total	19	10	10	10	10	19

Test No.: 943127

Test Article: CGA 329351 tech.

**SUMMARY OF MACROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20

**ORBITAL GLAND****NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**EXTRAORBITAL LACRIMAL GLAND****NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**ZYMBAL GLAND****NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**MUZZLE****NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

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Test No.: 943127

Test Article: CGA 329351 tech.

**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	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Treatment ended in observation period, selected	20	10	10	10	10	20
Examined macroscopically						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

**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 MACROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>SKIN</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>MAMMARY AREA</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>SPLEEN</b>						
Damaged during autopsy	(1)	(0)	(0)	(0)	(0)	(0)
<b>NO CHANGES OBSERVED</b>						
S1	9	10	10	10	10	10
S2	10	0	0	0	0	10
Total	19	10	10	10	10	20
<b>MESENTERIC LYMPH NODE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>AXILLARY LYMPH NODE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>STERNUM WITH BONE MARROW</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

Test No.: 943127

Test Article: CGA 329351 tech.

## SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>FEMUR WITH JOINT</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>SKELETAL MUSCLE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>TRACHEA</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>LUNG</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>HEART</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>AORTA</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20

**TONGUE**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**SUBMANDIBULAR SALIVARY GLAND**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**LIVER**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**PANCREAS**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**ESOPHAGUS**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**STOMACH**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>SMALL INTESTINE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>LARGE INTESTINE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>KIDNEY</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	9	0	0	0	0	10
Total	19	10	10	10	10	20
<b>SCARRING</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>RENAL PELVIS</b>						
<b>CALCULUS</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>URINARY BLADDER</b>						
<b>THICK</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	9	0	0	0	0	10
Total	19	10	10	10	10	20
<b>CALCULUS</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0

**SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>VAGINA</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>UTERUS</b>						
Damaged during autopsy	(1)	(0)	(0)	(0)	(0)	(0)
<b>NO CHANGES OBSERVED</b>						
S1	9	10	10	10	10	10
S2	10	0	0	0	0	10
Total	19	10	10	10	10	20
<b>OVARY</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>PITUITARY GLAND</b>						
Damaged during autopsy	(0)	(0)	(1)	(0)	(0)	(0)
<b>NO CHANGES OBSERVED</b>						
S1	10	10	9	10	10	10
S2	10	0	0	0	0	10
Total	20	10	9	10	10	20
<b>ADRENAL GLAND</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>THYROID WITH PARATHYROID GLAND</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

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Test No.: 943127

Test Article: CGA 329351 tech.

**SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
<b>THYMUS</b>						
<b>MOTTLED</b>						
S1	1	0	0	1	0	1
Total	1	0	0	1	0	1
<b>NO CHANGES OBSERVED</b>						
S1	9	10	10	9	10	9
S2	10	0	0	0	0	10
Total	19	10	10	9	10	19
<b>PERIPHERAL NERVE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>BRAIN</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>SPINAL CORD</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>EYE WITH OPTIC NERVE</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
<b>ORBITAL GLAND</b>						
<b>NO CHANGES OBSERVED</b>						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**SUMMARY OF MACROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20

**EXTRAORBITAL LACRIMAL GLAND**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**ZYMBAL GLAND**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**MUZZLE**

**NO CHANGES OBSERVED**

S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**ABDOMINAL WALL**

**MASS**

S2	1	0	0	0	0	0
Total	1	0	0	0	0	0

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#### 4.13.2. Microscopical findings

#### 4.13.3. Treatment-related microscopical findings

##### Liver

The treatment with the test article resulted in a dose-related occurrence of hepatocellular inclusion bodies in male rats. The inclusion bodies consisted of ring- or whorl-shaped eosinophilic particles, located within the cytoplasm of perilobular hepatocytes. The occurrence of these inclusions was sometimes associated with an enlargement of perilobular hepatocytes. These changes, observed in male groups 5 and 6 (625 and 1250 ppm, respectively) at the end of the treatment period (experimental group I), were no more found in the recovery group 6 (experimental group II), indicating the complete reversibility of these changes.

In females, no such hepatocellular inclusions were observed. However, the incidence of a minimal hepatocellular hypertrophy, located centrilobularly, was increased in groups 5 and 6 (625 and 1250 ppm, respectively) at the end of the treatment period (experimental group I). As the incidence of this finding in the recovery group 6 (experimental group II) was within the normal range seen in groups 1 to 4, it was concluded that the change was fully reversible.

The incidence and severity of these findings are shown in the table below:

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Incidence table of treatment-related microscopical findings in the liver

Group	1	2	3	4	5	6
Dose (ppm)	0	25	50	250	625	1250
Animals examined microscopically (Males, main groups, end of treatment)	10	10	10	10	10	10
Liver-hepatocyte: Cytoplasmic inclusion body						
-minimal	0	0	0	0	1	2
-moderate	0	0	0	0	0	1
Animals examined microscopically (Females, main groups, end of treatment)	10	10	10	10	10	10
Liver-hepatocyte: Hypertrophy						
-minimal	0	0	2	1	5	5
Animals examined microscopically (Females, recovery groups)	10					10
Liver-hepatocyte: Hypertrophy						
-minimal	0					1

4.13.4. Findings unrelated to treatment with the test article

The incidence of atrophy of the exocrine pancreas appeared slightly increased in female groups 5 and 6 (experimental group I). This finding, however, occurs spontaneously in rats of our colony, occasionally affecting large numbers of control animals as well. Therefore, no toxicological relevance was attributed to it.

Additionally, a variety of other changes was found in this study. They commonly occur in our colony of rats and neither their incidences nor their distribution and morphologic appearance gave any indication of a treatment-related association. In particular, the most frequent spontaneous lesions included fatty atrophy of the bone marrow, haemosiderosis and extramedullary haematopoiesis of the spleen, accumulation of foam cells in the lung, inflammatory lesions of the myocardium (males), lymphocytic infiltration of the liver, atrophy of the exocrine pancreas, nephrocalcinosis and atrophy of the renal tubules (females), precipitate in the urinary bladder (males), fatty change of the adrenal cortex (males), squamous metaplasia of the thyroid gland (females), and hyperplasia of the thymic epithelium.

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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	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Treatment ended in observation period, selected	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
Examined microscopically						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

=====  
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	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

**ORGANS AND TISSUES AS A WHOLE**

**NO CHANGES OBSERVED**

S2	5	0	0	0	0	2
Total	5	0	0	0	0	2

**BONE MARROW**

**FATTY ATROPHY**

S1	3	3	2	1	1	3
Total	3	3	2	1	1	3

**SPLEEN**

**HAEMOSIDEROSIS**

S1	2	5	3	5	5	4
Total	2	5	3	5	5	4

**EXTRAMEDULLARY HAEMATOPOIISIS**

S1	4	6	8	6	8	6
Total	4	6	8	6	8	6

**MESENTERIC LYMPH NODE**

**HYPOCELLULARITY**

S1	1	0	0	0	0	0
Total	1	0	0	0	0	0

**AXILLARY LYMPH NODE**

**LYMPHOID HYPERPLASIA**

S1	0	0	0	1	0	0
Total	0	0	0	1	0	0

**TRACHEA**

**MUCOUS HYPERSECRETION**

S1	0	0	0	1	0	0
Total	0	0	0	1	0	0

**LYMPHOCYTIC INFILTRATION**

S1	0	1	1	0	0	0
Total	0	1	1	0	0	0

**SUMMARY OF MICROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>LUNG</b>						
<b>MACROSCOPICAL CHANGE NOT OBSERVED</b>						
S1	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>HAEMORRHAGE</b>						
S1	1	2	1	2	1	1
Total	1	2	1	2	1	1
<b>LYMPHOCYTIC INFILTRATION</b>						
S1	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>HAEMOSIDEROSIS</b>						
S1	0	0	1	0	0	0
Total	0	0	1	0	0	0
<b>OSSEOUS METAPLASIA</b>						
S1	0	0	0	1	0	0
Total	0	0	0	1	0	0
<b>LUNG ALVEOLUS</b>						
<b>OEDEMA</b>						
S1	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>FOAM CELL</b>						
S1	4	5	7	7	5	8
Total	4	5	7	7	5	8
<b>LUNG BLOOD VESSEL</b>						
<b>CALCIFICATION</b>						
S1	0	0	0	3	0	1
Total	0	0	0	3	0	1
<b>MYOCARDIUM</b>						
<b>INFLAMMATION WITH FIBROSIS</b>						
S1	3	6	4	2	7	5
Total	3	6	4	2	7	5

**SUMMARY OF MICROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>LIVER</b>						
<b>DEVELOPMENTAL MALFORMATION</b>						
S1	0	0	0	1	0	0
Total	0	0	0	1	0	0
<b>INFLAMMATORY CELL INFILTRATION</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>LYMPHOCYTIC INFILTRATION</b>						
S1	2	3	4	4	3	3
S2	2	0	0	0	0	5
Total	4	3	4	4	3	8
<b>FATTY CHANGE</b>						
S1	0	0	1	0	1	0
S2	0	0	0	0	0	1
Total	0	0	1	0	1	1
<b>NECROSIS</b>						
S1	0	0	0	0	1	0
Total	0	0	0	0	1	0
<b>FOCUS OF CELLULAR CHANGE</b>						
S2	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>EXTRAMEDULLARY HAEMATOPOIESIS</b>						
S2	2	0	0	0	0	1
Total	2	0	0	0	0	1
<b>INTRAHEPATIC BILE DUCT</b>						
<b>CHOLANGIOFIBROSIS</b>						
S1	1	1	0	1	0	0
S2	1	0	0	0	0	0
Total	2	1	0	1	0	0
<b>LIVER HEPATOCYTE</b>						
<b>NECROSIS</b>						
S1	1	2	0	1	1	1
S2	1	0	0	0	0	1
Total	2	2	0	1	1	2

**SUMMARY OF MICROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>LIVER HEPATOCYTE (continued)</b>						
<b>CYTOPLASMIC VACUOLIZATION</b>						
S1	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>CYTOPLASMIC INCLUSION BODY</b>						
S1	0	0	0	0	1	3
Total	0	0	0	0	1	3
<b>HYPERTROPHY</b>						
S1	1	0	1	2	1	0
Total	1	0	1	2	1	0
<b>PANCREAS</b>						
No exam. for technical reason	0	0	0	0	0	1
<b>CHRONIC INFLAMMATION</b>						
S1	1	0	0	0	1	0
Total	1	0	0	0	1	0
<b>INFLAMMATORY CELL INFILTRATION</b>						
S1	0	0	0	3	1	2
Total	0	0	0	3	1	2
<b>EXOCRINE PANCREAS</b>						
<b>INFLAMMATORY CELL INFILTRATION</b>						
S1	1	0	1	0	0	0
Total	1	0	1	0	0	0
<b>NECROSIS</b>						
S1	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>ATROPHY</b>						
S1	0	1	1	0	4	1
Total	0	1	1	0	4	1
<b>HYPERPLASIA</b>						
S1	0	0	0	0	0	1
Total	0	0	0	0	0	1

**SUMMARY OF MICROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>NONGLANDULAR STOMACH</b>						
<b>INFLAMMATORY CELL INFILTRATION</b>						
S1	0	1	0	0	0	0
Total	0	1	0	0	0	0
<b>GASTRIC GLAND</b>						
<b>DILATATION</b>						
S1	0	0	0	1	0	0
Total	0	0	0	1	0	0
<b>SMALL INTESTINE PEYER'S PATCH</b>						
<b>CALCIFICATION</b>						
S1	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>LARGE INTESTINE</b>						
<b>PARASITE</b>						
S1	0	0	0	1	1	0
Total	0	0	0	1	1	0
<b>KIDNEY</b>						
<b>LYMPHOCYTTIC INFILTRATION</b>						
S1	0	0	1	1	0	0
Total	0	0	1	1	0	0
<b>RENAL TUBULE</b>						
<b>CAST</b>						
S1	1	0	2	4	1	1
Total	1	0	2	4	1	1
<b>HYALINE CHANGE</b>						
S1	1	0	0	0	1	0
Total	1	0	0	0	1	0
<b>CALCIFICATION</b>						
S1	0	1	0	0	0	0
Total	0	1	0	0	0	0
<b>ATROPHY</b>						
S1	1	1	1	2	1	0
Total	1	1	1	2	1	0



**SUMMARY OF MICROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

**RENAL PELVIS**

**CALCULUS**

S1	0	0	0	0	1	0
Total	0	0	0	0	1	0

**DILATATION**

S1	1	0	0	0	2	0
Total	1	0	0	0	2	0

**EPITHELIUM OF RENAL PELVIS**

**CALCIFICATION**

S1	1	0	0	0	0	0
Total	1	0	0	0	0	0

**HYPERPLASIA**

S1	1	0	0	1	1	0
Total	1	0	0	1	1	0

**URINARY BLADDER**

No exam. for technical reason

	1	0	0	0	0	1
--	---	---	---	---	---	---

**PRECIPITATE**

S1	3	3	2	2	3	1
S2	1	0	0	0	0	0
Total	4	3	2	2	3	1

**OEDEMA**

S1	1	0	0	0	0	0
Total	1	0	0	0	0	0

**INFLAMMATORY OEDEMA**

S1	2	0	1	0	0	0
Total	2	0	1	0	0	0

**INFLAMMATORY CELL INFILTRATION**

S1	0	0	0	1	1	0
Total	0	0	0	1	1	0

**EPITHELIUM OF URINARY BLADDER**

**HYPERPLASIA**

S1	0	0	0	0	1	0
Total	0	0	0	0	1	0

**SUMMARY OF MICROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

**TESTIS**

**TUBULAR ATROPHY**

S1	0	0	1	1	0	1
Total	0	0	1	1	0	1

**TESTIS SEMINIFEROUS TUBULE**

**IMPACTION**

S1	0	0	0	0	0	1
Total	0	0	0	0	0	1

**SPERMATIC GIANT CELL**

S1	0	0	1	0	0	0
Total	0	0	1	0	0	0

**EPIDIDYMIS**

**LYMPHOCYtic INFILTRATION**

S1	0	1	0	0	0	0
Total	0	1	0	0	0	0

**REDUCTION OF SPERMATOZOA**

S1	0	0	1	0	0	1
Total	0	0	1	0	0	1

**PITUITARY GLAND**

**CHOLESTEROL GRANULOMA**

S1	0	1	1	0	1	0
Total	0	1	1	0	1	0

**ADENOHYPHYSIS**

**DEVELOPMENTAL CYST**

S1	1	1	1	1	1	1
Total	1	1	1	1	1	1

**PITUITARY CELL**

**HYPERTROPHY**

S1	0	0	0	0	2	0
Total	0	0	0	0	2	0

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Test No.: 943127

Test Article: CGA 329351 tech.

**SUMMARY OF MICROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>ADRENAL CORTEX</b>						
<b>FATTY CHANGE</b>						
S1	5	3	4	3	3	6
Total	5	3	4	3	3	6
<b>ADRENAL MEDULLA</b>						
One organ, no exam.tech.reasons	(1)	(0)	(0)	(0)	(0)	(0)
<b>THYROID GLAND</b>						
<b>SQUAMOUS METAPLASIA</b>						
S1	0	1	0	0	0	1
Total	0	1	0	0	0	1
<b>THYROID FOLLICULAR EPITHELIUM</b>						
<b>HYPERTROPHY</b>						
S1	1	0	0	1	2	2
Total	1	0	0	1	2	2
<b>THYMUS</b>						
<b>HAEMORRHAGE</b>						
S1	0	0	1	0	0	0
Total	0	0	1	0	0	0
<b>ATROPHY</b>						
S1	0	0	0	0	1	0
Total	0	0	0	0	1	0
<b>THYMIC EPITHELIUM</b>						
<b>HYPERPLASIA</b>						
S1	1	2	2	0	1	0
Total	1	2	2	0	1	0
<b>BRAIN HYPOTHALAMUS</b>						
<b>DEVELOPMENTAL CYST</b>						
S1	0	0	0	1	0	0
Total	0	0	0	1	0	0

**SUMMARY OF MICROSCOPICAL FINDINGS IN MALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>OPTIC NERVE</b>						
One organ, not taken	(0)	(0)	(0)	(0)	(0)	(1)
<b>HAEMORRHAGE</b>						
Sl	0	0	0	0	1	0
Total	0	0	0	0	1	0
<b>DEMYELINATION</b>						
Sl	0	0	0	0	1	0
Total	0	0	0	0	1	0
<b>EYE</b>						
One organ, not taken	(0)	(0)	(0)	(0)	(0)	(1)

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Test No.: 943127

Test Article: CGA 329351 tech.

**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	6
Exposure : ppm	0	25	50	250	625	1250
-----	-----	-----	-----	-----	-----	-----
Animals initially in study	20	10	10	10	10	20
Treatment ended in observation period, <u>selected</u>	20	10	10	10	10	20
Examined macroscopically	20	10	10	10	10	20
Examined microscopically						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20

**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	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

**ORGANS AND TISSUES AS A WHOLE**

**NO CHANGES OBSERVED**

S2	3	0	0	0	0	5
Total	3	0	0	0	0	5

**MAMMARY GLAND**

**CARCINOMA**

S2	1	0	0	0	0	0
Total	1	0	0	0	0	0

**BONE MARROW**

**FATTY ATROPHY**

S1	4	5	3	3	3	5
Total	4	5	3	3	3	5

**SPLEEN**

**HAEMOSIDEROSIS**

S1	8	9	9	9	10	10
Total	8	9	9	9	10	10

**EXTRAMEDULLARY HAEMATOPOIESIS**

S1	7	6	9	7	4	4
Total	7	6	9	7	4	4

**MESENTERIC LYMPH NODE**

**EOSINOPHILIC INFILTRATION**

S1	1	0	0	1	0	0
Total	1	0	0	1	0	0

**HAEMOSIDEROSIS**

S1	0	0	0	0	0	1
Total	0	0	0	0	0	1

**LYMPHOID HYPERPLASIA**

S1	0	0	1	0	0	0
Total	0	0	1	0	0	0

**SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

**AXILLARY LYMPH NODE**

**CHRONIC REACTIVE HYPERPLASIA**

S1	0	1	0	0	0	1
Total	0	1	0	0	0	1

**LYMPHOID HYPERPLASIA**

S1	0	1	1	0	0	0
Total	0	1	1	0	0	0

**TRACHEA**

**MUCOUS HYPERSECRETION**

S1	1	0	1	1	0	1
Total	1	0	1	1	0	1

**LYMPHOCYtic INFILTRATION**

S1	1	0	0	1	0	0
Total	1	0	0	1	0	0

**LUNG**

**HAEMORRHAGE**

S1	0	2	1	1	1	1
Total	0	2	1	1	1	1

**INFLAMMATORY CELL INFILTRATION**

S1	1	0	0	0	0	0
Total	1	0	0	0	0	0

**LYMPHOCYtic INFILTRATION**

S1	0	0	1	1	0	0
Total	0	0	1	1	0	0

**OSSEOUS METAPLASIA**

S1	1	0	1	0	0	1
Total	1	0	1	0	0	1

**LUNG ALVEOLUS**

**FOAM CELL**

S1	6	9	8	5	6	5
Total	6	9	8	5	6	5

**SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>LUNG BLOOD VESSEL</b>						
<b>CALCIFICATION</b>						
S1	1	2	3	0	3	0
Total	1	2	3	0	3	0
<b>MYOCARDIUM</b>						
<b>INFLAMMATION WITH FIBROSIS</b>						
S1	1	3	1	0	1	2
Total	1	3	1	0	1	2
<b>SALIVARY GLAND</b>						
<b>CYTOPLASMIC VACUOLIZATION</b>						
S1	0	1	1	0	0	0
Total	0	1	1	0	0	0
<b>LIVER</b>						
<b>LYMPHOCYTTIC INFILTRATION</b>						
S1	4	5	4	4	7	4
S2	4	0	0	0	0	3
Total	8	5	4	4	7	7
<b>FATTY CHANGE</b>						
S1	1	3	0	1	1	1
S2	2	0	0	0	0	1
Total	3	3	0	1	1	2
<b>NECROSIS</b>						
S1	0	0	0	0	1	0
Total	0	0	0	0	1	0
<b>FOCUS OF CELLULAR CHANGE</b>						
S2	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>LIVER PORTAL TRACT</b>						
<b>EOSINOPHILIC INFILTRATION</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0



**SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>INTRAHEPATIC BILE DUCT</b>						
<b>CHOLANGIOFIBROSIS</b>						
S1	0	0	0	1	0	0
S2	0	0	0	0	0	1
Total	0	0	0	1	0	1
<b>LIVER HEPATOCYTE</b>						
<b>NECROSIS</b>						
S1	0	0	1	0	0	1
Total	0	0	1	0	0	1
<b>HYPERTROPHY</b>						
S1	0	0	2	1	5	5
S2	0	0	0	0	0	1
Total	0	0	2	1	5	6
<b>PANCREAS</b>						
<b>INFLAMMATORY CELL INFILTRATION</b>						
S1	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>LYMPHOCYTIC INFILTRATION</b>						
S1	0	0	1	0	0	0
Total	0	0	1	0	0	0
<b>EXOCRINE PANCREAS</b>						
<b>ATROPHY</b>						
S1	1	1	1	2	3	4
Total	1	1	1	2	3	4
<b>HYPERPLASIA</b>						
S1	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>STOMACH</b>						
No exam. for technical reason	0	0	1	0	0	0

**SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>NONGLANDULAR STOMACH</b>						
<b>CHRONIC INFLAMMATION</b>						
S1	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>INFLAMMATORY CELL INFILTRATION</b>						
S1	0	0	0	1	0	0
Total	0	0	0	1	0	0
<b>EPITHELIUM OF NONGLANDULAR STOMACH</b>						
<b>HYPERKERATOSIS</b>						
S1	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>LARGE INTESTINE</b>						
<b>LYMPHOCYtic INFILTRATION</b>						
S1	0	0	1	0	0	1
Total	0	0	1	0	0	1
<b>KIDNEY</b>						
<b>CHRONIC PYELONEPHRITIS</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>LYMPHOCYtic INFILTRATION</b>						
S1	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>NEPHROCALCINOSIS</b>						
S1	9	10	10	9	10	10
S2	1	0	0	0	0	0
Total	10	10	10	9	10	10
<b>RENAL TUBULE</b>						
<b>CAST</b>						
S1	2	2	0	1	0	1
Total	2	2	0	1	0	1
<b>ATROPHY</b>						
S1	1	3	3	3	2	3
Total	1	3	3	3	2	3

**SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>RENAL PELVIS</b>						
<b>CALCULUS</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>DILATATION</b>						
S1	1	0	0	0	1	0
Total	1	0	0	0	1	0
<b>URINARY BLADDER</b>						
<b>CALCULUS</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>INFLAMMATORY OEDEMA</b>						
S1	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>CHRONIC INFLAMMATION</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>INFLAMMATORY CELL INFILTRATION</b>						
S1	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>EPITHELIUM OF URINARY BLADDER</b>						
<b>PAPILLARY HYPERPLASIA</b>						
S2	1	0	0	0	0	0
Total	1	0	0	0	0	0
<b>UTERUS</b>						
<b>DILATATION</b>						
S1	1	1	1	1	2	2
Total	1	1	1	1	2	2
<b>FALLOPIAN TUBE</b>						
<b>HYPERPLASIA</b>						
S1	0	0	1	0	0	0
Total	0	0	1	0	0	0

**SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20
<b>ADENOHYPHYSIS</b>						
<b>DEVELOPMENTAL CYST</b>						
S1	2	1	0	1	1	1
Total	2	1	0	1	1	1
<b>ADRENAL CORTEX</b>						
<b>LYMPHOCYTIC INFILTRATION</b>						
S1	0	0	1	0	0	0
Total	0	0	1	0	0	0
<b>OSSEOUS METAPLASIA</b>						
S1	0	0	0	1	0	0
Total	0	0	0	1	0	0
<b>THYROID GLAND</b>						
<b>ACCESSORY THYMUS</b>						
S1	0	0	1	1	1	0
Total	0	0	1	1	1	0
<b>SQUAMOUS METAPLASIA</b>						
S1	2	1	0	3	1	2
Total	2	1	0	3	1	2
<b>THYROID FOLLICULAR EPITHELIUM</b>						
<b>HYPERTROPHY</b>						
S1	0	0	0	0	0	1
Total	0	0	0	0	0	1
<b>THYMUS</b>						
<b>HAEMORRHAGE</b>						
S1	1	0	0	1	0	1
Total	1	0	0	1	0	1
<b>ATROPHY</b>						
S1	0	0	1	1	0	0
Total	0	0	1	1	0	0

**SUMMARY OF MICROSCOPICAL FINDINGS IN FEMALES**

Group	1	2	3	4	5	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

**THYMIC EPITHELIUM**

**HYPERPLASIA**

S1	2	4	2	4	5	2
Total	2	4	2	4	5	2

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Test No.: 943127

Test Article: CGA 329351 tech.

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**5. APPENDIX A: STATISTICAL DATA**

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Test No.: 943127

Test Article: CGA 329351 tech.

5.1. Body weight (statistics)

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01

a/b ind. of diff. in loc./disp.

JONCKHEERE: +- if p<sub>J</sub> < 0.01

**Body weight (statistics) : males**  
(g/animal)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>week: -1</b>						
N	20	10	10	10	10	20
Mean	149.3	149.9	149.4	149.5	150.6	150.7
Median	147.2	150.8	146.7	147.3	143.6	149.6
IQ-Range	22.96	16.51	14.54	22.34	24.37	17.14
Min	131.0	132.8	135.4	133.0	134.7	133.3
Max	175.5	167.4	166.9	174.3	174.4	168.8
p <sub>L</sub>		0.957	0.460	0.995	0.730	0.727
p <sub>J</sub>		0.895	0.929	0.937	0.911	0.737
<b>week: 1</b>						
N	20	10	10	10	10	20
Mean	203.4	206.0	199.3	203.2	207.7	205.1
Median	204.6	201.3	196.8	200.2	199.5	207.0
IQ-Range	26.33	13.76	24.41	23.01	29.26	13.56
Min	169.5	185.8	178.0	173.7	186.7	172.0
Max	240.7	235.8	227.1	236.5	236.1	228.8
p <sub>L</sub>		0.403	0.824	0.907	0.936	0.621
p <sub>J</sub>		0.792	0.558	0.699	1.000	0.513
<b>week: 2</b>						
N	20	10	10	10	10	20
Mean	260.2	260.4	255.2	258.1	267.3	261.6
Median	262.2	252.9	251.2	258.6	261.8	265.0
IQ-Range	28.26	17.40	32.64	27.19	34.96	17.01
Min	220.7	235.0	230.0	222.0	241.0	220.8
Max	301.2	305.1	284.0	289.3	290.8	286.8
p <sub>L</sub>		0.777	0.798	0.662	0.730	0.326
p <sub>J</sub>		0.725	0.484	0.642	0.660	0.465
<b>week: 3</b>						
N	20	10	10	10	10	20
Mean	308.2	306.3	302.8	305.9	315.7	306.2
Median	310.9	298.8	296.0	315.5	313.2	308.7
IQ-Range	38.41	23.50	36.33	25.01	27.23	17.21
Min	259.1	268.4	270.8	261.6	289.1	258.7
Max	350.9	377.7	339.5	336.0	340.2	329.7
p <sub>L</sub>		0.824	0.645	0.456	0.175	0.179
p <sub>J</sub>		0.538	0.460	0.739	0.519	0.593

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 128

Test No.: 943127

Test Article: CGA 329351 tech.

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

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: 4 N	20	10	10	10	10	20
Mean	338.8	337.3	332.6	336.6	348.1	337.3
Median	342.2	333.5	326.4	345.9	348.5	344.7
IQ-Range	51.41	25.01	43.03	19.00	31.31	32.27
Min	235.5	287.9	292.5	285.8	317.0	279.9
Max	386.5	414.9	374.9	365.9	380.3	368.7
p_L		0.771	0.578	0.357	0.336	0.289
p_J		0.567	0.476	0.779	0.572	0.703
week: 5 N	20	10	10	10	10	20
Mean	367.8	367.3	359.9	366.6	377.6	367.5
Median	372.6	366.0	352.3	378.2	376.9	377.1
IQ-Range	54.05	34.69	53.83	30.16	28.81	38.40
Min	309.9	304.4	313.5	305.9	337.8	301.7
Max	423.1	455.0	411.6	394.5	413.1	407.2
p_L		0.876	0.771	0.779	0.429	0.517
p_J		0.628	0.476	0.861	0.581	0.629
week: 6 N	20	10	10	10	10	20
Mean	391.4	392.1	384.0	391.3	406.4	394.3
Median	395.6	385.8	379.1	404.4	408.2	408.1
IQ-Range	59.64	36.23	60.64	32.60	39.59	43.24
Min	329.3	325.3	337.1	323.4	367.8	315.9
Max	450.6	492.4	439.5	418.2	436.3	441.0
p_L		0.925	0.756	0.908	0.268	0.666
p_J		0.692	0.575	0.986	0.331	0.274
week: 7 N	20	10	10	10	10	20
Mean	408.4	409.7	398.0	408.1	426.5	410.9
Median	412.8	403.1	390.3	424.2	425.9	422.7
IQ-Range	66.22	38.01	63.41	31.63	54.26	50.66
Min	347.0	341.3	345.8	331.5	383.8	326.5
Max	469.5	520.6	455.8	440.4	461.1	458.6
p_L		0.910	0.730	0.925	0.290	0.819
p_J		0.692	0.430	0.930	0.293	0.342
week: 8 N	20	10	10	10	10	20
Mean	430.0	430.3	420.6	430.8	451.8	432.1
Median	434.1	422.4	411.0	446.4	449.9	446.1
IQ-Range	66.63	39.99	68.87	41.77	45.07	54.11
Min	365.4	349.9	369.5	345.0	409.5	347.5
Max	502.1	549.0	485.8	467.6	492.7	478.7
p_L		0.896	0.836	0.886	0.163	0.809
p_J		0.758	0.492	0.958	0.207	0.317



Test No.: 943127

Test Article: CGA 329351 tech.

**Body weight (statistics): males**  
(g/animal)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: 9 N	20	10	10	10	10	20
Mean	445.5	445.9	436.0	449.0	470.8	448.5
Median	444.7	438.8	423.5	470.7	473.6	462.2
IQ-Range	70.42	35.71	83.69	44.13	35.53	54.61
Min	377.1	370.0	384.3	357.5	426.1	353.6
Max	525.1	567.8	498.8	495.5	518.8	498.0
p_L		0.950	0.792	0.886	0.223	0.856
p_J		0.758	0.492	0.986	0.212	0.342
week: 10 N	20	10	10	10	10	20
Mean	457.3	461.5	447.1	462.7	487.0	462.7
Median	456.5	453.4	432.4	483.8	491.7	477.6
IQ-Range	67.01	25.11	83.99	53.61	33.56	54.82
Min	388.5	373.5	392.2	366.2	442.6	362.7
Max	538.1	589.2	523.3	516.4	534.3	516.4
p_L		0.900	0.756	0.719	0.096	0.791
p_J		0.895	0.476	0.958	0.159	0.274
week: 11 N	20	10	10	10	10	20
Mean	470.8	477.0	460.2	479.0	503.2	476.8
Median	468.6	468.0	444.7	499.3	503.8	486.8
IQ-Range	65.51	29.14	81.20	59.00	34.93	58.17
Min	396.2	387.1	406.0	379.3	453.4	372.4
Max	559.6	606.1	540.9	537.4	558.2	533.6
p_L		0.995	0.756	0.552	0.127	0.777
p_J		0.965	0.524	0.833	0.137	0.274
week: 12 N	20	10	10	10	10	20
Mean	482.2	490.7	470.8	486.3	513.9	487.2
Median	480.2	478.1	451.5	503.8	520.0	494.6
IQ-Range	62.58	22.07	81.87	67.43	38.03	58.45
Min	412.0	394.5	416.7	387.6	459.8	379.9
Max	581.3	618.3	556.2	544.7	577.5	550.0
p_L		0.962	0.403	0.665	0.145	0.724
p_J		0.930	0.524	0.916	0.163	0.285
week: 13 N	20	10	10	10	10	20
Mean	492.7	503.8	481.1	500.5	527.1	497.7
Median	487.4	493.0	459.8	518.1	531.6	500.2
IQ-Range	54.35	25.13	88.44	66.81	46.21	68.29
Min	423.3	405.9	432.5	397.3	475.9	380.3
Max	586.4	634.6	569.5	571.3	589.6	565.4
p_L		0.896	0.352	0.292	0.128	0.669
p_J		0.758	0.558	0.752	0.121	0.238

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

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
recovery						
week: 14	N	10				10
	Mean	510.4				494.9
	Median	519.2				514.9
	IQ-Range	84.56				76.91
	Min	420.4				400.4
	Max	585.4				551.0
	p_L					0.719
	p_J					0.473
week: 15	N	10				10
	Mean	524.2				505.1
	Median	534.0				528.9
	IQ-Range	69.46				83.04
	Min	432.8				411.0
	Max	604.5				564.1
	p_L					0.589
	p_J					0.406
week: 16	N	10				10
	Mean	537.2				523.3
	Median	542.1				548.1
	IQ-Range	66.79				82.90
	Min	444.8				425.1
	Max	621.4				582.0
	p_L					0.975
	p_J					0.821
week: 17	N	10				10
	Mean	547.3				535.3
	Median	556.3				560.8
	IQ-Range	66.83				86.42
	Min	456.3				435.6
	Max	629.0				594.5
	p_L					0.977
	p_J					0.880

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Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01

a/b ind. of diff. in loc./disp.

JONCKHEERE: +- if p<sub>J</sub> < 0.01

**Body weight (statistics): females**  
(g/animal)

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
week: -1 N	20	10	10	10	10	20
Mean	135.0	135.0	135.2	135.1	135.7	135.0
Median	136.8	131.7	132.1	134.1	138.2	129.2
IQ-Range	13.16	14.76	16.30	10.04	17.23	21.21
Min	123.2	123.8	123.7	122.6	124.2	124.7
Max	151.6	148.4	159.2	146.0	150.5	153.8
p <sub>L</sub>		0.976	0.692	0.567	0.552	0.340
p <sub>J</sub>		0.895	0.809	0.951	0.859	0.929
week: 1 N	20	10	10	10	10	20
Mean	160.2	163.9	159.2	166.5	167.2	162.6
Median	160.1	163.7	162.4	163.4	170.1	161.8
IQ-Range	16.72	20.70	26.39	22.37	30.41	24.11
Min	140.8	145.3	132.5	140.5	145.4	138.3
Max	195.9	181.2	182.8	190.4	189.6	187.3
p <sub>L</sub>		0.564	0.416	0.518	0.103	0.638
p <sub>J</sub>		0.291	0.684	0.370	0.198	0.471
week: 2 N	20	10	10	10	10	20
Mean	189.9	195.0	191.0	199.0	197.0	190.7
Median	193.0	195.4	193.0	196.7	200.3	188.9
IQ-Range	19.41	26.16	21.20	32.63	41.07	27.05
Min	159.1	159.8	171.9	169.9	167.6	158.3
Max	226.2	222.1	211.4	231.5	229.8	228.0
p <sub>L</sub>		0.496	0.951	0.418	0.073	0.887
p <sub>J</sub>		0.428	0.665	0.370	0.281	0.760
week: 3 N	20	10	10	10	10	20
Mean	213.2	216.3	219.3	220.7	225.4	216.8
Median	213.2	214.8	218.0	214.3	233.6	217.3
IQ-Range	27.68	18.70	44.69	42.51	40.00	27.04
Min	173.9	194.0	191.3	184.5	191.0	177.3
Max	254.0	257.3	257.4	261.3	253.5	250.3
p <sub>L</sub>		0.925	0.439	0.730	0.086	0.824
p <sub>J</sub>		0.860	0.721	0.527	0.216	0.432

Test No.: 943127

Test Article: CGA 329351 tech.

**Body weight (statistics): females**  
(g/animal)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: 4 N	20	10	10	10	10	20
Mean	228.8	237.6	241.3	241.8	245.2	232.7
Median	226.7	234.6	241.3	230.9	256.4	230.9
IQ-Range	21.43	24.47	47.84	35.57	42.51	32.21
Min	193.1	213.3	206.1	217.7	198.2	186.7
Max	282.9	277.3	295.7	294.8	280.9	269.7
p_L		0.424	0.051	0.590	0.007 *	0.201
p_J		0.379	0.262	0.194	0.064	0.373
week: 5 N	20	10	10	10	10	20
Mean	241.8	252.5	250.5	262.0	261.1	248.5
Median	237.2	251.3	254.8	253.6	269.9	249.9
IQ-Range	25.74	38.66	51.40	46.01	55.74	29.93
Min	202.0	225.9	213.2	229.5	223.2	195.2
Max	300.7	293.1	280.2	311.9	293.7	297.3
p_L		0.520	0.180	0.181	0.070	0.430
p_J		0.291	0.308	0.076	0.039	0.242
week: 6 N	20	10	10	10	10	20
Mean	254.8	263.8	265.4	273.0	271.8	260.3
Median	252.4	255.0	266.4	265.6	285.1	261.2
IQ-Range	26.68	31.57	48.16	49.11	61.32	30.51
Min	207.4	236.8	230.5	231.7	230.7	210.2
Max	313.2	318.8	313.3	334.1	307.0	323.2
p_L		0.630	0.261	0.205	0.046	0.528
p_J		0.356	0.333	0.145	0.109	0.401
week: 7 N	20	10	10	10	10	20
Mean	263.2	272.8	275.7	279.6	280.5	266.1
Median	260.4	268.8	280.2	270.6	290.7	263.3
IQ-Range	35.02	31.50	55.20	49.38	56.73	40.62
Min	212.7	250.1	239.1	241.1	239.0	213.8
Max	317.9	319.8	312.6	345.5	312.8	303.8
p_L		0.605	0.280	0.326	0.163	0.867
p_J		0.333	0.252	0.160	0.098	0.617
week: 8 N	20	10	10	10	10	20
Mean	275.2	284.3	284.2	290.1	289.6	277.2
Median	273.9	274.2	292.7	279.3	300.6	274.7
IQ-Range	35.51	32.74	42.96	55.71	66.29	39.96
Min	221.7	261.7	247.1	251.2	246.1	218.1
Max	327.8	333.2	315.4	357.3	326.0	330.5
p_L		0.530	0.604	0.370	0.094	0.904
p_J		0.379	0.308	0.203	0.146	0.659

Test No.: 943127

Test Article: CGA 329351 tech.

**Body weight (statistics): females**  
(g/animal)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: 9 N	20	10	10	10	10	20
Mean	282.2	289.4	286.3	293.5	296.8	285.7
Median	277.2	279.8	295.8	286.6	308.6	285.5
IQ-Range	37.10	37.87	44.46	45.20	67.64	52.04
Min	228.6	254.7	244.2	257.4	254.3	220.7
Max	335.7	336.3	324.8	364.5	331.5	327.9
p_L		0.754	0.545	0.710	0.250	0.699
p_J		0.481	0.610	0.461	0.242	0.508
week: 10 N	20	10	10	10	10	20
Mean	290.0	297.7	296.1	302.0	306.5	289.9
Median	291.8	291.6	301.1	291.3	315.6	292.8
IQ-Range	32.47	45.09	47.49	49.57	62.63	47.24
Min	233.3	268.2	253.1	260.2	254.4	224.6
Max	343.2	348.0	339.2	369.2	342.4	328.3
p_L		0.857	0.415	0.561	0.051	0.519
p_J		0.598	0.593	0.516	0.242	0.832
week: 11 N	20	10	10	10	10	20
Mean	293.8	301.2	304.3	312.6	308.9	294.4
Median	294.6	292.3	315.2	306.8	323.7	292.8
IQ-Range	27.16	36.54	50.36	60.57	60.74	53.59
Min	242.5	273.7	261.4	261.6	264.7	231.0
Max	337.7	354.8	345.3	382.7	345.1	355.1
p_L		0.869	0.073	0.205	0.039	0.289
p_J		0.692	0.346	0.135	0.090	0.626
week: 12 N	20	10	10	10	10	20
Mean	294.2	302.2	299.6	309.9	310.2	299.0
Median	295.0	291.1	313.0	305.5	316.3	301.4
IQ-Range	31.12	38.96	52.80	61.19	59.93	53.77
Min	244.0	273.0	260.1	269.0	266.1	229.4
Max	348.2	353.4	336.6	380.9	345.7	350.2
p_L		0.708	0.080	0.222	0.175	0.288
p_J		0.481	0.593	0.325	0.159	0.435
week: 13 N	20	10	10	10	10	20
Mean	301.9	310.1	307.0	312.6	319.3	305.9
Median	304.5	304.5	314.6	303.9	327.9	307.5
IQ-Range	28.34	41.67	40.26	52.80	62.79	53.82
Min	252.3	278.2	260.7	274.0	276.9	232.1
Max	352.1	360.3	358.3	385.2	355.3	364.4
p_L		0.818	0.204	0.679	0.146	0.207
p_J		0.598	0.575	0.499	0.239	0.561

Test No.: 943127

Test Article: CGA 329351 tech.

**Body weight (statistics): females**  
 (g/animal)

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>recovery</b>						
week: 14	N	10				10
	Mean	308.0				309.3
	Median	300.6				312.8
	IQ-Range	29.94				41.27
	Min	280.7				262.0
	Max	353.0				335.2
	p_L					0.912
	p_J					0.762
week: 15	N	10				10
	Mean	315.6				320.2
	Median	309.7				328.2
	IQ-Range	26.67				38.94
	Min	298.7				267.4
	Max	343.4				355.3
	p_L					0.216
	p_J					0.597
week: 16	N	10				10
	Mean	321.2				331.0
	Median	317.1				338.0
	IQ-Range	29.49				41.76
	Min	301.5				262.9
	Max	346.4				379.8
	p_L					0.347
	p_J					0.257
week: 17	N	10				10
	Mean	328.7				332.5
	Median	324.0				334.4
	IQ-Range	33.47				24.39
	Min	292.5				272.1
	Max	359.3				363.0
	p_L					0.497
	p_J					0.364

Test No.: 943127

Test Article: CGA 329351 tech.

5.2. Food consumption (statistics)

Statistical tests and flags used:

JONCKHEERE: +- if p<sub>J</sub> < 0.05Food consumption (statistics, determined cagewise) : males  
(g/animal/week)

Dose (ppm)		group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: -1	N	4	2	2	2	2	4
	Mean	132.1	137.3	133.7	132.5	138.0	140.3
	p <sub>J</sub>			0.417	1.000	0.572	0.066
week: 1	N	4	2	2	2	2	4
	Mean	145.0	147.8	150.9	145.9	154.5	156.7
	p <sub>J</sub>			0.787	1.000	0.396	0.034 +
week: 2	N	4	2	2	2	2	4
	Mean	187.1	174.6	178.4	178.3	189.3	190.2
	p <sub>J</sub>			0.787	0.851	0.480	0.118
week: 3	N	4	2	2	2	2	4
	Mean	174.2	170.7	173.2	173.3	179.3	177.9
	p <sub>J</sub>			0.787	0.851	0.480	0.311
week: 4	N	4	2	2	2	2	4
	Mean	192.4	186.4	182.1	188.2	195.0	195.7
	p <sub>J</sub>			0.417	0.452	1.000	0.434
week: 5	N	4	2	2	2	2	4
	Mean	188.9	180.7	173.7	185.4	191.2	182.0
	p <sub>J</sub>			0.105	0.188	0.777	0.854
week: 6	N	4	2	2	2	2	4
	Mean	191.8	188.4	179.2	189.7	200.8	190.1
	p <sub>J</sub>			0.105	0.188	1.000	0.782
week: 7	N	4	2	2	2	2	4
	Mean	200.8	197.1	191.0	197.0	209.2	198.8
	p <sub>J</sub>			0.176	0.260	0.888	0.854
week: 8	N	4	2	2	2	2	4
	Mean	187.9	179.1	179.8	189.3	201.3	192.6
	p <sub>J</sub>			0.176	0.707	0.396	0.197

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 136

Test No.: 943127

Test Article: CGA 329351 tech.

Food consumption (statistics, determined cagewise) : males  
(g/animal/week)

Dose (ppm)	group 0	group 1 25	group 2 50	group 3 250	group 4 625	group 5 1250	group 6
week: 9 N	4	2	2	2	2	4	
Mean	173.6	166.0	168.0	182.9	199.0	177.0	
p_J			0.417	0.707	0.090	0.231	
week: 10 N	4	2	2	2	2	4	
Mean	179.1	178.3	174.3	187.0	197.2	187.7	
p_J			0.417	0.851	0.203	0.118	
week: 11 N	4	2	2	2	2	4	
Mean	184.6	192.2	180.8	193.2	204.0	192.4	
p_J			1.000	0.707	0.157	0.197	
week: 12 N	4	2	2	2	2	4	
Mean	171.6	176.6	166.3	179.0	194.1	175.2	
p_J			0.589	0.851	0.120	0.357	
week: 13 N	4	2	2	2	2	4	
Mean	187.3	190.7	182.7	192.4	208.2	192.1	
p_J			0.589	0.851	0.203	0.357	
recovery							
week: 14 N	2					2	
Mean	180.7					180.1	
p_J							
week: 15 N	2					2	
Mean	197.5					203.7	
p_J							
week: 16 N	2					2	
Mean	190.5					197.3	
p_J							
week: 17 N	2					2	
Mean	196.5					203.6	
p_J							

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 137

Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:  
 JONCKHEERE: +- if p\_J < 0.05

Food consumption (statistics, determined cagewise) : females  
 (g/animal/week)

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
0	0	25	50	250	625	1250
week: -1 N	4	2	2	2	2	4
Mean	104.2	106.3	105.7	109.2	113.4	106.9
p_J			0.176	0.015	+ 0.001	+ 0.066
week: 1 N	4	2	2	2	2	4
Mean	106.9	116.6	112.9	117.8	121.1	112.9
p_J			0.058	0.015	+ 0.003	+ 0.098
week: 2 N	4	2	2	2	2	4
Mean	131.0	132.1	132.4	139.6	133.4	136.1
p_J			0.589	0.133	0.322	0.231
week: 3 N	4	2	2	2	2	4
Mean	128.7	131.2	143.0	132.8	139.9	133.0
p_J			0.417	0.260	0.120	0.231
week: 4 N	4	2	2	2	2	4
Mean	140.5	147.4	140.7	154.8	157.3	144.5
p_J			0.589	0.060	0.007	+ 0.167
week: 5 N	4	2	2	2	2	4
Mean	136.8	124.8	132.0	133.8	150.2	123.8
p_J			0.279	0.452	0.777	0.782
week: 6 N	4	2	2	2	2	4
Mean	142.9	144.1	137.5	144.5	149.3	134.5
p_J			0.279	0.707	1.000	0.231
week: 7 N	4	2	2	2	2	4
Mean	151.4	148.4	148.6	142.8	151.2	141.5
p_J			0.589	0.188	0.480	0.167
week: 8 N	4	2	2	2	2	4
Mean	137.7	136.0	120.6	134.9	144.5	133.9
p_J			0.058	0.188	0.671	1.000
week: 9 N	4	2	2	2	2	4
Mean	130.4	123.7	115.8	133.1	145.1	124.1
p_J			0.015	- 0.348	0.480	0.782

Test No.: 943127

Test Article: CGA 329351 tech.

**Food consumption (statistics, determined cagewise) : females**  
(g/animal/week)

Dose (ppm)		group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: 10	N	4	2	2	2	2	4
	Mean	147.0	127.9	132.2	142.2	144.8	126.7
	P_J			0.417	0.348	0.120	1.000
week: 11	N	4	2	2	2	2	4
	Mean	130.4	126.8	125.2	129.8	136.3	128.2
	P_J			0.176	0.348	0.572	0.927
week: 12	N	4	2	2	2	2	4
	Mean	122.9	128.9	110.4	119.8	133.5	125.4
	P_J			0.589	0.348	0.572	0.713
week: 13	N	4	2	2	2	2	4
	Mean	133.5	136.2	128.2	126.2	145.1	133.0
	P_J			0.589	0.133	0.777	1.000
	recovery						
week: 14	N	2					2
	Mean	115.3					120.6
	P_J						
week: 15	N	2					2
	Mean	135.7					146.8
	P_J						
week: 16	N	2					2
	Mean	136.5					145.1
	P_J						
week: 17	N	2					2
	Mean	144.2					135.4
	P_J						

Test No.: 943127

Test Article: CGA 329351 tech.

5.3. Water consumption (statistics)

Statistical tests and flags used:

JONCKHEERE: +- if p\_J &lt; 0.05

Water consumption (statistics, determined cagewise) : males  
(g/animal/week)

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
week: -1 N	4	2	2	2	2	4
Mean	172.5	176.1	168.6	168.4	177.8	181.3
p_J			0.589	0.573	0.671	0.927
week: 1 N	4	2	2	2	2	4
Mean	208.0	207.6	197.2	215.7	205.2	208.5
p_J			0.787	0.707	1.000	0.927
week: 2 N	4	2	2	2	2	4
Mean	241.5	235.0	213.6	244.9	246.5	233.2
p_J			0.279	0.573	0.888	0.854
week: 3 N	4	2	2	2	2	4
Mean	264.4	270.1	238.5	290.0	276.4	235.3
p_J			0.589	0.573	0.396	0.311
week: 4 N	4	2	2	2	2	4
Mean	267.9	277.6	244.7	285.7	284.9	248.2
p_J			0.417	0.851	0.480	0.519
week: 5 N	4	2	2	2	2	4
Mean	267.6	274.5	246.6	310.9	291.7	262.3
p_J			0.279	0.573	0.396	0.927
week: 6 N	4	2	2	2	2	4
Mean	277.0	295.3	268.4	297.9	302.5	262.7
p_J			1.000	0.452	0.157	0.713
week: 7 N	4	2	2	2	2	4
Mean	273.7	271.0	255.4	294.8	335.3	265.0
p_J			0.417	0.573	0.090	0.645
week: 8 N	4	2	2	2	2	4
Mean	279.3	292.2	274.4	325.0	310.7	278.2
p_J			0.787	0.091	0.090	0.461

Water consumption (statistics, determined cagewise) : males  
 (g/animal/week)

Dose (ppm)		group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
week: 9	N	4	2	2	2	2	4
	Mean	270.6	282.2	263.6	321.3	301.0	255.9
	p_J			1.000	0.188	0.157	0.854
week: 10	N	4	2	2	2	2	4
	Mean	278.6	307.7	273.1	314.7	331.2	273.2
	p_J			0.787	0.260	0.066	0.782
week: 11	N	4	2	2	2	2	4
	Mean	234.9	292.7	250.2	291.8	288.3	260.7
	p_J			0.279	0.060	0.024 +	0.167
week: 12	N	4	2	2	2	2	4
	Mean	267.4	288.3	245.1	256.0	300.4	250.6
	p_J			0.787	0.573	0.572	0.645
week: 13	N	4	2	2	2	2	4
	Mean	236.4	284.1	230.5	277.0	277.8	249.3
	p_J			0.787	0.188	0.120	0.581
recovery							
week: 14	N	2					2
	Mean	194.5					210.4
	p_J						
week: 15	N	2					2
	Mean	250.5					238.1
	p_J						
week: 16	N	2					2
	Mean	244.3					243.5
	p_J						
week: 17	N	2					2
	Mean	229.6					238.6
	p_J						

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 141

Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:  
 JONCKHEERE: +- if p<sub>J</sub> < 0.05

Water consumption (statistics, determined cagewise) : females  
 (g/animal/week)

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
week: -1 N	4	2	2	2	2	4
Mean	155.5	161.8	156.3	158.9	163.4	145.8
p <sub>J</sub>			0.589	0.707	0.621	0.550
week: 1 N	4	2	2	2	2	4
Mean	174.7	184.2	163.7	196.1	187.5	175.4
p <sub>J</sub>			1.000	0.452	0.358	0.747
week: 2 N	4	2	2	2	2	4
Mean	191.8	190.6	206.6	195.4	180.5	180.0
p <sub>J</sub>			0.417	0.348	0.777	0.461
week: 3 N	4	2	2	2	2	4
Mean	204.1	200.7	218.9	203.1	216.4	201.0
p <sub>J</sub>			0.589	0.851	0.777	0.890
week: 4 N	4	2	2	2	2	4
Mean	222.6	216.4	232.3	245.6	231.7	210.8
p <sub>J</sub>			0.787	0.348	0.322	0.747
week: 5 N	4	2	2	2	2	4
Mean	207.3	200.1	213.9	210.1	218.4	209.8
p <sub>J</sub>			0.589	0.452	0.258	0.231
week: 6 N	4	2	2	2	2	4
Mean	223.3	196.8	232.3	229.5	218.0	212.8
p <sub>J</sub>			0.787	0.573	0.777	0.782
week: 7 N	4	2	2	2	2	4
Mean	219.1	195.6	243.1	192.7	212.4	196.0
p <sub>J</sub>			0.417	0.573	0.671	0.269
week: 8 N	4	2	2	2	2	4
Mean	212.6	205.7	240.5	212.6	229.5	217.1
p <sub>J</sub>			0.417	0.452	0.671	0.519
week: 9 N	4	2	2	2	2	4
Mean	213.3	177.5	198.9	206.2	218.0	192.2
p <sub>J</sub>			0.417	1.000	0.777	0.927

Test No.: 943127

Test Article: CGA 329351 tech.

Water consumption (statistics, determined cagewise) : females  
(g/animal/week)

Dose (ppm)	group 0	group 1	group 2	group 3	group 4	group 5	group 6
week: 10 N	4	2	2	2	2	4	
Mean	225.3	213.5	216.3	241.5	237.1	198.0	
p_J			0.589	0.452	0.322	0.461	
week: 11 N	4	2	2	2	2	4	
Mean	205.4	188.6	200.6	207.6	222.1	203.9	
p_J			0.589	0.851	0.724	0.581	
week: 12 N	4	2	2	2	2	4	
Mean	193.0	181.9	225.3	181.9	215.4	204.1	
p_J			0.279	0.851	0.396	0.311	
week: 13 N	4	2	2	2	2	4	
Mean	205.0	216.7	206.0	199.6	226.1	205.1	
p_J			1.000	0.573	0.777	0.927	
recovery							
week: 14 N	2					2	
Mean	192.4					186.1	
p_J							
week: 15 N	2					2	
Mean	226.1					223.1	
p_J							
week: 16 N	2					2	
Mean	231.6					245.4	
p_J							
week: 17 N	2					2	
Mean	234.2					190.8	
p_J							

5.4. Hematology (statistics)

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

Hematology (statistics) : males

dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
RBC (T/l)						
week: 14 N	20	10	10	10	10	20
Mean	8.533	8.649	8.327	8.428	8.515	8.500
Median	8.555	8.605	8.290	8.440	8.525	8.505
IQ-Range	0.565	0.180	0.160	0.580	0.390	0.445
Min	8.010	8.330	8.120	7.830	8.050	7.620
Max	9.350	9.060	8.780	8.950	8.950	9.120
p <sub>L</sub>		0.072	0.066	0.852	0.746	0.836
p <sub>J</sub>		0.379	0.181	0.173	0.404	0.773
week: 18 N	10					10
Mean	8.726					8.635
Median	8.705					8.690
IQ-Range	0.300					0.540
Min	8.310					8.130
Max	9.020					9.010
p <sub>L</sub>						0.415
p <sub>J</sub>						0.597
Hb (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	9.615	9.760	9.560	9.710	9.580	9.545
Median	9.650	9.800	9.550	9.650	9.700	9.500
IQ-Range	0.400	0.100	0.500	0.400	0.400	0.350
Min	9.200	9.400	9.300	9.300	9.100	9.100
Max	9.900	10.00	9.900	10.10	9.800	10.30
p <sub>L</sub>		0.240	0.715	0.720	0.881	0.459
p <sub>J</sub>		0.113	0.929	0.706	0.844	0.128
week: 18 N	10					10
Mean	9.620					9.520
Median	9.650					9.600
IQ-Range	0.200					0.300
Min	9.200					9.000
Max	9.900					10.10
p <sub>L</sub>						0.544
p <sub>J</sub>						0.345

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Hct (l)						
week: 14 N	20	10	10	10	10	20
Mean	0.433	0.445	0.432	0.438	0.432	0.434
Median	0.433	0.447	0.432	0.437	0.433	0.435
IQ-Range	0.015	0.010	0.022	0.020	0.017	0.016
Min	0.418	0.435	0.419	0.416	0.408	0.411
Max	0.451	0.458	0.445	0.455	0.443	0.466
p_L		0.016	0.633	0.448	0.992	0.699
p_J		0.004 +	0.656	0.429	0.901	0.614
week: 18 N	10					10
Mean	0.444					0.443
Median	0.449					0.441
IQ-Range	0.016					0.028
Min	0.428					0.421
Max	0.457					0.468
p_L						0.214
p_J						0.910
MCV (fl)						
week: 14 N	20	10	10	10	10	20
Mean	50.82	51.43	51.87	52.06	50.69	51.17
Median	50.75	51.35	51.75	52.45	50.65	50.55
IQ-Range	2.400	1.800	2.000	2.600	1.100	1.450
Min	48.20	49.60	50.50	49.60	48.30	49.70
Max	52.90	52.90	54.10	55.20	52.50	55.80
p_L		0.324	0.154	0.133	0.278	0.488
p_J		0.253	0.058	0.028	0.466	0.845
week: 18 N	10					10
Mean	50.93					51.29
Median	51.25					51.10
IQ-Range	1.400					0.900
Min	49.50					50.00
Max	52.00					53.70
p_L						0.823
p_J						0.623



Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics): males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
RDW (1)						
week: 14 N	20	10	10	10	10	20
Mean	0.137	0.127	0.131	0.129	0.126	0.130
Median	0.131	0.127	0.129	0.130	0.126	0.128
IQ-Range	0.022	0.006	0.004	0.012	0.007	0.011
Min	0.117	0.120	0.119	0.116	0.116	0.117
Max	0.224	0.139	0.164	0.143	0.134	0.147
p_L		0.207	0.421	0.498	0.186	0.553
p_J		0.141	0.285	0.370	0.163	0.484
week: 18 N	10					10
Mean	0.129					0.130
Median	0.125					0.129
IQ-Range	0.014					0.010
Min	0.122					0.120
Max	0.149					0.138
p_L						0.413
p_J						0.427
MCH (fmol)						
week: 14 N	20	10	10	10	10	20
Mean	1.128	1.128	1.147	1.152	1.126	1.123
Median	1.130	1.140	1.135	1.160	1.125	1.110
IQ-Range	0.065	0.060	0.030	0.060	0.010	0.045
Min	1.050	1.080	1.120	1.090	1.090	1.080
Max	1.180	1.170	1.210	1.210	1.160	1.210
p_L		0.958	0.183	0.249	0.070	0.699
p_J		0.947	0.366	0.097	0.617	0.333
week: 18 N	10					10
Mean	1.103					1.104
Median	1.095					1.105
IQ-Range	0.040					0.020
Min	1.070					1.070
Max	1.140					1.160
p_L						0.685
p_J						0.940

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (statistics): males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
MCHC (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	22.18	21.94	22.12	22.14	22.22	21.97
Median	22.15	22.02	22.11	22.22	22.29	21.97
IQ-Range	0.295	0.540	0.190	0.340	0.350	0.415
Min	21.76	21.17	21.93	21.88	21.87	21.38
Max	23.15	22.29	22.26	22.40	22.64	22.56
p_L		0.305	0.334	0.883	0.250	0.074
p_J		0.153	0.437	0.826	0.430	0.289
week: 18 N	10					10
Mean	21.66					21.52
Median	21.59					21.51
IQ-Range	0.320					0.240
Min	21.20					21.04
Max	22.23					22.15
p_L						0.544
p_J						0.290
HDW (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	1.654	1.637	1.891	1.734	1.722	1.778
Median	1.515	1.545	1.930	1.665	1.620	1.685
IQ-Range	0.410	0.120	0.620	0.480	0.340	0.575
Min	1.420	1.430	1.500	1.460	1.470	1.440
Max	2.150	2.190	2.320	2.240	2.180	2.340
p_L		0.708	0.063	0.406	0.096	0.362
p_J		0.809	0.038	0.075	0.075	0.090
week: 18 N	10					10
Mean	1.503					1.696
Median	1.445					1.690
IQ-Range	0.150					0.490
Min	1.370					1.390
Max	1.740					2.040
p_L						0.159
p_J						0.112

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Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics): males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
WBC (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	10.76	11.14	11.48	12.12	12.92	12.87
Median	10.97	11.03	10.78	12.72	12.61	12.94
IQ-Range	2.920	1.730	4.330	3.420	3.150	3.225
Min	7.270	8.310	8.710	9.060	10.03	8.130
Max	13.60	13.68	14.65	14.55	16.10	17.61
p_L		0.649	0.789	0.080	0.077	0.012
p_J		0.628	0.575	0.165	0.016	0.001 +
week: 18 N	10					10
Mean	10.39					10.31
Median	10.08					9.585
IQ-Range	2.310					2.160
Min	8.410					9.020
Max	12.83					12.50
p_L						0.955
p_J						0.762
Neut (1)						
week: 14 N	20	10	10	10	10	20
Mean	0.166	0.180	0.185	0.179	0.259	0.189
Median	0.160	0.175	0.182	0.165	0.269	0.164
IQ-Range	0.054	0.086	0.038	0.134	0.100	0.115
Min	0.111	0.095	0.104	0.089	0.097	0.069
Max	0.275	0.340	0.253	0.304	0.378	0.362
p_L		0.551	0.275	0.305	0.003 *	0.241
p_J		0.792	0.226	0.409	0.008 +	0.143
week: 18 N	10					10
Mean	0.183					0.164
Median	0.166					0.147
IQ-Range	0.088					0.044
Min	0.138					0.110
Max	0.237					0.301
p_L						0.394
p_J						0.199

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Eos (1)						
week: 14	N 20	10	10	10	10	20
Mean	0.016	0.014	0.012	0.019	0.014	0.012
Median	0.013	0.016	0.011	0.012	0.015	0.010
IQ-Range	0.007	0.008	0.008	0.011	0.008	0.007
Min	0.005	0.008	0.005	0.009	0.007	0.004
Max	0.075	0.023	0.019	0.070	0.023	0.023
p_L		0.655	0.644	0.916	0.876	0.582
p_J		0.660	0.524	0.937	0.895	0.375
week: 18	N 10					10
Mean	0.016					0.013
Median	0.014					0.009
IQ-Range	0.012					0.017
Min	0.009					0.005
Max	0.025					0.024
p_L						0.032
p_J						0.076
Baso (1)						
week: 14	N 20	10	10	10	10	20
Mean	0.004	0.004	0.004	0.004	0.004	0.004
Median	0.003	0.005	0.004	0.004	0.004	0.004
IQ-Range	0.001	0.002	0.002	0.002	0.002	0.002
Min	0.002	0.003	0.002	0.003	0.003	0.002
Max	0.006	0.006	0.005	0.005	0.006	0.006
p_L		0.194	0.433	0.235	0.649	0.559
p_J		0.135	0.169	0.102	0.214	0.453
week: 18	N 10					10
Mean	0.004					0.004
Median	0.004					0.004
IQ-Range	0.001					0.001
Min	0.002					0.003
Max	0.005					0.005
p_L						0.336
p_J						0.226

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Lympho (1)						
week: 14 N	20	10	10	10	10	20
Mean	0.707	0.702	0.692	0.700	0.618	0.685
Median	0.711	0.715	0.703	0.722	0.628	0.700
IQ-Range	0.082	0.070	0.063	0.155	0.119	0.111
Min	0.608	0.562	0.610	0.587	0.500	0.518
Max	0.799	0.781	0.785	0.803	0.778	0.790
p_L		0.751	0.262	0.859	0.023	0.644
p_J		0.912	0.476	0.745	0.030	0.154
week: 18 N	10					10
Mean	0.688					0.699
Median	0.707					0.709
IQ-Range	0.086					0.065
Min	0.627					0.581
Max	0.733					0.783
p_L						0.931
p_J						0.821
Mono (1)						
week: 14 N	20	10	10	10	10	20
Mean	0.062	0.060	0.069	0.061	0.065	0.067
Median	0.059	0.057	0.074	0.055	0.058	0.066
IQ-Range	0.021	0.022	0.029	0.020	0.028	0.021
Min	0.041	0.045	0.045	0.046	0.047	0.047
Max	0.097	0.080	0.091	0.099	0.091	0.100
p_L		0.689	0.344	0.926	0.911	0.492
p_J		0.843	0.308	0.772	0.599	0.254
week: 18 N	10					10
Mean	0.060					0.066
Median	0.058					0.065
IQ-Range	0.009					0.010
Min	0.046					0.052
Max	0.078					0.086
p_L						0.359
p_J						0.186

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics): males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Luc (1)						
week: 14	N 20	10	10	10	10	20
Mean	0.046	0.040	0.039	0.038	0.040	0.043
Median	0.044	0.043	0.038	0.039	0.041	0.041
IQ-Range	0.016	0.015	0.015	0.008	0.003	0.018
Min	0.031	0.026	0.024	0.026	0.036	0.028
Max	0.067	0.051	0.058	0.045	0.050	0.061
p_L		0.603	0.192	0.134	0.054	0.604
p_J		0.322	0.106	0.043	0.065	0.323
week: 18	N 10					10
Mean	0.049					0.054
Median	0.050					0.056
IQ-Range	0.015					0.022
Min	0.032					0.032
Max	0.070					0.069
p_L						0.508
p_J						0.273
Neut (G/l)						
week: 14	N 20	10	10	10	10	20
Mean	1.788	1.989	2.172	2.189	3.367	2.447
Median	1.650	1.850	1.865	1.775	3.335 a	1.960
IQ-Range	0.725	0.880	0.890	1.790	1.810	1.490
Min	1.060	0.970	1.110	0.920	1.070	1.070
Max	3.200	3.790	3.710	3.890	4.930	5.400
p_L		0.753	0.455	0.665	0.001 *	0.220
p_J		0.481	0.207	0.265	0.003 +	0.016
week: 18	N 10					10
Mean	1.900					1.732
Median	1.790					1.525
IQ-Range	0.820					0.530
Min	1.280					0.990
Max	2.740					3.770
p_L						0.460
p_J						0.226

Rematology (statistics) : males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Eos (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	0.173	0.163	0.122	0.237	0.178	0.145
Median	0.120	0.150	0.120	0.160	0.170	0.145
IQ-Range	0.090	0.110	0.050	0.090	0.130	0.075
Min	0.050	0.080	0.070	0.080	0.100	0.030
Max	0.920	0.310	0.170	0.930	0.270	0.240
p_L		0.708	0.651	0.556	0.324	0.737
p_J		0.441	0.869	0.466	0.143	0.362
week: 18 N	10					10
Mean	0.169					0.130
Median	0.150					0.080
IQ-Range	0.120					0.150
Min	0.110					0.050
Max	0.250					0.290
p_L						0.005 *
p_J						0.082
Baso (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	0.038	0.044	0.042	0.050	0.051	0.052
Median	0.040	0.045	0.040	0.050	0.050	0.050
IQ-Range	0.010	0.030	0.020	0.030	0.020	0.020
Min	0.020	0.020	0.020	0.030	0.030	0.010
Max	0.070	0.060	0.070	0.070	0.080	0.100
p_L		0.311	0.479	0.088	0.075	0.042
p_J		0.218	0.285	0.049	0.014	0.008 +
week: 18 N	10					10
Mean	0.037					0.043
Median	0.040					0.040
IQ-Range	0.010					0.020
Min	0.020					0.030
Max	0.060					0.060
p_L						0.597
p_J						0.326

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Lympho (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	7.607	7.832	7.907	8.435	7.942	8.797
Median	7.600	7.895	7.915	8.245	8.495	8.535
IQ-Range	2.020	2.010	1.540	1.780	2.460	1.600
Min	5.100	5.520	5.840	6.410	5.610	5.170
Max	10.53	10.13	10.23	10.71	9.580	13.08
p_L		0.869	0.735	0.385	0.733	0.133
p_J		0.692	0.593	0.226	0.237	0.029
week: 18 N	10					10
Mean	7.159					7.157
Median	7.155					7.130
IQ-Range	1.630					0.460
Min	5.610					6.100
Max	9.280					8.580
p_L						0.190
p_J						0.940
Mono (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	0.660	0.663	0.798	0.744	0.853	0.890
Median	0.610	0.650	0.780	0.670	0.750	0.820
IQ-Range	0.180	0.190	0.330	0.210	0.450	0.395
Min	0.410	0.500	0.390	0.510	0.470	0.430
Max	1.070	0.960	1.290	1.440	1.390	1.770
p_L		0.596	0.139	0.730	0.175	0.047
p_J		0.676	0.130	0.200	0.055	0.006 +
week: 18 N	10					10
Mean	0.620					0.681
Median	0.585					0.630
IQ-Range	0.090					0.280
Min	0.530					0.520
Max	0.800					0.970
p_L						0.447
p_J						0.345



Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (statistics) : males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Luc (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	0.492	0.442	0.440	0.464	0.526	0.542
Median	0.490	0.435	0.435	0.480	0.515	0.520
IQ-Range	0.145	0.130	0.200	0.200	0.180	0.215
Min	0.260	0.330	0.280	0.240	0.360	0.350
Max	0.750	0.610	0.650	0.620	0.800	0.790
p_L		0.520	0.512	0.714	0.768	0.589
p_J		0.312	0.231	0.471	0.772	0.156
week: 18 N	10					10
Mean	0.500					0.560
Median	0.525					0.585
IQ-Range	0.230					0.200
Min	0.330					0.310
Max	0.650					0.740
p_L						0.259
p_J						0.364
Plt (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	971.1	916.4	935.1	976.7	931.0	991.7
Median	993.0	905.5	945.0	1007	950.0	1001
IQ-Range	118.5	52.00	173.0	122.0	144.0	90.00
Min	676.0	690.0	790.0	819.0	740.0	750.0
Max	1116	1081	1055	1102	1109	1091
p_L		0.325	0.590	0.991	0.502	0.566
p_J		0.135	0.169	0.673	0.462	0.425
week: 18 N	10					10
Mean	998.7					1037
Median	1011					1033
IQ-Range	82.00					76.00
Min	808.0					918.0
Max	1108					1153
p_L						0.676
p_J						0.406

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics): males

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
PT(CS) (sec)						
week: 14 N	20	10	10	10	10	20
Mean	32.58	32.54	36.49	34.43	34.23	36.65
Median	32.95	33.73	35.98	35.14	33.77	36.75 a
IQ-Range	5.260	3.350	3.950	3.900	4.950	3.180
Min	21.80	23.77	32.84	25.89	29.24	28.47
Max	39.38	35.82	42.21	39.65	38.63	42.28
p_L		0.511	0.052	0.358	0.694	0.004 *
p_J		0.860	0.020	0.023	0.079	0.000 +
week: 18 N		10				9
Mean		35.01				36.71
Median		35.24				36.04
IQ-Range		6.120				5.660
Min		25.74				31.91
Max		41.11				41.79
p_L						0.593
p_J						0.462

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Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

**Hematology (statistics) : females**

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
RBC (T/L)						
week: 14 N	20	10	10	10	10	20
Mean	7.812	7.601	7.713	7.836	7.721	7.579
Median	7.900	7.550	7.595	7.805	7.830	7.545
IQ-Range	0.683	0.520	0.720	0.890	0.610	0.365
Min	7.280	7.150	7.080	7.240	7.170	7.000
Max	8.470	8.050	8.270	8.520	8.190	8.280
p <sub>L</sub>		0.207	0.711	0.465	0.759	0.036
p <sub>J</sub>		0.118	0.468	0.979	0.844	0.231
week: 18 N	10					10
Mean	7.898					7.870
Median	7.770					7.840
IQ-Range	0.530					0.310
Min	7.460					7.570
Max	8.520					8.290
p <sub>L</sub>						0.278
p <sub>J</sub>						0.910
Hb (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	9.380	9.230	9.310	9.260	9.280	9.185
Median	9.350	9.200	9.300	9.350	9.350	9.200
IQ-Range	0.575	0.600	0.600	0.300	0.300	0.400
Min	8.900	8.700	8.900	8.700	8.600	8.500
Max	10.10	9.700	9.900	9.700	9.800	9.600
p <sub>L</sub>		0.581	0.879	0.631	0.637	0.185
p <sub>J</sub>		0.356	0.492	0.471	0.572	0.163
week: 18 N	10					10
Mean	9.575					9.600
Median	9.500					9.550
IQ-Range	0.300					0.300
Min	9.300					9.400
Max	10.20					10.10
p <sub>L</sub>						0.801
p <sub>J</sub>						0.678

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics): females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Hct						
(1)						
week: 14 N	20	10	10	10	10	20
Mean	0.426	0.418	0.418	0.418	0.420	0.418
Median	0.422	0.412	0.414	0.417	0.421	0.417
IQ-Range	0.021	0.035	0.030	0.014	0.019	0.021
Min	0.409	0.397	0.396	0.401	0.393	0.392
Max	0.457	0.442	0.454	0.438	0.438	0.440
p_L		0.058	0.124	0.596	0.719	0.300
p_J		0.153	0.083	0.152	0.281	0.233
week: 18 N	10					10
Mean	0.446					0.443
Median	0.446					0.441
IQ-Range	0.021					0.011
Min	0.426					0.424
Max	0.479					0.468
p_L						0.792
p_J						0.521
MCV						
(fl)						
week: 14 N	20	10	10	10	10	20
Mean	54.57	55.05	54.22	53.48	54.39	55.14
Median	54.60	55.20	54.45	53.50	54.40	55.50
IQ-Range	2.900	2.100	2.400	3.300	2.500	1.050
Min	51.60	51.50	51.50	50.60	51.70	52.20
Max	57.80	57.60	57.20	56.90	56.50	58.20
p_L		0.701	0.807	0.254	0.861	0.175
p_J		0.468	0.799	0.194	0.314	0.519
week: 18 N	10					10
Mean	56.57					56.32
Median	56.65					56.50
IQ-Range	2.000					0.900
Min	53.10					54.70
Max	59.70					57.90
p_L						0.283
p_J						0.650

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (statistics): females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
RDW (1)						
week: 14 N	20	10	10	10	10	20
Mean	0.128	0.121	0.131	0.134	0.126	0.130
Median	0.123	0.123	0.122	0.122	0.126	0.127
IQ-Range	0.020	0.012	0.027	0.017	0.019	0.014
Min	0.112	0.112	0.113	0.112	0.113	0.113
Max	0.173	0.134	0.185	0.236	0.139	0.172
p_L		0.485	0.669	0.910	0.906	0.429
p_J		0.235	0.619	0.719	0.937	0.272
week: 18 N	10					10
Mean	0.129					0.118
Median	0.124					0.119
IQ-Range	0.018					0.006
Min	0.117					0.113
Max	0.147					0.123
p_L						0.025
p_J						0.007
MCH (fmol)						
week: 14 N	20	10	10	10	10	20
Mean	1.200	1.217	1.208	1.183	1.205	1.213
Median	1.195	1.220	1.200	1.185	1.203	1.220
IQ-Range	0.037	0.030	0.060	0.080	0.040	0.017
Min	1.130	1.140	1.140	1.110	1.140	1.130
Max	1.260	1.290	1.260	1.260	1.260	1.260
p_L		0.489	0.882	0.415	0.724	0.047
p_J		0.235	0.422	0.617	0.793	0.380
week: 18 N	10					10
Mean	1.214					1.219
Median	1.215					1.220
IQ-Range	0.060					0.020
Min	1.150					1.180
Max	1.270					1.240
p_L						0.150
p_J						0.791

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics): females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
MCHC (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	22.01	22.10	22.26	22.13	22.14	21.99
Median	21.95	22.07	22.35	22.13	22.03	21.90
IQ-Range	0.625	0.270	0.500	0.790	0.590	0.440
Min	21.59	21.66	21.47	21.50	21.72	21.50
Max	22.48	22.71	22.66	22.70	22.70	22.65
p_L		0.155	0.140	0.221	0.527	0.764
p_J		0.495	0.054	0.131	0.191	0.919
week: 18 N	10					10
Mean	21.45					21.67
Median	21.46					21.59
IQ-Range	0.520					0.500
Min	20.89					21.32
Max	22.16					22.20
p_L						0.361
p_J						0.226
HDW (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	1.525	1.508	1.582	1.568	1.428	1.586
Median	1.478	1.330	1.495	1.460	1.300	1.600
IQ-Range	0.515	0.640	0.630	0.560	0.320	0.500
Min	1.200	1.180	1.210	1.250	1.240	1.260
Max	1.970	1.950	2.110	2.060	1.920	2.020
p_L		0.661	0.894	0.701	0.483	0.579
p_J		0.660	0.750	0.568	0.895	0.522
week: 18 N	10					10
Mean	1.532					1.497
Median	1.515					1.500
IQ-Range	0.480					0.420
Min	1.210					1.190
Max	1.975					1.890
p_L						0.963
p_J						0.791

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (statistics): females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
WBC (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	7.180	7.023	7.524	5.897	6.762	6.971
Median	6.535	6.800	7.820	5.390	6.510	6.975
IQ-Range	2.600	1.920	2.260	1.980	1.790	1.510
Min	4.210	4.920	4.440	4.590	4.180	4.460
Max	16.90	9.430	11.25	8.980	8.870	10.13
p_L		0.545	0.590	0.382	0.624	0.403
p_J		0.758	0.340	0.434	0.613	0.889
week: 18 N	10					10
Mean	7.064					6.539
Median	5.955					6.400
IQ-Range	2.100					1.680
Min	4.900					5.040
Max	15.23					7.840
p_L						0.451
p_J						0.496
Neut (I)						
week: 14 N	20	10	10	10	10	20
Mean	0.132	0.126	0.143	0.162	0.131	0.128
Median	0.116	0.127	0.124	0.144	0.128	0.124
IQ-Range	0.046	0.060	0.102	0.052	0.073	0.036
Min	0.073	0.053	0.078	0.088	0.061	0.067
Max	0.376	0.199	0.238	0.282	0.225	0.270
p_L		0.654	0.172	0.170	0.644	0.979
p_J		0.792	0.476	0.082	0.250	0.799
week: 18 N	10					10
Mean	0.190					0.122
Median	0.119					0.112
IQ-Range	0.038					0.039
Min	0.097					0.085
Max	0.598					0.220
p_L						0.346
p_J						0.257





Test No.: 943127  
 Test Article: CGA 329351 tech.

Hematology (statistics): females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Lympho (1)						
week: 14 N	20	10	10	10	10	20
Mean	0.736	0.752	0.738	0.717	0.746	0.754
Median	0.751	0.754	0.746	0.726	0.748	0.759
IQ-Range	0.039	0.066	0.122	0.061	0.070	0.070
Min	0.520	0.658	0.645	0.608	0.654	0.598
Max	0.796	0.849	0.821	0.808	0.818	0.820
p_L		0.370	0.194	0.326	0.234	0.204
p_J		0.553	0.859	0.330	0.674	0.463
week: 18 N	10					10
Mean	0.684					0.760
Median	0.739					0.777
IQ-Range	0.063					0.054
Min	0.310					0.652
Max	0.821					0.816
p_L						0.248
p_J						0.096
Mono (1)						
week: 14 N	20	10	10	10	10	20
Mean	0.069	0.063	0.059	0.058	0.062	0.064
Median	0.065	0.067	0.063	0.054	0.062	0.059
IQ-Range	0.027	0.019	0.019	0.015	0.024	0.028
Min	0.040	0.043	0.044	0.045	0.044	0.045
Max	0.108	0.080	0.069	0.086	0.086	0.097
p_L		0.746	0.188	0.358	0.730	0.615
p_J		0.613	0.212	0.085	0.184	0.375
week: 18 N	10					10
Mean	0.067					0.063
Median	0.061					0.059
IQ-Range	0.041					0.019
Min	0.033					0.048
Max	0.102					0.079
p_L						0.059
p_J						0.910

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Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics): females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Luc (1)						
week: 14 N	20	10	10	10	10	20
Mean	0.043	0.040	0.040	0.042	0.041	0.037
Median	0.045	0.041	0.040	0.043	0.040	0.035
IQ-Range	0.018	0.008	0.010	0.012	0.015	0.008
Min	0.030	0.029	0.024	0.028	0.029	0.028
Max	0.064	0.051	0.052	0.054	0.055	0.057
p_L		0.066	0.226	0.392	0.608	0.094
p_J		0.455	0.366	0.604	0.631	0.040
week: 18 N	10					10
Mean	0.041					0.039
Median	0.041					0.040
IQ-Range	0.009					0.017
Min	0.031					0.028
Max	0.049					0.048
p_L						0.407
p_J						0.496
Neut (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	1.081	0.884	1.102	1.003	0.869	0.877
Median	0.765	0.785	0.875	0.895	0.830	0.805
IQ-Range	0.400	0.330	0.750	0.380	0.380	0.275
Min	0.405	0.370	0.480	0.400	0.390	0.460
Max	6.350	1.580	2.680	2.540	1.345	1.530
p_L		0.924	0.613	0.807	0.913	0.453
p_J		0.741	0.380	0.445	0.590	0.665
week: 18 N	10					10
Mean	1.714					0.777
Median	0.850					0.720
IQ-Range	0.320					0.160
Min	0.540					0.540
Max	9.105					1.340
p_L						0.237
p_J						0.571



Hematology (statistics) : females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Lympho (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	5.157	5.284	5.535	4.188	5.069	5.264
Median	4.910	5.080	5.690	3.805	4.930	5.160
IQ-Range	1.972	1.430	1.650	1.470	1.400	1.245
Min	3.200	3.530	2.930	3.440	3.220	3.280
Max	8.780	7.370	7.250	5.460	7.080	7.280
p_L		0.662	0.570	0.257	0.996	0.476
p_J		0.567	0.268	0.375	0.524	0.815
week: 18 N	10					10
Mean	4.515					4.991
Median	4.160					4.975
IQ-Range	0.920					1.770
Min	3.460					3.740
Max	7.080					6.320
p_L						0.481
p_J						0.226
Mono (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	0.498	0.446	0.443	0.337	0.414	0.452
Median	0.435	0.440	0.410	0.305	0.445	0.415
IQ-Range	0.290	0.270	0.210	0.120	0.080	0.275
Min	0.200	0.270	0.280	0.250	0.200	0.240
Max	1.045	0.620	0.770	0.570	0.610	0.850
p_L		0.937	0.507	0.107	0.250	0.781
p_J		0.775	0.684	0.038	0.171	0.430
week: 18 N	10					10
Mean	0.446					0.405
Median	0.390					0.410
IQ-Range	0.300					0.080
Min	0.260					0.300
Max	0.805					0.550
p_L						0.042
p_J						0.970

Test No.: 943127  
 Test Article: CGA 329351 tech.

Hematology (statistics): females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Luc (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	0.307	0.283	0.292	0.243	0.272	0.256
Median	0.295	0.260	0.285	0.235	0.263	0.245
IQ-Range	0.153	0.120	0.110	0.060	0.070	0.070
Min	0.140	0.200	0.180	0.180	0.160	0.150
Max	0.540	0.400	0.420	0.390	0.350	0.520
p_L		0.753	0.368	0.124	0.141	0.047
p_J		0.982	0.929	0.288	0.454	0.153
week: 18 N	10					10
Mean	0.275					0.246
Median	0.245					0.245
IQ-Range	0.050					0.040
Min	0.210					0.180
Max	0.475					0.300
p_L						0.919
p_J						0.705
Plt (G/l)						
week: 14 N	20	10	10	10	10	20
Mean	1004	1015	982.4	985.3	994.1	995.1
Median	993.5	1023	992.0	970.0	1004	1022
IQ-Range	75.50	86.00	205.0	204.0	118.0	93.75
Min	899.0	894.0	832.0	824.0	800.5	848.0
Max	1187	1124	1119	1173	1136	1173
p_L		0.763	0.133	0.191	0.889	0.670
p_J		0.644	0.789	0.545	0.718	0.829
week: 18 N	10					10
Mean	1028					964.9
Median	1027					927.5
IQ-Range	200.0					222.0
Min	764.0					743.0
Max	1396					1173
p_L						0.625
p_J						0.450

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (statistics): females

dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
PT(CS) (sec)						
week: 14 N	20	10	10	10	10	20
Mean	28.99	28.88	28.95	28.54	27.97	26.15
Median	29.11	28.64	29.17	28.57	27.92	26.40 a
IQ-Range	3.500	2.520	4.270	0.880	2.080	2.355
Min	22.84	24.59	22.84	26.27	24.41	19.86
Max	33.87	33.98	32.29	30.32	31.81	28.99
p_L		0.933	0.848	0.052	0.366	0.004 *
p_J		0.792	0.970	0.680	0.216	0.000 -
week: 18 N	9					10
Mean	27.10					27.43
Median	26.80					27.40
IQ-Range	3.040					5.500
Min	24.05					23.14
Max	30.83					31.31
p_L						0.638
p_J						0.806

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5.5. Blood chemistry (statistics)

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Gluc (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	8.365	8.098	7.678	7.672	7.610	7.815
Median	8.415	8.080	7.525	7.670	7.570	7.660
IQ-Range	0.830	1.170	1.170	0.980	1.060	1.335
Min	7.470	6.480	6.330	6.100	6.640	6.830
Max	9.390	9.360	10.04	8.890	8.510	9.740
p <sub>L</sub>		0.405	0.007 *	0.080	0.021	0.007 *
p <sub>J</sub>		0.481	0.030	0.015	0.005	0.010
week: 18 N	10					10
Mean	8.734					9.575
Median	8.710					9.645
IQ-Range	1.420					1.620
Min	7.750					7.670
Max	9.600					11.98
p <sub>L</sub>						0.054
p <sub>J</sub>						0.082
Urea (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	5.701	5.684	6.049	5.563	5.612	5.675
Median	5.855	5.685	6.155	5.530	5.700	5.780
IQ-Range	0.685	1.150	0.830	0.970	0.670	1.075
Min	4.085	4.800	4.590	4.860	4.470	4.860
Max	6.690	6.960	7.080	6.510	6.540	7.020
p <sub>L</sub>		0.703	0.142	0.662	0.868	0.663
p <sub>J</sub>		0.792	0.241	0.972	0.727	0.629
week: 18 N	10					10
Mean	5.889					5.465
Median	5.975					5.380
IQ-Range	0.300					0.240
Min	4.290					5.080
Max	6.870					6.320
p <sub>L</sub>						0.058
p <sub>J</sub>						0.019

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 168

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Creat-e (umol/l)						
week: 14 N	20	10	10	10	10	20
Mean	55.15	56.23	60.70	59.42	59.30	61.91
Median	56.05	57.35	61.65	58.70	58.10	61.40 a
IQ-Range	6.450	3.400	7.800	10.40	9.300	6.950
Min	46.70	50.00	52.10	52.30	52.90	53.50
Max	59.50	58.60	67.90	69.10	67.20	69.30
p_L		0.182	0.004 *	0.055	0.133	0.000 *
p_J		0.725	0.014	0.006 +	0.007 +	0.000 +
week: 18 N	10					10
Mean	56.82					57.05
Median	57.30					56.65
IQ-Range	5.700					2.600
Min	50.90					52.20
Max	63.10					66.80
p_L						0.638
p_J						0.791
Bili-tot (umol/l)						
week: 14 N	20	10	10	10	10	20
Mean	2.093	1.995	2.190	2.189	1.947	2.103
Median	2.070	1.950	2.190	2.190	2.070	2.190
IQ-Range	0.855	0.490	0.980	0.480	0.730	0.730
Min	1.220	1.700	1.700	1.460	1.460	1.460
Max	3.160	2.430	2.680	2.920	2.680	3.890
p_L		0.025	0.617	0.285	0.430	0.269
p_J		0.708	0.647	0.445	0.890	0.796
week: 18 N	10					10
Mean	2.016					2.264
Median	2.090					1.970
IQ-Range	0.490					0.490
Min	1.480					1.970
Max	2.460					3.200
p_L						0.629
p_J						0.427



Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Prot (g/l)						
week: 14 N	20	10	10	10	10	20
Mean	66.31	67.86	66.07	67.05	68.52	66.91
Median	66.39	66.99	65.59	66.32	68.09	67.03
IQ-Range	3.435	2.140	2.300	2.750	2.220	2.750
Min	61.58	65.00	63.75	63.69	63.39	64.50
Max	70.59	72.68	70.84	70.87	75.82	70.15
p_L		0.243	0.744	0.353	0.158	0.306
p_J		0.218	0.919	0.826	0.139	0.306
week: 18 N	10					10
Mean	68.99					67.22
Median	69.18					67.73
IQ-Range	2.370					2.620
Min	67.13					64.96
Max	71.43					69.01
p_L						0.127
p_J						0.064
Alb (g/l)						
week: 14 N	20	10	10	10	10	20
Mean	35.31	35.77	35.19	35.31	35.49	35.35
Median	35.32	35.67	35.02	35.33	35.56	35.43
IQ-Range	1.185	0.870	1.290	1.150	1.720	1.735
Min	33.30	33.95	33.71	33.88	33.28	33.40
Max	37.31	38.22	38.09	37.62	37.22	36.75
p_L		0.612	0.738	0.943	0.616	0.728
p_J		0.322	0.839	0.706	0.927	0.842
week: 18 N	10					10
Mean	36.11					36.20
Median	36.34					36.54
IQ-Range	1.460					1.380
Min	34.55					34.62
Max	37.85					37.17
p_L						0.892
p_J						0.650

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 170

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Glob (g/l)						
week: 14 N	20	10	10	10	10	20
Mean	31.00	32.09	30.88	31.74	33.03	31.56
Median	31.25	31.84	30.24	31.41	32.24	31.66
IQ-Range	3.680	1.820	1.800	2.060	1.610	1.495
Min	28.15	30.05	28.95	29.27	30.11	29.01
Max	35.22	35.47	33.53	35.06	38.60	33.70
p_L		0.252	0.411	0.418	0.110	0.087
p_J		0.159	0.721	0.429	0.050	0.184
week: 18 N	10					10
Mean	32.88					31.02
Median	33.41					30.86
IQ-Range	1.720					1.400
Min	29.88					29.73
Max	34.39					32.24
p_L						0.012
p_J						0.007
A/G (l)						
week: 14 N	20	10	10	10	10	20
Mean	1.144	1.117	1.142	1.115	1.078	1.122
Median	1.135	1.120	1.150	1.135	1.080	1.110
IQ-Range	0.100	0.060	0.100	0.080	0.070	0.075
Min	0.980	1.040	1.050	1.010	0.960	1.040
Max	1.300	1.170	1.210	1.180	1.170	1.240
p_L		0.419	0.995	0.564	0.059	0.413
p_J		0.379	0.909	0.493	0.043	0.091
week: 18 N	10					10
Mean	1.101					1.168
Median	1.090					1.165
IQ-Range	0.070					0.050
Min	1.020					1.140
Max	1.260					1.210
p_L						0.007 *
p_J						0.007 +

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Chol (mmol/l)						
week: 14	N 20	10	10	10	10	20
Mean	1.916	2.005	1.883	2.010	1.993	1.914
Median	1.888	1.920	1.905	2.015	1.975	1.905
IQ-Range	0.465	0.630	0.290	0.490	0.400	0.380
Min	1.360	1.410	1.260	1.450	1.730	1.350
Max	2.825	2.540	2.550	2.730	2.390	2.630
p_L		0.678	0.888	0.699	0.477	0.811
p_J		0.481	0.789	0.533	0.415	0.747
week: 18	N 10					10
Mean	2.250					2.086
Median	2.095					2.040
IQ-Range	0.730					0.480
Min	1.650					1.690
Max	3.270					2.800
p_L						0.715
p_J						0.496
Na+ (mmol/l)						
week: 14	N 20	10	10	10	10	20
Mean	142.6	142.4	142.9	141.9	141.7	142.0
Median	142.8	142.3	142.8	141.9	141.8	142.0
IQ-Range	1.650	0.600	0.900	1.150	2.050	2.025
Min	141.2	141.7	141.9	140.2	139.7	139.4
Max	143.9	143.3	144.8	144.0	144.8	144.6
p_L		0.025	0.486	0.370	0.173	0.262
p_J		0.468	0.647	0.243	0.028	0.019
week: 18	N 10					10
Mean	144.0					143.0
Median	144.3					143.4
IQ-Range	1.400					1.400
Min	142.1					141.2
Max	145.3					144.0
p_L						0.125
p_J						0.070

Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
K+ (mmol/l)						
week: 14	N 20	10	10	10	10	20
Mean	3.664	3.595	3.594	3.673	3.435	3.446
Median	3.615	3.590	3.630	3.695	3.385	3.415
IQ-Range	0.290	0.210	0.370	0.210	0.200	0.265
Min	3.260	3.350	3.290	3.360	3.150	3.170
Max	4.800	3.840	3.940	3.960	3.730	3.750
p_L		0.626	0.962	0.608	0.085	0.033
p_J		0.692	0.684	0.680	0.134	0.002
week: 18	N 10					10
Mean	3.586					3.477
Median	3.585					3.440
IQ-Range	0.110					0.340
Min	3.130					3.190
Max	3.970					3.800
p_L						0.222
p_J						0.406
Ca++ (mmol/l)						
week: 14	N 20	10	10	10	10	20
Mean	2.632	2.651	2.608	2.643	2.664	2.647
Median	2.635	2.640	2.600	2.640	2.665	2.655
IQ-Range	0.085	0.060	0.050	0.070	0.060	0.085
Min	2.540	2.570	2.560	2.580	2.540	2.530
Max	2.710	2.760	2.700	2.700	2.740	2.760
p_L		0.611	0.451	0.578	0.312	0.704
p_J		0.468	0.366	0.951	0.281	0.238
week: 18	N 10					10
Mean	2.668					2.612
Median	2.650					2.600
IQ-Range	0.070					0.060
Min	2.570					2.570
Max	2.760					2.670
p_L						0.113
p_J						0.038

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Test Article: CGA 329351 tech.

## Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Cl- (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	99.96	97.58	99.14	99.92	98.85	99.08
Median	99.85	97.45 a	99.30	100.0	98.70	98.95
IQ-Range	2.050	1.600	1.700	2.400	1.100	2.350
Min	97.20	96.20	97.30	97.40	96.70	96.10
Max	102.7	98.90	100.4	102.0	100.0	101.9
p_L		0.001 *	0.242	0.981	0.086	0.291
p_J		0.000 -	0.048	0.752	0.415	0.492
week: 18 N	10					10
Mean	103.7					103.7
Median	104.0					103.9
IQ-Range	1.100					0.500
Min	101.3					101.2
Max	106.0					105.2
p_L						0.548
p_J						0.821
PO4-in (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	1.645	1.691	1.715	1.780	1.818	1.772
Median	1.630	1.680	1.725	1.770	1.790 a	1.775
IQ-Range	0.150	0.180	0.340	0.150	0.220	0.265
Min	1.430	1.520	1.430	1.670	1.630	1.430
Max	1.900	1.870	1.940	1.930	2.040	2.160
p_L		0.587	0.093	0.016	0.008 *	0.026
p_J		0.333	0.217	0.011	0.001 +	0.001 +
week: 18 N	10					10
Mean	1.562					1.472
Median	1.560					1.440
IQ-Range	0.130					0.190
Min	1.370					1.270
Max	1.780					1.680
p_L						0.255
p_J						0.186

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
ASAT (GOT) (U/l)						
week: 14 N	20	10	10	10	10	20
Mean	59.66	66.06	61.09	70.35	75.41	59.62
Median	57.50	64.00	57.50	64.00	61.20	57.80
IQ-Range	11.55	11.20	8.700	21.10	14.30	10.90
Min	44.10	52.80	50.30	42.90	47.80	44.70
Max	95.10	106.3	82.60	121.2	233.3	85.10
p_L		0.364	0.777	0.237	0.737	0.961
p_J		0.166	0.602	0.414	0.594	0.792
week: 18 N	10					10
Mean	60.95					62.75
Median	60.55					57.75
IQ-Range	12.40					13.70
Min	48.50					54.70
Max	76.40					83.30
p_L						0.846
p_J						0.623
ALAT (GPT) (U/l)						
week: 14 N	20	10	10	10	10	20
Mean	35.99	41.98	34.20	39.84	48.98	35.11
Median	35.55	35.90	34.10	37.80	34.80	32.60
IQ-Range	8.900	14.00	3.700	12.60	6.700	6.650
Min	25.90	28.10	29.60	24.40	22.20	20.00
Max	47.40	91.80	39.20	80.70	181.8	60.70
p_L		0.720	0.119	0.662	0.987	0.710
p_J		0.644	0.760	0.930	0.885	0.418
week: 18 N	10					10
Mean	37.61					34.29
Median	36.65					32.20
IQ-Range	11.80					12.60
Min	28.10					23.70
Max	47.40					48.90
p_L						0.302
p_J						0.212

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
ALP (U/l)						
week: 14 N	20	10	10	10	10	20
Mean	80.82	87.55	83.16	77.06	71.83	73.58
Median	80.85	83.25	77.60	77.15	71.40	69.30
IQ-Range	12.80	25.90	36.90	20.00	13.20	22.40
Min	54.40	60.00	49.85	62.50	58.30	44.20
Max	122.0	119.7	130.1	93.80	85.60	96.10
p_L		0.608	0.462	0.798	0.157	0.290
p_J		0.416	0.859	0.648	0.122	0.056
week: 18 N	10					10
Mean	76.21					79.88
Median	73.70					81.30
IQ-Range	18.60					14.90
Min	56.10					63.90
Max	94.90					90.10
p_L						0.430
p_J						0.650
GGT (U/l)						
week: 14 N	20	10	10	10	10	20
Mean	0.000	0.000	0.000	0.000	0.000	0.000
Median	0.000	0.000	0.000	0.000	0.000	0.000
IQ-Range	0.000	0.000	0.000	0.000	0.000	0.000
Min	0.000	0.000	0.000	0.000	0.000	0.000
Max	0.000	0.000	0.000	0.000	0.000	0.000
p_L		1.000	1.000	1.000	1.000	1.000
p_J		1.000	1.000	1.000	1.000	1.000
week: 18 N	10					10
Mean	0.250					0.000
Median	0.000					0.000
IQ-Range	0.000					0.000
Min	0.000					0.000
Max	2.500					0.000
p_L						0.368
p_J						0.705

Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01

a/b ind. of diff. in loc./disp.

JONCKHEERE: +- if p<sub>J</sub> < 0.01

**Blood chemistry (statistics): females**

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
<b>Gluc (mmol/l)</b>						
week: 14	N 20	10	10	10	10	20
Mean	7.731	7.883	7.404	7.643	7.699	7.604
Median	7.655	7.700	7.455	7.630	7.980	7.500
IQ-Range	0.750	0.780	0.830	0.590	0.870	1.175
Min	6.530	6.980	5.920	6.670	6.560	6.120
Max	9.120	9.390	8.110	8.880	8.370	8.960
p <sub>L</sub>		0.921	0.590	0.865	0.798	0.340
p <sub>J</sub>		0.692	0.445	0.482	0.859	0.668
week: 18	N 10					10
Mean	7.709					8.014
Median	7.645					8.020
IQ-Range	1.350					1.250
Min	6.890					6.080
Max	8.970					9.190
p <sub>L</sub>						0.589
p <sub>J</sub>						0.326
<b>Urea (mmol/l)</b>						
week: 14	N 20	10	10	10	10	20
Mean	7.409	6.856	6.711	6.980	7.226	6.997
Median	6.870	6.765	6.720	6.945	7.085	7.080
IQ-Range	1.110	1.670	1.280	1.270	2.010	1.550
Min	5.680	5.870	5.350	5.320	5.260	5.260
Max	16.83	8.030	8.090	8.270	9.120	8.790
p <sub>L</sub>		0.789	0.709	0.998	0.317	0.603
p <sub>J</sub>		0.567	0.366	0.752	0.828	0.728
week: 18	N 10					10
Mean	7.852					7.102
Median	7.065					7.035
IQ-Range	0.700					0.950
Min	6.110					5.870
Max	15.58					8.880
p <sub>L</sub>						0.603
p <sub>J</sub>						0.850



Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Creat-e (umol/l)						
week: 14 N	20	10	10	10	10	20
Mean	57.44	58.17	58.19	57.35	58.25	56.93
Median	56.80	57.70	57.95	56.60	58.10	57.65
IQ-Range	8.650	4.200	7.600	6.100	13.70	6.250
Min	49.70	49.20	50.00	48.90	49.20	50.00
Max	70.20	68.50	70.50	67.20	70.50	63.40
p_L		0.433	0.750	0.848	0.462	0.522
p_J		0.613	0.610	0.861	0.787	0.949
week: 18 N	10					10
Mean	62.35					60.40
Median	61.80					61.95
IQ-Range	2.000					7.500
Min	53.10					54.40
Max	75.00					67.50
p_L						0.991
p_J						0.910
Bili-tot (umol/l)						
week: 14 N	20	10	10	10	10	20
Mean	3.286	3.037	2.718	2.577	2.979	2.600
Median	3.070	2.955	2.600	2.600 a	3.190	2.600 a
IQ-Range	1.060	0.710	0.470	0.480	0.710	0.825
Min	2.600	2.360	2.130	1.890	2.130	1.660
Max	4.490	4.850	3.310	3.550	3.550	3.310
p_L		0.392	0.036	0.007 *	0.403	0.004 *
p_J		0.194	0.013	0.001 -	0.023	0.001 -
week: 18 N	10					10
Mean	2.679					2.360
Median	2.700					2.460
IQ-Range	0.990					0.980
Min	1.720					1.720
Max	3.200					3.200
p_L						0.405
p_J						0.186

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Prot (g/l)						
week: 14 N	20	10	10	10	10	20
Mean	66.44	66.12	65.99	66.32	69.28	67.82
Median	66.21	65.76	65.92	66.29	69.93	67.59
IQ-Range	1.660	3.260	4.620	4.410	4.760	2.955
Min	61.91	63.52	63.17	62.38	65.36	64.81
Max	72.15	69.44	70.01	71.08	73.27	70.31
p_L		0.341	0.212	0.283	0.015	0.041
p_J		0.428	0.314	0.556	0.132	0.015
week: 18 N	10					10
Mean	70.21					69.29
Median	70.14					69.07
IQ-Range	2.560					3.690
Min	66.82					64.65
Max	78.65					73.23
p_L						0.795
p_J						0.762
Alb (g/l)						
week: 14 N	20	10	10	10	10	20
Mean	36.72	36.65	36.77	36.59	38.03	37.20
Median	36.57	36.73	36.67	36.21	38.13	37.23
IQ-Range	1.765	2.020	1.950	2.690	2.260	1.370
Min	34.19	34.59	35.44	34.55	36.16	35.41
Max	39.40	38.82	38.77	38.71	39.83	38.78
p_L		0.995	0.847	0.501	0.064	0.301
p_J		0.965	0.909	0.854	0.110	0.068
week: 18 N	10					10
Mean	37.50					37.43
Median	37.52					37.61
IQ-Range	0.870					0.750
Min	36.01					35.55
Max	38.45					39.02
p_L						0.989
p_J						1.000

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Glob (g/l)						
week: 14 N	20	10	10	10	10	20
Mean	29.72	29.47	29.23	29.74	31.25	30.62
Median	29.64	29.26	28.76	29.70	31.13	30.62
IQ-Range	1.230	1.430	2.440	2.230	1.930	2.225
Min	26.93	28.17	27.55	27.83	28.34	28.47
Max	33.30	30.62	31.87	32.37	33.49	33.59
p_L		0.907	0.424	0.802	0.030	0.114
p_J		0.792	0.321	0.654	0.099	0.008 +
week: 18 N	10					10
Mean	32.70					31.86
Median	32.35					32.07
IQ-Range	2.810					2.520
Min	29.72					28.39
Max	40.94					34.87
p_L						0.944
p_J						0.762
A/G (1)						
week: 14 N	20	10	10	10	10	20
Mean	1.239	1.244	1.260	1.232	1.219	1.216
Median	1.235	1.250	1.260	1.240	1.220	1.225
IQ-Range	0.080	0.070	0.050	0.070	0.050	0.070
Min	1.030	1.180	1.150	1.150	1.140	1.090
Max	1.350	1.310	1.330	1.280	1.310	1.360
p_L		0.482	0.200	0.536	0.452	0.416
p_J		0.947	0.408	0.937	0.239	0.034
week: 18 N	10					10
Mean	1.157					1.179
Median	1.160					1.185
IQ-Range	0.130					0.090
Min	0.920					1.100
Max	1.260					1.280
p_L						0.972
p_J						0.821

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 180

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Chol (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	2.104	2.148	2.349	2.224	2.508	2.578
Median	2.120	2.210	2.130	2.315	2.400	2.530 a
IQ-Range	0.640	0.580	0.650	0.450	0.510	0.370
Min	1.490	1.590	1.470	1.540	1.930	2.160
Max	2.760	2.830	3.590	2.650	3.390	3.405
p_L		0.940	0.814	0.605	0.065	0.001 *
p_J		0.725	0.460	0.276	0.031	0.000 +
week: 18 N	10					10
Mean	2.254					2.338
Median	2.155					2.325
IQ-Range	0.160					0.220
Min	1.880					1.660
Max	3.340					3.110
p_L						0.468
p_J						0.241
Na+ (mmol/l)						
week: 14 N	20	10	10	10	10	20
Mean	143.3	143.5	143.1	143.2	143.2	143.1
Median	143.5	143.6	143.2	143.4	143.1	143.0
IQ-Range	0.900	1.000	1.400	0.600	1.400	1.050
Min	139.9	141.9	142.2	140.9	142.1	141.5
Max	145.5	144.5	144.1	144.4	144.9	145.5
p_L		0.872	0.641	0.553	0.671	0.406
p_J		0.676	0.468	0.389	0.290	0.097
week: 18 N	10					10
Mean	144.0					144.0
Median	143.4					144.0
IQ-Range	1.400					1.300
Min	141.2					142.6
Max	150.1					145.3
p_L						0.403
p_J						0.326

Test No.: 943127  
 Test Article: CGA 329351 tech.

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
K+						
(mmol/l)						
week: 14	N 20	10	10	10	10	20
Mean	2.810	2.857	2.911	2.853	2.739	2.806
Median	2.830	2.820	2.940	2.830	2.760	2.840
IQ-Range	0.265	0.310	0.180	0.120	0.340	0.320
Min	2.317	2.530	2.600	2.590	2.143	2.310
Max	3.140	3.410	3.140	3.280	3.150	3.170
p_L		0.793	0.370	0.380	0.627	0.863
p_J		0.878	0.247	0.545	0.793	0.668
week: 18	N 10					10
Mean	3.123					2.952
Median	3.115					2.980
IQ-Range	0.590					0.150
Min	2.720					2.575
Max	3.470					3.250
p_L						0.239
p_J						0.212
Ca++						
(mmol/l)						
week: 14	N 20	10	10	10	10	20
Mean	2.576	2.540	2.532	2.544	2.577	2.568
Median	2.580	2.535	2.520	2.530	2.595	2.570
IQ-Range	0.080	0.050	0.080	0.080	0.050	0.075
Min	2.480	2.480	2.460	2.510	2.470	2.480
Max	2.680	2.590	2.590	2.590	2.630	2.680
p_L		0.098	0.113	0.160	0.840	0.824
p_J		0.068	0.017	0.037	0.636	0.812
week: 18	N 10					10
Mean	2.590					2.565
Median	2.590					2.575
IQ-Range	0.060					0.070
Min	2.480					2.490
Max	2.760					2.600
p_L						0.222
p_J						0.385

Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>Cl-</b> (mmol/l)						
week: 14	N 20	10	10	10	10	20
Mean	100.3	100.8	99.81	101.5	99.57	99.32
Median	99.90	100.9	99.70	101.0	99.80	99.60
IQ-Range	1.850	1.400	1.500	3.200	3.100	1.700
Min	97.10	98.85	98.20	98.20	97.50	97.00
Max	103.8	102.0	102.4	109.4	101.4	101.1
p_L		0.223	0.646	0.516	0.754	0.192
p_J		0.244	0.628	0.833	0.486	0.035
week: 18	N 10					10
Mean	105.8					106.3
Median	105.1					106.2
IQ-Range	1.900					1.700
Min	102.4					104.3
Max	112.8					108.7
p_L						0.280
p_J						0.212
<b>PO4-in</b> (mmol/l)						
week: 14	N 20	10	10	10	10	20
Mean	1.411	1.436	1.461	1.382	1.436	1.392
Median	1.405	1.415	1.420	1.300	1.380	1.390
IQ-Range	0.235	0.300	0.240	0.350	0.320	0.310
Min	1.040	1.070	1.230	1.110	1.090	1.110
Max	2.140	1.830	1.660	1.710	1.750	1.700
p_L		0.931	0.609	0.375	0.720	0.948
p_J		0.708	0.373	0.965	0.767	0.845
week: 18	N 10					10
Mean	1.312					1.205
Median	1.305					1.245
IQ-Range	0.250					0.350
Min	1.110					0.970
Max	1.520					1.610
p_L						0.288
p_J						0.199

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
ASAT (GOT) (U/l)						
week: 14 N	20	10	10	10	10	20
Mean	56.21	55.11	55.55	61.36	55.78	53.50
Median	55.30	55.60	51.90	57.75	52.80	51.85
IQ-Range	13.35	11.20	9.400	21.80	11.80	10.85
Min	41.00	44.70	42.30	39.80	44.70	42.30
Max	80.20	65.90	93.20	127.1	70.80	75.20
p_L		0.869	0.791	0.139	0.985	0.734
p_J		1.000	0.558	0.765	0.885	0.463
week: 18 N	10					10
Mean	78.81					52.45
Median	60.00					52.80
IQ-Range	13.60					10.50
Min	46.00					42.30
Max	246.1					60.30
p_L						0.068
p_J						0.031
ALAT (GPT) (U/l)						
week: 14 N	20	10	10	10	10	20
Mean	32.43	30.37	28.51	34.05	27.62	26.00
Median	29.60	30.00	26.30	31.10	27.05	23.70 a
IQ-Range	8.900	8.100	8.200	7.400	7.400	5.850
Min	20.70	21.50	20.00	17.00	19.30	18.50
Max	58.50	41.50	40.00	86.65	37.00	40.70
p_L		0.925	0.197	0.903	0.191	0.007 *
p_J		0.725	0.185	0.389	0.146	0.002 -
week: 18 N	10					10
Mean	36.73					22.38
Median	26.70					23.35
IQ-Range	14.80					6.600
Min	19.30					14.10
Max	121.4					28.10
p_L						0.123
p_J						0.064

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
ALP (U/l)						
week: 14 N	20	10	10	10	10	20
Mean	48.08	47.26	47.08	48.24	38.41	43.33
Median	44.80	45.65	44.10	41.70	38.70	40.95
IQ-Range	20.05	13.80	16.00	20.80	15.20	11.85
Min	31.80	38.30	30.70	34.60	25.80	30.40
Max	68.20	62.00	71.00	71.80	50.10	77.70
p_L		0.675	0.926	0.962	0.112	0.400
p_J		0.930	0.829	0.888	0.115	0.051
week: 18 N	10					10
Mean	47.22					46.05
Median	43.25					40.70
IQ-Range	16.10					13.00
Min	30.15					34.90
Max	79.40					91.00
p_L						0.823
p_J						0.545
GGT (U/l)						
week: 14 N	20	10	10	10	10	20
Mean	0.208	0.000	0.000	0.000	0.000	0.000
Median	0.000	0.000	0.000	0.000	0.000	0.000
IQ-Range	0.000	0.000	0.000	0.000	0.000	0.000
Min	0.000	0.000	0.000	0.000	0.000	0.000
Max	4.150	0.000	0.000	0.000	0.000	0.000
p_L		0.607	0.607	0.607	0.607	0.368
p_J		0.826	0.799	0.792	0.793	0.799
week: 18 N	10					10
Mean	1.193					0.000
Median	0.000					0.000
IQ-Range	0.000					0.000
Min	0.000					0.000
Max	7.433					0.000
p_L						0.123
p_J						0.450



5.6. Urine analysis (statistics)

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

Urine analysis (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Volume (ml)						
week: 14 N	20	10	10	10	10	20
Mean	5.925	6.960	5.860	6.990	7.210	6.710
Median	5.500	6.550	6.300	7.250	7.250	6.350
IQ-Range	2.800	3.800	2.800	3.100	1.800	2.900
Min	2.200	4.400	3.100	3.700	5.200	4.100
Max	9.800	10.40	7.800	10.80	10.30	11.00
p <sub>L</sub>		0.468	0.987	0.502	0.131	0.386
p <sub>J</sub>		0.244	0.656	0.272	0.075	0.160
week: 18 N	10					10
Mean	6.610					7.000
Median	6.550					7.750
IQ-Range	1.700					2.500
Min	3.900					3.600
Max	8.500					9.200
p <sub>L</sub>						0.195
p <sub>J</sub>						0.496
Rel dens (1)						
week: 14 N	20	10	10	10	10	20
Mean	1.047	1.043	1.043	1.041	1.045	1.043
Median	1.048	1.042	1.042	1.039	1.045	1.045
IQ-Range	0.011	0.017	0.011	0.011	0.009	0.009
Min	1.036	1.032	1.032	1.032	1.031	1.031
Max	1.059	1.054	1.051	1.051	1.052	1.054
p <sub>L</sub>		0.427	0.483	0.138	0.511	0.170
p <sub>J</sub>		0.235	0.150	0.034	0.180	0.300
week: 18 N	10					10
Mean	1.038					1.040
Median	1.038					1.040
IQ-Range	0.012					0.013
Min	1.030					1.029
Max	1.048					1.048
p <sub>L</sub>						0.769
p <sub>J</sub>						0.473

Test No.: 943127

Test Article: CGA 329351 tech.

Urine analysis (statistics) : males

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
pH						
(1)						
week: 14	N 20	10	10	10	10	20
Mean	6.450	6.500	6.600	6.900	6.750	6.700
Median	6.500	6.500	6.500	6.750	7.000	6.500
IQ-Range	0.250	0.000	0.500	0.500	0.500	0.500
Min	6.000	6.000	6.000	6.000	6.000	6.000
Max	7.000	7.000	7.000	8.500	7.000	8.500
p_L		0.922	0.484	0.068	0.039	0.230
p_J		0.725	0.308	0.049	0.012	0.069
week: 18	N 10					10
Mean	6.800					7.025
Median	6.750					7.000
IQ-Range	0.500					1.000
Min	6.000					6.000
Max	7.500					8.250
p_L						0.678
p_J						0.545

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Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

**Urine analysis (statistics): females**

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
Volume (ml)						
week: 14 N	20	10	10	10	10	20
Mean	5.265	3.630	5.790	5.130	4.160	5.700
Median	4.450	3.550	4.750	5.350	4.900	5.450
IQ-Range	2.700	2.400	2.900	3.000	2.500	3.850
Min	2.200	1.400	3.400	2.100	1.000	2.000
Max	13.40	6.200	10.40	8.200	6.000	9.800
p <sub>L</sub>		0.096	0.514	0.878	0.755	0.544
p <sub>J</sub>		0.053	0.869	0.623	0.937	0.279
week: 18 N	10					10
Mean	5.690					5.040
Median	4.900					5.000
IQ-Range	2.400					2.000
Min	3.200					3.300
Max	11.90					7.200
p <sub>L</sub>						0.963
p <sub>J</sub>						0.791
Rel dens (1)						
week: 14 N	20	10	10	10	10	20
Mean	1.039	1.047	1.035	1.039	1.043	1.034
Median	1.038	1.047	1.037	1.034	1.041	1.033
IQ-Range	0.007	0.016	0.006	0.011	0.007	0.013
Min	1.019	1.028	1.024	1.029	1.032	1.022
Max	1.074	1.070	1.046	1.061	1.066	1.056
p <sub>L</sub>		0.045	0.377	0.151	0.615	0.090
p <sub>J</sub>		0.033	0.693	0.434	0.974	0.064
week: 18 N	10					10
Mean	1.033					1.033
Median	1.034					1.033
IQ-Range	0.010					0.008
Min	1.016					1.027
Max	1.042					1.048
p <sub>L</sub>						0.596
p <sub>J</sub>						0.623

Urine analysis (statistics) : females

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
pH (1)						
week: 14	N 20	10	10	10	10	20
Mean	6.575	6.350	6.750	6.350	6.400	6.800
Median	6.500	6.000	6.750	6.000	6.500	6.500
IQ-Range	0.250	0.500	0.500	0.500	0.500	0.500
Min	6.000	6.000	6.000	6.000	6.000	6.000
Max	9.000	7.500	7.500	7.500	7.000	9.000
p_L		0.116	0.232	0.116	0.888	0.473
p_J		0.235	0.575	0.642	0.636	0.344
week: 18	N 10					10
Mean	6.700					6.650
Median	6.500					6.500
IQ-Range	0.000					0.500
Min	6.000					6.500
Max	8.500					7.000
p_L						0.691
p_J						0.597

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5.7. Organ weights (statistics)

5.7.1. Organ weights (statistics): 1. sacrifice

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

Organ weights (statistics): males week 14

Dose (ppm)		group 1	group 2	group 3	group 4	group 5	group 6
		0	25	50	250	625	1250
Body (g)	N	10	10	10	10	10	10
	Mean	454.5	485.1	458.8	479.7	501.7	473.9
	Median	451.3	476.9	440.4	495.3	506.0	477.3
	IQ-Range	57.83	27.83	75.64	59.50	36.39	55.10
	Min	398.4	388.2	411.3	381.1	446.2	367.0
	Max	495.3	607.8	547.7	544.6	556.4	532.4
	p <sub>L</sub>		0.526	0.748	0.054	0.017	0.289
	p <sub>J</sub>		0.257	0.939	0.299	0.020	0.072
	Heart (g)	N	10	10	10	10	10
Mean		1.383	1.414	1.326	1.454	1.436	1.416
Median		1.309	1.390	1.305	1.496	1.398	1.450
IQ-Range		0.277	0.251	0.217	0.265	0.162	0.202
Min		1.218	1.130	1.171	1.212	1.288	1.192
Max		1.696	1.811	1.579	1.660	1.642	1.597
p <sub>L</sub>			0.833	0.758	0.655	0.109	0.625
p <sub>J</sub>			0.545	0.594	0.426	0.194	0.216
Liver (g)		N	10	10	10	10	10
	Mean	18.35	19.44	16.50	19.54	20.33	18.69
	Median	18.18	19.10	17.02	19.46	20.29	19.19
	IQ-Range	2.571	4.147	3.597	2.395	2.378	1.999
	Min	15.69	15.26	13.25	15.51	17.13	11.52
	Max	22.35	24.10	21.31	23.23	24.62	21.84
	p <sub>L</sub>		0.531	0.251	0.460	0.109	0.551
	p <sub>J</sub>		0.406	0.138	0.772	0.094	0.158

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Test No.: 943127

Test Article: CGA 329351 tech.

Organ weights (statistics): males week 14

Dose (ppm)		group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>Kidney (both)</b>							
(g)	N	10	10	10	10	10	10
	Mean	2.896	3.108	2.857	2.979	3.185	3.070
	Median	2.814	3.117	2.876	2.920	3.230	3.095
	IQ-Range	0.302	0.673	0.229	0.568	0.311	0.383
	Min	2.611	2.537	2.433	2.456	2.768	2.702
	Max	3.302	3.719	3.322	3.384	3.770	3.395
	p_L		0.166	0.899	0.718	0.090	0.248
	p_J		0.257	0.820	0.828	0.124	0.090
<b>Adrenal (both)</b>							
(mg)	N	10	10	10	10	10	10
	Mean	70.38	77.81	70.71	74.49	74.98	72.21
	Median	72.30	77.70	68.75	69.80	75.15	70.75
	IQ-Range	18.90	16.60	22.00	24.80	10.50	13.70
	Min	56.00	55.50	55.40	56.30	65.30	56.90
	Max	96.10	97.20	88.10	90.30	84.00	89.00
	p_L		0.394	0.899	0.902	0.289	0.739
	p_J		0.257	0.879	0.904	0.614	0.887
<b>Thymus</b>							
(mg)	N	10	10	10	10	10	10
	Mean	544.5	491.6	452.8	512.3	497.9	443.7
	Median	555.6	535.5	433.8	470.7	495.9	472.5
	IQ-Range	80.90	160.7	181.0	247.9	103.3	151.8
	Min	419.8	276.0	313.5	289.6	366.3	261.8
	Max	699.6	616.7	591.6	838.6	704.7	566.2
	p_L		0.652	0.111	0.109	0.271	0.125
	p_J		0.597	0.087	0.228	0.281	0.105
<b>Testis (both)</b>							
(g)	N	10	10	10	10	10	10
	Mean	3.881	3.874	3.625	4.052	3.994	3.694
	Median	4.056	3.639	3.684	4.063	4.068	3.736
	IQ-Range	0.754	0.803	0.327	0.315	0.401	0.422
	Min	3.336	3.323	2.221	3.537	3.560	2.906
	Max	4.307	4.990	3.975	4.485	4.503	4.222
	p_L		0.811	0.027	0.474	0.708	0.230
	p_J		0.821	0.494	0.334	0.146	0.876
<b>Spleen</b>							
(g)	N	10	10	10	10	10	10
	Mean	0.782	0.800	0.727	0.833	0.785	0.778
	Median	0.771	0.763	0.718	0.855	0.817	0.765
	IQ-Range	0.103	0.130	0.098	0.067	0.155	0.121
	Min	0.688	0.639	0.642	0.701	0.652	0.634
	Max	0.881	1.126	0.863	0.920	0.960	0.955
	p_L		0.741	0.251	0.288	0.316	0.811
	p_J		0.880	0.148	0.398	0.538	0.736

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

Organ weights (statistics): females week 14

Dose (ppm)		group 1	group 2	group 3	group 4	group 5	group 6
		0	25	50	250	625	1250
Body (g)	N	10	10	10	10	10	10
	Mean	277.3	287.3	285.5	291.7	290.3	268.0
	Median	281.2	281.3	289.7	278.6	299.1	265.7
	IQ-Range	32.74	35.36	41.53	47.09	65.58	38.77
	Min	232.6	257.4	244.0	255.9	243.4	216.6
	Max	301.2	334.2	340.1	360.9	327.2	308.4
	p <sub>L</sub> p <sub>J</sub>		0.655 0.364	0.829 0.790	0.758 0.629	0.095 0.538	0.617 0.543
Heart (g)	N	10	10	10	10	10	10
	Mean	0.946	0.963	0.927	0.956	0.966	0.930
	Median	0.951	0.961	0.914	0.955	0.993	0.919
	IQ-Range	0.074	0.076	0.108	0.135	0.186	0.170
	Min	0.831	0.892	0.798	0.789	0.827	0.699
	Max	1.037	1.025	1.089	1.120	1.100	1.132
	p <sub>L</sub> p <sub>J</sub>		0.823 0.545	0.403 0.470	0.389 0.847	0.165 0.632	0.312 0.938
Liver (g)	N	10	10	10	10	10	10
	Mean	10.22	10.30	10.26	11.16	11.37	10.41
	Median	10.56	10.53	9.765	10.84	11.08	10.37
	IQ-Range	1.892	1.010	2.637	2.917	1.399	1.414
	Min	8.404	9.311	8.753	9.151	9.753	8.313
	Max	12.56	10.84	12.38	14.87	12.99	12.61
	p <sub>L</sub> p <sub>J</sub>		0.625 0.545	0.944 0.820	0.395 0.347	0.035 0.014	0.891 0.123
Kidney (both) (g)	N	10	10	10	10	10	10
	Mean	1.927	2.094	1.997	2.037	2.171	2.004
	Median	1.926	2.068	1.986	1.981	2.222	2.012
	IQ-Range	0.285	0.293	0.186	0.396	0.434	0.302
	Min	1.618	1.794	1.810	1.740	1.769	1.697
	Max	2.295	2.553	2.263	2.479	2.482	2.482
	p <sub>L</sub> p <sub>J</sub>		0.239 0.131	0.278 0.494	0.463 0.579	0.075 0.101	0.700 0.325

## 3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 192

Test No.: 943127

Test Article: CGA 329351 tech.

## Organ weights (statistics): females week 14

Dose (ppm)		group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Adrenal (both) (mg)	N	10	10	10	10	10	10
	Mean	86.36	92.81	84.91	90.73	93.58	83.99
	Median	84.10	92.45	83.80	91.60	95.55	82.30
	IQ-Range	16.90	10.50	12.30	24.90	19.50	18.30
	Min	75.30	74.70	76.20	71.30	76.00	70.20
	Max	101.6	112.2	101.7	107.5	106.0	107.3
	p_L		0.394	0.561	0.530	0.304	0.473
	p_J		0.199	0.704	0.754	0.274	0.861
Thymus (mg)	N	10	10	10	10	10	10
	Mean	354.4	351.3	345.4	305.4	375.2	340.5
	Median	328.0	385.1	342.6	309.0	376.8	320.8
	IQ-Range	134.3	195.7	66.10	103.7	65.80	115.2
	Min	244.3	235.6	242.4	222.7	291.3	238.4
	Max	561.0	461.2	439.8	389.1	482.0	462.4
	p_L		0.316	0.811	0.676	0.351	0.892
	p_J		1.000	0.909	0.237	0.864	0.943
Ovary (both) (mg)	N	10	10	10	10	10	10
	Mean	157.8	165.0	164.1	169.5	165.5	152.3
	Median	161.6	166.8	167.5	166.7	152.8	144.6
	IQ-Range	42.80	11.60	26.90	55.10	45.80	31.40
	Min	119.1	130.1	131.6	129.4	134.1	119.7
	Max	205.9	192.2	202.7	218.0	213.8	214.6
	p_L		0.275	0.230	0.513	0.750	0.530
	p_J		0.597	0.704	0.484	0.681	0.509
Spleen (g)	N	10	10	10	10	10	10
	Mean	0.532	0.537	0.587	0.570	0.559	0.558
	Median	0.518	0.542	0.588	0.559	0.552	0.547
	IQ-Range	0.067	0.041	0.107	0.112	0.178	0.074
	Min	0.451	0.463	0.445	0.449	0.420	0.465
	Max	0.630	0.605	0.782	0.733	0.685	0.673
	p_L		0.758	0.239	0.351	0.312	0.545
	p_J		0.496	0.074	0.135	0.281	0.351



5.7.2. Organ weights (statistics): 2. sacrifice (recovery)

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.

Organ weights (statistics): males week 18

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
Body (g)	N	10				10
	Mean	522.3				505.9
	Median	527.2				526.6
	IQ-Range	71.10				95.80
	Min	432.3				412.4
	Max	605.0				564.5
	p <sub>L</sub>					0.944
Heart (g)	N	10				10
	Mean	1.531				1.460
	Median	1.561				1.518
	IQ-Range	0.140				0.280
	Min	1.276				1.048
	Max	1.661				1.646
	p <sub>L</sub>					0.496
Liver (g)	N	10				10
	Mean	19.26				19.43
	Median	18.60				19.44
	IQ-Range	2.955				4.717
	Min	15.43				15.08
	Max	24.41				26.55
	p <sub>L</sub>					0.986
Kidney (both) (g)	N	10				10
	Mean	3.174				3.137
	Median	3.137				3.184
	IQ-Range	0.234				0.512
	Min	2.895				2.372
	Max	3.766				3.873
	p <sub>L</sub>					0.653

Test No.: 943127

Test Article: CGA 329351 tech.

Organ weights (statistics): males week 18

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>Adrenal (both)</b>						
(mg) N	10					10
Mean	77.77					65.87
Median	76.15					62.70
IQ-Range	22.60					13.70
Min	48.50					50.30
Max	126.7					93.60
p_L						0.297
<b>Thymus</b>						
(mg) N	10					10
Mean	530.7					464.0
Median	531.3					499.6
IQ-Range	171.2					272.0
Min	324.4					280.1
Max	748.3					640.1
p_L						0.380
<b>Testis (both)</b>						
(g) N	10					10
Mean	3.792					4.047
Median	3.808					4.005
IQ-Range	0.327					0.367
Min	2.705					3.573
Max	4.201					4.619
p_L						0.545
<b>Spleen</b>						
(g) N	10					10
Mean	0.772					0.817
Median	0.770					0.774
IQ-Range	0.165					0.106
Min	0.622					0.591
Max	0.917					1.234
p_L						0.774

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Test No.: 943127

Test Article: CGA 329351 tech.

Statistical tests and flags used:

LEPAGE: \* if p\_L &lt; 0.01

a/b ind. of diff. in loc./disp.

**Organ weights (statistics): females week 18**

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
<b>Body (g)</b>						10
N	10					309.0
Mean	305.2					312.8
Median	306.3					37.84
IQ-Range	20.10					254.1
Min	260.2					339.2
Max	324.7					0.046
p_L						
<b>Heart (g)</b>						10
N	10					1.006
Mean	1.015					1.021
Median	1.022					0.108
IQ-Range	0.070					0.781
Min	0.932					1.103
Max	1.147					0.861
p_L						
<b>Liver (g)</b>						10
N	10					10.89
Mean	10.27					10.69
Median	10.05					2.588
IQ-Range	1.187					8.683
Min	9.204					13.23
Max	11.81					0.377
p_L						
<b>Kidney (both) (g)</b>						10
N	10					2.066
Mean	2.180					1.998
Median	2.021					0.369
IQ-Range	0.364					1.757
Min	1.838					2.378
Max	3.380					0.569
p_L						
<b>Adrenal (both) (mg)</b>						10
N	10					87.84
Mean	94.03					83.60
Median	95.65					12.50
IQ-Range	18.80					71.60
Min	68.40					115.3
Max	111.9					0.638
p_L						

Organ weights (statistics): females week 18

Dose (ppm)		group 1	group 2	group 3	group 4	group 5	group 6
		0	25	50	250	625	1250
Thymus (mg)	N	10					10
	Mean	277.1					313.1
	Median	221.4					303.0
	IQ-Range	154.0					107.5
	Min	124.8					210.8
	Max	490.8					419.6
	p_L						0.060
Ovary (both) (mg)	N	10					10
	Mean	170.6					170.1
	Median	167.5					158.0
	IQ-Range	41.10					62.60
	Min	144.0					135.7
	Max	207.0					237.4
	p_L						0.530
Spleen (g)	N	10					10
	Mean	0.558					0.577
	Median	0.536					0.560
	IQ-Range	0.093					0.161
	Min	0.464					0.445
	Max	0.755					0.693
	p_L						0.869

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5.7.3. Organ to body weight ratios (statistics):  
 1. sacrifice

Statistical tests and flags used:

LEPAGE: \* if  $p_L < 0.01$   
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if  $p_J < 0.01$

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

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
<b>Heart (o/oo)</b>						
N	10	10	10	10	10	10
Mean	3.041	2.915	2.896	3.037	2.865	3.000
Median	3.044	2.900	2.901	3.073	2.870	2.966
IQ-Range	0.286	0.180	0.122	0.185	0.367	0.478
Min	2.675	2.741	2.572	2.895	2.648	2.714
Max	3.426	3.223	3.291	3.225	3.154	3.410
p <sub>L</sub>		0.252	0.079	0.554	0.211	0.859
p <sub>J</sub>		0.257	0.183	0.612	0.549	0.887
<b>Liver (o/oo)</b>						
N	10	10	10	10	10	10
Mean	40.29	40.02	35.87	40.73	40.54	39.30
Median	39.90	39.57	35.50	40.97	41.09	39.07
IQ-Range	3.039	2.466	5.550	2.248	4.265	4.176
Min	36.71	35.26	30.48	36.84	33.57	31.39
Max	45.15	43.22	40.64	43.83	44.98	43.36
p <sub>L</sub>		0.955	0.020	0.693	0.784	0.644
p <sub>J</sub>		0.762	0.003	0.682	0.549	0.678
<b>Kidney (both) (o/oo)</b>						
N	10	10	10	10	10	10
Mean	6.373	6.420	6.243	6.236	6.347	6.510
Median	6.392	6.486	6.279	6.248	6.332	6.391
IQ-Range	0.302	0.462	0.611	0.541	0.366	0.711
Min	5.821	5.661	5.674	5.553	5.553	5.882
Max	6.845	6.810	6.811	7.099	7.027	7.362
p <sub>L</sub>		0.595	0.693	0.468	0.977	0.677
p <sub>J</sub>		0.496	0.704	0.347	0.516	0.948
<b>Adrenal (both) (o/oo)</b>						
N	10	10	10	10	10	10
Mean	0.155	0.162	0.154	0.155	0.150	0.153
Median	0.152	0.162	0.151	0.158	0.157	0.153
IQ-Range	0.050	0.032	0.027	0.020	0.027	0.035
Min	0.113	0.117	0.127	0.122	0.123	0.114
Max	0.194	0.204	0.188	0.177	0.167	0.178
p <sub>L</sub>		0.715	0.315	0.237	0.355	0.294
p <sub>J</sub>		0.496	0.939	0.809	0.462	0.501

Test No.: 943127

Test Article: CGA 329351 tech.

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

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>Thymus</b>						
(o/oo) N	10	10	10	10	10	10
Mean	1.199	1.002	0.999	1.061	0.997	0.945
Median	1.183	1.035	1.019	1.067	0.979	0.998
IQ-Range	0.207	0.174	0.393	0.347	0.174	0.396
Min	0.909	0.711	0.616	0.740	0.718	0.552
Max	1.436	1.252	1.308	1.646	1.414	1.225
p_L		0.063	0.151	0.249	0.082	0.102
p_J		0.019	0.048	0.162	0.081	0.042
<b>Testis (both)</b>						
(o/oo) N	10	10	10	10	10	10
Mean	8.552	8.014	8.009	8.515	8.001	7.826
Median	8.534	7.656	8.450	8.146	7.854	8.043
IQ-Range	1.375	1.212	1.150	1.026	0.914	0.803
Min	7.437	6.968	4.364	7.722	6.751	6.090
Max	9.661	9.584	9.625	10.17	10.09	8.917
p_L		0.378	0.889	0.912	0.319	0.111
p_J		0.174	0.648	0.828	0.402	0.136
<b>Spleen</b>						
(o/oo) N	10	10	10	10	10	10
Mean	1.724	1.643	1.591	1.745	1.573	1.652
Median	1.739	1.650	1.555	1.760	1.524	1.662
IQ-Range	0.131	0.120	0.192	0.178	0.323	0.301
Min	1.488	1.440	1.384	1.587	1.291	1.307
Max	1.966	1.852	1.889	1.866	2.072	2.012
p_L		0.297	0.174	0.931	0.187	0.347
p_J		0.174	0.033	0.904	0.313	0.422

Statistical tests and flags used:  
 LEPAGE: \* if p<sub>L</sub> < 0.01  
 a/b ind. of diff. in loc./disp.  
 JONCKHEERE: +- if p<sub>J</sub> < 0.01

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

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>Heart (o/oo)</b>						
N	10	10	10	10	10	10
Mean	3.427	3.372	3.262	3.289	3.336	3.464
Median	3.381	3.356	3.275	3.256	3.320	3.455
IQ-Range	0.332	0.381	0.360	0.395	0.167	0.404
Min	3.131	2.776	2.860	2.954	3.051	3.109
Max	4.082	3.842	3.665	3.754	3.652	3.790
p <sub>L</sub>		0.774	0.474	0.153	0.784	0.652
p <sub>J</sub>		0.705	0.254	0.247	0.441	0.746
<b>Liver (o/oo)</b>						
N	10	10	10	10	10	10
Mean	36.83	35.98	35.99	38.23	39.38	38.84
Median	37.23	35.62	36.85	39.27	40.16	38.46
IQ-Range	4.069	2.987	4.013	5.245	3.157	2.567
Min	31.76	32.35	30.53	33.34	33.29	36.21
Max	41.78	38.71	39.92	44.72	42.65	41.60
p <sub>L</sub>		0.360	0.427	0.351	0.109	0.172
p <sub>J</sub>		0.450	0.470	0.469	0.019	0.006 +
<b>Kidney (both) (o/oo)</b>						
N	10	10	10	10	10	10
Mean	6.946	7.337	7.064	6.998	7.496	7.489
Median	7.047	7.247	7.268	7.098	7.476	7.623
IQ-Range	1.142	1.430	1.399	0.739	0.379	1.218
Min	6.168	6.103	5.613	6.206	6.469	6.507
Max	7.619	8.967	7.870	7.702	8.467	8.185
p <sub>L</sub>		0.317	0.451	0.543	0.187	0.160
p <sub>J</sub>		0.364	0.568	0.962	0.252	0.062
<b>Adrenal (both) (o/oo)</b>						
N	10	10	10	10	10	10
Mean	0.314	0.324	0.301	0.311	0.325	0.314
Median	0.302	0.330	0.280	0.312	0.331	0.317
IQ-Range	0.042	0.065	0.082	0.036	0.062	0.056
Min	0.250	0.263	0.246	0.274	0.249	0.253
Max	0.407	0.378	0.396	0.381	0.374	0.353
p <sub>L</sub>		0.715	0.351	0.829	0.751	0.892
p <sub>J</sub>		0.496	0.447	0.754	0.669	0.678

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

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
<b>Thymus</b> (o/oo) N	10	10	10	10	10	10
Mean	1.276	1.226	1.222	1.045	1.294	1.272
Median	1.202	1.202	1.207	1.059	1.304	1.331
IQ-Range	0.370	0.580	0.454	0.160	0.115	0.434
Min	0.841	0.850	0.922	0.840	0.957	0.928
Max	1.866	1.792	1.683	1.275	1.473	1.583
p_L		0.644	0.723	0.139	0.176	0.989
p_J		0.821	0.820	0.128	0.986	0.569
<b>Ovary (both)</b> (o/oo) N	10	10	10	10	10	10
Mean	0.576	0.580	0.582	0.587	0.572	0.567
Median	0.586	0.608	0.554	0.523	0.579	0.558
IQ-Range	0.218	0.142	0.124	0.196	0.130	0.060
Min	0.411	0.427	0.436	0.406	0.444	0.482
Max	0.811	0.700	0.790	0.769	0.672	0.696
p_L		0.750	0.479	0.912	0.829	0.075
p_J		0.650	0.909	0.847	0.932	0.938
<b>Spleen</b> (o/oo) N	10	10	10	10	10	10
Mean	1.922	1.879	2.089	1.972	1.934	2.094
Median	1.905	1.890	2.110	1.881	1.961	2.095
IQ-Range	0.309	0.230	0.676	0.422	0.493	0.295
Min	1.700	1.616	1.511	1.468	1.409	1.808
Max	2.207	2.245	2.993	2.793	2.316	2.487
p_L		0.793	0.159	0.466	0.466	0.174
p_J		0.496	0.676	0.885	0.864	0.218

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5.7.4. Organ to body weight ratios (statistics):  
 2. sacrifice (recovery)

Statistical tests and flags used:

LEPAGE: \* if p<sub>L</sub> < 0.01

a/b ind. of diff. in loc./disp.

Organ to body weight ratios (statistics): males week 18

Dose (ppm)	group 1 0	group 2 25	group 3 50	group 4 250	group 5 625	group 6 1250
Heart (o/oo) N	10					10
Mean	2.945					2.881
Median	2.956					2.919
IQ-Range	0.401					0.258
Min	2.578					2.541
Max	3.322					3.342
p <sub>L</sub>						0.496
Liver (o/oo) N	10					10
Mean	36.80					38.29
Median	36.87					37.50
IQ-Range	2.296					3.161
Min	32.43					33.14
Max	40.35					48.41
p <sub>L</sub>						0.750
Kidney (both) (o/oo) N	10					10
Mean	6.105					6.209
Median	6.073					6.123
IQ-Range	0.469					0.339
Min	5.548					5.558
Max	7.393					7.698
p <sub>L</sub>						0.774
Adrenal (both) (o/oo) N	10					10
Mean	0.149					0.131
Median	0.147					0.138
IQ-Range	0.044					0.051
Min	0.091					0.092
Max	0.236					0.166
p <sub>L</sub>						0.633

Organ to body weight ratios (statistics): males week 18

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
Thymus (o/oo) N	10					10
Mean	1.034					0.919
Median	1.008					0.918
IQ-Range	0.229					0.459
Min	0.645					0.557
Max	1.731					1.471
p_L						0.715
Testis (both) (o/oo) N	10					10
Mean	7.265					8.056
Median	7.260					8.034
IQ-Range	0.684					1.065
Min	6.258					7.087
Max	8.244					9.352
p_L						0.096
Spleen (o/oo) N	10					10
Mean	1.478					1.616
Median	1.497					1.539
IQ-Range	0.203					0.308
Min	1.237					1.357
Max	1.626					2.250
p_L						0.095

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Organ to body weight ratios (statistics): females week 18

Dose (ppm)	group 1	group 2	group 3	group 4	group 5	group 6
	0	25	50	250	625	1250
Ovary (both)						10
(o/oo) N	10					0.550
Mean	0.561					0.539
Median	0.540					0.158
IQ-Range	0.147					0.450
Min	0.470					0.720
Max	0.719					0.723
p_L						
Spleen						10
(o/oo) N	10					1.878
Mean	1.846					1.886
Median	1.687					0.365
IQ-Range	0.382					1.413
Min	1.484					2.311
Max	2.899					0.784
p_L						

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**6. APPENDIX B: INDIVIDUAL DATA**

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**6.1. In-life observations (individuals)**

- : clinical sign observed until scheduled sacrifice
- \* : clinical sign observed until early death
- l, r : left, right, resp.

**Antemortem findings (individuals): males group 1 : 0 ppm**

No.	Finding	start day	end day
01	no findings noted		
02	no findings noted		
03	no findings noted		
04	no findings noted		
05	no findings noted		
06	no findings noted		
07	eye, exudate right	31	59
08	no findings noted		
09	no findings noted		
10	no findings noted		
11	no findings noted		
12	no findings noted		
13	no findings noted		
14	no findings noted		
15	no findings noted		
16	no findings noted		
17	no findings noted		
18	no findings noted		
19	no findings noted		
20	skin lesion neck	31	59

**Antemortem findings (individuals): males group 2 : 25 ppm**

No.	Finding	start day	end day
21	no findings noted		
22	no findings noted		
23	no findings noted		
24	no findings noted		
25	no findings noted		
26	no findings noted		
27	no findings noted		
28	skin lesion neck	38	52

Antemortem findings (individuals) : males group 2 : 25 ppm

No.	Finding	start day	end day
29	no findings noted		
30	no findings noted		

Antemortem findings (individuals) : males group 3 : 50 ppm

No.	Finding	start day	end day
31	no findings noted		
32	no findings noted		
33	no findings noted		
34	no findings noted		
35	no findings noted		
36	no findings noted		
37	no findings noted		
38	no findings noted		
39	no findings noted		
40	no findings noted		

Antemortem findings (individuals) : males group 4 : 250 ppm

No.	Finding	start day	end day
41	no findings noted		
42	no findings noted		
43	no findings noted		
44	hair loss abdomen	52	-
45	hair loss abdomen	80	-
46	no findings noted		
47	no findings noted		
48	no findings noted		
49	no findings noted		
50	no findings noted		

Antemortem findings (individuals) : males group 5 : 625 ppm

No.	Finding	start day	end day
51	no findings noted		
52	no findings noted		
53	no findings noted		
54	no findings noted		
55	no findings noted		
56	no findings noted		
57	no findings noted		
58	no findings noted		
59	no findings noted		
60	no findings noted		

Antemortem findings (individuals) : males group 6 : 1250 ppm

No.	Finding	start day	end day
61	no findings noted		
62	no findings noted		
63	no findings noted		
64	no findings noted		
65	no findings noted		
66	no findings noted		
67	no findings noted		
68	no findings noted		
69	no findings noted		
70	no findings noted		
71	no findings noted		
72	no findings noted		
73	no findings noted		
74	no findings noted		
75	no findings noted		
76	no findings noted		
77	no findings noted		
78	no findings noted		
79	no findings noted		
80	no findings noted		



Antemortem findings (individuals) : females group 1 : 0 ppm

No.	Finding	start day	end day
81	no findings noted		
82	no findings noted		
83	no findings noted		
84	no findings noted		
85	no findings noted		
86	no findings noted		
87	no findings noted		
88	no findings noted		
89	no findings noted		
90	no findings noted		
91	no findings noted		
92	no findings noted		
93	no findings noted		
94	mass, 1-1cm diam	abdominal 87	
95	no findings noted		
96	no findings noted		
97	no findings noted		
98	no findings noted		
99	no findings noted		
100	no findings noted		

Antemortem findings (individuals) : females group 2 : 25 ppm

No.	Finding	start day	end day
101	no findings noted		
102	no findings noted		
103	no findings noted		
104	no findings noted		
105	no findings noted		
106	no findings noted		
107	no findings noted		
108	no findings noted		
109	no findings noted		
110	no findings noted		

Antemortem findings (individuals) : females group 3 : 50 ppm

No.	Finding	start day	end day
111	no findings noted		
112	no findings noted		
113	no findings noted		
114	no findings noted		
115	no findings noted		
116	no findings noted		
117	no findings noted		
118	no findings noted		
119	no findings noted		
120	no findings noted		

Antemortem findings (individuals) : females group 4 : 250 ppm

No.	Finding	start day	end day
121	no findings noted		
122	no findings noted		
123	no findings noted		
124	no findings noted		
125	no findings noted		
126	no findings noted		
127	no findings noted		
128	no findings noted		
129	no findings noted		
130	no findings noted		

Antemortem findings (individuals) : females group 5 : 625 ppm

No.	Finding	start day	end day
131	no findings noted		
132	no findings noted		
133	no findings noted		
134	no findings noted		
135	no findings noted		
136	no findings noted		
137	no findings noted		

Antemortem findings (individuals) : females group 5 : 625 ppm

No.	Finding	start day	end day
138	no findings noted		
139	no findings noted		
140	no findings noted		

Antemortem findings (individuals) : females group 6 : 1250 ppm

No.	Finding	start day	end day
141	no findings noted		
142	no findings noted		
143	no findings noted		
144	no findings noted		
145	no findings noted		
146	no findings noted		
147	no findings noted		
148	no findings noted		
149	no findings noted		
150	no findings noted		
151	no findings noted		
152	no findings noted		
153	no findings noted		
154	no findings noted		
155	no findings noted		
156	no findings noted		
157	no findings noted		
158	no findings noted		
159	no findings noted		
160	no findings noted		

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6.2. Mortality (individuals)

Mortality (individuals) : males group 1 : 0 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
1	1	25 Jan 95	14	93	yes	Sacrifice 1
2	1	25 Jan 95	14	93	yes	Sacrifice 1
3	1	25 Jan 95	14	93	yes	Sacrifice 1
4	1	25 Jan 95	14	93	yes	Sacrifice 1
5	1	25 Jan 95	14	93	yes	Sacrifice 1
6	2	25 Jan 95	14	93	yes	Sacrifice 1
7	2	25 Jan 95	14	93	yes	Sacrifice 1
8	2	25 Jan 95	14	93	yes	Sacrifice 1
9	2	25 Jan 95	14	93	yes	Sacrifice 1
10	2	25 Jan 95	14	93	yes	Sacrifice 1
11	3	22 Feb 95	18	121	yes	Sacrifice 2
12	3	22 Feb 95	18	121	yes	Sacrifice 2
13	3	22 Feb 95	18	121	yes	Sacrifice 2
14	3	22 Feb 95	18	121	yes	Sacrifice 2
15	3	22 Feb 95	18	121	yes	Sacrifice 2
16	4	22 Feb 95	18	121	yes	Sacrifice 2
17	4	22 Feb 95	18	121	yes	Sacrifice 2
18	4	22 Feb 95	18	121	yes	Sacrifice 2
19	4	22 Feb 95	18	121	yes	Sacrifice 2
20	4	22 Feb 95	18	121	yes	Sacrifice 2

Mortality (individuals) : males group 2 : 25 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
21	5	25 Jan 95	14	93	yes	Sacrifice 1
22	5	25 Jan 95	14	93	yes	Sacrifice 1
23	5	25 Jan 95	14	93	yes	Sacrifice 1
24	5	25 Jan 95	14	93	yes	Sacrifice 1
25	5	25 Jan 95	14	93	yes	Sacrifice 1
26	6	25 Jan 95	14	93	yes	Sacrifice 1
27	6	25 Jan 95	14	93	yes	Sacrifice 1
28	6	25 Jan 95	14	93	yes	Sacrifice 1
29	6	25 Jan 95	14	93	yes	Sacrifice 1
30	6	25 Jan 95	14	93	yes	Sacrifice 1

Mortality (individuals) : males group 3 : 50 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
31	7	26 Jan 95	14	94	yes	Sacrifice 1
32	7	26 Jan 95	14	94	yes	Sacrifice 1
33	7	26 Jan 95	14	94	yes	Sacrifice 1
34	7	26 Jan 95	14	94	yes	Sacrifice 1
35	7	26 Jan 95	14	94	yes	Sacrifice 1
36	8	25 Jan 95	14	93	yes	Sacrifice 1
37	8	25 Jan 95	14	93	yes	Sacrifice 1
38	8	25 Jan 95	14	93	yes	Sacrifice 1
39	8	25 Jan 95	14	93	yes	Sacrifice 1
40	8	25 Jan 95	14	93	yes	Sacrifice 1

Mortality (individuals) : males group 4 : 250 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
41	9	25 Jan 95	14	93	yes	Sacrifice 1
42	9	25 Jan 95	14	93	yes	Sacrifice 1
43	9	25 Jan 95	14	93	yes	Sacrifice 1
44	9	25 Jan 95	14	93	yes	Sacrifice 1
45	9	25 Jan 95	14	93	yes	Sacrifice 1
46	10	25 Jan 95	14	93	yes	Sacrifice 1
47	10	26 Jan 95	14	94	yes	Sacrifice 1
48	10	26 Jan 95	14	94	yes	Sacrifice 1
49	10	25 Jan 95	14	93	yes	Sacrifice 1
50	10	26 Jan 95	14	94	yes	Sacrifice 1

Mortality (individuals) : males group 5 : 625 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
51	11	25 Jan 95	14	93	yes	Sacrifice 1
52	11	25 Jan 95	14	93	yes	Sacrifice 1
53	11	25 Jan 95	14	93	yes	Sacrifice 1
54	11	25 Jan 95	14	93	yes	Sacrifice 1
55	11	25 Jan 95	14	93	yes	Sacrifice 1
56	12	26 Jan 95	14	94	yes	Sacrifice 1
57	12	26 Jan 95	14	94	yes	Sacrifice 1
58	12	26 Jan 95	14	94	yes	Sacrifice 1

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 214  
 Test No.: 943127  
 Test Article: CGA 329351 tech.

Mortality (individuals) : males group 5 : 625 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
59	12	26 Jan 95	14	94	yes	Sacrifice 1
60	12	26 Jan 95	14	94	yes	Sacrifice 1

Mortality (individuals) : males group 6 : 1250 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
61	13	25 Jan 95	14	93	yes	Sacrifice 1
62	13	25 Jan 95	14	93	yes	Sacrifice 1
63	13	25 Jan 95	14	93	yes	Sacrifice 1
64	13	25 Jan 95	14	93	yes	Sacrifice 1
65	13	25 Jan 95	14	93	yes	Sacrifice 1
66	14	25 Jan 95	14	93	yes	Sacrifice 1
67	14	25 Jan 95	14	93	yes	Sacrifice 1
68	14	25 Jan 95	14	93	yes	Sacrifice 1
69	14	25 Jan 95	14	93	yes	Sacrifice 1
70	14	25 Jan 95	14	93	yes	Sacrifice 1
71	15	22 Feb 95	18	121	yes	Sacrifice 2
72	15	22 Feb 95	18	121	yes	Sacrifice 2
73	15	22 Feb 95	18	121	yes	Sacrifice 2
74	15	22 Feb 95	18	121	yes	Sacrifice 2
75	15	22 Feb 95	18	121	yes	Sacrifice 2
76	16	22 Feb 95	18	121	yes	Sacrifice 2
77	16	22 Feb 95	18	121	yes	Sacrifice 2
78	16	22 Feb 95	18	121	yes	Sacrifice 2
79	16	22 Feb 95	18	121	yes	Sacrifice 2
80	16	22 Feb 95	18	121	yes	Sacrifice 2

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 215  
 Test No.: 943127  
 Test Article: CGA 329351 tech.

Mortality (individuals) : females group 1 : 0 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
81	17	26 Jan 95	14	94	yes	Sacrifice 1
82	17	26 Jan 95	14	94	yes	Sacrifice 1
83	17	26 Jan 95	14	94	yes	Sacrifice 1
84	17	26 Jan 95	14	94	yes	Sacrifice 1
85	17	26 Jan 95	14	94	yes	Sacrifice 1
86	18	27 Jan 95	14	95	yes	Sacrifice 1
87	18	27 Jan 95	14	95	yes	Sacrifice 1
88	18	27 Jan 95	14	95	yes	Sacrifice 1
89	18	27 Jan 95	14	95	yes	Sacrifice 1
90	18	27 Jan 95	14	95	yes	Sacrifice 1
91	19	22 Feb 95	18	121	yes	Sacrifice 2
92	19	22 Feb 95	18	121	yes	Sacrifice 2
93	19	22 Feb 95	18	121	yes	Sacrifice 2
94	19	22 Feb 95	18	121	yes	Sacrifice 2
95	19	22 Feb 95	18	121	yes	Sacrifice 2
96	20	23 Feb 95	18	122	yes	Sacrifice 2
97	20	23 Feb 95	18	122	yes	Sacrifice 2
98	20	23 Feb 95	18	122	yes	Sacrifice 2
99	20	23 Feb 95	18	122	yes	Sacrifice 2
100	20	23 Feb 95	18	122	yes	Sacrifice 2

Mortality (individuals) : females group 2 : 25 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
101	21	26 Jan 95	14	94	yes	Sacrifice 1
102	21	26 Jan 95	14	94	yes	Sacrifice 1
103	21	26 Jan 95	14	94	yes	Sacrifice 1
104	21	26 Jan 95	14	94	yes	Sacrifice 1
105	21	26 Jan 95	14	94	yes	Sacrifice 1
106	22	26 Jan 95	14	94	yes	Sacrifice 1
107	22	26 Jan 95	14	94	yes	Sacrifice 1
108	22	26 Jan 95	14	94	yes	Sacrifice 1
109	22	26 Jan 95	14	94	yes	Sacrifice 1
110	22	26 Jan 95	14	94	yes	Sacrifice 1

Mortality (individuals) : females group 3 : 50 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
111	23	26 Jan 95	14	94	yes	Sacrifice 1
112	23	26 Jan 95	14	94	yes	Sacrifice 1
113	23	26 Jan 95	14	94	yes	Sacrifice 1
114	23	26 Jan 95	14	94	yes	Sacrifice 1
115	23	26 Jan 95	14	94	yes	Sacrifice 1
116	24	27 Jan 95	14	95	yes	Sacrifice 1
117	24	27 Jan 95	14	95	yes	Sacrifice 1
118	24	27 Jan 95	14	95	yes	Sacrifice 1
119	24	27 Jan 95	14	95	yes	Sacrifice 1
120	24	27 Jan 95	14	95	yes	Sacrifice 1

Mortality (individuals) : females group 4 : 250 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
121	25	26 Jan 95	14	94	yes	Sacrifice 1
122	25	26 Jan 95	14	94	yes	Sacrifice 1
123	25	26 Jan 95	14	94	yes	Sacrifice 1
124	25	26 Jan 95	14	94	yes	Sacrifice 1
125	25	26 Jan 95	14	94	yes	Sacrifice 1
126	26	27 Jan 95	14	95	yes	Sacrifice 1
127	26	27 Jan 95	14	95	yes	Sacrifice 1
128	26	27 Jan 95	14	95	yes	Sacrifice 1
129	26	27 Jan 95	14	95	yes	Sacrifice 1
130	26	27 Jan 95	14	95	yes	Sacrifice 1

Mortality (individuals) : females group 5 : 625 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
131	27	26 Jan 95	14	94	yes	Sacrifice 1
132	27	26 Jan 95	14	94	yes	Sacrifice 1
133	27	26 Jan 95	14	94	yes	Sacrifice 1
134	27	26 Jan 95	14	94	yes	Sacrifice 1
135	27	26 Jan 95	14	94	yes	Sacrifice 1
136	28	26 Jan 95	14	94	yes	Sacrifice 1
137	28	26 Jan 95	14	94	yes	Sacrifice 1
138	28	26 Jan 95	14	94	yes	Sacrifice 1



3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 217  
 Test No.: 943127  
 Test Article: CGA 329351 tech.

Mortality (individuals) : females group 5 : 625 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
139	28	26 Jan 95	14	94	yes	Sacrifice 1
140	28	26 Jan 95	14	94	yes	Sacrifice 1

Mortality (individuals) : females group 6 : 1250 ppm

Animal number	cage	date of death	study week	study day	necropsy	type of death
141	29	26 Jan 95	14	94	yes	Sacrifice 1
142	29	26 Jan 95	14	94	yes	Sacrifice 1
143	29	26 Jan 95	14	94	yes	Sacrifice 1
144	29	26 Jan 95	14	94	yes	Sacrifice 1
145	29	26 Jan 95	14	94	yes	Sacrifice 1
146	30	26 Jan 95	14	94	yes	Sacrifice 1
147	30	26 Jan 95	14	94	yes	Sacrifice 1
148	30	26 Jan 95	14	94	yes	Sacrifice 1
149	30	26 Jan 95	14	94	yes	Sacrifice 1
150	30	26 Jan 95	14	94	yes	Sacrifice 1
151	31	22 Feb 95	18	121	yes	Sacrifice 2
152	31	22 Feb 95	18	121	yes	Sacrifice 2
153	31	22 Feb 95	18	121	yes	Sacrifice 2
154	31	22 Feb 95	18	121	yes	Sacrifice 2
155	31	22 Feb 95	18	121	yes	Sacrifice 2
156	32	23 Feb 95	18	122	yes	Sacrifice 2
157	32	23 Feb 95	18	122	yes	Sacrifice 2
158	32	23 Feb 95	18	122	yes	Sacrifice 2
159	32	23 Feb 95	18	122	yes	Sacrifice 2
160	32	23 Feb 95	18	122	yes	Sacrifice 2

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6.3. Bodyweight (individuals)

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

	Animal no									
	1	2	3	4	5	6	7	8	9	10
week: -1	167.9	151.2	151.3	140.8	153.2	136.9	136.1	136.6	142.0	143.6
1	230.5	206.8	207.5	203.2	206.0	189.4	169.5	175.2	189.1	199.1
2	297.5	266.0	272.5	271.0	262.5	241.0	221.9	220.7	242.5	254.7
3	340.6	322.8	324.3	327.9	299.5	286.7	274.5	259.1	283.3	288.7
4	372.6	353.6	354.5	362.1	317.8	314.8	313.9	290.1	301.1	304.1
5	382.9	379.2	383.1	402.5	334.1	341.5	346.7	320.6	320.5	330.2
6	395.0	404.0	406.6	432.0	358.0	365.9	363.2	349.4	334.6	352.5
7	400.7	418.9	420.3	450.1	370.8	379.5	387.7	366.5	348.4	370.7
8	413.3	441.7	430.3	472.6	386.7	398.0	403.5	391.9	365.4	396.3
9	426.5	453.4	449.2	481.2	404.7	408.3	429.1	406.7	377.1	407.9
10	439.3	466.5	462.4	485.7	416.0	417.7	442.4	418.4	388.5	421.2
11	458.3	479.8	470.6	494.9	432.4	426.7	458.5	434.7	396.2	432.3
12	464.4	493.0	480.0	508.5	446.9	440.0	468.8	450.4	412.0	446.0
13	475.2	506.7	502.7	511.9	460.7	450.4	480.0	463.5	423.3	452.8

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

	Animal no									
	11	12	13	14	15	16	17	18	19	20
week: -1	163.0	149.0	175.5	163.3	140.0	161.7	161.1	145.5	131.0	136.9
1	223.8	211.9	240.7	222.1	198.3	206.5	227.1	196.2	173.5	191.9
2	274.7	280.3	301.2	272.9	256.8	261.9	286.9	249.1	221.3	248.6
3	324.2	348.1	350.9	313.1	313.3	308.7	341.7	292.9	263.1	300.5
4	369.5	385.5	386.5	338.6	345.8	338.0	375.4	320.4	285.5	346.9
5	398.3	423.1	420.9	368.4	371.1	374.0	415.1	348.5	309.9	385.3
6	430.8	450.6	446.7	395.2	395.9	396.0	439.4	373.4	329.3	409.8
7	460.3	469.5	467.0	417.1	410.1	415.5	450.4	385.7	347.0	432.6
8	472.8	502.1	497.1	440.7	438.0	440.0	488.8	398.6	368.1	454.9
9	488.2	525.1	511.9	453.4	440.3	461.5	509.5	419.0	382.1	475.8
10	506.2	538.1	526.0	466.5	450.5	472.3	517.3	428.9	393.1	487.9
11	518.7	559.6	538.2	483.9	466.5	476.0	538.8	441.4	404.4	503.3
12	526.0	581.3	541.2	501.1	480.4	486.4	545.5	447.0	414.6	510.5
13	535.3	586.4	554.5	515.6	482.9	491.9	557.3	461.2	425.6	515.0

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 219  
 Test No.: 943127  
 Test Article: CGA 329351 tech.

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

	11	12	13	14	Animal no		17	18	19	20
					15	16				
recovery										
week: 14	531.8	585.4	554.6	513.6	484.9	470.0	557.5	460.9	420.4	524.7
15	546.2	604.5	560.8	530.3	494.1	491.3	570.9	473.0	432.8	537.7
16	549.7	621.4	576.7	538.6	509.9	510.7	586.5	488.3	444.8	545.7
17	559.4	629.0	583.0	557.7	516.1	521.3	599.1	496.3	456.3	554.9

Body weight (individuals) : males group 2 : 25 ppm  
 (g/animal)

	21	22	23	24	Animal no		27	28	29	30
					25	26				
week: -1	167.4	145.4	141.5	155.3	135.4	147.4	154.1	132.8	161.5	158.0
1	225.2	196.8	199.8	203.4	185.8	199.6	202.9	198.4	235.8	212.2
2	291.9	257.7	252.2	250.9	235.0	244.6	247.6	253.6	305.1	265.0
3	357.9	305.0	298.5	281.5	268.4	298.3	274.1	302.3	377.7	299.1
4	398.0	333.0	334.6	311.4	287.9	334.0	296.3	336.4	414.9	326.2
5	438.4	362.1	369.8	339.3	304.4	373.9	312.6	370.0	455.0	347.7
6	468.6	376.3	395.2	362.1	325.3	398.3	331.3	393.7	492.4	377.8
7	489.0	379.8	412.9	385.1	341.3	417.9	344.3	408.7	520.6	397.5
8	519.3	400.0	424.0	412.3	362.7	440.0	349.9	424.7	549.0	420.9
9	531.7	415.8	442.9	422.1	374.6	451.5	370.0	448.2	567.8	434.6
10	554.2	439.5	456.0	439.9	387.1	464.6	373.5	460.2	589.2	450.7
11	572.2	451.6	471.0	464.4	400.4	480.7	387.1	471.2	606.1	465.1
12	587.2	476.7	475.7	479.1	413.1	497.7	394.5	487.6	618.3	477.1
13	605.4	487.9	493.7	492.4	421.3	509.5	405.9	503.5	634.6	484.3

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 220  
 Test No.: 943127  
 Test Article: CGA 329351 tech.

Body weight (individuals) : males  
 (g/animal)

group 3 : 50 ppm

	Animal no									
	31	32	33	34	35	36	37	38	39	40
week: -1	140.0	166.4	147.2	142.4	135.4	157.0	146.4	166.9	146.9	145.2
1	178.0	220.3	195.6	184.5	179.2	208.9	206.2	227.1	198.0	195.2
2	230.0	282.3	250.6	236.0	232.3	268.7	265.9	284.0	251.5	250.9
3	286.6	339.5	284.5	270.8	292.1	308.0	322.9	331.9	291.2	300.0
4	319.1	374.9	307.0	292.5	327.1	325.7	362.1	366.1	319.5	332.1
5	349.9	411.6	327.6	313.5	360.1	341.3	399.7	395.1	345.3	354.7
6	378.4	439.5	343.0	337.1	379.8	364.1	427.4	424.7	365.8	380.8
7	386.6	455.8	358.6	345.8	399.9	374.3	447.8	437.8	379.6	394.0
8	409.5	485.8	377.4	369.5	418.4	394.7	478.1	463.6	396.6	412.4
9	422.6	498.8	390.6	384.3	439.1	402.5	496.5	486.2	414.8	424.4
10	435.7	523.3	398.1	392.2	446.3	415.4	508.8	499.3	422.8	429.1
11	450.2	540.9	414.7	406.0	464.1	427.2	517.4	508.4	434.1	439.2
12	459.6	556.2	425.0	416.7	483.9	437.4	525.4	519.3	443.3	441.6
13	467.7	569.5	436.3	432.5	488.1	445.2	536.0	533.7	451.9	450.0

Body weight (individuals) : males  
 (g/animal)

group 4 : 250 ppm

	Animal no									
	41	42	43	44	45	46	47	48	49	50
week: -1	151.3	164.2	139.0	161.3	174.3	137.1	133.0	151.1	143.5	139.9
1	208.6	215.1	192.1	218.4	236.5	189.7	173.7	198.0	201.8	198.6
2	259.1	273.4	248.7	272.4	289.3	245.2	222.0	244.0	268.5	258.0
3	315.3	316.4	300.4	315.6	336.0	295.9	261.6	275.4	320.9	321.3
4	346.3	345.4	343.5	348.8	365.9	333.2	285.8	287.3	352.2	357.9
5	389.7	377.4	375.3	378.9	394.5	359.4	305.9	306.6	388.2	389.6
6	416.0	402.6	404.7	404.0	417.1	384.5	323.4	323.8	418.0	418.2
7	440.4	422.2	425.8	422.5	430.1	398.5	331.5	343.6	428.9	437.4
8	462.1	445.6	455.4	442.2	460.9	419.1	345.0	362.8	447.3	467.6
9	480.6	470.5	476.9	458.4	474.2	432.7	357.5	372.8	470.9	495.5
10	500.6	484.0	492.5	475.8	490.1	438.8	366.2	378.8	483.6	516.4
11	522.8	496.3	509.2	493.0	511.4	452.4	379.3	385.7	502.3	537.4
12	532.7	497.4	525.2	495.9	521.8	457.7	389.8	387.6	510.3	544.7
13	553.1	512.6	535.8	517.1	530.5	469.0	397.3	398.8	519.1	571.3

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 221  
 Test No.: 943127  
 Test Article: CGA 329351 tech.

Body weight (individuals) : males  
 (g/animal)

group 5 : 625 ppm

	Animal no									
	51	52	53	54	55	56	57	58	59	60
week: -1	172.7	139.2	163.6	158.2	142.3	174.4	136.2	139.9	134.7	144.9
1	233.6	191.5	224.4	213.3	186.7	236.1	195.1	200.2	198.9	197.7
2	290.8	253.3	288.2	275.6	241.0	290.3	250.1	261.7	261.9	259.6
3	333.8	306.0	340.2	322.0	289.1	333.2	300.3	316.9	309.4	306.5
4	364.5	337.4	380.3	354.2	317.0	366.6	323.9	361.4	342.8	333.2
5	391.9	365.7	413.1	375.3	337.8	402.7	346.1	394.5	378.5	370.0
6	411.2	398.4	436.3	405.2	367.8	431.9	373.6	435.5	411.8	392.3
7	423.6	423.5	457.5	428.2	383.8	457.1	392.7	461.1	434.8	402.8
8	446.9	449.9	478.4	449.9	409.5	475.7	416.9	492.7	468.0	430.6
9	469.3	477.8	497.1	465.2	426.3	487.0	426.1	518.8	487.8	452.3
10	485.7	497.7	516.1	472.8	445.8	501.4	442.6	534.3	503.7	470.1
11	494.7	512.9	530.5	490.3	461.4	521.3	453.4	558.2	522.1	487.1
12	510.1	531.1	538.6	497.3	465.8	530.0	459.8	577.5	533.5	495.4
13	523.5	552.2	552.1	509.2	475.9	539.7	478.1	589.6	544.4	505.9

Body weight (individuals) : males  
 (g/animal)

group 6 : 1250 ppm

	Animal no									
	61	62	63	64	65	66	67	68	69	70
week: -1	133.3	144.5	148.3	158.7	157.7	163.8	168.8	156.1	164.7	136.1
1	172.0	202.6	207.7	225.3	206.4	223.1	228.8	216.2	215.8	185.3
2	220.8	253.3	270.5	284.8	262.3	280.6	286.8	271.0	268.1	234.8
3	258.7	302.9	329.5	329.7	302.9	328.4	317.6	307.1	312.7	281.3
4	279.9	342.4	368.7	355.9	325.0	368.7	358.1	332.8	346.9	313.4
5	301.7	376.1	407.2	390.4	354.5	400.9	388.1	355.5	372.8	339.2
6	315.9	406.1	441.0	420.0	380.9	422.3	426.8	380.1	399.4	366.8
7	326.5	422.3	458.6	437.6	387.6	444.9	456.8	395.0	412.2	381.8
8	347.5	435.0	478.7	461.9	407.4	464.9	478.6	416.3	425.7	404.6
9	353.6	444.3	494.8	479.1	423.5	493.0	498.0	436.7	444.9	422.6
10	362.7	454.2	509.9	489.9	439.3	508.1	516.4	449.4	454.8	434.8
11	372.4	470.6	522.4	505.9	457.4	526.2	533.6	463.7	464.3	441.7
12	379.9	480.3	535.0	517.9	466.1	539.0	545.8	476.4	474.0	454.4
13	380.3	492.2	556.1	524.3	472.9	536.1	557.4	488.6	486.1	462.5

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 222

Test No.: 943127  
 Test Article: CGA 329351 tech.

Body weight (individuals) : males group 6 : 1250 ppm  
 (g/animal)

	Animal no									
	71	72	73	74	75	76	77	78	79	80
week: -1	142.5	149.8	135.9	161.5	147.5	149.9	139.3	149.4	143.3	162.0
1	203.9	210.9	186.5	202.6	205.6	208.1	176.3	211.7	200.1	214.0
2	265.2	270.4	248.5	258.7	264.8	264.9	224.9	275.6	254.5	270.9
3	308.3	301.8	307.9	292.1	319.4	311.1	258.7	325.7	309.0	319.8
4	334.3	320.7	347.5	316.1	351.8	341.4	282.0	357.2	348.3	354.4
5	372.7	343.9	384.8	342.4	381.4	378.2	303.0	387.1	379.3	389.9
6	408.2	364.3	409.9	358.3	413.6	408.0	321.5	412.3	411.5	419.8
7	425.7	377.8	432.6	373.4	442.6	423.2	336.4	428.2	421.9	433.1
8	452.5	393.1	458.3	393.5	470.0	451.1	355.9	449.5	442.8	454.8
9	474.5	404.5	476.2	410.7	488.9	473.4	364.4	463.4	462.7	461.8
10	489.1	416.4	488.2	419.0	515.2	493.9	375.6	479.3	481.6	475.9
11	499.5	426.9	507.7	433.7	533.6	507.7	388.0	489.0	506.2	484.6
12	512.8	428.5	516.5	446.0	550.0	518.2	395.2	491.9	519.2	497.2
13	527.7	441.5	532.5	454.6	565.4	535.8	402.8	492.8	536.7	507.6
recovery										
week: 14	524.3	439.6	534.8	454.9	551.0	531.8	400.4	480.6	526.4	505.5
15	537.1	442.8	544.3	458.9	564.1	541.9	411.0	493.0	537.0	520.9
16	555.0	451.7	568.3	477.1	582.0	560.0	425.1	517.5	553.9	542.4
17	567.1	459.1	584.7	483.0	594.5	569.4	435.6	537.5	564.9	556.8

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

	Animal no									
	81	82	83	84	85	86	87	88	89	90
week: -1	138.0	140.6	126.4	135.8	138.4	124.4	141.6	123.2	127.1	129.5
1	160.8	159.4	142.3	166.5	165.4	146.1	158.9	140.8	149.4	147.3
2	196.3	194.4	159.1	188.2	186.1	174.4	198.4	161.9	183.2	178.2
3	221.1	212.0	184.1	225.8	203.6	195.5	240.6	173.9	208.0	199.6
4	233.5	224.9	193.1	250.3	226.9	203.2	244.1	196.4	216.8	216.8
5	233.0	233.7	202.0	257.6	235.3	221.5	242.8	226.6	222.1	231.8
6	257.5	253.7	207.4	267.6	245.9	235.8	269.5	222.2	237.1	232.5
7	262.5	254.9	212.7	286.4	260.0	234.4	274.5	237.9	247.0	243.8
8	275.4	266.2	221.7	295.1	265.5	244.4	304.4	261.2	259.9	256.0
9	308.3	266.3	228.6	292.0	277.2	257.9	335.6	244.6	261.0	261.6
10	304.2	276.5	233.3	297.0	278.6	267.5	320.6	253.6	272.3	273.7
11	290.9	278.5	242.5	312.4	284.3	265.3	317.8	276.0	280.7	270.2
12	300.9	279.5	244.0	312.0	280.4	263.2	318.3	274.1	283.1	275.3
13	309.4	275.8	252.3	315.8	307.1	271.8	319.9	268.3	304.9	276.7

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

	Animal no									
	91	92	93	94	95	96	97	98	99	100
week: -1	145.7	138.9	137.7	126.2	151.6	127.7	133.4	148.7	126.5	139.3
1	169.9	161.0	176.7	149.1	195.9	162.7	158.3	173.7	156.4	163.5
2	195.5	177.7	209.8	168.3	226.2	191.6	195.1	209.5	194.9	209.0
3	215.5	208.1	236.3	195.9	254.0	216.6	214.4	227.8	198.7	231.5
4	224.5	226.5	244.0	226.2	282.9	227.2	229.0	240.2	225.2	244.7
5	237.8	237.6	270.4	219.3	300.7	245.8	236.7	253.5	256.5	271.7
6	251.2	247.5	291.5	245.0	313.2	262.2	258.1	267.6	244.8	286.5
7	263.8	259.1	289.4	241.4	317.9	260.8	267.6	299.3	255.9	295.2
8	272.3	277.1	297.1	249.7	327.8	279.4	280.7	301.8	267.5	301.3
9	277.2	281.0	311.5	266.0	335.7	288.2	275.8	294.2	273.2	307.6
10	287.2	283.4	322.7	272.4	343.2	299.4	296.5	306.9	300.2	311.0
11	294.4	295.9	331.9	283.8	337.7	301.9	303.2	306.3	294.8	307.2
12	296.6	297.5	327.7	276.5	348.2	293.4	301.7	306.2	284.2	320.4
13	293.8	301.4	346.0	295.5	352.1	308.4	294.5	304.1	311.4	329.1
recovery										
week: 14	291.3	299.6	345.0	280.7	353.0	302.7	293.3	301.6	291.3	321.2
15	300.2	317.3	343.4	298.7	339.1	310.7	308.6	308.1	301.4	328.1
16	304.4	317.2	339.3	301.5	346.4	309.9	315.0	317.0	319.6	341.3
17	326.7	323.4	359.3	292.5	351.9	318.4	314.9	318.6	324.7	356.7

Body weight (individuals): females group 2 : 25 ppm  
 (g/animal)

	Animal no									
	101	102	103	104	105	106	107	108	109	110
week: -1	133.1	148.4	128.5	123.8	147.1	130.3	143.3	126.4	139.6	130.0
1	168.8	174.7	163.4	145.3	181.2	152.9	173.6	162.8	152.6	163.9
2	211.3	220.7	191.6	159.8	222.1	172.4	199.2	186.8	185.1	201.2
3	226.3	220.5	217.8	194.0	257.3	197.9	224.6	206.6	205.9	211.8
4	244.8	248.8	230.7	225.4	277.3	213.3	257.9	214.8	224.4	238.4
5	255.6	270.7	247.4	230.3	293.1	225.9	279.3	235.3	232.0	255.2
6	268.7	279.1	258.7	239.3	318.8	236.8	289.8	248.0	247.6	251.4
7	274.6	287.2	264.1	255.7	319.8	252.8	294.4	250.1	256.0	273.5
8	290.2	301.2	271.0	268.5	333.2	268.5	308.6	261.7	262.8	277.4
9	297.0	309.1	279.8	274.0	336.3	269.7	321.9	271.2	254.7	279.9
10	308.0	317.7	290.2	272.6	348.0	272.1	323.3	284.2	268.2	292.9
11	317.0	317.7	290.4	282.5	354.8	279.5	321.1	281.2	273.7	294.3
12	311.9	323.7	290.5	284.7	353.4	285.0	327.1	280.8	273.0	291.7
13	316.2	332.2	302.2	290.8	360.3	288.6	335.0	290.5	278.2	306.7

Body weight (individuals): females group 3 : 50 ppm  
 (g/animal)

	Animal no									
	111	112	113	114	115	116	117	118	119	120
week: -1	142.4	159.2	125.1	135.2	126.1	134.0	130.2	123.7	149.7	126.4
1	182.8	176.6	144.3	170.7	151.3	169.2	162.3	132.5	162.5	139.9
2	204.7	211.4	181.5	194.9	179.6	200.8	191.0	174.0	199.7	171.9
3	253.5	257.4	192.4	237.1	206.6	224.3	211.8	192.3	226.3	191.3
4	288.3	295.7	206.1	252.0	217.3	248.7	234.0	206.4	256.1	208.2
5	277.6	280.2	213.2	265.0	235.0	268.0	244.7	226.2	279.6	215.1
6	299.2	313.3	235.0	276.2	245.4	285.0	268.5	236.9	264.3	230.5
7	303.2	312.6	251.7	284.2	242.9	308.6	290.3	248.0	276.2	239.1
8	311.1	303.4	272.5	291.4	252.0	315.4	293.9	260.4	294.5	247.1
9	305.9	324.8	258.9	297.5	261.6	315.0	294.1	261.4	299.9	244.2
10	317.2	322.8	275.0	312.6	269.4	339.2	299.2	269.7	303.0	253.1
11	318.8	324.2	284.6	332.2	273.8	345.3	317.7	272.8	312.6	261.4
12	320.2	328.7	267.4	310.2	266.7	336.6	319.4	270.5	315.7	260.1
13	319.4	356.5	265.7	314.9	282.3	358.3	314.2	279.2	318.3	260.7



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

	Animal no									
	121	122	123	124	125	126	127	128	129	130
week: -1	141.7	146.0	134.5	134.3	122.6	132.1	130.2	133.9	144.4	131.6
1	173.1	188.7	164.4	156.8	140.5	179.2	150.1	159.3	190.4	162.3
2	217.9	231.5	186.6	199.4	169.9	198.6	194.7	175.1	231.5	185.2
3	246.9	261.3	219.7	214.4	184.5	212.5	214.1	204.4	248.6	200.0
4	258.2	294.8	243.4	228.4	222.7	226.6	233.3	217.7	274.2	218.2
5	288.3	311.9	254.6	249.0	242.3	252.5	264.0	229.5	293.7	233.6
6	319.0	334.1	261.2	260.8	238.2	269.9	277.1	231.7	293.6	244.5
7	302.3	345.5	268.6	272.7	241.1	265.3	291.6	246.5	309.3	252.9
8	318.0	357.3	270.4	281.3	251.2	277.4	305.0	259.8	318.2	262.3
9	308.9	364.5	279.2	290.7	257.4	282.5	308.3	260.9	319.1	263.7
10	349.0	369.2	285.1	297.6	272.4	283.9	312.7	260.2	321.9	267.6
11	346.7	382.7	298.7	319.9	296.6	285.0	315.0	274.1	345.6	261.6
12	342.8	380.9	302.0	308.9	269.0	281.6	320.7	277.9	339.1	276.2
13	345.0	385.2	300.6	307.1	274.0	291.5	320.4	284.2	337.0	280.3

Body weight (individuals) : females group 5 : 625 ppm  
 (g/animal)

	Animal no									
	131	132	133	134	135	136	137	138	139	140
week: -1	124.8	128.5	136.5	144.6	140.8	139.9	124.7	150.5	124.2	142.1
1	145.4	154.9	176.3	186.2	172.5	167.6	145.8	181.9	151.5	189.6
2	170.1	181.0	211.3	216.4	199.6	201.0	175.3	217.6	167.6	229.8
3	191.0	222.0	237.2	253.5	233.0	242.9	193.6	234.1	202.9	243.6
4	198.2	250.3	259.1	280.9	260.1	258.6	200.3	254.2	217.5	272.5
5	223.2	246.5	271.3	286.3	289.1	268.5	225.1	276.8	230.6	293.7
6	237.9	243.1	283.1	297.6	287.1	307.0	233.3	299.3	230.7	299.2
7	242.3	261.1	288.5	312.5	293.0	299.7	239.0	306.4	249.6	312.8
8	247.0	275.0	299.2	326.0	303.3	301.9	246.1	325.8	252.8	319.0
9	254.3	281.4	306.8	326.9	310.4	316.0	258.6	326.3	255.2	331.5
10	266.0	312.2	319.1	329.9	303.0	330.2	267.6	342.4	254.4	339.8
11	269.4	324.0	323.3	333.5	302.4	328.8	267.1	345.1	264.7	330.2
12	266.1	296.9	326.6	340.5	310.5	322.0	280.6	345.7	268.3	344.7
13	276.9	287.8	355.3	343.8	313.8	341.9	294.7	350.6	277.2	351.3

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 Test No.: 943127  
 Test Article: CGA 329351 tech.

Body weight (individuals) : females group 6 : 1250 ppm  
 (g/animal)

	Animal no									
	141	142	143	144	145	146	147	148	149	150
week: -1	126.4	124.7	146.6	125.0	125.2	139.5	150.4	125.8	125.1	129.9
1	152.3	138.3	178.5	149.2	154.2	171.5	179.4	162.1	148.9	157.9
2	181.8	158.3	203.0	167.6	178.2	205.3	220.2	195.7	175.3	195.7
3	199.5	177.3	220.4	182.9	195.2	241.7	239.6	220.5	213.0	225.4
4	230.1	186.7	245.7	203.3	211.8	254.7	247.1	234.7	231.7	228.2
5	244.2	195.2	252.4	219.5	221.6	268.2	260.4	258.1	232.0	238.4
6	252.9	210.2	259.1	224.4	231.3	301.9	286.5	274.7	239.2	247.4
7	263.6	213.8	261.9	231.5	240.9	303.8	285.0	271.4	239.7	251.8
8	275.8	218.1	275.0	238.2	252.4	312.3	288.9	272.5	244.7	261.9
9	279.3	220.7	282.7	255.4	257.2	319.4	295.0	288.3	256.5	266.2
10	287.8	224.6	297.8	266.5	259.6	320.4	310.4	307.8	264.8	268.9
11	286.1	231.0	298.2	259.6	262.2	323.7	320.1	306.3	267.3	266.7
12	297.0	229.4	306.1	261.2	268.4	331.5	319.3	305.8	266.2	275.8
13	292.1	232.1	304.4	271.0	274.6	335.4	314.8	310.6	278.6	281.9

Body weight (individuals) : females group 6 : 1250 ppm  
 (g/animal)

	Animal no									
	151	152	153	154	155	156	157	158	159	160
week: -1	127.4	141.2	124.9	153.8	127.8	148.3	146.9	149.9	128.6	132.0
1	149.5	163.3	145.6	187.3	161.5	168.1	184.7	180.1	157.2	163.2
2	172.2	189.1	176.1	228.0	181.8	197.4	206.8	205.6	188.7	186.9
3	197.9	212.6	211.1	250.3	217.8	225.5	239.0	238.9	216.8	210.9
4	210.6	215.9	222.0	269.7	247.6	223.8	259.1	260.0	252.4	219.6
5	222.6	251.4	238.3	297.3	265.5	248.5	264.8	277.2	270.9	243.8
6	226.4	270.4	250.9	323.2	263.3	269.7	272.9	283.4	266.9	250.5
7	239.4	279.2	254.9	300.1	289.0	262.6	294.4	293.7	281.6	263.0
8	246.6	296.3	265.9	309.1	295.6	274.5	330.5	313.0	297.9	273.8
9	249.0	299.8	268.3	317.6	324.7	292.6	327.9	321.4	309.9	282.6
10	249.8	303.4	277.6	328.3	319.7	282.4	323.4	319.5	309.1	276.6
11	254.7	301.1	285.1	355.1	321.1	284.0	328.9	329.0	319.8	287.3
12	260.8	309.3	286.0	350.2	323.0	291.1	328.7	348.1	335.2	286.1
13	261.4	316.7	287.3	345.8	332.8	312.2	356.8	364.4	352.0	293.6
recovery										
week: 14	262.0	307.8	281.9	333.4	335.2	299.2	329.1	334.6	317.8	292.2
15	267.4	300.8	291.6	355.3	354.9	302.0	333.5	339.8	328.7	327.6
16	262.9	310.8	308.7	379.8	340.4	324.4	340.1	352.5	336.0	353.9
17	272.1	324.0	323.0	363.0	348.3	328.0	335.9	355.1	333.0	342.9

6.4. Food consumption (individuals)

Food consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 1 : 0 ppm

	Cage no			
	1	2	3	4
week: -1	139.1	122.7	139.3	127.4
1	158.5	130.9	153.2	137.4
2	203.1	172.2	201.1	171.9
3	183.3	158.9	190.1	164.5
4	198.1	178.3	210.3	182.9
5	194.2	177.8	204.7	179.0
6	191.4	183.5	208.0	184.5
7	196.6	194.4	215.0	196.9
8	188.4	176.7	199.7	186.9
9	180.1	158.6	184.6	171.0
10	183.8	164.5	193.9	174.0
11	183.8	169.0	206.9	178.8
12	180.5	161.2	185.0	159.7
13	194.7	177.0	202.7	174.8
recovery				
week: 14			199.2	162.1
15			203.5	191.5
16			197.9	183.0
17			200.6	192.4

Food consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 2 : 25 ppm

	Cage no	
	5	6
week: -1	135.1	139.5
1	146.4	149.1
2	171.9	177.2
3	167.7	173.7
4	182.1	190.7
5	179.2	182.2
6	188.8	188.0

Food consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 2 : 25 ppm

	Cage no	
	5	6
7	194.3	199.9
8	175.8	182.3
9	162.2	169.7
10	176.8	179.8
11	191.0	193.4
12	176.3	176.9
13	190.8	190.5

Food consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 3 : 50 ppm

	Cage no	
	7	8
week: -1	126.6	140.7
1	145.0	156.9
2	177.3	179.5
3	171.3	175.1
4	178.3	185.9
5	172.7	174.7
6	178.3	180.1
7	186.9	195.1
8	177.4	182.2
9	160.4	175.6
10	174.7	173.8
11	184.5	177.1
12	168.5	164.1
13	182.0	183.3

Food consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 4 : 250 ppm

week:	Cage no	
	9	10
-1	138.8	126.1
1	151.8	139.9
2	186.5	170.1
3	183.8	162.9
4	202.5	173.9
5	198.8	171.9
6	203.5	175.9
7	210.0	184.0
8	200.9	177.6
9	192.6	173.3
10	198.7	175.2
11	203.6	182.8
12	184.6	173.3
13	201.2	183.6

Food consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 5 : 625 ppm

week:	Cage no	
	11	12
-1	136.2	139.9
1	154.1	155.0
2	188.9	189.7
3	180.9	177.6
4	190.5	199.5
5	188.1	194.3
6	195.1	206.6
7	204.2	214.2
8	196.0	206.5
9	194.1	204.0
10	190.7	203.8
11	200.5	207.4
12	185.6	202.5
13	199.6	216.8

Food consumption (individuals, determined cagewise) : males  
 (g/animal/week) group 6 : 1250 ppm

	Cage no			
	13	14	15	16
week: -1	142.5	142.3	136.6	139.9
1	156.6	159.8	154.4	156.2
2	187.0	188.7	191.0	194.2
3	178.7	173.5	177.7	181.6
4	197.4	194.0	190.5	201.0
5	180.6	178.8	183.0	185.6
6	182.2	193.9	192.8	191.7
7	192.9	197.6	201.2	203.6
8	190.2	195.4	196.9	187.8
9	164.9	189.4	180.1	173.5
10	182.0	190.5	187.2	190.9
11	184.4	196.3	196.1	192.6
12	161.2	182.0	179.3	178.3
13	181.8	198.0	192.7	195.9
recovery				
week: 14			185.1	175.2
15			204.1	203.3
16			197.4	197.3
17			203.4	203.8

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Food consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 1 : 0 ppm

	Cage no			
	17	18	19	20
week: -1	105.3	101.0	104.1	106.5
1	103.5	102.8	109.8	111.3
2	125.3	129.8	133.3	135.8
3	127.5	135.4	132.8	119.0
4	139.6	135.8	145.4	141.4
5	135.2	133.9	139.8	138.4
6	134.8	138.5	152.0	146.2
7	145.5	151.6	149.9	158.5
8	138.7	141.3	138.4	132.5
9	131.1	134.3	130.6	125.7
10	126.6	124.0	129.9	207.4
11	132.8	134.9	133.6	120.2
12	125.8	119.1	127.6	119.0
13	143.9	129.5	133.2	127.7
recovery				
week: 14			124.0	106.7
15			134.0	137.4
16			129.3	143.8
17			144.6	143.7

Food consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 2 : 25 ppm

	Cage no	
	21	22
week: -1	106.7	106.0
1	122.5	110.6
2	137.0	127.1
3	135.4	127.1
4	150.8	143.9
5	127.6	122.0
6	145.8	142.4
7	154.1	142.6
8	138.7	133.3
9	127.2	120.3
10	124.2	131.5
11	127.4	126.1
12	128.4	129.3

Food consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 2 : 25 ppm

	Cage no	
	21	22
13	133.4	139.1

Food consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 3 : 50 ppm

	Cage no	
	23	24
week: -1	104.3	107.1
1	113.0	112.9
2	138.2	126.5
3	157.4	128.7
4	135.6	145.8
5	119.4	144.7
6	133.9	141.1
7	141.3	155.8
8	116.8	124.3
9	115.8	115.9
10	131.4	133.1
11	118.4	131.9
12	102.2	118.7
13	125.3	131.0

Food consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 4 : 250 ppm

	Cage no	
	25	26
week: -1	109.3	109.0
1	118.2	117.3
2	142.9	136.4
3	136.1	129.4
4	153.4	156.2
5	112.0	155.6
6	140.7	148.2
7	137.4	148.2
8	133.6	136.2



Food consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 4 : 250 ppm

	Cage no	
	25	26
9	139.2	127.1
10	156.6	127.7
11	130.8	128.8
12	117.0	122.6
13	123.9	128.4

Food consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 5 : 625 ppm

	Cage no	
	27	28
week: -1	113.0	113.9
1	121.0	121.1
2	134.6	132.3
3	144.7	135.1
4	158.7	155.8
5	136.8	163.6
6	138.2	160.3
7	151.0	151.5
8	145.1	144.0
9	147.8	142.5
10	147.4	142.2
11	138.9	133.7
12	128.8	138.2
13	145.4	144.9

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3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 234

Test No.: 943127

Test Article: CGA 329351 tech.

Food consumption (individuals, determined cagewise) : females  
(g/animal/week)

group 6 : 1250 ppm

	Cage no			
	29	30	31	32
week: -1	98.78	103.9	107.9	117.0
1	105.8	116.9	110.7	118.1
2	122.0	145.2	135.0	142.4
3	117.9	140.7	134.2	139.3
4	130.2	143.3	151.8	152.8
5	137.7	95.38	172.5	89.48
6	120.0	137.4	136.1	144.7
7	128.6	139.9	143.0	154.5
8	119.6	129.0	137.4	149.7
9	121.2	127.6	121.0	126.5
10	120.3	131.1	134.1	121.5
11	117.4	128.4	132.3	134.8
12	111.4	124.4	121.9	143.9
13	126.6	132.9	130.8	141.6
recovery				
week: 14			119.8	121.4
15			142.3	151.3
16			143.9	146.3
17			138.4	132.5

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6.5. Water consumption (individuals)

Water consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 1 : 0 ppm

	Cage no			
	1	2	3	4
week: -1	195.2	150.6	187.3	156.8
1	239.7	176.7	224.4	191.2
2	274.7	206.1	264.5	220.6
3	308.4	239.1	271.2	239.0
4	315.1	236.5	269.6	250.2
5	309.9	253.2	272.0	235.3
6	295.8	249.2	302.5	260.4
7	300.3	267.8	278.7	248.1
8	308.6	246.4	296.8	265.6
9	326.8	214.5	296.9	244.0
10	322.0	252.8	296.8	242.6
11	226.5	228.2	261.4	223.3
12	289.4	244.9	282.2	253.0
13	260.0	235.2	261.0	189.6
recovery				
week: 14			217.7	171.4
15			272.2	228.8
16			249.1	239.5
17			243.3	215.9

Water consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 2 : 25 ppm

	Cage no	
	5	6
week: -1	168.1	184.1
1	203.6	211.5
2	236.0	233.9
3	288.5	251.7
4	306.6	248.6
5	297.9	251.1
6	312.6	278.0

Water consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 2 : 25 ppm

	Cage no	
	5	6
7	282.8	259.1
8	319.6	264.7
9	300.0	264.5
10	336.1	279.3
11	321.4	263.9
12	316.1	260.4
13	298.9	269.2

Water consumption (individuals, determined cagewise) : males  
 (g/animal/week)

group 3 : 50 ppm

	Cage no	
	7	8
week: -1	154.4	182.8
1	179.3	215.0
2	197.5	229.7
3	218.7	258.3
4	226.8	262.5
5	243.7	249.6
6	272.7	264.0
7	248.8	262.1
8	266.8	282.0
9	261.8	265.4
10	283.4	262.8
11	250.5	249.9
12	227.1	263.2
13	224.8	236.2

Water consumption (individuals, determined cagewise) : males  
 (g/animal/week) group 4 : 250 ppm

	Cage no	
	9	10
week: -1	185.2	151.5
1	226.4	205.0
2	273.8	216.0
3	300.6	279.4
4	307.7	263.6
5	315.7	306.2
6	299.6	296.1
7	294.8	294.7
8	320.2	329.8
9	306.7	335.9
10	327.7	301.7
11	285.9	297.8
12	278.7	233.2
13	279.9	274.1

Water consumption (individuals, determined cagewise) : males  
 (g/animal/week) group 5 : 625 ppm

	Cage no	
	11	12
week: -1	181.9	173.7
1	209.2	201.3
2	254.8	238.3
3	280.4	272.4
4	291.3	278.5
5	301.9	281.6
6	308.1	296.8
7	371.4	299.1
8	314.4	306.9
9	303.5	298.5
10	304.5	357.8
11	298.2	278.5
12	280.4	320.3
13	260.1	295.4

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Water consumption (individuals, determined cagewise) : males  
(g/animal/week)

group 6 : 1250 ppm

	Cage no			
	13	14	15	16
week: -1	178.2	175.8	210.1	160.9
1	195.0	212.5	233.8	192.6
2	229.5	235.3	251.7	216.2
3	208.3	235.2	266.8	231.0
4	244.3	238.4	277.3	232.8
5	262.9	274.9	276.7	234.7
6	273.6	262.8	274.8	239.8
7	270.6	277.0	284.7	227.8
8	275.0	287.3	322.7	227.9
9	228.6	282.1	286.3	226.5
10	261.7	279.6	318.9	232.8
11	210.3	304.4	293.9	234.4
12	234.9	279.6	268.7	219.1
13	220.9	294.8	263.2	218.4
recovery				
week: 14			235.3	185.4
15			248.2	227.9
16			253.3	233.7
17			258.9	218.3

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Test No.: 943127

Test Article: CGA 329351 tech.

Water consumption (individuals, determined cagewise) : females  
(g/animal/week)

group 1 : 0 ppm

	Cage no			
	17	18	19	20
week: -1	150.8	149.1	151.8	170.5
1	161.3	148.4	192.4	196.7
2	178.5	185.1	188.7	214.8
3	184.8	190.4	224.7	216.6
4	223.2	193.1	245.7	228.5
5	184.5	186.6	218.3	239.7
6	210.4	185.8	254.1	243.0
7	220.5	196.3	209.9	249.6
8	200.9	201.7	231.7	215.9
9	190.3	192.9	236.5	233.5
10	222.6	198.7	250.9	229.2
11	200.6	168.8	219.9	232.3
12	176.4	156.2	212.2	227.2
13	195.3	182.7	234.5	207.3
recovery				
week: 14			199.9	184.8
15			241.4	210.8
16			234.9	228.3
17			236.2	232.1

Water consumption (individuals, determined cagewise) : females  
(g/animal/week)

group 2 : 25 ppm

	Cage no	
	21	22
week: -1	161.1	162.4
1	200.8	167.6
2	210.6	170.7
3	219.9	181.4
4	213.6	219.2
5	199.1	201.1
6	186.6	206.9
7	180.4	210.9
8	201.2	210.3
9	194.7	160.3
10	191.2	235.8
11	210.0	167.2
12	177.7	186.1

Water consumption (individuals, determined cagewise) : females  
 (g/animal/week) group 2 : 25 ppm

	Cage no	
	21	22
13	246.4	187.0

Water consumption (individuals, determined cagewise) : females  
 (g/animal/week) group 3 : 50 ppm

	Cage no	
	23	24
week: -1	158.8	153.9
1	174.7	152.7
2	223.3	190.0
3	244.6	193.2
4	245.4	219.1
5	210.1	217.6
6	251.0	213.5
7	263.3	223.0
8	270.1	211.0
9	209.9	188.0
10	224.8	207.8
11	212.4	188.7
12	247.5	203.0
13	228.1	184.0

Water consumption (individuals, determined cagewise) : females  
 (g/animal/week) group 4 : 250 ppm

	Cage no	
	25	26
week: -1	141.1	176.7
1	173.3	218.8
2	190.5	200.2
3	186.6	219.5
4	232.3	259.0
5	200.4	219.8
6	224.1	234.8
7	180.2	205.2
8	204.1	221.1



Water consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 4 : 250 ppm

		Cage no	
		25	26
	9	196.3	216.2
	10	241.8	241.2
	11	198.8	216.4
	12	174.9	188.9
	13	172.6	226.7

Water consumption (individuals, determined cagewise) : females  
 (g/animal/week)

group 5 : 625 ppm

		Cage no	
		27	28
week: -1		149.1	177.7
	1	182.6	192.4
	2	183.5	177.5
	3	217.0	215.7
	4	239.3	224.1
	5	217.3	219.5
	6	223.7	212.2
	7	233.9	190.9
	8	259.6	199.4
	9	246.8	189.1
	10	259.1	215.0
	11	245.4	198.8
	12	241.4	189.4
	13	249.9	202.3

Water consumption (individuals, determined cagewise) : females  
 (g/animal/week)  
 group 6 : 1250 ppm

	Cage no			
	29	30	31	32
week: -1	119.3	157.6	161.0	145.3
1	146.4	183.4	187.6	184.1
2	152.3	197.3	192.2	178.2
3	147.0	217.0	216.4	223.6
4	180.2	224.1	224.3	214.7
5	164.9	220.8	217.5	236.1
6	176.0	220.8	245.4	209.0
7	164.0	217.3	195.8	206.9
8	169.5	221.6	229.5	247.9
9	164.1	195.4	195.9	213.2
10	171.5	203.1	235.2	182.0
11	152.3	218.3	232.8	212.4
12	138.3	250.3	218.3	209.3
13	150.8	195.2	241.9	232.4
<b>recovery</b>				
week: 14			200.9	171.4
15			231.4	214.8
16			242.5	248.4
17			198.2	183.3

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6.6. Ophthalmological examinations (individuals)

% : unilateral  
 n.d. : not determined

Ophthalmological examination (individuals) : males  
 Day -6 (October 19, 1994) group 1 : 0 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
001	normal	absent	normal	present	none
002	normal	absent	normal	present	none
003	normal	absent	normal	present	none
004	normal	absent	normal	present	none
005	normal	absent	normal	present	none
006	normal	absent	normal	present	none
007	normal	absent	normal	present	none
008	normal	absent	normal	present	none
009	normal	absent	normal	present	none
010	normal	absent	normal	present	none
011	normal	absent	normal	present	none
012	normal	absent	normal	present	none
013	normal	absent	normal	present	none
014	normal	absent	normal	present	none
015	normal	absent	normal	present	none
016	normal	absent	normal	present	none
017	normal	absent	normal	present	none
018	normal	absent	normal	present	none
019	normal	absent	normal	present	none
020	normal	absent	normal	present	none

Ophthalmological examination (individuals) : males  
 Day -6 (October 19, 1994) group 6 : 1250 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
061	normal	absent	normal	present	none
062	normal	absent	normal	present	none
063	normal	absent	normal	present	none
064	normal	absent	normal	present	none
065	normal	absent	normal	present	none
066	normal	absent	normal	present	none
067	normal	absent	normal	present	none
068	normal	absent	normal	present	none

Ophthalmological examination (individuals) : males  
 Day -6 (October 19, 1994) group 6 : 1250 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
069	normal	absent	normal	present	none
070	normal	absent	normal	present	none
071	normal	absent	normal	present	none
072	normal	absent	normal	present	none
073	normal	absent	normal	present	none
074	normal	absent	normal	present	none
075	normal	absent	normal	present	none
076	normal	absent	normal	present	none
077	normal	absent	normal	present	none
078	normal	absent	normal	present	none
079	normal	absent	normal	present	none
080	normal	absent	normal	present	none

Ophthalmological examination (individuals) : males  
 Day 87 (week 13 / January 19, 1995) group 1 : 0 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
001	normal	absent	normal	present	none
002	normal	absent	normal	present	none
003	normal	absent	normal	present	none
004	normal	absent	normal	present	none
005	normal	absent	normal	present	none
006	normal	absent	normal	present	none
007	normal	absent	normal	present	none
008	normal	absent	normal	present	none
009	normal	absent	normal	present	none
010	normal	absent	normal	present	none
011	normal	absent	normal	present	none
012	normal	absent	normal	present	none
013	normal	absent	normal	present	none
014	normal	absent	normal	present	none
015	normal	absent	normal	present	none
016	normal	absent	normal	present	none
017	normal	absent	normal	present	none
018	normal	absent	normal	present	none
019	normal	absent	normal	present	none
020	normal	absent	normal	present	none

Test No.: 943127

Test Article: CGA 329351 tech.

Ophthalmological examination (individuals) : males  
 Day 87 (week 13 / January 19, 1995) group 6 : 1250 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
061	normal	absent	normal	present	none
062	normal	absent	normal	present	none
063	normal	absent	normal	present	none
064	normal	absent	normal	present	none
065	normal	absent	normal	present	none
066	normal	absent	normal	present	none
067	normal	absent	normal	present	none
068	normal	absent	normal	present	none
069	normal	absent	normal	present	none
070	normal	absent	normal	present	none
071	normal	absent	normal	present	none
072	normal	absent	normal	present	none
073	normal	absent	normal	present	none
074	normal	absent	normal	present	none
075	normal	absent	normal	present	none
076	normal	absent	normal	present	none
077	normal	absent	normal	present	none
078	normal	absent	normal	present	none
079	normal	absent	normal	present	none
080	normal	absent	normal	present	none

Ophthalmological examination (individuals) : males  
 Day 115 (week 17 / February 16, 1995) group 1 : 0 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
011	normal	absent	normal	present	none
012	normal	absent	normal	present	none
013	normal	absent	normal	present	none
014	normal	absent	normal	present	none
015	normal	absent	normal	present	none
016	normal	absent	normal	present	none
017	normal	absent	normal	present	none
018	normal	absent	normal	present	none
019	normal	absent	normal	present	none
020	normal	absent	normal	present	none

Test No.: 943127

Test Article: CGA 329351 tech.

Ophthalmological examination (individuals) : males  
 Day 115 (week 17 / February 16, 1995) group 6 : 1250 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
071	normal	absent	normal	present	none
072	normal	absent	normal	present	none
073	normal	absent	normal	present	none
074	normal	absent	normal	present	none
075	normal	absent	normal	present	none
076	normal	absent	normal	present	none
077	normal	absent	normal	present	none
078	normal	absent	normal	present	none
079	normal	absent	normal	present	none
080	normal	absent	normal	present	none

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Test No.: 943127

Test Article: CGA 329351 tech.

Ophthalmological examination (individuals) : females  
 Day -6 (October 19, 1994) group 1 : 0 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
081	normal	absent	normal	present	none
082	normal	absent	normal	present	none
083	normal	absent	normal	present	none
084	normal	absent	normal	present	none
085	normal	absent	normal	present	none
086	normal	absent	normal	present	none
087	normal	absent	normal	present	none
088	normal	absent	normal	present	none
089	normal	absent	normal	present	none
090	normal	absent	normal	present	none
091	normal	absent	normal	present	none
092	normal	absent	normal	present	none
093	normal	absent	normal	present	none
094	normal	absent	normal	present	none
095	normal	absent	normal	present	none
096	normal	absent	normal	present	none
097	normal	absent	normal	present	none
098	normal	absent	normal	present	none
099	normal	absent	normal	present	none
100	normal	absent	normal	present	none

Ophthalmological examination (individuals) : females  
 Day -6 (October 19, 1994) group 6 : 1250 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
141	normal	absent	normal	present	none
142	normal	absent	normal	present	none
143	normal	absent	normal	present	none
144	normal	absent	normal	present	none
145	normal	absent	normal	present	none
146	normal	absent	normal	present	none
147	normal	absent	normal	present	none
148	normal	absent	normal	present	none
149	normal	absent	normal	present	none
150	normal	absent	normal	present	none
151	normal	absent	normal	present	none
152	normal	absent	normal	present	none
153	normal	absent	normal	present	none
154	normal	absent	normal	present	none
155	normal	absent	normal	present	none
156	normal	absent	normal	present	none

Test No.: 943127

Test Article: CGA 329351 tech.

Ophthalmological examination (individuals) : females  
 Day -6 (October 19, 1994) group 6 : 1250 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
157	normal	absent	normal	present	none
158	normal	absent	normal	present	none
159	normal	absent	normal	present	none
160	normal	absent	normal	present	none

Ophthalmological examination (individuals) : females  
 Day 87 (week 13 / January 19, 1995) group 1 : 0 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
081	normal	absent	normal	present	none
082	normal	absent	normal	present	none
083	normal	absent	normal	present	none
084	normal	absent	normal	present	none
085	normal	absent	normal	present	none
086	normal	absent	normal	present	none
087	normal	absent	normal	present	none
088	normal	absent	normal	present	none
089	normal	absent	normal	present	none
090	normal	absent	normal	present	none
091	normal	absent	normal	present	none
092	normal	absent	normal	present	none
093	normal	absent	normal	present	none
094	normal	absent	normal	present	none
095	normal	absent	normal	present	none
096	normal	absent	normal	present	none
097	normal	absent	normal	present	none
098	normal	absent	normal	present	none
099	normal	absent	normal	present	none
100	normal	absent	normal	present	none



Test No.: 943127

Test Article: CGA 329351 tech.

Ophthalmological examination (individuals) : females  
 Day 87 (week 13 / January 19, 1995) group 6 : 1250 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
141	normal	absent	normal	present	none
142	normal	absent	normal	present	none
143	normal	absent	normal	present	none
144	normal	absent	normal	present	none
145	normal	absent	normal	present	none
146	normal	absent	normal	present	none
147	normal	absent	normal	present	none
148	normal	absent	normal	present	none
149	normal	absent	normal	present	none
150	normal	absent	normal	present	none
151	normal	absent	normal	present	none
152	normal	absent	normal	present	none
153	normal	absent	normal	present	none
154	normal	absent	normal	present	none
155	normal	absent	normal	present	none
156	normal	absent	normal	present	none
157	normal	absent	normal	present	none
158	normal	absent	normal	present	none
159	normal	absent	normal	present	none
160	normal	absent	normal	present	none

Ophthalmological examination (individuals) : females  
 Day 115 (week 17 / February 16, 1995) group 1 : 0 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
091	normal	absent	normal	present	none
092	normal	absent	normal	present	none
093	normal	absent	normal	present	none
094	normal	absent	normal	present	none
095	normal	absent	normal	present	none
096	normal	absent	normal	present	none
097	normal	absent	normal	present	none
098	normal	absent	normal	present	none
099	normal	absent	normal	present	none
100	normal	absent	normal	present	none

Test No.: 943127

Test Article: CGA 329351 tech.

Ophthalmological examination (individuals) : females  
Day 115 (week 17 / February 16, 1995) group 6 : 1250 ppm

Animal number	eyelid(s) and surrounds	exudate	eye(s) and/or color	pupil(s) reaction	remarks
151	normal	absent	normal	present	none
152	normal	absent	normal	present	none
153	normal	absent	normal	present	none
154	normal	absent	normal	present	none
155	normal	absent	normal	present	none
156	normal	absent	normal	present	none
157	normal	absent	normal	present	none
158	normal	absent	normal	present	none
159	normal	absent	normal	present	none
160	normal	absent	normal	present	none

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6.7. Hematology (individuals)

Hematology (individuals): males

group 1  
0 ppm

		Animal no									
		1	2	3	4	5	6	7	8	9	10
RBC (T/l)											
week:	14	8.010	8.650	8.080	9.350	8.080	8.040	8.480	8.220	8.230	8.310
Hb (mmol/l)											
week:	14	9.400	9.400	9.400	9.800	9.300	9.200	9.600	9.400	9.700	9.800
Hct (l)											
week:	14	0.424	0.429	0.425	0.451	0.423	0.418	0.431	0.424	0.435	0.423
MCV (fl)											
week:	14	52.90	49.60	52.70	48.20	52.30	51.90	50.80	51.60	52.80	50.90
RDW (l)											
week:	14	0.224	0.150	0.149	0.145	0.135	0.130	0.120	0.129	0.125	0.119
MCH (fmol)											
week:	14	1.170	1.090	1.170	1.050	1.150	1.140	1.130	1.140	1.180	1.180
MCHC (mmol/l)											
week:	14	22.17	21.96	22.15	21.76	21.92	21.95	22.30	22.09	22.34	23.15
HDW (mmol/l)											
week:	14	2.150	1.440	1.950	1.470	2.150	1.940	1.450	2.010	1.560	1.480
WBC (G/l)											
week:	14	7.490	8.390	12.24	11.06	9.980	13.60	13.18	11.63	12.46	11.09

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 1  
0 ppm

		Animal no									
		1	2	3	4	5	6	7	8	9	10
Neut	(1)										
week:	14	0.141	0.134	0.168	0.212	0.138	0.235	0.111	0.132	0.132	0.157
Eos	(1)										
week:	14	0.016	0.006	0.075	0.010	0.018	0.014	0.005	0.017	0.010	0.010
Baso	(1)										
week:	14	0.002	0.002	0.003	0.004	0.004	0.003	0.006	0.003	0.004	0.004
Lympho	(1)										
week:	14	0.719	0.767	0.669	0.609	0.750	0.665	0.799	0.739	0.762	0.696
Mono	(1)										
week:	14	0.054	0.059	0.043	0.097	0.057	0.044	0.041	0.062	0.055	0.095
Luc	(1)										
week:	14	0.067	0.031	0.042	0.067	0.034	0.039	0.038	0.048	0.036	0.039
Neut	(G/l)										
week:	14	1.060	1.130	2.050	2.350	1.380	3.200	1.460	1.530	1.650	1.740
Eos	(G/l)										
week:	14	0.120	0.050	0.920	0.110	0.180	0.190	0.070	0.200	0.120	0.110
Baso	(G/l)										
week:	14	0.020	0.020	0.040	0.040	0.040	0.040	0.070	0.030	0.050	0.040
Lympho	(G/l)										
week:	14	5.380	6.440	8.190	6.740	7.480	9.040	10.53	8.590	9.490	7.720
Mono	(G/l)										
week:	14	0.410	0.490	0.530	1.070	0.570	0.600	0.540	0.720	0.690	1.050

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (individuals): males

group 1  
0 ppm

		Animal no									
		1	2	3	4	5	6	7	8	9	10
Luc (G/l)											
week:	14	0.500	0.260	0.510	0.750	0.340	0.530	0.500	0.550	0.450	0.430
Plt (G/l)											
week:	14	1026	956.0	676.0	1002	941.0	984.0	1069	824.0	1097	885.0
PT(CS) (sec)											
week:	14	32.14	31.77	29.20	25.52	21.80	30.27	29.03	29.45	32.42	33.05

Hematology (individuals): males

group 1  
0 ppm

		Animal no									
		11	12	13	14	15	16	17	18	19	20
RBC (T/l)											
week:	14	8.760	8.860	8.460	8.440	8.960	8.810	8.840	8.770	8.670	8.630
	18	8.910	8.940	8.610	8.310	9.020	8.680	8.720	8.810	8.690	8.570
Hb (mmol/l)											
week:	14	9.900	9.600	9.800	9.800	9.700	9.900	9.900	9.700	9.600	9.400
	18	9.800	9.600	9.700	9.500	9.700	9.700	9.900	9.600	9.500	9.200
Hct (l)											
week:	14	0.437	0.430	0.440	0.440	0.442	0.447	0.446	0.439	0.435	0.426
	18	0.457	0.443	0.448	0.428	0.453	0.450	0.449	0.451	0.435	0.429
MCV (fl)											
week:	14	49.80	48.50	52.00	52.20	49.30	50.70	50.50	50.00	50.20	49.40
	18	51.30	49.50	52.00	51.50	50.20	51.90	51.50	51.20	50.10	50.10
RDW (l)											
week:	14	0.129	0.132	0.117	0.146	0.131	0.123	0.130	0.122	0.138	0.146
	18	0.149	0.136	0.122	0.122	0.127	0.125	0.136	0.124	0.122	0.124

Test No.: 943127

Test Article: CGA 329351 tech.

## Rematology (individuals): males

group 1  
0 ppm

		Animal no									
		11	12	13	14	15	16	17	18	19	20
MCH	(fmol)										
week:	14	1.130	1.080	1.160	1.160	1.080	1.120	1.120	1.100	1.110	1.090
	18	1.100	1.070	1.120	1.140	1.080	1.120	1.140	1.090	1.090	1.080
MCHC	(mmol/l)										
week:	14	22.62	22.30	22.22	22.23	21.87	22.14	22.26	22.01	22.02	22.15
	18	21.42	21.61	21.57	22.23	21.52	21.63	22.03	21.20	21.84	21.53
HDW	(mmol/l)										
week:	14	1.710	1.620	1.460	1.490	1.460	1.540	1.810	1.420	1.490	1.470
	18	1.660	1.590	1.440	1.450	1.420	1.440	1.740	1.370	1.480	1.440
WBC	(G/l)										
week:	14	10.78	12.23	9.230	10.87	8.940	10.67	13.27	7.270	11.38	9.400
	18	9.770	12.83	9.280	11.59	8.410	10.39	9.760	8.870	12.38	10.57
Neut	(1)										
week:	14	0.204	0.165	0.251	0.275	0.168	0.133	0.124	0.164	0.162	0.114
	18	0.234	0.146	0.138	0.237	0.169	0.163	0.159	0.234	0.210	0.140
Eos	(1)										
week:	14	0.023	0.012	0.009	0.011	0.014	0.014	0.020	0.013	0.005	0.011
	18	0.025	0.015	0.012	0.011	0.013	0.023	0.025	0.020	0.009	0.011
Baso	(1)										
week:	14	0.003	0.003	0.003	0.004	0.003	0.003	0.005	0.003	0.005	0.003
	18	0.003	0.005	0.003	0.004	0.004	0.004	0.004	0.004	0.004	0.002
Lympho	(1)										
week:	14	0.660	0.693	0.623	0.608	0.668	0.742	0.731	0.702	0.747	0.787
	18	0.627	0.723	0.733	0.628	0.667	0.722	0.721	0.637	0.692	0.733
Mono	(1)										
week:	14	0.052	0.066	0.068	0.059	0.079	0.063	0.077	0.074	0.044	0.048
	18	0.055	0.060	0.065	0.069	0.078	0.056	0.056	0.063	0.046	0.056

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 1  
0 ppm

		Animal no									
		11	12	13	14	15	16	17	18	19	20
Luc											
(1)											
week:	14	0.058	0.061	0.047	0.043	0.067	0.045	0.044	0.045	0.036	0.037
	18	0.056	0.051	0.049	0.052	0.070	0.032	0.035	0.042	0.041	0.058
Neut											
(G/l)											
week:	14	2.200	2.020	2.320	2.990	1.500	1.420	1.650	1.190	1.850	1.070
	18	2.290	1.880	1.280	2.740	1.420	1.700	1.550	2.070	2.600	1.470
Eos											
(G/l)											
week:	14	0.240	0.140	0.080	0.120	0.130	0.150	0.270	0.090	0.060	0.100
	18	0.250	0.190	0.120	0.120	0.110	0.240	0.250	0.180	0.110	0.120
Baso											
(G/l)											
week:	14	0.030	0.040	0.030	0.040	0.030	0.030	0.060	0.020	0.050	0.030
	18	0.030	0.060	0.020	0.040	0.030	0.040	0.040	0.040	0.050	0.020
Lympho											
(G/l)											
week:	14	7.120	8.470	5.750	6.610	5.970	7.910	9.700	5.100	8.500	7.400
	18	6.120	9.280	6.810	7.280	5.610	7.500	7.030	5.650	8.560	7.750
Mono											
(G/l)											
week:	14	0.560	0.800	0.620	0.650	0.710	0.670	1.020	0.540	0.500	0.450
	18	0.530	0.770	0.600	0.800	0.650	0.580	0.550	0.560	0.570	0.590
Luc											
(G/l)											
week:	14	0.630	0.750	0.430	0.460	0.600	0.480	0.580	0.330	0.410	0.350
	18	0.550	0.650	0.460	0.600	0.590	0.330	0.340	0.370	0.500	0.610
Plt											
(G/l)											
week:	14	853.0	1008	921.0	1065	939.0	1116	1006	956.0	1046	1051
	18	861.0	1029	987.0	1059	992.0	1108	1086	808.0	988.0	1069
PT(CS)											
(sec)											
week:	14	35.60	34.00	39.38	37.45	34.31	34.64	32.85	34.45	37.41	36.80
	18	34.89	34.56	41.11	37.58	31.94	35.58	32.06	25.74	38.42	38.18

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 2  
25 ppm

		Animal no									
		21	22	23	24	25	26	27	28	29	30
RBC (T/l)											
week:	14	8.630	8.960	8.580	8.520	8.660	8.510	8.700	9.060	8.330	8.540
Hb (mmol/l)											
week:	14	10.00	9.700	9.400	9.800	10.00	9.800	9.800	9.800	9.700	9.600
Hct (l)											
week:	14	0.449	0.458	0.435	0.448	0.447	0.446	0.439	0.450	0.441	0.436
MCV (fl)											
week:	14	52.00	51.10	50.60	52.60	51.60	52.40	50.40	49.60	52.90	51.10
RDW (l)											
week:	14	0.128	0.139	0.136	0.127	0.121	0.123	0.120	0.126	0.129	0.123
MCH (fmol)											
week:	14	1.160	1.080	1.090	1.150	1.150	1.150	1.120	1.080	1.170	1.130
MCHC (mmol/l)											
week:	14	22.29	21.17	21.61	21.93	22.27	22.01	22.25	21.71	22.03	22.11
HDW (mmol/l)											
week:	14	1.520	1.430	2.190	1.630	1.550	1.430	1.550	1.540	2.020	1.510
WBC (G/l)											
week:	14	10.14	8.310	13.68	12.76	11.16	10.90	11.93	11.41	10.20	10.86
Neut (l)											
week:	14	0.216	0.199	0.145	0.191	0.340	0.217	0.110	0.130	0.095	0.159
Eos (l)											
week:	14	0.010	0.017	0.023	0.017	0.020	0.009	0.008	0.017	0.008	0.014



Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 2  
25 ppm

		Animal no									
		21	22	23	24	25	26	27	28	29	30
Baso (1)											
week:	14	0.003	0.003	0.005	0.003	0.003	0.005	0.005	0.006	0.005	0.004
Lympho (1)											
week:	14	0.678	0.664	0.741	0.709	0.562	0.672	0.746	0.742	0.781	0.721
Mono (1)											
week:	14	0.049	0.073	0.056	0.053	0.045	0.051	0.080	0.058	0.074	0.059
Luc (1)											
week:	14	0.043	0.044	0.031	0.026	0.031	0.046	0.051	0.048	0.037	0.043
Neut (G/l)											
week:	14	2.190	1.650	1.980	2.440	3.790	2.360	1.310	1.480	0.970	1.720
Eos (G/l)											
week:	14	0.110	0.140	0.310	0.210	0.220	0.100	0.100	0.200	0.080	0.160
Baso (G/l)											
week:	14	0.030	0.020	0.060	0.040	0.030	0.050	0.060	0.060	0.050	0.040
Lympho (G/l)											
week:	14	6.880	5.520	10.13	9.050	6.270	7.330	8.890	8.460	7.960	7.830
Mono (G/l)											
week:	14	0.500	0.610	0.770	0.680	0.500	0.560	0.960	0.660	0.750	0.640
Luc (G/l)											
week:	14	0.440	0.370	0.430	0.330	0.350	0.500	0.610	0.540	0.380	0.470
Plt (G/l)											
week:	14	1081	690.0	1031	898.0	907.0	904.0	859.0	949.0	948.0	897.0

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 2  
25 ppm

		Animal no									
		21	22	23	24	25	26	27	28	29	30
PT(CS)											
(sec)											
week:	14	23.77	35.82	33.13	31.27	34.14	33.32	35.16	34.62	29.78	34.39

## Hematology (individuals): males

group 3  
50 ppm

		Animal no									
		31	32	33	34	35	36	37	38	39	40
RBC											
(T/l)											
week:	14	8.440	8.290	8.210	8.360	8.140	8.370	8.290	8.780	8.120	8.270
Hb											
(mmol/l)											
week:	14	9.800	9.300	9.900	9.700	9.600	9.500	9.400	9.800	9.300	9.300
Hct											
(l)											
week:	14	0.445	0.420	0.445	0.437	0.433	0.431	0.423	0.444	0.422	0.419
MCV											
(fl)											
week:	14	52.70	50.70	54.10	52.30	53.20	51.50	51.00	50.50	52.00	50.70
RDW											
(l)											
week:	14	0.119	0.164	0.126	0.129	0.126	0.138	0.128	0.124	0.129	0.130
MCH											
(fmol)											
week:	14	1.160	1.120	1.210	1.160	1.170	1.130	1.130	1.120	1.140	1.130
MCHC											
(mmol/l)											
week:	14	22.05	22.07	22.25	22.15	22.09	21.93	22.24	22.13	21.98	22.26

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 3  
50 ppm

		Animal no									
		31	32	33	34	35	36	37	38	39	40
HDW (mmol/l)	week: 14	1.500	2.320	2.010	1.530	1.930	2.230	2.230	1.620	1.610	1.930
WBC (G/l)	week: 14	10.80	10.74	14.53	9.790	9.050	11.69	14.12	8.710	14.65	10.76
Neut (1)	week: 14	0.169	0.104	0.178	0.141	0.207	0.185	0.248	0.196	0.253	0.173
Eos (1)	week: 14	0.012	0.014	0.008	0.016	0.017	0.009	0.005	0.019	0.008	0.007
Baso (1)	week: 14	0.005	0.004	0.005	0.002	0.005	0.004	0.004	0.003	0.004	0.003
Lympho (1)	week: 14	0.709	0.785	0.704	0.722	0.646	0.699	0.610	0.705	0.640	0.701
Mono (1)	week: 14	0.075	0.046	0.077	0.073	0.067	0.080	0.091	0.045	0.051	0.082
Luc (1)	week: 14	0.031	0.047	0.029	0.046	0.058	0.024	0.042	0.033	0.044	0.034
Neut (G/l)	week: 14	1.820	1.110	2.590	1.380	1.870	2.170	3.510	1.700	3.710	1.860
Eos (G/l)	week: 14	0.130	0.150	0.110	0.150	0.150	0.100	0.080	0.170	0.110	0.070
Baso (G/l)	week: 14	0.050	0.040	0.070	0.020	0.040	0.040	0.050	0.020	0.060	0.030

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (individuals): males

group 3  
50 ppm

		Animal no									
		31	32	33	34	35	36	37	38	39	40
Lympho (G/l)	week: 14	7.660	8.440	10.23	7.070	5.840	8.170	8.610	6.130	9.380	7.540
Mono (G/l)	week: 14	0.810	0.500	1.110	0.710	0.600	0.930	1.290	0.390	0.750	0.890
Luc (G/l)	week: 14	0.330	0.500	0.420	0.450	0.530	0.280	0.590	0.280	0.650	0.370
Plt (G/l)	week: 14	1053	973.0	920.0	790.0	855.0	1028	845.0	862.0	1055	970.0
PT(CS) (sec)	week: 14	39.80	34.15	35.17	36.26	35.70	32.84	38.10	33.84	36.87	42.21

Hematology (individuals): males

group 4  
250 ppm

		Animal no									
		41	42	43	44	45	46	47	48	49	50
RBC (T/l)	week: 14	8.170	8.630	8.110	8.290	7.830	8.690	8.590	8.920	8.950	8.100
Hb (mmol/l)	week: 14	9.900	9.700	9.500	9.500	9.300	10.10	9.600	10.10	9.800	9.600
Hct (l)	week: 14	0.451	0.436	0.426	0.435	0.416	0.455	0.431	0.452	0.444	0.437

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Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 4  
250 ppm

		Animal no									
		41	42	43	44	45	46	47	48	49	50
MCV (fl)											
week:	14	55.20	50.50	52.50	52.50	53.10	52.40	50.10	50.70	49.60	54.00
RDW (1)											
week:	14	0.143	0.135	0.132	0.136	0.129	0.123	0.126	0.116	0.121	0.130
MCH (fmol)											
week:	14	1.210	1.120	1.170	1.150	1.190	1.170	1.110	1.130	1.090	1.180
MCHC (mmol/l)											
week:	14	21.91	22.20	22.24	21.88	22.37	22.25	22.23	22.40	22.04	21.88
HDW (mmol/l)											
week:	14	1.500	1.700	1.630	1.980	2.240	1.480	1.700	1.460	1.500	2.150
WBC (G/l)											
week:	14	10.38	12.62	14.03	14.55	10.41	10.10	13.44	9.060	12.81	13.80
Neut (1)											
week:	14	0.173	0.144	0.104	0.253	0.089	0.157	0.251	0.193	0.304	0.117
Eos (1)											
week:	14	0.009	0.014	0.011	0.009	0.020	0.010	0.070	0.009	0.013	0.024
Baso (1)											
week:	14	0.004	0.004	0.005	0.005	0.005	0.003	0.003	0.003	0.004	0.005
Lympho (1)											
week:	14	0.724	0.737	0.764	0.595	0.803	0.719	0.605	0.708	0.587	0.760
Mono (1)											
week:	14	0.052	0.055	0.072	0.099	0.049	0.070	0.046	0.060	0.050	0.054

Hematology (individuals): males

group 4  
 250 ppm

		Animal no									
		41	42	43	44	45	46	47	48	49	50
Luc (1)											
week:	14	0.039	0.045	0.044	0.039	0.035	0.041	0.026	0.027	0.043	0.039
Neut (G/l)											
week:	14	1.800	1.820	1.460	3.680	0.920	1.580	3.370	1.750	3.890	1.620
Eos (G/l)											
week:	14	0.090	0.180	0.160	0.130	0.200	0.110	0.930	0.080	0.160	0.330
Baso (G/l)											
week:	14	0.040	0.050	0.070	0.070	0.050	0.030	0.040	0.030	0.050	0.070
Lympho (G/l)											
week:	14	7.520	9.300	10.71	8.650	8.360	7.260	8.130	6.410	7.520	10.49
Mono (G/l)											
week:	14	0.530	0.700	1.010	1.440	0.510	0.710	0.610	0.540	0.640	0.750
Luc (G/l)											
week:	14	0.410	0.570	0.620	0.570	0.370	0.420	0.350	0.240	0.550	0.540
Plt (G/l)											
week:	14	1024	1102	1009	1057	926.0	921.0	862.0	819.0	1004	1043
PT(CS) (sec)											
week:	14	39.65	36.28	31.00	36.05	32.38	25.89	34.54	35.26	38.23	35.02

Hematology (individuals): males

group 5  
625 ppm

		Animal no									
		51	52	53	54	55	56	57	58	59	60
RBC	(T/l)										
week:	14	8.400	8.820	8.320	8.710	8.050	8.610	8.190	8.440	8.950	8.660
Hb	(mmol/l)										
week:	14	9.400	9.800	9.300	9.800	9.100	9.700	9.500	9.700	9.800	9.700
Hct	(l)										
week:	14	0.431	0.441	0.421	0.439	0.408	0.432	0.424	0.443	0.433	0.443
MCV	(fl)										
week:	14	51.30	50.00	50.70	50.40	50.60	50.20	51.80	52.50	48.30	51.10
RDW	(l)										
week:	14	0.132	0.131	0.123	0.124	0.134	0.124	0.116	0.127	0.125	0.128
MCH	(fmol)										
week:	14	1.120	1.110	1.120	1.130	1.130	1.120	1.160	1.150	1.090	1.130
MCHC	(mmol/l)										
week:	14	21.88	22.26	22.06	22.34	22.32	22.38	22.41	21.87	22.64	22.03
HDW	(mmol/l)										
week:	14	1.910	1.680	1.610	1.620	2.030	1.620	1.470	2.180	1.570	1.530
WBC	(G/l)										
week:	14	13.04	11.04	10.03	12.08	14.19	15.68	14.05	12.18	16.10	10.76
Neut	(l)										
week:	14	0.378	0.097	0.274	0.219	0.210	0.310	0.263	0.187	0.276	0.373
Eos	(l)										
week:	14	0.008	0.022	0.016	0.015	0.014	0.008	0.007	0.023	0.016	0.012

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 5  
625 ppm

		Animal no									
		51	52	53	54	55	56	57	58	59	60
Baso (1) week:	14	0.003	0.005	0.003	0.003	0.003	0.005	0.004	0.006	0.004	0.003
Lympho (1) week:	14	0.500	0.778	0.625	0.630	0.675	0.556	0.639	0.690	0.567	0.521
Mono (1) week:	14	0.069	0.059	0.047	0.091	0.056	0.081	0.050	0.053	0.086	0.055
Luc (1) week:	14	0.041	0.038	0.036	0.041	0.042	0.040	0.038	0.041	0.050	0.036
Neut (G/l) week:	14	4.930	1.070	2.750	2.640	2.980	4.860	3.690	2.280	4.450	4.020
Eos (G/l) week:	14	0.110	0.250	0.160	0.180	0.190	0.130	0.100	0.270	0.270	0.120
Baso (G/l) week:	14	0.040	0.060	0.030	0.040	0.050	0.080	0.050	0.070	0.060	0.030
Lympho (G/l) week:	14	6.520	8.590	6.270	7.620	9.580	8.720	8.980	8.400	9.130	5.610
Mono (G/l) week:	14	0.900	0.660	0.470	1.100	0.800	1.270	0.700	0.650	1.390	0.590
Luc (G/l) week:	14	0.530	0.420	0.360	0.500	0.600	0.620	0.540	0.500	0.800	0.390
Plt. (G/l) week:	14	928.0	1041	954.0	977.0	810.0	946.0	740.0	1109	972.0	833.0



Hematology (individuals): males

group 5  
625 ppm

		51	52	53	54	Animal no		57	58	59	60
PT(CS) (sec) week:	14	37.28	32.36	29.50	33.94	32.38	37.31	38.04	29.24	33.60	38.63

Hematology (individuals): males

group 6  
1250 ppm

		61	62	63	64	Animal no		67	68	69	70
RBC (T/l) week:	14	8.290	8.490	8.720	8.740	8.700	8.280	8.660	7.620	8.140	8.380
Hb (mmol/l) week:	14	9.800	9.500	9.700	9.500	9.700	9.300	9.400	9.200	9.500	9.600
Hct (l) week:	14	0.440	0.424	0.440	0.437	0.442	0.416	0.436	0.425	0.431	0.427
MCV (fl) week:	14	53.10	50.00	50.40	50.00	50.80	50.20	50.40	55.80	53.00	51.00
RDW (l) week:	14	0.128	0.138	0.125	0.147	0.136	0.127	0.128	0.135	0.144	0.123
MCH (fmol) week:	14	1.180	1.120	1.110	1.080	1.110	1.120	1.090	1.210	1.170	1.150
MCHC (mmol/l) week:	14	22.32	22.44	22.08	21.69	21.88	22.37	21.61	21.73	22.09	22.56

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## Hematology (individuals): males

group 6  
1250 ppm

		Animal no									
		61	62	63	64	65	66	67	68	69	70
HDW (mmol/l)	week: 14	2.060	1.720	1.440	1.440	1.540	1.740	1.650	2.340	2.230	1.580
WBC (G/l)	week: 14	16.57	11.27	13.54	12.99	14.06	8.130	12.88	11.92	14.93	17.61
Neut (1)	week: 14	0.069	0.173	0.165	0.246	0.113	0.243	0.347	0.112	0.362	0.123
Eos (1)	week: 14	0.010	0.015	0.012	0.011	0.014	0.022	0.009	0.020	0.007	0.010
Baso (1)	week: 14	0.006	0.003	0.004	0.003	0.005	0.003	0.003	0.005	0.003	0.005
Lympho (1)	week: 14	0.790	0.727	0.704	0.646	0.778	0.636	0.538	0.776	0.518	0.718
Mono (1)	week: 14	0.093	0.047	0.060	0.054	0.050	0.053	0.059	0.051	0.077	0.100
Luc (1)	week: 14	0.033	0.035	0.055	0.040	0.040	0.043	0.045	0.036	0.033	0.043
Neut (G/l)	week: 14	1.150	1.950	2.230	3.200	1.590	1.970	4.460	1.330	5.400	2.160
Eos (G/l)	week: 14	0.160	0.170	0.160	0.140	0.200	0.180	0.110	0.240	0.100	0.180
Baso (G/l)	week: 14	0.100	0.030	0.060	0.040	0.070	0.020	0.040	0.060	0.050	0.090

Hematology (individuals): males

group 6  
1250 ppm

		Animal no									
		61	62	63	64	65	66	67	68	69	70
Lympho (G/l)											
week:	14	13.08	8.200	9.530	8.390	10.94	5.170	6.930	9.240	7.740	12.65
Mono (G/l)											
week:	14	1.540	0.530	0.820	0.700	0.700	0.430	0.750	0.610	1.150	1.770
Luc (G/l)											
week:	14	0.540	0.390	0.740	0.520	0.570	0.350	0.580	0.430	0.500	0.750
Plt (G/l)											
week:	14	750.0	1052	1019	969.0	947.0	1006	916.0	1031	989.0	1088
PT(CS) (sec)											
week:	14	36.88	38.46	35.32	36.62	28.47	35.37	41.09	34.91	35.68	42.28

Hematology (individuals): males

group 6  
1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
RBC (T/l)											
week:	14	9.120	8.900	8.660	8.520	8.220	8.860	8.820	8.410	8.080	8.390
	18	9.010	8.880	8.630	8.750	8.350	8.890	9.010	8.280	8.130	8.420
Hb (mmol/l)											
week:	14	10.30	10.10	9.600	9.400	9.100	9.700	9.600	9.200	9.500	9.200
	18	10.10	9.900	9.600	9.600	9.300	9.600	9.600	9.000	9.400	9.100
Hct (l)											
week:	14	0.466	0.457	0.430	0.440	0.411	0.444	0.447	0.421	0.434	0.421
	18	0.468	0.460	0.432	0.444	0.429	0.457	0.453	0.421	0.437	0.427

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 6  
1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
MCV	(fl)										
week:	14	51.10	51.30	49.70	51.70	50.00	50.10	50.70	50.00	53.70	50.30
	18	52.00	51.70	50.00	50.80	51.40	51.40	50.30	50.80	53.70	50.80
RDW	(1)										
week:	14	0.117	0.118	0.125	0.136	0.136	0.126	0.118	0.128	0.130	0.137
	18	0.127	0.124	0.127	0.135	0.136	0.125	0.120	0.138	0.131	0.135
MCH	(fmol)										
week:	14	1.130	1.130	1.110	1.110	1.100	1.090	1.080	1.090	1.170	1.100
	18	1.120	1.110	1.110	1.100	1.110	1.080	1.070	1.090	1.160	1.090
MCHC	(mmol/l)										
week:	14	22.04	22.06	22.25	21.45	22.04	21.81	21.38	21.78	21.87	21.89
	18	21.63	21.48	22.15	21.69	21.57	21.04	21.28	21.42	21.53	21.39
HDW	(mmol/l)										
week:	14	1.490	1.470	1.500	2.090	2.080	1.580	1.440	1.930	2.060	2.180
	18	1.450	1.490	1.420	1.910	1.940	1.470	1.390	1.890	1.960	2.040
WBC	(G/l)										
week:	14	11.27	15.26	11.00	15.31	12.46	13.42	12.79	9.420	13.41	9.180
	18	9.520	9.020	9.640	11.33	12.13	12.50	9.530	9.040	11.19	9.170
Neut	(1)										
week:	14	0.157	0.298	0.155	0.240	0.139	0.229	0.210	0.114	0.130	0.162
	18	0.151	0.110	0.142	0.194	0.133	0.301	0.128	0.143	0.162	0.177
Eos	(1)										
week:	14	0.010	0.008	0.006	0.006	0.012	0.010	0.008	0.004	0.017	0.023
	18	0.008	0.009	0.007	0.007	0.024	0.006	0.011	0.005	0.024	0.024
Baso	(1)										
week:	14	0.004	0.004	0.003	0.006	0.003	0.004	0.003	0.004	0.004	0.002
	18	0.005	0.004	0.004	0.003	0.005	0.005	0.004	0.004	0.005	0.003

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): males

group 6  
1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
Lympho (1)											
week:	14	0.696	0.586	0.713	0.604	0.739	0.634	0.670	0.789	0.753	0.692
	18	0.720	0.783	0.731	0.645	0.707	0.581	0.756	0.711	0.691	0.666
Mono (1)											
week:	14	0.072	0.072	0.072	0.093	0.067	0.065	0.078	0.049	0.067	0.064
	18	0.060	0.058	0.061	0.086	0.070	0.052	0.068	0.068	0.076	0.061
Luc (1)											
week:	14	0.061	0.032	0.052	0.052	0.040	0.057	0.031	0.041	0.028	0.057
	18	0.056	0.036	0.056	0.065	0.061	0.054	0.032	0.069	0.043	0.069
Neut (G/l)											
week:	14	1.770	4.540	1.700	3.680	1.730	3.070	2.690	1.070	1.750	1.490
	18	1.440	0.990	1.370	2.190	1.610	3.770	1.220	1.290	1.820	1.620
Eos (G/l)											
week:	14	0.110	0.130	0.070	0.090	0.150	0.130	0.100	0.030	0.230	0.210
	18	0.080	0.080	0.070	0.080	0.290	0.070	0.100	0.050	0.260	0.220
Baso (G/l)											
week:	14	0.050	0.060	0.030	0.090	0.040	0.060	0.040	0.040	0.060	0.010
	18	0.050	0.040	0.030	0.040	0.060	0.060	0.040	0.030	0.050	0.030
Lympho (G/l)											
week:	14	7.850	8.950	7.840	9.250	9.210	8.510	8.560	7.430	10.10	6.360
	18	6.850	7.060	7.050	7.310	8.580	7.260	7.200	6.430	7.730	6.100
Mono (G/l)											
week:	14	0.820	1.100	0.790	1.420	0.840	0.880	1.000	0.460	0.900	0.580
	18	0.570	0.520	0.580	0.970	0.850	0.650	0.650	0.610	0.850	0.560
Luc. (G/l)											
week:	14	0.680	0.480	0.570	0.790	0.500	0.770	0.400	0.380	0.370	0.520
	18	0.530	0.320	0.540	0.740	0.740	0.680	0.310	0.630	0.480	0.630

Hematology (individuals): males

group 6  
 1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
Plt (G/l)	week: 14	995.0	994.0	888.0	958.0	1090	1091	1012	938.0	1068	1033
	18	1020	1011	918.0	1045	1153	1073	1019	937.0	1104	1087
PT(CS) (sec)	week: 14	35.67	38.59	39.12	32.25	35.58	36.91	38.98	37.64	34.86	38.27
	18	n.d.	39.23	41.79	34.77	39.80	40.32	32.42	34.14	31.91	36.04

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Hematology (individuals): females

group 1  
0 ppm

		Animal no									
		81	82	83	84	85	86	87	88	89	90
RBC (T/l)	week: 14	8.190	7.920	8.060	7.800	7.375	7.910	7.980	7.530	7.890	8.120
Hb (mmol/l)	week: 14	9.800	9.500	10.10	9.500	9.050	9.400	9.600	9.000	8.900	9.700
Hct (l)	week: 14	0.442	0.435	0.456	0.425	0.409	0.431	0.426	0.415	0.413	0.436
MCV (fl)	week: 14	53.90	54.90	56.60	54.60	55.45	54.50	53.40	55.10	52.30	53.80
RDW (l)	week: 14	0.173	0.147	0.120	0.134	0.124	0.137	0.132	0.123	0.116	0.112
MCH (fmol)	week: 14	1.190	1.200	1.260	1.220	1.220	1.190	1.200	1.190	1.130	1.190
MCHC (mmol/l)	week: 14	22.14	21.83	22.22	22.35	22.03	21.87	22.44	21.63	21.60	22.23
HDW (mmol/l)	week: 14	1.340	1.950	1.590	1.230	1.555	1.400	1.230	1.780	1.240	1.200
WBC (G/l)	week: 14	6.470	9.960	8.020	5.890	5.530	6.040	6.600	8.090	4.210	5.190
Neut (l)	week: 14	0.144	0.172	0.101	0.089	0.073	0.149	0.116	0.086	0.116	0.121
Eos (l)	week: 14	0.007	0.029	0.019	0.012	0.010	0.015	0.016	0.014	0.018	0.016

Hematology (individuals): females

group 1  
0 ppm

		Animal no									
		81	82	83	84	85	86	87	88	89	90
Baso (1) week:	14	0.002	0.003	0.005	0.004	0.003	0.003	0.005	0.003	0.002	0.002
Lympho (1) week:	14	0.758	0.707	0.733	0.758	0.757	0.726	0.746	0.796	0.762	0.761
Mono (1) week:	14	0.052	0.046	0.093	0.083	0.098	0.060	0.067	0.069	0.051	0.068
Luc (1) week:	14	0.037	0.044	0.049	0.053	0.061	0.047	0.049	0.032	0.050	0.032
Neut (G/l) week:	14	0.930	1.710	0.810	0.520	0.405	0.900	0.770	0.700	0.490	0.630
Eos (G/l) week:	14	0.040	0.290	0.150	0.070	0.055	0.090	0.110	0.110	0.080	0.080
Baso (G/l) week:	14	0.010	0.030	0.040	0.030	0.015	0.020	0.040	0.020	0.010	0.010
Lympho (G/l) week:	14	4.900	7.040	5.880	4.470	4.185	4.390	4.920	6.440	3.200	3.950
Mono (G/l) week:	14	0.340	0.450	0.750	0.490	0.540	0.360	0.440	0.560	0.220	0.350
Luc (G/l) week:	14	0.240	0.440	0.390	0.310	0.335	0.280	0.330	0.260	0.210	0.170
Plt (G/l) week:	14	1046	972.0	949.0	957.0	1065	905.0	964.0	1026	899.0	995.0



Hematology (individuals): females

group 1  
0 ppm

		Animal no									
		81	82	83	84	85	86	87	88	89	90
PT(CS) (sec)	week: 14	28.15	28.68	22.84	29.53	30.31	27.44	33.87	31.41	27.18	30.27

Hematology (individuals): females

group 1  
0 ppm

		Animal no									
		91	92	93	94	95	96	97	98	99	100
RBC (T/l)	week: 14	8.470	7.890	7.300	7.300	8.030	8.360	7.430	7.300	8.110	7.280
	18	8.170	7.960	7.570	7.685	7.850	8.430	7.690	7.640	8.520	7.460
Hb (mmol/l)	week: 14	9.700	9.300	9.100	8.950	9.300	10.00	9.400	8.900	9.200	9.200
	18	9.700	9.500	9.400	9.350	9.300	10.20	9.600	9.400	9.800	9.500
Hct (l)	week: 14	0.450	0.416	0.422	0.411	0.415	0.457	0.417	0.413	0.421	0.410
	18	0.458	0.444	0.452	0.448	0.426	0.479	0.444	0.432	0.453	0.429
MCV (fl)	week: 14	53.10	52.70	57.80	56.20	51.60	54.60	56.10	56.50	51.90	56.30
	18	56.00	55.80	59.70	58.20	54.30	56.80	57.80	56.50	53.10	57.50
RDW (l)	week: 14	0.116	0.115	0.116	0.129	0.114	0.141	0.122	0.127	0.149	0.122
	18	0.145	0.117	0.138	0.130	0.125	0.122	0.120	0.120	0.147	0.123
MCH (fmol)	week: 14	1.150	1.180	1.250	1.225	1.150	1.190	1.260	1.220	1.130	1.260
	18	1.190	1.190	1.250	1.220	1.180	1.210	1.250	1.230	1.150	1.270

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Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (individuals): females

group 1  
0 ppm

		Animal no									
		91	92	93	94	95	96	97	98	99	100
MCHC	(mmol/l)										
week:	14	21.59	22.37	21.69	21.79	22.34	21.81	22.48	21.67	21.75	22.39
	18	21.19	21.35	20.89	20.90	21.73	21.34	21.56	21.68	21.71	22.16
HDW	(mmol/l)										
week:	14	1.310	1.270	1.630	1.925	1.340	1.260	1.970	1.780	1.590	1.910
	18	1.230	1.210	1.540	1.975	1.360	1.260	1.720	1.740	1.490	1.790
WBC	(G/l)										
week:	14	5.400	4.430	7.030	16.90	7.140	6.260	8.510	8.040	9.380	4.520
	18	5.350	5.150	5.900	15.23	4.900	5.660	7.450	8.610	6.010	6.380
Neut	(1)										
week:	14	0.100	0.106	0.101	0.376	0.169	0.116	0.124	0.111	0.111	0.168
	18	0.101	0.115	0.114	0.598	0.115	0.152	0.122	0.097	0.151	0.337
Eos	(1)										
week:	14	0.013	0.020	0.012	0.007	0.019	0.011	0.017	0.014	0.023	0.029
	18	0.010	0.015	0.010	0.005	0.021	0.009	0.022	0.012	0.022	0.022
Baso	(1)										
week:	14	0.004	0.001	0.003	0.005	0.002	0.006	0.005	0.004	0.005	0.002
	18	0.002	0.001	0.003	0.003	0.002	0.003	0.003	0.004	0.002	0.002
Lympho	(1)										
week:	14	0.790	0.757	0.734	0.520	0.719	0.774	0.709	0.791	0.696	0.726
	18	0.749	0.737	0.735	0.310	0.746	0.740	0.774	0.821	0.686	0.543
Mono	(1)										
week:	14	0.063	0.070	0.103	0.062	0.060	0.060	0.082	0.040	0.108	0.044
	18	0.094	0.083	0.102	0.053	0.067	0.053	0.034	0.033	0.099	0.054
Luc	(1)										
week:	14	0.030	0.046	0.047	0.031	0.031	0.034	0.064	0.040	0.058	0.031
	18	0.044	0.049	0.035	0.031	0.048	0.041	0.044	0.033	0.040	0.041

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): females

group 1  
0 ppm

		Animal no									
		91	92	93	94	95	96	97	98	99	100
Neut (G/l) week:	14	0.540	0.470	0.710	6.350	1.210	0.720	1.060	0.890	1.040	0.760
	18	0.540	0.590	0.670	9.105	0.560	0.860	0.910	0.840	0.910	2.150
Eos (G/l) week:	14	0.070	0.090	0.080	0.120	0.130	0.070	0.140	0.110	0.220	0.130
	18	0.060	0.080	0.060	0.075	0.110	0.050	0.170	0.110	0.130	0.140
Baso (G/l) week:	14	0.020	0.010	0.020	0.080	0.010	0.040	0.040	0.030	0.040	0.010
	18	0.010	0.010	0.020	0.050	0.010	0.020	0.020	0.030	0.010	0.010
Lympho (G/l) week:	14	4.270	3.360	5.160	8.780	5.130	4.850	6.040	6.360	6.530	3.280
	18	4.010	3.800	4.340	4.720	3.650	4.190	5.770	7.080	4.130	3.460
Mono (G/l) week:	14	0.340	0.310	0.730	1.045	0.430	0.370	0.700	0.320	1.010	0.200
	18	0.500	0.430	0.600	0.805	0.330	0.300	0.260	0.280	0.600	0.350
Luc (G/l) week:	14	0.160	0.200	0.330	0.515	0.220	0.210	0.540	0.320	0.540	0.140
	18	0.230	0.250	0.210	0.475	0.240	0.230	0.330	0.280	0.240	0.260
Plt (G/l) week:	14	1102	903.0	1018	1110	1013	969.0	992.0	1187	987.0	1026
	18	1098	887.0	1048	1396	1006	1089	952.0	1144	898.0	764.0
PT(CS) (sec) week:	14	31.31	32.11	26.63	26.92	29.77	30.08	28.26	24.82	27.79	32.35
	18	25.17	26.22	27.70	24.05	29.83	30.83	26.80	n.d.	28.21	25.11

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Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (individuals): females

group 2  
25 ppm

		Animal no									
		101	102	103	104	105	106	107	108	109	110
RBC (T/l)											
week:	14	7.880	7.380	7.690	8.050	7.410	7.250	7.150	7.900	7.910	7.390
Hb (mmol/l)											
week:	14	9.700	8.800	9.400	9.700	9.100	9.300	9.000	9.000	9.600	8.700
Hct (l)											
week:	14	0.442	0.397	0.422	0.442	0.411	0.410	0.412	0.407	0.442	0.397
MCV (fl)											
week:	14	56.00	53.90	54.90	54.90	55.50	56.60	57.60	51.50	55.80	53.80
RDW (l)											
week:	14	0.112	0.126	0.115	0.114	0.124	0.124	0.121	0.113	0.131	0.134
MCH (fmol)											
week:	14	1.230	1.200	1.230	1.200	1.230	1.290	1.260	1.140	1.210	1.180
MCHC (mmol/l)											
week:	14	21.98	22.19	22.37	21.92	22.15	22.71	21.88	22.16	21.66	21.94
HDW (mmol/l)											
week:	14	1.270	1.950	1.370	1.260	1.760	1.900	1.910	1.290	1.180	1.190
WBC (G/l)											
week:	14	6.660	7.930	6.010	8.840	7.740	5.630	9.430	6.130	4.920	6.940
Neut (l)											
week:	14	0.152	0.199	0.126	0.089	0.168	0.092	0.109	0.128	0.142	0.053
Eos (l)											
week:	14	0.021	0.015	0.020	0.014	0.016	0.014	0.005	0.024	0.016	0.013

Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): females

group 2  
25 ppm

		Animal no									
		101	102	103	104	105	106	107	108	109	110
Baso (1) week:	14	0.004	0.003	0.003	0.004	0.002	0.003	0.003	0.002	0.003	0.003
Lympho (1) week:	14	0.741	0.658	0.734	0.782	0.700	0.792	0.781	0.766	0.716	0.849
Mono (1) week:	14	0.054	0.073	0.080	0.068	0.069	0.054	0.065	0.044	0.080	0.043
Luc (1) week:	14	0.029	0.051	0.037	0.043	0.044	0.045	0.036	0.036	0.042	0.039
Neut (G/l) week:	14	1.010	1.580	0.760	0.790	1.300	0.520	1.030	0.780	0.700	0.370
Eos (G/l) week:	14	0.140	0.120	0.120	0.120	0.130	0.080	0.050	0.140	0.080	0.090
Baso (G/l) week:	14	0.030	0.030	0.020	0.040	0.010	0.020	0.030	0.020	0.010	0.020
Lympho (G/l) week:	14	4.940	5.220	4.410	6.910	5.420	4.460	7.370	4.690	3.530	5.890
Mono (G/l) week:	14	0.360	0.580	0.480	0.600	0.540	0.310	0.620	0.270	0.400	0.300
Luc (G/l) week:	14	0.200	0.400	0.220	0.380	0.340	0.250	0.340	0.220	0.210	0.270
Plt- (G/l) week:	14	894.0	980.0	957.0	1124	1043	1040	1114	1021	953.0	1025

Hematology (individuals): females

group 2  
25 ppm

		Animal no									
		101	102	103	104	105	106	107	108	109	110
PT(CS) (sec)											
week:	14	30.20	26.01	27.68	33.98	29.15	32.17	27.75	28.65	28.63	24.59

Hematology (individuals): females

group 3  
50 ppm

		Animal no									
		111	112	113	114	115	116	117	118	119	120
RBC (T/l)											
week:	14	7.410	7.500	7.080	8.180	7.330	8.270	7.690	7.430	8.110	8.130
Hb (mmol/l)											
week:	14	8.900	9.400	8.900	9.700	9.100	9.900	9.000	9.300	9.600	9.300
Hct (l)											
week:	14	0.397	0.415	0.405	0.454	0.405	0.438	0.396	0.413	0.435	0.420
MCV (fl)											
week:	14	53.60	55.30	57.20	55.40	55.20	53.00	51.50	55.60	53.70	51.70
RDW (l)											
week:	14	0.185	0.155	0.116	0.118	0.113	0.118	0.126	0.127	0.113	0.143
MCH (fmol)											
week:	14	1.200	1.250	1.260	1.190	1.240	1.200	1.160	1.250	1.190	1.140
MCHC (mmol/l)											
week:	14	22.32	22.66	22.04	21.47	22.37	22.54	22.59	22.50	22.11	22.01

Hematology (individuals): females

group 3  
50 ppm

		Animal no									
		111	112	113	114	115	116	117	118	119	120
HDW (mmol/l)	week: 14	2.110	2.060	1.540	1.450	1.560	1.380	1.260	1.940	1.210	1.310
WBC (G/l)	week: 14	8.320	8.070	11.25	7.570	6.130	6.500	8.390	8.610	4.440	5.960
Neut (1)	week: 14	0.080	0.176	0.238	0.085	0.078	0.123	0.187	0.125	0.214	0.123
Eos (1)	week: 14	0.016	0.019	0.009	0.021	0.012	0.013	0.013	0.020	0.021	0.035
Baso (1)	week: 14	0.003	0.005	0.005	0.006	0.001	0.004	0.003	0.003	0.002	0.002
Lympho (1)	week: 14	0.817	0.680	0.645	0.821	0.802	0.755	0.702	0.761	0.660	0.737
Mono (1)	week: 14	0.048	0.068	0.069	0.044	0.063	0.067	0.064	0.048	0.062	0.054
Luc (1)	week: 14	0.036	0.052	0.035	0.024	0.045	0.039	0.032	0.042	0.041	0.049
Neut (G/l)	week: 14	0.670	1.420	2.680	0.640	0.480	0.800	1.570	1.080	0.950	0.730
Eos (G/l)	week: 14	0.130	0.150	0.100	0.160	0.070	0.080	0.100	0.180	0.090	0.210
Baso (G/l)	week: 14	0.030	0.040	0.060	0.040	0.010	0.030	0.020	0.020	0.010	0.010

Hematology (individuals): females

group 3  
50 ppm

		Animal no									
		111	112	113	114	115	116	117	118	119	120
Lympho (G/l)											
week:	14	6.800	5.490	7.250	6.210	4.920	4.910	5.890	6.560	2.930	4.390
Mono (G/l)											
week:	14	0.400	0.550	0.770	0.330	0.390	0.430	0.540	0.420	0.280	0.320
Luc (G/l)											
week:	14	0.300	0.420	0.390	0.180	0.280	0.250	0.270	0.360	0.180	0.290
Plt (G/l)											
week:	14	1090	1119	986.0	893.0	832.0	1096	885.0	877.0	998.0	1048
PT(CS) (sec)											
week:	14	28.88	26.70	31.89	29.46	29.46	28.64	32.29	22.84	31.80	27.53

Hematology (individuals): females

group 4  
250 ppm

		Animal no									
		121	122	123	124	125	126	127	128	129	130
RBC (T/l)											
week:	14	8.010	8.520	8.470	7.380	7.330	7.600	7.460	8.270	8.080	7.240
Hb (mmol/l)											
week:	14	9.400	9.700	9.400	8.900	8.700	9.400	9.100	9.300	9.600	9.100
Hct (l)											
week:	14	0.416	0.431	0.438	0.401	0.403	0.413	0.418	0.425	0.426	0.412



Test No.: 943127

Test Article: CGA 329351 tech.

## Hematology (individuals): females

group 4  
250 ppm

		Animal no									
		121	122	123	124	125	126	127	128	129	130
MCV (fl)											
week:	14	51.90	50.60	51.70	54.30	55.00	54.30	56.00	51.40	52.70	56.90
RDW (1)											
week:	14	0.135	0.134	0.113	0.120	0.121	0.236	0.131	0.112	0.117	0.122
MCH (fmol)											
week:	14	1.180	1.140	1.110	1.200	1.180	1.230	1.220	1.120	1.190	1.260
MCHC (mmol/l)											
week:	14	22.70	22.48	21.56	22.19	21.50	22.65	21.76	21.81	22.55	22.07
HDW (mmol/l)											
week:	14	1.280	1.380	1.290	1.850	1.860	1.450	2.060	1.250	1.470	1.790
WBC (G/l)											
week:	14	7.220	4.690	5.290	5.280	5.530	6.940	4.960	4.590	8.980	5.490
Neut (1)											
week:	14	0.181	0.141	0.193	0.198	0.145	0.142	0.142	0.088	0.282	0.104
Eos (1)											
week:	14	0.013	0.029	0.017	0.014	0.048	0.018	0.013	0.018	0.015	0.007
Baso (1)											
week:	14	0.003	0.002	0.004	0.001	0.003	0.002	0.002	0.002	0.004	0.002
Lympho (1)											
week:	14	0.700	0.733	0.687	0.678	0.718	0.748	0.734	0.757	0.608	0.808
Mono (1)											
week:	14	0.049	0.052	0.055	0.073	0.048	0.045	0.061	0.086	0.063	0.047

Hematology (individuals): females

group 4  
 250 ppm

		Animal no									
		121	122	123	124	125	126	127	128	129	130
Luc (1) week:	14	0.054	0.041	0.045	0.036	0.039	0.044	0.048	0.049	0.028	0.032
Neut (G/l) week:	14	1.310	0.660	1.020	1.040	0.800	0.990	0.700	0.400	2.540	0.570
Eos (G/l) week:	14	0.100	0.140	0.090	0.070	0.270	0.130	0.070	0.080	0.130	0.040
Baso (G/l) week:	14	0.020	0.010	0.020	0.010	0.010	0.010	0.010	0.010	0.040	0.010
Lympho (G/l) week:	14	5.050	3.440	3.630	3.580	3.970	5.200	3.640	3.470	5.460	4.440
Mono (G/l) week:	14	0.350	0.250	0.290	0.380	0.260	0.310	0.300	0.400	0.570	0.260
Luc (G/l) week:	14	0.390	0.190	0.240	0.190	0.220	0.300	0.240	0.230	0.250	0.180
Plt (G/l) week:	14	957.0	903.0	1011	824.0	1173	923.0	1107	983.0	848.0	1124
PT(CS) (sec) week:	14	28.94	29.12	28.39	28.75	29.74	26.27	27.37	28.24	28.28	30.32

Hematology (individuals): females

group 5  
 625 ppm

	Animal no										
		131	132	133	134	135	136	137	138	139	140
RBC (T/l)											
week:	14	8.030	8.020	7.410	7.940	7.500	7.290	8.190	7.770	7.890	7.170
Hb (mmol/l)											
week:	14	9.800	9.400	9.200	9.400	9.500	8.800	9.300	9.300	9.500	8.600
Hct (l)											
week:	14	0.438	0.434	0.419	0.430	0.423	0.405	0.423	0.411	0.419	0.393
MCV (fl)											
week:	14	54.60	54.10	56.50	54.20	56.40	55.60	51.70	52.90	53.10	54.80
RDW (l)											
week:	14	0.132	0.128	0.115	0.138	0.117	0.122	0.113	0.139	0.136	0.124
MCH (fmol)											
week:	14	1.220	1.180	1.250	1.180	1.260	1.210	1.140	1.200	1.205	1.200
MCHC (mmol/l)											
week:	14	22.37	21.73	22.03	21.83	22.42	21.72	22.03	22.70	22.65	21.90
HDW (mmol/l)											
week:	14	1.290	1.240	1.600	1.280	1.280	1.720	1.290	1.310	1.345	1.920
WBC (G/l)											
week:	14	7.120	8.870	6.290	6.730	4.180	8.650	7.760	6.100	5.970	5.950
Neut (l)											
week:	14	0.092	0.112	0.061	0.132	0.137	0.089	0.165	0.123	0.225	0.175
Eos (l)											
week:	14	0.018	0.013	0.015	0.019	0.005	0.016	0.024	0.021	0.027	0.015

Hematology (individuals): females

group 5  
 625 ppm

		Animal no									
		131	132	133	134	135	136	137	138	139	140
Baso (1) week:	14	0.003	0.003	0.004	0.004	0.002	0.003	0.002	0.003	0.003	0.002
Lympho (1) week:	14	0.767	0.787	0.792	0.725	0.770	0.818	0.717	0.729	0.654	0.701
Mono (1) week:	14	0.086	0.051	0.073	0.068	0.048	0.044	0.056	0.074	0.049	0.067
Luc (1) week:	14	0.034	0.035	0.055	0.052	0.038	0.029	0.035	0.050	0.043	0.041
Neut (G/l) week:	14	0.660	0.990	0.390	0.890	0.570	0.770	1.280	0.750	1.345	1.040
Eos (G/l) week:	14	0.130	0.110	0.090	0.130	0.020	0.140	0.190	0.130	0.160	0.090
Baso (G/l) week:	14	0.020	0.030	0.020	0.030	0.010	0.030	0.020	0.020	0.020	0.010
Lympho (G/l) week:	14	5.460	6.980	4.980	4.880	3.220	7.080	5.570	4.440	3.905	4.170
Mono (G/l) week:	14	0.610	0.450	0.460	0.460	0.200	0.380	0.440	0.450	0.295	0.400
Luc (G/l) week:	14	0.240	0.310	0.340	0.350	0.160	0.250	0.270	0.300	0.255	0.240
Plt (G/l) week:	14	986.0	905.0	1017	1033	927.0	1045	1136	991.0	800.5	1100

Hematology (individuals): females

group 5  
625 ppm

		Animal no									
		131	132	133	134	135	136	137	138	139	140
PT(CS)											
(sec)											
week:	14	25.81	29.22	31.81	27.14	28.15	27.27	27.71	28.12	24.41	30.07

Hematology (individuals): females

group 6  
1250 ppm

		Animal no									
		141	142	143	144	145	146	147	148	149	150
RBC											
(T/l)											
week:	14	7.580	8.280	7.530	7.500	7.750	7.000	8.090	7.620	7.320	7.220
Hb											
(mmol/l)											
week:	14	9.100	9.400	9.200	9.200	9.400	8.500	9.600	9.300	8.900	8.900
Hct											
(l)											
week:	14	0.421	0.433	0.420	0.411	0.432	0.398	0.440	0.410	0.407	0.392
MCV											
(fl)											
week:	14	55.50	52.20	55.70	54.80	55.80	56.80	54.40	53.80	55.60	54.20
RDW											
(l)											
week:	14	0.136	0.172	0.126	0.146	0.131	0.136	0.136	0.115	0.138	0.126
MCH											
(fmol)											
week:	14	1.200	1.130	1.220	1.230	1.210	1.225	1.190	1.220	1.220	1.230
MCHC											
(mmol/l)											
week:	14	21.51	21.72	21.90	22.44	21.65	21.50	21.83	22.64	21.89	22.65

Hematology (individuals): females

group 6  
 1250 ppm

		Animal no									
		141	142	143	144	145	146	147	148	149	150
HDW (mmol/l)	week: 14	1.320	1.510	1.930	1.900	1.280	1.750	1.290	1.310	1.670	2.020
WBC (G/l)	week: 14	7.390	7.110	5.820	10.13	6.260	5.765	7.220	7.590	4.980	6.540
Neut (1)	week: 14	0.108	0.123	0.124	0.149	0.108	0.087	0.141	0.110	0.136	0.168
Eos (1)	week: 14	0.017	0.028	0.019	0.015	0.021	0.010	0.015	0.012	0.012	0.015
Baso (1)	week: 14	0.002	0.005	0.003	0.003	0.002	0.002	0.003	0.002	0.002	0.002
Lympho (1)	week: 14	0.791	0.726	0.775	0.714	0.793	0.812	0.714	0.790	0.719	0.741
Mono (1)	week: 14	0.047	0.084	0.045	0.084	0.045	0.051	0.096	0.056	0.074	0.046
Luc (1)	week: 14	0.034	0.033	0.035	0.035	0.031	0.039	0.031	0.030	0.057	0.029
Neut (G/l)	week: 14	0.800	0.870	0.720	1.510	0.680	0.500	1.020	0.840	0.680	1.100
Eos (G/l)	week: 14	0.120	0.200	0.110	0.150	0.130	0.060	0.110	0.090	0.060	0.100
Baso (G/l)	week: 14	0.020	0.040	0.020	0.030	0.010	0.015	0.020	0.010	0.010	0.010

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 287

Test No.: 943127

Test Article: CGA 329351 tech.

Hematology (individuals): females

group 6  
1250 ppm

		Animal no									
		141	142	143	144	145	146	147	148	149	150
Lympho (G/l) week:	14	5.850	5.160	4.510	7.240	4.960	4.680	5.160	5.990	3.580	4.840
Mono (G/l) week:	14	0.350	0.600	0.260	0.850	0.280	0.290	0.690	0.420	0.370	0.300
Luc (G/l) week:	14	0.250	0.240	0.200	0.350	0.190	0.225	0.220	0.230	0.280	0.190
Plt (G/l) week:	14	952.0	1032	1041	1023	859.0	1038	1021	1031	991.0	1074
PT (CS) (sec) week:	14	26.07	25.45	27.51	28.57	25.90	19.86	27.20	25.33	27.50	23.48

Hematology (individuals): females

group 6  
1250 ppm

		Animal no									
		151	152	153	154	155	156	157	158	159	160
RBC (T/l) week:	14	7.170	7.560	7.920	7.450	7.570	7.880	7.420	7.830	7.430	7.450
	18	7.570	7.840	8.050	7.740	7.910	8.290	7.840	7.790	7.580	8.090
Hb (mmol/l) week:	14	8.800	9.300	9.200	9.000	9.200	9.600	9.100	9.600	9.400	9.000
	18	9.400	9.600	9.500	9.400	9.700	10.10	9.400	9.600	9.400	9.900
Hct (l) week:	14	0.398	0.420	0.413	0.413	0.423	0.434	0.411	0.432	0.432	0.413
	18	0.424	0.447	0.443	0.439	0.447	0.468	0.429	0.436	0.439	0.459

Hematology (individuals): females

group 6  
 1250 ppm

		Animal no										
		151	152	153	154	155	156	157	158	159	160	
MCV (fl)	week:	14	55.60	55.50	52.20	55.50	55.80	55.10	55.40	55.10	58.20	55.50
		18	56.00	57.10	55.10	56.70	56.60	56.40	54.70	55.90	57.90	56.80
RDW (1)	week:	14	0.136	0.122	0.136	0.121	0.115	0.122	0.127	0.124	0.113	0.124
		18	0.120	0.119	0.114	0.123	0.121	0.115	0.113	0.121	0.116	0.118
MCH (fmol)	week:	14	1.220	1.230	1.170	1.210	1.220	1.210	1.220	1.230	1.260	1.210
		18	1.240	1.220	1.180	1.210	1.230	1.220	1.200	1.230	1.240	1.220
MCHC (mmol/l)	week:	14	22.02	22.15	22.38	21.77	21.85	22.06	22.04	22.22	21.68	21.88
		18	22.20	21.42	21.49	21.40	21.75	21.66	21.92	22.05	21.32	21.52
HDW (mmol/l)	week:	14	1.530	1.760	1.260	1.780	1.340	1.330	1.860	1.850	1.270	1.750
		18	1.450	1.580	1.190	1.700	1.320	1.220	1.790	1.890	1.280	1.550
WBC (G/l)	week:	14	6.140	4.460	9.100	6.510	8.280	7.150	9.110	7.360	6.840	5.670
		18	5.840	5.680	6.840	6.080	7.520	6.460	7.840	7.750	6.340	5.040
Neut (1)	week:	14	0.130	0.156	0.090	0.140	0.079	0.113	0.146	0.109	0.067	0.270
		18	0.161	0.130	0.104	0.220	0.091	0.127	0.093	0.085	0.085	0.119
Eos (1)	week:	14	0.010	0.020	0.014	0.030	0.007	0.012	0.012	0.009	0.015	0.008
		18	0.011	0.016	0.015	0.022	0.021	0.014	0.014	0.009	0.018	0.010
Baso (1)	week:	14	0.001	0.002	0.004	0.002	0.003	0.003	0.003	0.003	0.003	0.001
		18	0.003	0.002	0.003	0.003	0.003	0.002	0.003	0.005	0.003	0.003



Hematology (individuals): females

group 6  
 1250 ppm

		Animal no										
		151	152	153	154	155	156	157	158	159	160	
Lympho (1)	week:	14	0.761	0.736	0.800	0.756	0.820	0.734	0.703	0.779	0.816	0.598
		18	0.703	0.751	0.799	0.652	0.781	0.773	0.796	0.816	0.783	0.742
Mono (1)	week:	14	0.057	0.053	0.059	0.045	0.058	0.097	0.079	0.064	0.062	0.073
		18	0.074	0.053	0.048	0.061	0.073	0.056	0.056	0.054	0.071	0.079
Luc (1)	week:	14	0.041	0.033	0.033	0.028	0.033	0.041	0.057	0.035	0.036	0.049
		18	0.048	0.048	0.031	0.042	0.031	0.028	0.039	0.031	0.041	0.048
Neut (G/l)	week:	14	0.800	0.700	0.820	0.910	0.660	0.810	1.320	0.800	0.460	1.530
		18	0.940	0.740	0.710	1.340	0.690	0.820	0.730	0.660	0.540	0.600
Eos (G/l)	week:	14	0.060	0.090	0.130	0.190	0.060	0.090	0.110	0.070	0.110	0.050
		18	0.070	0.090	0.110	0.130	0.160	0.090	0.110	0.070	0.110	0.050
Baso (G/l)	week:	14	0.010	0.010	0.030	0.010	0.030	0.020	0.030	0.020	0.020	0.010
		18	0.020	0.010	0.020	0.020	0.020	0.010	0.020	0.040	0.020	0.010
Lympho (G/l)	week:	14	4.670	3.280	7.280	4.920	6.790	5.250	6.400	5.730	5.580	3.400
		18	4.100	4.260	5.470	3.960	5.870	4.990	6.240	6.320	4.960	3.740
Mono (G/l)	week:	14	0.350	0.240	0.540	0.290	0.480	0.690	0.720	0.470	0.430	0.410
		18	0.430	0.300	0.330	0.370	0.550	0.360	0.440	0.420	0.450	0.400
Luc (G/l)	week:	14	0.250	0.150	0.300	0.180	0.270	0.290	0.520	0.260	0.240	0.280
		18	0.280	0.270	0.210	0.250	0.230	0.180	0.300	0.240	0.260	0.240

Hematology (individuals): females

group 6  
 1250 ppm

		Animal no									
		151	152	153	154	155	156	157	158	159	160
Plt (G/l)	week: 14	898.0	848.0	957.0	1045	970.0	939.0	1050	1173	1033	927.0
	18	743.0	913.0	942.0	888.0	1141	879.0	1044	1173	1101	825.0
PT(CS) (sec)	week: 14	26.45	26.34	21.35	28.59	25.84	26.61	25.11	28.99	27.98	28.82
	18	31.31	28.84	27.58	23.90	27.22	31.12	26.53	23.14	24.56	30.06

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6.8. Blood chemistry (individuals)

Blood chemistry (individuals): males

group 1  
0 ppm

	Animal no										
		1	2	3	4	5	6	7	8	9	10
Gluc (mmol/l) week: 14		8.190	7.470	8.490	8.800	7.750	8.460	9.010	8.900	8.010	7.810
Urea (mmol/l) week: 14		5.470	5.500	5.260	5.650	4.860	5.930	5.990	4.085	5.170	5.650
Creat-e (umol/l) week: 14		52.00	54.30	57.70	52.10	52.30	49.90	58.80	46.70	58.90	59.50
Bili-tot (umol/l) week: 14		1.700	1.220	3.160	1.700	2.430	2.680	1.460	2.430	2.190	1.950
Prot (g/l) week: 14		70.59	65.67	62.28	67.09	65.72	65.08	63.19	64.00	61.58	67.95
Alb (g/l) week: 14		36.75	34.56	33.37	35.71	35.72	36.76	35.04	35.37	33.30	35.57
Glob (g/l) week: 14		33.84	31.11	28.91	31.38	30.00	28.32	28.15	28.63	28.28	32.38
A/G (1) week: 14		1.090	1.110	1.150	1.140	1.190	1.300	1.240	1.240	1.180	1.100
Chol (mmol/l) week: 14		2.370	1.940	1.935	2.370	1.800	1.840	1.990	1.540	1.470	1.620



Blood chemistry (individuals): males

group 1  
0 ppm

		Animal no									
		11	12	13	14	15	16	17	18	19	20
Gluc (mmol/l)	week: 14	8.370	9.390	7.810	7.900	8.470	8.650	8.690	9.110	8.080	7.930
	18	7.800	9.600	8.550	7.750	8.870	9.080	9.570	9.600	8.150	8.370
Urea (mmol/l)	week: 14	6.690	6.410	5.900	5.960	6.110	6.110	5.810	5.050	5.930	6.480
	18	6.080	6.870	5.960	6.410	5.780	6.050	5.960	4.290	5.500	5.990
Creat-e (umol/l)	week: 14	58.30	51.50	57.60	58.90	52.10	57.70	59.10	53.40	57.10	55.00
	18	56.90	50.90	58.90	63.10	51.00	59.00	62.00	53.30	57.70	55.40
Bili-tot (umol/l)	week: 14	2.680	1.460	2.680	2.680	1.700	1.950	2.190	1.700	1.460	2.430
	18	1.970	1.480	1.970	2.210	2.210	2.210	2.210	1.720	1.720	2.460
Prot (g/l)	week: 14	68.00	70.45	65.25	66.64	66.14	69.90	67.37	68.53	63.05	67.64
	18	68.87	71.43	67.27	67.13	67.49	70.95	69.71	69.86	69.49	67.69
Alb (g/l)	week: 14	35.46	37.31	34.51	35.24	36.04	34.68	35.89	35.22	34.40	35.27
	18	34.82	37.85	35.10	34.55	37.61	36.56	36.37	36.38	35.60	36.30
Glob (g/l)	week: 14	32.54	33.14	30.74	31.40	30.10	35.22	31.48	33.31	28.65	32.37
	18	34.05	33.58	32.17	32.58	29.88	34.39	33.34	33.48	33.89	31.39
A/G (l)	week: 14	1.090	1.130	1.120	1.120	1.200	0.980	1.140	1.060	1.200	1.090
	18	1.020	1.130	1.090	1.060	1.260	1.060	1.090	1.090	1.050	1.160
Chol (mmol/l)	week: 14	2.120	2.300	1.690	1.750	2.120	1.770	2.825	1.990	1.360	1.510
	18	2.130	2.630	1.830	2.040	2.520	2.060	3.270	2.560	1.810	1.650

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (individuals): males

group 1  
0 ppm

		Animal no									
		11	12	13	14	15	16	17	18	19	20
Na+	(mmol/l)										
week:	14	143.9	141.6	143.0	143.6	143.6	142.8	143.3	143.2	143.2	143.3
	18	144.6	143.3	145.3	144.7	144.7	142.1	144.8	143.1	143.5	143.9
K+	(mmol/l)										
week:	14	3.520	3.430	3.750	3.570	3.720	3.980	3.740	3.850	3.780	3.660
	18	3.550	3.590	3.530	3.500	3.130	3.970	3.770	3.580	3.640	3.600
Ca++	(mmol/l)										
week:	14	2.690	2.650	2.560	2.580	2.690	2.690	2.700	2.660	2.540	2.620
	18	2.630	2.680	2.640	2.640	2.660	2.750	2.760	2.710	2.640	2.570
Cl-	(mmol/l)										
week:	14	98.70	97.20	98.90	99.70	101.9	100.1	98.10	100.8	98.90	100.5
	18	104.7	103.1	106.0	104.2	104.2	101.3	103.6	103.8	101.4	104.2
PO4-in	(mmol/l)										
week:	14	1.830	1.540	1.620	1.630	1.750	1.580	1.670	1.560	1.710	1.610
	18	1.780	1.450	1.640	1.620	1.540	1.510	1.580	1.370	1.630	1.500
ASAT (GOT)	(U/l)										
week:	14	50.30	60.30	67.10	65.90	72.70	60.90	58.40	57.20	50.30	44.10
	18	76.40	62.10	64.60	68.40	52.80	54.70	59.00	48.50	67.10	55.90
ALAT (GPT)	(U/l)										
week:	14	39.20	31.80	41.50	37.80	47.40	28.90	37.00	30.40	31.10	25.90
	18	47.40	34.10	44.40	40.00	32.60	31.80	38.50	28.10	44.40	34.80
ALP	(U/l)										
week:	14	75.50	86.80	75.50	82.00	83.90	76.60	54.40	76.60	83.90	65.10
	18	69.60	85.60	74.40	71.80	89.60	88.20	56.10	73.00	94.90	58.90
GGT	(U/l)										
week:	14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	18	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	2.500	0.000

Blood chemistry (individuals): males

group 2  
25 ppm

		Animal no									
		21	22	23	24	25	26	27	28	29	30
Gluc (mmol/l)	week: 14	8.990	8.060	8.790	7.880	6.480	7.620	7.180	8.100	9.360	8.520
Urea (mmol/l)	week: 14	4.890	6.320	5.530	5.960	5.840	4.800	6.960	4.960	6.110	5.470
Creat-e (umol/l)	week: 14	56.40	58.50	57.70	57.60	58.00	53.80	58.60	54.60	57.10	50.00
Bili-tot (umol/l)	week: 14	1.700	1.700	2.190	2.190	2.430	1.700	1.950	1.950	2.190	1.950
Prot (g/l)	week: 14	67.75	65.89	71.76	66.31	65.00	66.75	67.20	66.78	72.68	68.45
Alb (g/l)	week: 14	35.77	35.57	38.22	34.86	34.95	33.95	35.51	35.80	37.21	35.82
Glob (g/l)	week: 14	31.98	30.32	33.54	31.45	30.05	32.80	31.69	30.98	35.47	32.63
A/G (l)	week: 14	1.120	1.170	1.140	1.110	1.160	1.040	1.120	1.160	1.050	1.100
Chol (mmol/l)	week: 14	2.370	1.410	1.740	1.840	2.000	2.480	1.740	2.160	2.540	1.770
Na+ (mmol/l)	week: 14	142.9	142.0	142.3	142.3	142.2	142.5	143.3	142.6	142.0	141.7
K+ (mmol/l)	week: 14	3.820	3.350	3.840	3.550	3.490	3.630	3.440	3.480	3.660	3.690

Blood chemistry (individuals): males

group 2  
25 ppm

		Animal no									
		21	22	23	24	25	26	27	28	29	30
Ca++ (mmol/l)	week: 14	2.690	2.590	2.690	2.670	2.570	2.650	2.630	2.630	2.760	2.630
Cl- (mmol/l)	week: 14	97.40	98.80	98.40	96.80	96.20	98.90	96.60	98.00	97.20	97.50
PO4-in (mmol/l)	week: 14	1.830	1.690	1.550	1.870	1.670	1.600	1.770	1.630	1.780	1.520
ASAT (GOT) (U/l)	week: 14	64.00	106.3	54.70	59.00	69.60	68.40	64.00	57.20	52.80	64.60
ALAT (GPT) (U/l)	week: 14	28.10	91.80	30.40	37.00	40.70	44.40	33.30	48.90	30.40	34.80
ALP (U/l)	week: 14	80.30	75.50	76.90	115.2	86.20	119.7	93.00	67.30	60.00	101.4
GGT (U/l)	week: 14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): males

group 3  
50 ppm

		Animal no									
		31	32	33	34	35	36	37	38	39	40
Gluc (mmol/l)	week: 14	7.420	10.04	6.330	7.390	7.950	7.910	8.720	6.780	7.630	6.610



Blood chemistry (individuals): males

group 3  
50 ppm

		Animal no									
		31	32	33	34	35	36	37	38	39	40
Urea (mmol/l)	week: 14	7.080	5.680	5.870	5.350	6.510	4.590	6.660	6.170	6.140	6.440
Creat-e (umol/l)	week: 14	60.60	52.10	67.90	57.00	62.70	64.80	54.00	62.70	59.10	66.10
Bili-tot (umol/l)	week: 14	1.950	2.430	1.700	1.700	1.700	2.680	2.430	2.680	1.950	2.680
Prot (g/l)	week: 14	64.70	70.84	65.36	66.17	64.56	64.03	63.75	66.86	68.62	65.81
Alb (g/l)	week: 14	35.47	38.09	33.71	36.06	34.36	33.75	34.80	34.95	35.09	35.65
Glob (g/l)	week: 14	29.23	32.75	31.65	30.11	30.20	30.28	28.95	31.91	33.53	30.16
A/G (1)	week: 14	1.210	1.160	1.070	1.200	1.140	1.110	1.200	1.100	1.050	1.180
Chol (mmol/l)	week: 14	2.110	2.550	1.960	1.500	1.850	1.820	1.750	1.990	2.040	1.260
Na+ (mmol/l)	week: 14	142.6	141.9	142.4	143.3	142.5	143.1	142.9	143.8	142.0	144.8
K+ (mmol/l)	week: 14	3.370	3.380	3.600	3.290	3.740	3.940	3.440	3.750	3.660	3.770
Ca++ (mmol/l)	week: 14	2.600	2.690	2.600	2.570	2.560	2.620	2.560	2.700	2.600	2.580

Blood chemistry (individuals): males

group 3  
50 ppm

		Animal no									
		31	32	33	34	35	36	37	38	39	40
Cl-	(mmol/l)										
week:	14	98.00	97.30	98.60	99.90	99.40	99.20	100.4	100.3	98.30	100.0
PO4-in	(mmol/l)										
week:	14	1.630	1.430	1.940	1.500	1.920	1.820	1.560	1.840	1.610	1.900
ASAT (GOT)	(U/l)										
week:	14	57.80	51.60	57.20	54.70	50.30	82.60	63.40	57.80	54.70	80.80
ALAT (GPT)	(U/l)										
week:	14	39.20	30.40	34.10	34.10	31.80	29.60	34.80	33.30	35.50	39.20
ALP	(U/l)										
week:	14	104.2	71.60	76.30	109.9	49.85	58.60	84.80	67.30	78.90	130.1
GGT	(U/l)										
week:	14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): males

group 4  
250 ppm

		Animal no									
		41	42	43	44	45	46	47	48	49	50
Gluc	(mmol/l)										
week:	14	7.290	8.890	8.260	7.340	7.960	7.380	6.390	6.100	8.840	8.270
Urea	(mmol/l)										
week:	14	4.920	6.140	4.860	5.380	5.810	5.590	6.510	5.960	5.470	4.990

Blood chemistry (individuals): males

group 4  
250 ppm

		Animal no									
		41	42	43	44	45	46	47	48	49	50
Creat-e (umol/l)	week: 14	58.30	53.80	52.30	64.30	61.30	59.10	69.10	64.20	53.50	58.30
Bili-tot (umol/l)	week: 14	1.460	2.190	1.700	2.190	2.430	2.190	1.950	2.430	2.430	2.920
Prot (g/l)	week: 14	68.56	66.14	70.87	65.81	65.75	66.00	66.50	63.69	66.61	70.59
Alb (g/l)	week: 14	35.77	35.26	37.62	33.88	35.02	35.40	35.68	34.42	34.53	35.53
Glob (g/l)	week: 14	32.79	30.88	33.25	31.93	30.73	30.60	30.82	29.27	32.08	35.06
A/G (1)	week: 14	1.090	1.140	1.130	1.060	1.140	1.160	1.160	1.180	1.080	1.010
Chol (mmol/l)	week: 14	2.130	2.050	2.730	1.760	2.250	1.980	1.560	1.450	1.760	2.430
Na+ (mmol/l)	week: 14	141.9	142.2	141.8	144.0	141.0	141.7	140.2	141.9	143.4	140.9
K+ (mmol/l)	week: 14	3.570	3.620	3.360	3.460	3.760	3.740	3.650	3.960	3.780	3.830
Ca++ (mmol/l)	week: 14	2.650	2.700	2.690	2.610	2.600	2.630	2.660	2.580	2.630	2.680
Cl- (mmol/l)	week: 14	101.4	99.00	100.8	102.0	100.4	101.4	97.80	99.40	99.60	97.40

Blood chemistry (individuals): males

group 4  
250 ppm

		Animal no									
		41	42	43	44	45	46	47	48	49	50
PO4-in (mmol/l)	week: 14	1.680	1.700	1.670	1.860	1.790	1.850	1.930	1.740	1.830	1.750
ASAT (GOT) (U/l)	week: 14	64.00	57.20	51.60	72.70	42.90	66.50	121.2	114.3	64.00	49.10
ALAT (GPT) (U/l)	week: 14	44.40	28.90	28.90	37.80	24.40	37.80	41.50	80.70	34.80	39.20
ALP (U/l)	week: 14	93.80	73.50	76.60	85.90	62.50	92.70	79.20	77.70	62.80	65.90
GGT (U/l)	week: 14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): males

group 5  
625 ppm

		Animal no									
		51	52	53	54	55	56	57	58	59	60
Gluc (mmol/l)	week: 14	6.850	6.640	8.070	7.440	8.420	7.010	8.510	8.020	7.530	7.610
Urea (mmol/l)	week: 14	5.810	4.860	5.680	5.500	5.720	6.540	6.290	5.960	5.290	4.470
Creat-e (umol/l)	week: 14	55.80	67.00	55.50	60.30	60.40	64.80	67.20	53.20	55.90	52.90

Blood chemistry (individuals): males

group 5  
625 ppm

		Animal no									
		51	52	53	54	55	56	57	58	59	60
Bili-tot ( $\mu\text{mol/l}$ ) week: 14		2.190	1.460	2.680	2.190	1.950	2.190	1.460	2.190	1.460	1.700
Prot (g/l) week: 14		66.70	69.56	67.34	67.64	67.53	68.64	63.39	75.82	70.01	68.53
Alb (g/l) week: 14		34.62	36.17	35.01	35.86	36.45	35.26	33.28	37.22	34.66	36.38
Glob (g/l) week: 14		32.08	33.39	32.33	31.78	31.08	33.38	30.11	38.60	35.35	32.15
A/G (1) week: 14		1.080	1.080	1.080	1.130	1.170	1.060	1.110	0.960	0.980	1.130
Chol (mmol/l) week: 14		1.760	1.990	2.290	1.730	1.790	2.040	1.790	2.390	2.190	1.960
Na+ (mmol/l) week: 14		140.2	142.3	141.7	142.1	144.8	141.5	139.7	142.0	139.7	142.6
K+ (mmol/l) week: 14		3.350	3.540	3.550	3.350	3.560	3.350	3.360	3.410	3.150	3.730
Ca++ (mmol/l) week: 14		2.650	2.710	2.660	2.650	2.620	2.670	2.540	2.740	2.670	2.730
Cl- (mmol/l) week: 14		98.40	96.70	99.50	98.60	100.0	98.50	98.60	99.60	99.80	98.80
PO4-in (mmol/l) week: 14		2.040	1.630	1.690	1.770	1.690	1.910	2.030	1.770	1.810	1.840

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 302

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (individuals): males

group 5  
625 ppm

		Animal no									
		51	52	53	54	55	56	57	58	59	60
ASAT (GOT) (U/l)	week: 14	63.40	47.80	59.70	48.50	62.10	60.30	233.3	49.10	62.80	67.10
ALAT (GPT) (U/l)	week: 14	34.10	24.40	40.00	22.20	33.30	35.50	181.8	34.10	45.20	39.20
ALP (U/l)	week: 14	58.30	68.50	58.30	74.70	80.80	73.50	67.60	85.60	69.30	81.70
GGT (U/l)	week: 14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): males

group 6  
1250 ppm

		Animal no									
		61	62	63	64	65	66	67	68	69	70
Gluc (mmol/l)	week: 14	6.830	7.430	7.010	7.000	8.560	8.060	7.260	7.420	6.850	7.790
Urea (mmol/l)	week: 14	4.960	5.810	5.230	6.050	6.720	6.200	6.570	6.140	5.930	7.020
Creat-e (umol/l)	week: 14	63.10	64.80	58.60	60.40	69.30	57.00	66.00	61.80	69.10	68.80
Bili-tot (umol/l)	week: 14	3.890	1.700	2.190	1.700	1.460	1.700	1.950	2.430	2.190	1.700

Blood chemistry (individuals): males

group 6  
 1250 ppm

		Animal no									
		61	62	63	64	65	66	67	68	69	70
Prot (g/l)											
week:	14	64.50	67.11	68.42	65.81	66.36	67.50	67.75	68.17	66.53	64.64
Alb (g/l)											
week:	14	35.49	35.26	36.55	35.75	34.59	35.36	35.05	36.63	34.40	34.02
Glob (g/l)											
week:	14	29.01	31.85	31.87	30.06	31.77	32.14	32.70	31.54	32.13	30.62
A/G (1)											
week:	14	1.220	1.110	1.150	1.190	1.090	1.100	1.070	1.160	1.070	1.110
Chol (mmol/l)											
week:	14	1.350	1.980	1.940	1.870	2.150	2.210	1.390	1.810	2.140	1.420
Na+ (mmol/l)											
week:	14	142.1	139.4	142.3	143.0	140.0	144.2	141.6	141.8	141.7	140.8
K+ (mmol/l)											
week:	14	3.320	3.175	3.410	3.410	3.510	3.730	3.330	3.620	3.710	3.210
Ca++ (mmol/l)											
week:	14	2.660	2.650	2.700	2.580	2.570	2.620	2.590	2.650	2.640	2.570
Cl- (mmol/l)											
week:	14	99.00	98.90	100.1	101.9	96.70	98.10	99.70	100.3	100.5	99.20
PO4-in (mmol/l)											
week:	14	1.830	1.590	1.710	1.430	1.970	1.690	1.800	1.900	1.440	2.160
ASAT (GOT) (U/l)											
week:	14	72.10	57.80	58.40	85.10	76.40	47.80	62.80	44.70	57.80	64.00

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (individuals): males

group 6  
1250 ppm

		Animal no									
		61	62	63	64	65	66	67	68	69	70
ALAT (GPT) (U/l)											
week:	14	41.50	33.30	34.10	60.70	44.40	29.60	31.80	31.10	26.70	30.40
ALP (U/l)											
week:	14	65.60	67.00	71.60	82.50	53.50	44.20	92.70	63.40	87.30	62.80
GGT (U/l)											
week:	14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

## Blood chemistry (individuals): males

group 6  
1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
Gluc (mmol/l)											
week:	14	7.700	7.620	7.590	8.420	7.960	8.520	6.890	8.660	9.740	8.980
	18	9.660	8.220	9.760	8.820	10.73	10.44	7.670	8.840	9.630	11.98
Urea (mmol/l)											
week:	14	5.020	5.170	5.020	5.810	5.750	5.840	5.590	4.920	4.890	4.860
	18	5.080	5.440	5.650	6.320	5.260	5.320	5.380	5.530	5.380	5.290
Creat-e (umol/l)											
week:	14	60.70	65.20	61.00	57.70	62.10	53.50	65.20	60.70	57.90	55.30
	18	54.70	61.10	55.10	56.90	57.30	56.40	66.80	57.10	52.90	52.20
Bili-tot (umol/l)											
week:	14	1.460	2.430	1.700	2.430	2.190	2.190	2.190	1.700	2.430	2.430
	18	1.970	1.970	1.970	1.970	1.970	1.970	2.210	2.460	3.200	2.950
Prot (g/l)											
week:	14	68.53	64.72	68.78	66.95	67.31	70.15	65.08	65.17	68.31	66.48
	18	68.90	65.10	68.51	68.31	66.03	69.01	64.96	65.89	67.77	67.69



Blood chemistry (individuals): males

group 6  
 1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
Alb	(g/l)										
week:	14	34.93	33.40	35.93	36.39	36.07	36.45	34.24	33.77	36.00	36.75
	18	37.17	35.37	36.77	36.34	35.39	36.77	34.62	35.81	36.74	37.00
Glob	(g/l)										
week:	14	33.60	31.32	32.85	30.56	31.24	33.70	30.84	31.40	32.31	29.73
	18	31.73	29.73	31.74	31.97	30.64	32.24	30.34	30.08	31.03	30.69
A/G	(1)										
week:	14	1.040	1.070	1.090	1.190	1.150	1.080	1.110	1.080	1.110	1.240
	18	1.170	1.190	1.160	1.140	1.160	1.140	1.140	1.190	1.180	1.210
Chol	(mmol/l)										
week:	14	1.760	1.770	1.710	2.330	2.630	2.160	1.920	1.770	2.070	1.890
	18	2.030	1.690	1.820	2.330	2.800	2.190	1.900	1.750	2.050	2.300
Na+	(mmol/l)										
week:	14	144.6	142.6	140.6	141.7	143.4	142.8	143.1	140.4	142.2	141.0
	18	143.6	143.9	143.9	143.5	141.2	144.0	142.9	143.3	142.5	141.3
K+	(mmol/l)										
week:	14	3.350	3.580	3.480	3.400	3.750	3.420	3.600	3.170	3.300	3.450
	18	3.310	3.800	3.380	3.270	3.680	3.350	3.650	3.190	3.640	3.500
Ca++	(mmol/l)										
week:	14	2.680	2.660	2.680	2.690	2.720	2.760	2.610	2.530	2.700	2.670
	18	2.670	2.580	2.620	2.610	2.650	2.650	2.590	2.570	2.590	2.590
Cl-	(mmol/l)										
week:	14	97.20	98.00	97.90	100.5	98.70	96.10	98.30	100.9	98.80	100.8
	18	101.2	103.9	103.4	103.8	103.5	104.0	104.7	104.0	103.7	105.2
PO4-in	(mmol/l)										
week:	14	1.940	1.950	1.760	1.720	1.650	2.000	1.790	1.560	1.890	1.660
	18	1.680	1.550	1.360	1.390	1.380	1.490	1.570	1.390	1.640	1.270

Blood chemistry (individuals): males

group 6  
 1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
ASAT (GOT)	(U/l)										
week:	14	78.30	58.40	52.20	55.90	60.90	56.50	48.50	52.80	45.40	56.50
	18	59.00	71.50	54.70	55.30	55.90	83.30	65.20	56.50	56.50	69.60
ALAT (GPT)	(U/l)										
week:	14	36.30	37.80	34.10	32.60	52.60	32.60	30.40	20.00	29.60	32.60
	18	31.10	42.90	33.30	27.40	41.50	48.90	34.10	23.70	28.90	31.10
ALP	(U/l)										
week:	14	86.50	66.50	84.80	91.80	96.10	81.70	85.60	58.60	65.40	63.90
	18	85.60	69.30	90.10	82.30	88.20	80.00	87.00	72.10	63.90	80.30
GGT	(U/l)										
week:	14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	18	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

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Blood chemistry (individuals): females		group 1 0 ppm									
		Animal no									
		81	82	83	84	85	86	87	88	89	90
Gluc (mmol/l)											
week:	14	8.000	7.980	7.670	9.120	7.590	6.530	7.920	7.320	8.160	8.560
Urea (mmol/l)											
week:	14	6.720	6.170	8.150	6.050	8.480	7.450	5.960	6.840	7.840	5.680
Creat-e (umol/l)											
week:	14	49.70	52.50	70.20	50.30	52.40	55.20	52.20	63.30	57.00	58.00
Bili-tot (umol/l)											
week:	14	2.600	3.070	4.020	3.070	3.070	2.600	2.840	3.550	2.600	3.780
Prot (g/l)											
week:	14	69.14	66.15	64.84	65.82	72.15	65.36	64.43	61.91	66.15	66.95
Alb (g/l)											
week:	14	38.43	36.26	36.71	37.75	39.40	36.07	35.64	34.98	37.16	37.67
Glob (g/l)											
week:	14	30.71	29.89	28.13	28.07	32.75	29.29	28.79	26.93	28.99	29.28
A/G (l)											
week:	14	1.250	1.210	1.310	1.340	1.200	1.230	1.240	1.300	1.280	1.290
Chol (mmol/l)											
week:	14	2.180	2.060	2.320	1.890	2.250	2.500	1.490	1.630	2.710	2.230
Na+ (mmol/l)											
week:	14	143.6	143.6	145.2	144.8	140.9	145.5	142.4	142.8	139.9	144.1
K+ (mmol/l)											
week:	14	2.990	2.560	2.610	2.680	2.730	2.317	2.700	2.740	2.980	2.930

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (individuals): females

group 1  
0 ppm

		Animal no									
		81	82	83	84	85	86	87	88	89	90
Ca++ (mmol/l)											
week:	14	2.680	2.610	2.600	2.580	2.640	2.510	2.480	2.540	2.610	2.490
Cl- (mmol/l)											
week:	14	103.0	100.9	99.60	102.8	99.90	99.90	103.8	100.7	97.10	102.5
PO4-in (mmol/l)											
week:	14	1.390	1.550	1.470	1.320	1.510	1.160	1.470	1.420	1.480	1.040
ASAT (GOT) (U/l)											
week:	14	55.30	61.50	64.00	42.30	41.00	60.30	49.10	54.10	55.30	50.30
ALAT (GPT) (U/l)											
week:	14	25.90	37.80	27.40	29.60	25.20	34.80	40.70	20.70	30.40	28.10
ALP (U/l)											
week:	14	68.20	33.00	59.20	47.30	66.80	44.80	42.30	31.80	63.10	40.80
GGT (U/l)											
week:	14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

## Blood chemistry (individuals): females

group 1  
0 ppm

		Animal no									
		91	92	93	94	95	96	97	98	99	100
Gluc (mmol/l)											
week:	14	8.470	7.750	6.950	6.750	7.490	7.140	7.480	7.640	8.760	7.340
	18	6.960	8.340	8.260	7.080	6.990	7.020	8.210	8.970	8.370	6.890

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (individuals): females

group 1  
0 ppm

		Animal no									
		91	92	93	94	95	96	97	98	99	100
Urea	(mmol/l)										
week:	14	7.200	6.140	6.840	16.83	7.360	6.540	6.630	6.900	7.480	6.930
	18	6.510	6.900	7.360	15.58	7.050	7.240	6.660	7.080	8.030	6.110
Creat-e	(umol/l)										
week:	14	58.80	53.10	51.80	67.30	59.50	60.00	56.60	53.90	64.80	62.20
	18	60.70	53.10	62.10	75.00	62.70	70.30	54.70	61.10	62.30	61.50
Bili-tot	(umol/l)										
week:	14	2.600	3.070	3.070	2.600	3.780	3.310	4.490	3.550	4.020	4.020
	18	2.700	2.210	3.200	2.700	3.200	1.720	2.950	2.700	3.200	2.210
Prot	(g/l)										
week:	14	66.45	66.21	66.21	67.49	67.06	66.02	67.44	67.49	66.51	64.98
	18	70.67	68.42	69.97	78.65	66.82	70.81	67.46	70.76	70.31	68.20
Alb	(g/l)										
week:	14	36.33	37.13	36.42	34.19	36.95	35.90	37.72	35.96	38.25	35.43
	18	37.47	38.03	37.22	37.71	37.10	38.30	37.57	37.16	38.45	36.01
Glob	(g/l)										
week:	14	30.12	29.08	29.79	33.30	30.11	30.12	29.72	31.53	28.26	29.55
	18	33.20	30.39	32.75	40.94	29.72	32.51	29.89	33.60	31.86	32.19
A/G	(1)										
week:	14	1.210	1.280	1.220	1.030	1.230	1.190	1.270	1.140	1.350	1.200
	18	1.130	1.250	1.140	0.920	1.250	1.180	1.260	1.110	1.210	1.120
Chol	(mmol/l)										
week:	14	1.640	1.920	2.520	1.980	1.730	2.240	1.760	2.760	2.490	1.770
	18	2.170	2.070	2.230	2.370	2.030	2.090	2.140	3.340	1.880	2.220
Na+	(mmol/l)										
week:	14	143.6	143.8	143.7	142.8	143.4	143.3	142.9	143.1	143.4	143.6
	18	141.2	142.6	143.4	150.1	143.4	144.0	143.8	142.5	145.6	143.0

Blood chemistry (individuals): females

group 1  
 0 ppm

		Animal no										
		91	92	93	94	95	96	97	98	99	100	
K+	(mmol/l)											
	week:	14	2.860	2.820	3.100	3.000	2.900	2.910	2.740	2.840	3.140	2.660
		18	3.450	2.990	3.260	3.470	3.210	3.020	2.720	2.860	2.800	3.450
Ca++	(mmol/l)											
	week:	14	2.580	2.510	2.610	2.620	2.630	2.550	2.600	2.580	2.570	2.520
		18	2.610	2.480	2.580	2.760	2.600	2.550	2.550	2.610	2.630	2.530
Cl-	(mmol/l)											
	week:	14	100.6	100.5	99.50	97.20	99.60	99.40	98.90	99.20	99.40	101.6
		18	102.4	104.8	103.3	112.8	105.9	105.3	106.2	104.3	104.9	107.6
PO4-in	(mmol/l)											
	week:	14	1.240	1.070	1.760	2.140	1.560	1.260	1.360	1.420	1.330	1.260
		18	1.190	1.110	1.310	1.520	1.300	1.150	1.490	1.440	1.300	1.310
ASAT (GOT)	(U/l)											
	week:	14	55.30	44.70	59.00	49.70	80.20	65.90	72.70	45.40	64.60	53.40
		18	60.30	59.70	64.00	51.60	246.1	67.70	78.90	46.00	59.70	54.10
ALAT (GPT)	(U/l)											
	week:	14	31.10	28.90	25.90	29.60	58.50	41.50	35.50	28.90	40.00	28.10
		18	28.90	40.70	26.70	22.20	121.4	26.70	37.00	19.30	23.70	20.70
AlP	(U/l)											
	week:	14	42.00	53.80	47.30	58.60	44.80	67.30	36.30	36.90	41.10	36.10
		18	53.80	48.50	46.20	59.70	37.70	79.40	37.20	40.30	39.20	30.15
GGT	(U/l)											
	week:	14	0.000	0.000	0.000	0.000	0.000	0.000	4.150	0.000	0.000	0.000
		18	0.000	0.000	0.000	4.500	0.000	0.000	7.433	0.000	0.000	0.000

Blood chemistry (individuals): females

group 2  
25 ppm

		Animal no									
		101	102	103	104	105	106	107	108	109	110
Gluc (mmol/l)	week: 14	8.070	7.470	9.390	7.640	7.310	6.980	8.250	7.760	8.480	7.480
Urea (mmol/l)	week: 14	5.870	7.630	6.690	5.960	6.840	8.030	7.170	5.930	6.630	7.810
Creat-e (umol/l)	week: 14	59.40	68.50	58.00	56.40	56.10	57.40	60.30	49.20	56.00	60.40
Bili-tot (umol/l)	week: 14	3.070	4.850	2.360	2.600	3.310	3.070	2.840	2.600	3.310	2.360
Prot (g/l)	week: 14	65.00	65.77	65.74	65.14	66.07	63.52	68.26	68.29	69.44	63.94
Alb (g/l)	week: 14	36.35	36.53	35.85	36.97	36.92	34.59	37.90	37.87	38.82	34.66
Glob (g/l)	week: 14	28.65	29.24	29.89	28.17	29.15	28.93	30.36	30.42	30.62	29.28
A/G (l)	week: 14	1.270	1.250	1.200	1.310	1.270	1.200	1.250	1.240	1.270	1.180
Chol (mmol/l)	week: 14	2.130	1.800	2.830	1.870	2.290	1.780	1.590	2.480	2.380	2.330
Na+ (mmol/l)	week: 14	143.1	144.1	143.1	144.1	143.1	144.5	144.0	141.9	143.5	143.6
K+ (mmol/l)	week: 14	2.730	2.760	2.530	2.880	2.910	2.580	2.680	2.990	3.100	3.410

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 312

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (individuals): females

group 2  
25 ppm

		Animal no									
		101	102	103	104	105	106	107	108	109	110
Ca++ (mmol/l)	week: 14	2.530	2.570	2.520	2.540	2.590	2.480	2.520	2.570	2.590	2.490
Cl- (mmol/l)	week: 14	100.2	98.85	100.2	101.6	101.0	100.4	101.2	100.8	101.8	102.0
PO4-in (mmol/l)	week: 14	1.460	1.650	1.250	1.070	1.460	1.370	1.830	1.300	1.370	1.600
ASAT (GOT) (U/l)	week: 14	55.30	65.90	56.50	64.60	49.10	60.30	55.90	44.70	45.40	53.40
ALAT (GPT) (U/l)	week: 14	28.10	32.60	41.50	35.50	23.00	31.10	21.50	28.90	34.80	26.70
ALP (U/l)	week: 14	50.40	39.20	53.00	62.00	38.30	60.60	39.20	44.50	46.80	38.60
GGT (U/l)	week: 14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): females

group 3  
50 ppm

		Animal no									
		111	112	113	114	115	116	117	118	119	120
Gluc (mmol/l)	week: 14	7.120	8.070	7.480	7.790	5.920	7.320	7.950	6.850	8.110	7.430



Blood chemistry (individuals): females

group 3  
50 ppm

		Animal no									
		111	112	113	114	115	116	117	118	119	120
Urea (mmol/l)	week: 14	6.570	7.240	8.090	5.960	7.510	6.570	7.080	6.870	5.870	5.350
Creat-e (umol/l)	week: 14	59.40	57.10	62.20	55.20	61.90	52.50	70.50	58.80	54.30	50.00
Bili-tot (umol/l)	week: 14	2.360	3.070	3.310	2.600	3.310	2.600	2.600	2.600	2.600	2.130
Prot (g/l)	week: 14	63.83	70.01	65.99	63.17	64.78	68.45	65.85	63.28	68.51	66.07
Alb (g/l)	week: 14	35.44	38.77	36.72	35.62	36.62	36.58	37.57	35.49	37.91	36.95
Glob (g/l)	week: 14	28.39	31.24	29.27	27.55	28.16	31.87	28.28	27.79	30.60	29.12
A/G (l)	week: 14	1.250	1.240	1.250	1.290	1.300	1.150	1.330	1.280	1.240	1.270
Chol (mmol/l)	week: 14	3.510	3.590	1.880	2.010	2.420	2.530	1.470	2.090	2.170	1.820
Na+ (mmol/l)	week: 14	143.8	142.9	144.1	143.4	143.7	142.3	142.2	142.7	143.4	142.2
K+ (mmol/l)	week: 14	2.930	2.870	2.600	3.090	3.000	3.050	2.610	3.140	2.950	2.870
Ca++ (mmol/l)	week: 14	2.520	2.590	2.490	2.580	2.570	2.590	2.460	2.500	2.500	2.520

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 314

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (individuals): females group 3  
50 ppm

		Animal no									
		111	112	113	114	115	116	117	118	119	120
Cl-	(mmol/l)										
week:	14	99.90	98.20	100.3	102.4	101.1	100.2	98.80	98.30	99.40	99.50
PO4-in	(mmol/l)										
week:	14	1.570	1.660	1.440	1.400	1.630	1.370	1.320	1.610	1.380	1.230
ASAT (GOT)	(U/l)										
week:	14	93.20	57.20	47.80	44.70	56.50	52.20	51.60	49.10	60.90	42.30
ALAT (GPT)	(U/l)										
week:	14	40.00	26.70	29.60	22.20	24.40	37.80	20.00	25.90	32.60	25.90
AlP	(U/l)										
week:	14	34.40	69.90	50.40	30.70	43.40	71.00	44.80	42.80	33.50	49.90
GGT	(U/l)										
week:	14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): females group 4  
250 ppm

		Animal no									
		121	122	123	124	125	126	127	128	129	130
Gluc	(mmol/l)										
week:	14	7.060	7.690	7.970	7.790	7.380	7.570	8.880	7.990	6.670	7.430
Urea	(mmol/l)										
week:	14	6.900	6.990	7.140	8.270	6.570	6.690	6.050	5.320	8.030	7.840

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (individuals): females

group 4  
250 ppm

		Animal no									
		121	122	123	124	125	126	127	128	129	130
Creat-e ( $\mu\text{mol/l}$ ) week: 14		56.10	55.70	55.20	67.20	57.10	58.30	51.00	48.90	62.70	61.30
Bili-tot ( $\mu\text{mol/l}$ ) week: 14		2.360	2.600	2.360	2.840	2.130	3.550	2.840	2.600	2.600	1.890
Prot ( $\text{g/l}$ ) week: 14		62.38	66.18	71.08	67.96	63.31	66.40	68.10	69.03	63.69	65.08
Alb ( $\text{g/l}$ ) week: 14		34.55	36.04	38.71	38.17	35.06	37.26	36.37	38.55	35.66	35.48
Glob ( $\text{g/l}$ ) week: 14		27.83	30.14	32.37	29.79	28.25	29.14	31.73	30.48	28.03	29.60
A/G (1) week: 14		1.240	1.200	1.200	1.280	1.240	1.280	1.150	1.260	1.270	1.200
Chol ( $\text{mmol/l}$ ) week: 14		2.470	2.020	2.530	1.540	2.300	2.360	2.650	1.840	2.330	2.200
Na+ ( $\text{mmol/l}$ ) week: 14		140.9	142.8	144.4	143.4	143.8	143.4	143.0	143.3	143.6	143.0
K+ ( $\text{mmol/l}$ ) week: 14		2.850	2.910	2.820	2.590	2.790	2.720	2.790	2.940	3.280	2.840
Ca++ ( $\text{mmol/l}$ ) week: 14		2.510	2.540	2.590	2.520	2.510	2.560	2.590	2.520	2.590	2.510
Cl- ( $\text{mmol/l}$ ) week: 14		98.20	100.2	102.3	99.70	101.8	99.10	103.2	109.4	98.80	102.3

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (individuals): females

group 4  
250 ppm

		Animal no									
		121	122	123	124	125	126	127	128	129	130
PO4-in (mmol/l)	week: 14	1.640	1.530	1.110	1.220	1.280	1.570	1.220	1.220	1.710	1.320
ASAT (GOT) (U/l)	week: 14	69.60	44.10	65.90	64.00	62.10	53.40	39.80	39.80	127.1	47.80
ALAT (GPT) (U/l)	week: 14	31.80	31.80	31.10	29.60	38.50	31.10	24.40	17.00	86.65	18.50
ALP (U/l)	week: 14	41.10	34.60	59.70	71.80	38.90	63.90	38.60	42.30	39.70	51.80
GGT (U/l)	week: 14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): females

group 5  
625 ppm

		Animal no									
		131	132	133	134	135	136	137	138	139	140
Gluc (mmol/l)	week: 14	6.590	6.560	8.370	7.360	7.440	8.190	8.290	8.010	8.230	7.950
Urea (mmol/l)	week: 14	8.330	6.510	6.170	6.320	7.900	6.690	7.480	5.260	8.480	9.120
Creat-e (umol/l)	week: 14	67.90	59.70	49.70	56.40	59.50	49.20	56.70	49.50	63.40	70.50

Test No.: 943127

Test Article: CGA 329351 tech.

## Blood chemistry (individuals): females

group 5  
625 ppm

		Animal no									
		131	132	133	134	135	136	137	138	139	140
Bili-tot ( $\mu\text{mol/l}$ )	week: 14	3.070	3.550	3.310	3.310	2.130	3.310	2.130	3.310	3.070	2.600
Prot (g/l)	week: 14	66.59	69.19	71.16	65.47	68.26	70.67	73.27	71.46	65.36	71.35
Alb (g/l)	week: 14	36.16	38.26	39.83	36.17	37.49	38.31	39.78	38.00	37.02	39.28
Glob (g/l)	week: 14	30.43	30.93	31.33	29.30	30.77	32.36	33.49	33.46	28.34	32.07
A/G (1)	week: 14	1.190	1.240	1.270	1.230	1.220	1.180	1.190	1.140	1.310	1.220
Chol ( $\text{mmol/l}$ )	week: 14	2.760	2.250	3.020	3.390	2.500	2.290	2.300	2.520	2.120	1.930
Na+ ( $\text{mmol/l}$ )	week: 14	142.2	144.2	142.8	143.4	142.9	143.2	144.9	142.5	142.1	143.9
K+ ( $\text{mmol/l}$ )	week: 14	2.880	2.920	2.820	3.150	2.700	2.540	2.143	2.690	2.970	2.580
Ca++ ( $\text{mmol/l}$ )	week: 14	2.560	2.630	2.620	2.560	2.470	2.600	2.610	2.590	2.530	2.600
Cl- ( $\text{mmol/l}$ )	week: 14	97.80	97.50	99.90	101.4	101.4	100.3	97.80	100.9	99.00	99.70
PO4-in ( $\text{mmol/l}$ )	week: 14	1.660	1.690	1.430	1.340	1.090	1.380	1.750	1.370	1.380	1.270

Blood chemistry (individuals): females

group 5  
625 ppm

		Animal no									
		131	132	133	134	135	136	137	138	139	140
ASAT (GOT)	(U/l)										
week:	14	59.00	51.00	47.80	66.50	52.80	52.80	62.10	44.70	70.80	50.30
ALAT (GPT)	(U/l)										
week:	14	37.00	26.70	23.70	27.40	24.40	31.10	23.70	31.80	31.10	19.30
ALP	(U/l)										
week:	14	38.00	25.80	35.80	31.30	46.50	48.20	50.10	28.70	39.40	40.30
GGT	(U/l)										
week:	14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): females

group 6  
1250 ppm

		Animal no									
		141	142	143	144	145	146	147	148	149	150
Gluc	(mmol/l)										
week:	14	7.490	6.830	7.130	7.290	6.910	8.370	6.120	7.270	7.330	8.040
Urea	(mmol/l)										
week:	14	6.600	5.840	7.570	8.790	6.630	6.900	8.480	7.200	8.120	8.570
Creat-e	(umol/l)										
week:	14	53.40	50.00	57.90	62.50	57.40	51.60	63.40	58.00	59.50	61.50
Bili-tot	(umol/l)										
week:	14	2.600	2.600	2.840	3.070	2.600	2.130	3.310	2.130	2.130	3.070

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 319

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (individuals): females

group 6  
1250 ppm

		Animal no									
		141	142	143	144	145	146	147	148	149	150
Prot	(g/l)										
week:	14	65.85	65.96	70.07	67.30	70.31	67.58	65.71	69.68	64.81	68.20
Alb	(g/l)										
week:	14	37.32	36.72	38.52	37.13	38.06	36.79	36.53	38.48	35.76	38.41
Glob	(g/l)										
week:	14	28.53	29.24	31.55	30.17	32.25	30.79	29.18	31.20	29.05	29.79
A/G	(l)										
week:	14	1.310	1.260	1.220	1.230	1.180	1.190	1.250	1.230	1.230	1.290
Chol	(mmol/l)										
week:	14	2.370	2.760	3.200	2.570	2.160	2.560	2.530	2.290	2.710	2.250
Na+	(mmol/l)										
week:	14	143.0	143.0	143.4	141.9	143.0	143.6	143.2	142.4	142.5	144.2
K+	(mmol/l)										
week:	14	2.880	2.830	3.040	2.920	3.170	2.760	3.100	3.030	2.680	2.310
Ca++	(mmol/l)										
week:	14	2.530	2.560	2.680	2.600	2.530	2.530	2.620	2.610	2.520	2.550
Cl-	(mmol/l)										
week:	14	100.2	98.10	97.30	99.80	99.70	100.3	99.00	100.2	101.1	97.90
PO4-in	(mmol/l)										
week:	14	1.700	1.400	1.570	1.380	1.190	1.320	1.640	1.160	1.110	1.460
ASAT (GOT)	(U/l)										
week:	14	56.50	46.00	54.70	42.30	57.20	46.00	65.20	53.40	55.90	47.20

Blood chemistry (individuals): females

group 6  
1250 ppm

		Animal no									
		141	142	143	144	145	146	147	148	149	150
ALAT (GPT) (U/l)	week: 14	23.70	18.50	23.00	29.60	23.70	25.90	28.10	23.70	23.00	27.40
ALP (U/l)	week: 14	40.80	34.60	41.40	35.20	41.70	68.70	38.60	35.20	44.20	33.20
GGT (U/l)	week: 14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Blood chemistry (individuals): females

group 6  
1250 ppm

		Animal no									
		151	152	153	154	155	156	157	158	159	160
Gluc (mmol/l)	week: 14	6.430	8.050	6.840	8.210	7.510	8.960	8.380	8.180	8.960	7.770
	18	6.080	8.640	8.990	8.810	7.200	9.190	7.630	8.180	7.560	7.860
Urea (mmol/l)	week: 14	6.960	5.290	7.330	5.260	6.350	7.930	5.410	6.050	7.420	7.240
	18	7.360	5.870	7.110	6.440	8.060	8.880	6.870	6.960	7.390	6.080
Creat-e (umol/l)	week: 14	54.80	58.60	57.00	54.80	52.20	59.10	51.90	53.10	59.50	62.40
	18	62.10	55.00	62.60	64.60	67.50	56.10	63.60	54.40	61.80	56.30
Bili-tot (umol/l)	week: 14	2.360	3.310	2.360	3.310	1.660	2.840	3.070	2.360	2.360	1.890
	18	2.700	3.200	1.970	2.950	1.720	1.720	2.700	2.460	1.720	2.460
Prot (g/l)	week: 14	67.44	67.25	67.60	67.22	68.15	68.70	70.20	69.41	69.90	65.08
	18	67.35	64.65	68.73	72.19	67.63	71.32	70.42	69.41	73.23	67.97



3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 321

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (individuals): females

group 6  
1250 ppm

		Animal no									
		151	152	153	154	155	156	157	158	159	160
Alb (g/l)	week: 14	36.97	38.78	37.38	35.41	36.65	37.94	36.61	37.41	37.75	35.41
	18	37.49	36.26	37.67	39.02	36.98	37.73	37.55	37.69	38.36	35.55
Glob (g/l)	week: 14	30.47	28.47	30.22	31.81	31.50	30.76	33.59	32.00	32.15	29.67
	18	29.86	28.39	31.06	33.17	30.65	33.59	32.87	31.72	34.87	32.42
A/G (1)	week: 14	1.210	1.360	1.240	1.110	1.160	1.230	1.090	1.170	1.170	1.190
	18	1.260	1.280	1.210	1.180	1.210	1.120	1.140	1.190	1.100	1.100
Chol (mmol/l)	week: 14	2.530	2.490	2.890	2.590	2.360	2.380	3.405	2.260	2.420	2.830
	18	2.330	2.320	2.150	2.300	2.040	1.660	2.740	2.360	3.110	2.370
Na+ (mmol/l)	week: 14	142.5	143.4	143.1	144.2	142.5	141.9	145.5	144.0	142.3	141.5
	18	144.1	145.3	143.7	145.3	143.8	144.3	142.6	142.7	144.7	143.4
K+ (mmol/l)	week: 14	2.600	2.540	2.770	3.000	2.860	2.580	2.920	2.850	2.690	2.590
	18	3.080	2.910	2.575	2.930	3.250	2.720	2.980	3.030	2.980	3.060
Ca++ (mmol/l)	week: 14	2.500	2.570	2.580	2.500	2.580	2.590	2.630	2.630	2.570	2.480
	18	2.600	2.590	2.490	2.530	2.600	2.560	2.560	2.600	2.600	2.520
Cl- (mmol/l)	week: 14	99.00	99.30	99.80	99.40	100.3	97.00	99.50	100.4	101.0	97.20
	18	104.9	108.4	106.6	106.6	105.4	108.7	104.3	105.3	107.0	105.8
PO4-in (mmol/l)	week: 14	1.290	1.310	1.610	1.240	1.440	1.550	1.570	1.440	1.190	1.260
	18	1.010	1.260	1.610	0.980	1.270	1.370	1.350	1.230	0.970	1.000

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 322

Test No.: 943127

Test Article: CGA 329351 tech.

Blood chemistry (individuals): females

group 6  
1250 ppm

		Animal no									
		151	152	153	154	155	156	157	158	159	160
ASAT (GOT) (U/l)	week: 14	47.20	54.10	67.70	47.80	75.20	46.00	46.00	42.90	50.30	68.40
	18	49.70	48.50	59.70	53.40	59.00	43.50	60.30	42.30	52.20	55.90
ALAT (GPT) (U/l)	week: 14	19.30	29.60	29.60	21.50	40.70	25.20	23.00	21.50	23.70	39.20
	18	19.30	25.20	19.30	21.50	28.10	14.10	25.90	19.30	25.20	25.90
ALP (U/l)	week: 14	34.40	41.10	37.50	30.40	77.70	37.50	48.20	45.90	50.10	50.10
	18	36.90	41.40	40.00	36.30	91.00	34.90	35.50	49.30	51.00	44.20
GGT (U/l)	week: 14	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	18	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

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6.9. Urine analysis (individuals)

Urine analysis (individuals): males group 1  
0 ppm

		Animal no									
		1	2	3	4	5	6	7	8	9	10
Volume (ml)											
week:	14	6.800	6.100	9.800	9.300	4.500	2.200	8.100	3.700	5.400	6.000
Rel dens (1)											
week:	14	1.042	1.037	1.036	1.036	1.058	1.045	1.036	1.055	1.039	1.050
pH (1)											
week:	14	6.500	6.500	7.000	7.000	6.500	6.500	6.500	6.000	6.500	6.500

Urine analysis (individuals): males group 1  
0 ppm

		Animal no									
		11	12	13	14	15	16	17	18	19	20
Volume (ml)											
week:	14	5.600	9.300	4.600	7.900	5.600	3.900	4.500	5.000	4.900	5.300
	18	4.900	6.100	6.500	6.400	7.900	7.500	8.500	7.800	3.900	6.600
Rel dens (1)											
week:	14	1.047	1.042	1.055	1.044	1.048	1.059	1.048	1.050	1.050	1.054
	18	1.046	1.030	1.041	1.048	1.037	1.033	1.034	1.032	1.045	1.038
pH (1)											
week:	14	6.000	7.000	6.000	6.500	6.500	6.500	6.000	6.500	6.500	6.000
	18	6.000	7.500	6.500	6.500	7.500	7.000	6.500	7.000	6.500	7.000

Test No.: 943127

Test Article: CGA 329351 tech.

Urine analysis (individuals): males

group 2  
25 ppm

		Animal no									
		21	22	23	24	25	26	27	28	29	30
Volume (ml)											
week:	14	10.30	4.500	5.300	9.100	7.000	6.900	4.400	6.200	10.40	5.500
Rel dens (1)											
week:	14	1.032	1.043	1.046	1.034	1.039	1.040	1.054	1.053	1.036	1.054
pH (1)											
week:	14	7.000	6.500	7.000	6.500	6.000	6.500	6.500	6.000	6.500	6.500

Urine analysis (individuals): males

group 3  
50 ppm

		Animal no									
		31	32	33	34	35	36	37	38	39	40
Volume (ml)											
week:	14	6.100	3.100	4.200	6.500	7.800	6.500	7.600	4.300	7.100	5.400
Rel dens (1)											
week:	14	1.041	1.050	1.051	1.039	1.039	1.042	1.035	1.048	1.032	1.050
pH (1)											
week:	14	6.500	6.500	6.500	7.000	6.500	6.500	6.500	6.000	7.000	7.000

Test No.: 943127

Test Article: CGA 329351 tech.

Urine analysis (individuals): males

group 4  
250 ppm

		Animal no									
		41	42	43	44	45	46	47	48	49	50
Volume (ml)											
week:	14	10.80	5.700	7.200	5.600	8.700	7.300	4.200	3.700	7.500	9.200
Rel dens (1)											
week:	14	1.040	1.042	1.038	1.046	1.035	1.032	1.050	1.051	1.037	1.034
pH (1)											
week:	14	7.500	7.000	7.000	6.500	7.000	6.500	6.000	6.500	6.500	8.500

Urine analysis (individuals): males

group 5  
625 ppm

		Animal no									
		51	52	53	54	55	56	57	58	59	60
Volume (ml)											
week:	14	8.100	5.200	6.600	5.200	7.400	7.300	6.300	8.500	10.30	7.200
Rel dens (1)											
week:	14	1.047	1.044	1.039	1.052	1.052	1.045	1.044	1.041	1.031	1.050
pH (1)											
week:	14	7.000	6.000	7.000	6.500	7.000	6.500	6.500	7.000	7.000	7.000

Urine analysis (individuals): males

group 6  
1250 ppm

		Animal no									
		61	62	63	64	65	66	67	68	69	70
Volume (ml)											
week:	14	4.100	9.400	11.00	4.800	5.100	7.000	9.300	7.400	4.600	5.100
Rel dens (1)											
week:	14	1.043	1.031	1.037	1.045	1.054	1.043	1.035	1.033	1.039	1.050
pH (1)											
week:	14	6.000	6.500	7.500	6.500	7.000	6.500	6.500	6.500	6.000	7.000

Urine analysis (individuals): males

group 6  
1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
Volume (ml)											
week:	14	6.800	5.900	7.500	5.200	8.900	8.600	5.200	7.100	5.500	5.700
	18	9.200	6.000	8.700	3.600	7.800	8.500	4.100	7.700	6.200	8.200
Rel dens (1)											
week:	14	1.043	1.046	1.045	1.050	1.038	1.045	1.045	1.048	1.052	1.047
	18	1.034	1.045	1.040	1.033	1.029	1.048	1.048	1.047	1.040	1.039
pH (1)											
week:	14	7.500	6.000	8.500	6.500	7.000	7.000	6.500	6.000	6.500	6.500
	18	8.250	6.500	7.000	7.000	7.000	8.000	6.000	6.500	6.500	7.500

Urine analysis (individuals): females group 1  
0 ppm

		Animal no									
		81	82	83	84	85	86	87	88	89	90
Volume (ml)											
week:	14	5.600	5.200	3.400	7.100	7.600	2.200	4.200	3.500	7.800	4.500
Rel dens (1)											
week:	14	1.032	1.034	1.045	1.035	1.037	1.074	1.038	1.041	1.041	1.040
pH (1)											
week:	14	6.500	6.500	6.500	6.500	6.500	6.000	6.000	6.000	6.500	6.500

Urine analysis (individuals): females group 1  
0 ppm

		Animal no									
		91	92	93	94	95	96	97	98	99	100
Volume (ml)											
week:	14	4.400	7.300	2.600	13.40	4.800	4.200	4.000	3.700	3.900	5.900
	18	3.800	4.300	7.100	11.90	4.700	6.700	5.000	4.800	3.200	5.400
Rel dens (1)											
week:	14	1.038	1.038	1.032	1.019	1.039	1.031	1.044	1.036	1.046	1.042
	18	1.024	1.035	1.040	1.016	1.039	1.030	1.041	1.032	1.042	1.033
pH (1)											
week:	14	6.500	6.000	6.500	9.000	7.000	6.000	6.500	6.500	6.500	7.500
	18	6.500	6.000	6.500	8.500	6.500	7.000	6.500	6.500	6.500	6.500

Urine analysis (individuals): females

group 2  
25 ppm

		Animal no									
		101	102	103	104	105	106	107	108	109	110
Volume (ml)											
week:	14	3.400	4.000	2.100	4.500	6.200	6.100	3.000	1.900	3.700	1.400
Rel dens (1)											
week:	14	1.045	1.055	1.070	1.043	1.037	1.028	1.049	1.056	1.039	1.052
pH (1)											
week:	14	6.000	7.000	6.000	6.500	6.500	6.000	7.500	6.000	6.000	6.000

Urine analysis (individuals): females

group 3  
50 ppm

		Animal no									
		111	112	113	114	115	116	117	118	119	120
Volume (ml)											
week:	14	6.800	7.600	4.400	3.900	4.700	10.40	4.800	3.400	7.300	4.600
Rel dens (1)											
week:	14	1.028	1.036	1.037	1.024	1.032	1.046	1.037	1.038	1.033	1.039
pH (1)											
week:	14	7.000	7.000	7.000	6.500	7.500	7.500	6.500	6.500	6.000	6.000



Urine analysis (individuals): females

group 4  
250 ppm

		Animal no									
		121	122	123	124	125	126	127	128	129	130
Volume (ml)											
week:	14	5.500	7.300	7.000	5.200	4.000	2.100	5.800	4.100	8.200	2.100
Rel dens (1)											
week:	14	1.033	1.034	1.042	1.033	1.043	1.054	1.029	1.032	1.030	1.061
pH (1)											
week:	14	6.000	6.500	7.000	7.500	6.000	6.000	6.000	6.000	6.500	6.000

Urine analysis (individuals): females

group 5  
625 ppm

		Animal no									
		131	132	133	134	135	136	137	138	139	140
Volume (ml)											
week:	14	4.800	5.200	1.000	3.900	5.000	2.500	2.700	6.000	5.100	5.400
Rel dens (1)											
week:	14	1.041	1.037	1.044	1.032	1.044	1.066	1.049	1.036	1.037	1.040
pH (1)											
week:	14	6.500	6.500	6.000	6.500	6.500	6.000	6.000	6.500	7.000	6.500

3-MONTH ORAL TOXICITY STUDY IN RATS (ADMINISTRATION IN FOOD) 330

Test No.: 943127

Test Article: CGA 329351 tech.

Urine analysis (individuals): females

group 6  
1250 ppm

		Animal no									
		141	142	143	144	145	146	147	148	149	150
Volume (ml)											
week:	14	2.700	2.000	4.000	7.700	3.400	9.800	6.000	4.700	5.400	5.100
Rel dens (1)											
week:	14	1.049	1.046	1.036	1.030	1.040	1.031	1.035	1.031	1.037	1.041
pH (1)											
week:	14	6.500	6.000	6.000	6.500	7.000	6.500	6.500	6.500	6.500	7.500

Urine analysis (individuals): females

group 6  
1250 ppm

		Animal no									
		151	152	153	154	155	156	157	158	159	160
Volume (ml)											
week:	14	2.200	5.500	5.000	7.400	8.100	9.100	9.100	7.000	2.900	6.900
	18	5.300	5.600	3.900	6.200	7.200	3.300	4.700	5.900	4.600	3.700
Rel dens (1)											
week:	14	1.056	1.039	1.037	1.031	1.022	1.024	1.026	1.024	1.022	1.026
	18	1.033	1.028	1.038	1.032	1.027	1.048	1.036	1.033	1.031	1.028
pH (1)											
week:	14	6.500	8.000	8.000	7.000	6.500	9.000	6.500	6.500	6.500	6.000
	18	6.500	6.500	6.500	7.000	7.000	7.000	6.500	6.500	6.500	6.500

















Test No.: 943127

Test Article: CGA 329351 tech.

Urine analysis (individuals): males

group 6  
1250 ppm

		Animal no									
		71	72	73	74	75	76	77	78	79	80
Blood	(score)										
week:	14	0	0	0	0	0	0	0	0	0	0
	18	0	0	0	0	0	0	0	0	0	0
UBG	(score)										
week:	14	0	0	0	0	0	0	0	0	0	0
	18	0	0	0	0	0	0	0	0	0	0

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Test No.: 943127

Test Article: CGA 329351 tech.

Urine analysis (individuals): females

group 1  
0 ppm

		Animal no									
		81	82	83	84	85	86	87	88	89	90
Color (choice)		N	N	N	N	N	N	N	N	N	N
week: 14		N	N	N	N	N	N	N	N	N	N
Prot (score)		+	+	++	+	++	++	+	+	+	+
week: 14		+	+	++	+	++	++	+	+	+	+
Gluc (score)		0	0	0	0	0	0	0	0	0	0
week: 14		0	0	0	0	0	0	0	0	0	0
Keto (score)		0	0	0	0	0	0	0	+	0	+
week: 14		0	0	0	0	0	0	0	+	0	+
Bili (score)		0	0	0	0	0	0	0	0	0	0
week: 14		0	0	0	0	0	0	0	0	0	0
Blood (score)		0	0	0	0	0	0	0	0	0	0
week: 14		0	0	0	0	0	0	0	0	0	0
UBG (score)		0	0	0	0	0	0	0	0	0	0
week: 14		0	0	0	0	0	0	0	0	0	0

Urine analysis (individuals): females

group 1  
0 ppm

		Animal no									
		91	92	93	94	95	96	97	98	99	100
Color (choice)		N	N	N	N	N	N	N	N	N	N
week: 14		N	N	N	N	N	N	N	N	N	N
week: 18		N	N	N	RB	N	N	N	N	N	N







Test No.: 943127

Test Article: CGA 329351 tech.

Urine analysis (individuals): females

group 4  
250 ppm

		Animal no									
		121	122	123	124	125	126	127	128	129	130
Keto	(score)										
week:	14	+	+	+	+	0	0	0	+	+	+
Bili	(score)										
week:	14	0	0	0	0	0	0	0	0	0	0
Blood	(score)										
week:	14	0	0	0	0	0	0	0	0	0	0
UBG	(score)										
week:	14	0	0	0	0	0	0	0	0	0	0

Urine analysis (individuals): females

group 5  
625 ppm

		Animal no									
		131	132	133	134	135	136	137	138	139	140
Color	(choice)										
week:	14	N	N	N	N	N	N	N	N	N	N
Prot	(score)										
week:	14	+	+	+++	+	+	++	+++	+	+	+
Gluc	(score)										
week:	14	0	0	0	0	0	0	0	0	0	0
Keto	(score)										
week:	14	+	+	+	+	0	0	0	+	0	+







Test No.: 943127

Test Article: CGA 329351 tech.

Urine analysis (individuals): females

group 6  
1250 ppm

		Animal no									
		151	152	153	154	155	156	157	158	159	160
Blood (score)	week: 14	0	0	0	0	0	0	0	0	0	0
	18	0	0	0	0	0	0	0	0	0	0
UBG (score)	week: 14	0	0	0	0	0	0	0	0	0	0
	18	0	0	0	0	0	0	0	0	0	0

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6.10. Organ weights and ratios (individuals)

6.10.1. Organ weights (individuals): 1. sacrifice

Organ weights (individuals) : males

group 1: 0 ppm

week 14

	Animal no									
	1	2	3	4	5	6	7	8	9	10
Body (g)	461.9	487.3	495.1	495.3	448.1	427.5	454.0	448.6	398.4	429.4
Heart (g)	1.574	1.303	1.696	1.557	1.280	1.293	1.370	1.218	1.228	1.315
Liver (g)	19.42	19.00	22.35	20.87	18.31	15.69	18.04	16.85	15.96	17.01
Kidney (both) (g)	2.971	3.029	3.227	3.302	2.846	2.782	2.783	2.611	2.727	2.679
Adrenal (both) (mg)	72.10	72.50	56.00	96.10	57.90	76.80	80.60	56.80	72.60	62.40
Thymus (mg)	419.8	699.6	550.3	530.5	500.1	563.4	596.1	560.8	442.9	581.0
Testis (both) (g)	4.004	4.307	4.160	4.109	3.362	4.130	4.225	3.336	3.775	3.406
Spleen (g)	0.688	0.735	0.865	0.818	0.881	0.740	0.783	0.838	0.711	0.758

Organ weights (individuals) : males

group 2 : 25 ppm

week 14

	Animal no									
	21	22	23	24	25	26	27	28	29	30
Body (g)	576.4	467.5	476.8	476.9	404.6	495.3	388.2	483.3	607.8	474.5
Heart (g)	1.580	1.321	1.484	1.335	1.170	1.446	1.130	1.558	1.811	1.307
Liver (g)	24.10	18.50	20.61	16.82	16.01	20.96	15.26	19.52	23.96	18.67
Kidney (both) (g)	3.719	3.047	2.981	2.700	2.537	3.373	2.641	3.234	3.659	3.186
Adrenal (both) (mg)	71.70	71.20	87.80	78.00	82.60	77.40	64.20	92.50	97.20	55.50
Thymus (mg)	616.7	436.4	597.1	551.2	291.7	535.6	276.0	535.3	601.8	474.4
Testis (both) (g)	4.990	3.588	3.551	3.323	3.405	4.329	3.720	3.691	4.613	3.526
Spleen (g)	0.946	0.776	0.750	0.843	0.639	0.713	0.657	0.808	1.126	0.739

Organ weights (individuals) : males

group 3 : 50 ppm

week 14

	Animal no									
	31	32	33	34	35	36	37	38	39	40
Body (g)	445.9	547.7	413.0	411.3	453.1	431.5	508.9	507.2	434.1	434.9
Heart (g)	1.301	1.579	1.171	1.204	1.343	1.420	1.309	1.453	1.284	1.193
Liver (g)	17.58	21.31	14.16	13.36	15.12	16.47	17.76	18.31	17.65	13.25
Kidney (both) (g)	2.875	3.322	2.597	2.433	2.957	2.939	3.004	2.878	2.836	2.728

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## Organ weights (individuals) : males

group 3 : 50 ppm

week 14

	Animal no									
	31	32	33	34	35	36	37	38	39	40
Adrenal (both) (mg)	61.50	83.50	68.40	60.40	85.30	69.10	70.50	88.10	64.90	55.40
Thymus (mg)	369.4	421.2	492.7	446.3	362.5	411.3	313.5	591.6	550.4	568.9
Testis (both) (g)	3.946	3.607	3.975	3.706	3.953	3.662	2.221	3.905	3.619	3.659
Spleen (g)	0.691	0.758	0.780	0.642	0.674	0.745	0.772	0.863	0.689	0.656

## Organ weights (individuals) : males

group 4 : 250 ppm

week 14

	Animal no									
	41	42	43	44	45	46	47	48	49	50
Body (g)	530.0	489.2	509.6	489.7	510.3	450.8	381.1	391.1	500.8	544.6
Heart (g)	1.660	1.437	1.583	1.502	1.491	1.312	1.229	1.212	1.543	1.577
Liver (g)	23.23	21.20	19.28	19.64	18.80	18.89	15.97	15.51	20.21	22.65
Kidney (both) (g)	3.369	2.888	3.017	2.719	2.951	2.886	2.456	2.776	3.384	3.344
Adrenal (both) (mg)	86.00	70.70	90.30	68.90	89.10	68.90	56.30	64.30	60.90	89.50
Thymus (mg)	439.6	544.9	838.6	681.9	388.4	501.8	389.2	289.6	412.2	637.1
Testis (both) (g)	4.315	3.870	4.485	3.891	4.108	4.044	3.537	3.979	4.082	4.205
Spleen (g)	0.879	0.883	0.881	0.814	0.847	0.835	0.711	0.701	0.920	0.864

Organ weights (individuals) : males

group 5 : 625 ppm week 14

	Animal no									
	51	52	53	54	55	56	57	58	59	60
Body (g)	501.8	529.4	510.2	498.4	463.3	510.6	446.2	556.4	518.7	482.3
Heart (g)	1.525	1.415	1.363	1.320	1.382	1.610	1.369	1.642	1.446	1.288
Liver (g)	20.52	21.86	17.13	19.11	19.74	20.68	20.07	24.62	21.49	18.10
Kidney (both) (g)	3.209	3.307	3.357	2.768	2.787	3.266	3.135	3.770	3.251	2.997
Adrenal (both) (mg)	72.90	68.30	78.90	79.00	75.80	82.60	74.50	68.50	84.00	65.30
Thymus (mg)	545.5	483.4	366.3	704.7	536.4	504.5	433.1	413.1	503.1	488.7
Testis (both) (g)	4.181	3.574	3.785	3.780	3.560	4.245	4.503	3.974	4.162	4.178
Spleen (g)	0.840	0.700	0.659	0.695	0.960	0.854	0.850	0.845	0.794	0.652

Organ weights (individuals) : males

group 6 : 1250 ppm week 14

	Animal no									
	61	62	63	64	65	66	67	68	69	70
Body (g)	367.0	477.2	527.0	499.7	444.7	499.8	532.4	477.4	474.6	439.0
Heart (g)	1.251	1.542	1.446	1.454	1.459	1.509	1.597	1.399	1.307	1.192
Liver (g)	11.52	18.12	21.84	19.95	19.28	19.10	20.30	20.12	18.00	18.65
Kidney (both) (g)	2.702	3.395	3.100	3.167	3.087	3.218	3.317	2.835	3.090	2.785

Organ weights (individuals) : males

	group 6 : 1250 ppm				week 14					
	61	62	63	64	Animal no		67	68	69	70
Adrenal (both) (mg)	64.00	79.60	72.80	56.90	65	66	80.30	65.90	68.70	68.10
Thymus (mg)	449.6	351.5	561.7	317.7	498.5	566.2	495.4	430.8	261.8	503.3
Testis (both) (g)	3.272	2.906	4.222	4.102	3.604	3.868	3.928	3.535	3.956	3.545
Spleen (g)	0.701	0.801	0.921	0.723	0.760	0.822	0.696	0.770	0.955	0.634

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Organ weights (individuals) : females

group 1 : 0 ppm

week 14

	Animal no									
	81	82	83	84	85	86	87	88	89	90
Body (g)	295.0	271.8	232.6	297.3	300.7	265.3	301.2	253.9	290.6	264.6
Heart (g)	0.953	0.969	0.949	0.985	1.010	0.831	1.037	0.916	0.912	0.901
Liver (g)	11.42	10.50	8.823	9.719	12.56	10.62	10.71	8.789	10.62	8.404
Kidney (both) (g)	1.820	1.929	1.748	1.977	2.287	1.923	2.295	1.618	2.033	1.637
Adrenal (both) (mg)	92.00	101.6	94.60	83.10	75.30	77.70	98.40	80.50	85.10	75.30
Thymus (mg)	309.2	290.7	283.5	428.1	561.0	355.0	346.8	300.7	244.3	425.0
Ovary (both) (mg)	175.6	156.6	166.5	134.7	123.7	119.1	181.1	205.9	137.3	177.5
Spleen (g)	0.579	0.584	0.513	0.513	0.630	0.451	0.538	0.471	0.519	0.518

Organ weights (individuals) : females

group 2 : 25 ppm

week 14

	Animal no									
	101	102	103	104	105	106	107	108	109	110
Body (g)	298.6	304.7	277.9	268.9	334.2	269.4	307.1	269.7	257.4	284.7
Heart (g)	0.924	1.004	0.946	1.025	0.928	0.928	0.976	0.892	0.989	1.014
Liver (g)	10.42	10.63	10.76	9.742	10.81	10.03	10.75	9.311	9.747	10.84
Kidney (both) (g)	1.920	1.933	2.013	2.113	2.040	1.794	2.226	2.097	2.250	2.553



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## Organ weights (individuals) : females

group 2 : 25 ppm week 14

	Animal no									
	101	102	103	104	105	106	107	108	109	110
Adrenal (both) (mg)	112.2	97.10	96.80	85.00	87.90	101.8	87.00	74.70	88.10	97.50
Thymus (mg)	440.4	258.9	445.9	240.5	389.7	244.7	380.4	235.6	461.2	416.0
Ovary (both) (mg)	168.3	130.1	192.2	165.2	161.4	188.6	144.5	168.5	159.8	171.4
Spleen (g)	0.557	0.516	0.540	0.469	0.540	0.605	0.589	0.463	0.543	0.555

## Organ weights (individuals) : females

group 3 : 50 ppm week 14

	Animal no									
	111	112	113	114	115	116	117	118	119	120
Body (g)	298.2	332.5	244.0	292.8	261.3	340.1	286.7	256.7	294.4	248.2
Heart (g)	1.016	0.951	0.855	0.876	0.887	1.089	0.874	0.941	0.982	0.798
Liver (g)	11.91	12.36	9.269	9.876	9.863	12.38	8.753	9.666	9.479	9.062
Kidney (both) (g)	2.263	2.105	1.810	1.856	2.022	1.909	1.940	2.020	2.095	1.953
Adrenal (both) (mg)	78.40	90.70	84.90	84.00	93.00	83.60	76.20	101.7	80.20	76.40
Thymus (mg)	438.3	306.6	349.2	285.0	439.8	354.7	328.8	336.0	372.7	242.4
Ovary (both) (mg)	177.3	145.0	167.2	167.8	167.8	175.5	148.6	202.7	157.7	131.6
Spleen (g)	0.624	0.541	0.562	0.473	0.782	0.635	0.614	0.670	0.445	0.528

Organ weights (individuals) : females

group 4 : 250 ppm week 14

	Animal no									
	121	122	123	124	125	126	127	128	129	130
Body (g)	332.5	360.9	273.7	282.8	255.9	274.5	293.5	266.9	314.0	262.5
Heart (g)	1.069	1.120	0.992	0.839	0.961	0.950	0.900	0.789	1.035	0.906
Liver (g)	14.87	12.62	10.71	9.458	10.96	9.151	11.57	9.317	12.38	10.54
Kidney (both) (g)	2.479	2.240	1.948	1.832	1.971	1.992	2.078	1.740	2.244	1.844
Adrenal (both) (mg)	107.5	103.7	104.3	77.40	71.30	88.70	94.50	84.00	97.10	78.80
Thymus (mg)	364.3	389.1	294.0	360.6	324.2	256.9	306.3	224.3	311.6	222.7
Ovary (both) (mg)	135.0	187.7	197.8	149.0	182.1	142.7	151.3	129.4	218.0	201.8
Spleen (g)	0.610	0.530	0.471	0.500	0.589	0.529	0.612	0.449	0.673	0.733

Organ weights (individuals) : females

group 5 : 625 ppm week 14

	Animal no									
	131	132	133	134	135	136	137	138	139	140
Body (g)	251.7	270.6	318.3	314.0	284.3	319.0	253.4	327.2	243.4	321.0
Heart (g)	0.828	0.988	1.053	1.031	0.982	1.100	0.845	0.998	0.827	1.010
Liver (g)	10.73	10.85	12.16	12.99	11.46	12.83	10.76	10.89	9.753	11.28
Kidney (both) (g)	1.769	1.950	2.379	2.367	2.407	2.385	1.862	2.482	2.035	2.077

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## Organ weights (individuals) : females

group 5 : 625 ppm

week 14

	Animal no									
	131	132	133	134	135	136	137	138	139	140
Adrenal (both) (mg)	83.40	101.1	90.00	106.0	102.9	105.5	76.00	101.2	89.90	79.80
Thymus (mg)	341.0	397.2	304.6	429.8	356.4	402.8	340.4	482.0	291.3	406.2
Ovary (both) (mg)	134.1	152.0	141.5	163.6	191.0	213.8	151.0	145.2	153.6	208.9
Spleen (g)	0.577	0.528	0.685	0.598	0.658	0.661	0.420	0.461	0.480	0.518

## Organ weights (individuals) : females

group 6 : 1250 ppm

week 14

	Animal no									
	141	142	143	144	145	146	147	148	149	150
Body (g)	274.9	216.6	289.6	248.4	256.1	308.4	292.1	286.8	250.8	256.4
Heart (g)	1.029	0.699	1.097	0.818	0.892	1.132	0.908	0.937	0.860	0.930
Liver (g)	11.44	8.313	11.16	9.417	9.747	12.61	10.58	10.58	10.15	10.10
Kidney (both) (g)	2.243	1.704	2.136	1.697	1.835	2.482	1.986	1.866	2.053	2.039
Adrenal (both) (mg)	92.60	76.40	95.20	70.20	74.30	107.3	86.50	72.60	86.70	78.10
Thymus (mg)	283.2	301.1	268.6	340.4	238.4	398.4	462.4	419.9	297.3	395.4
Ovary (both) (mg)	143.4	139.7	158.8	119.7	129.0	214.6	170.0	166.9	135.5	145.7
Spleen (g)	0.673	0.465	0.524	0.618	0.506	0.576	0.597	0.532	0.539	0.554

6.10.2. Organ weights (individuals): 2. sacrifice (recovery)

Organ weights (individuals) : males

group 1 : 0 ppm

week 18

	Animal no									
	11	12	13	14	15	16	17	18	19	20
Body (g)	537.3	605.0	563.8	530.2	503.0	492.7	564.0	470.5	432.3	524.2
Heart (g)	1.591	1.560	1.470	1.647	1.383	1.552	1.610	1.563	1.276	1.661
Liver (g)	20.83	24.41	20.62	18.67	18.22	18.52	20.96	17.88	15.43	17.00
Kidney (both) (g)	2.985	3.766	3.387	3.145	2.895	3.111	3.129	2.910	3.196	3.218
Adrenal (both) (mg)	126.7	86.00	63.40	48.50	72.00	88.90	84.90	56.20	70.80	80.30
Thymus (mg)	548.9	618.8	433.5	536.1	324.4	486.9	447.6	636.1	748.3	526.4
Testis (both) (g)	3.978	4.194	4.201	3.773	3.831	4.062	3.784	3.735	2.705	3.662
Spleen (g)	0.705	0.878	0.869	0.839	0.622	0.794	0.917	0.746	0.627	0.725

Organ weights (individuals) : males

group 6 : 1250 ppm week 18

	Animal no									
	71	72	73	74	75	76	77	78	79	80
Body (g)	533.2	437.5	548.3	452.5	564.5	548.3	412.4	503.1	538.7	520.0
Heart (g)	1.518	1.462	1.636	1.220	1.646	1.618	1.048	1.338	1.592	1.519
Liver (g)	20.16	15.08	20.22	15.82	18.71	26.55	15.63	18.71	20.54	22.90
Kidney (both) (g)	3.236	2.871	3.384	2.749	3.138	3.384	2.372	3.873	3.150	3.217
Adrenal (both) (mg)	58.80	61.70	50.30	68.50	93.60	56.70	63.70	82.20	52.80	70.40
Thymus (mg)	589.6	347.3	550.0	292.6	567.3	640.1	606.5	280.1	449.1	317.6
Testis (both) (g)	4.047	4.092	3.886	3.756	4.518	4.619	3.826	3.573	3.964	4.194
Spleen (g)	0.772	0.848	0.893	0.752	0.775	1.234	0.591	0.850	0.744	0.706

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Test No.: 943127

Test Article: CGA 329351 tech.

Organ weights (individuals) : females

group 1 :	0 ppm				week 18					
	Animal no									
	91	92	93	94	95	96	97	98	99	100
Body (g)	306.4	299.7	323.6	260.2	319.8	306.3	311.0	303.4	296.8	324.7
Heart (g)	0.956	1.064	1.027	1.017	1.147	1.031	0.986	1.028	0.932	0.961
Liver (g)	9.901	9.204	10.88	10.21	9.838	10.51	11.81	9.689	9.617	11.04
Kidney (both) (g)	1.930	1.877	2.241	3.380	2.059	1.838	2.238	1.984	1.861	2.392
Adrenal (both) (mg)	81.20	68.40	103.1	89.80	84.60	85.00	111.9	103.4	101.5	111.4
Thymus (mg)	392.6	224.6	490.8	213.2	124.8	204.5	360.6	218.2	334.9	206.6
Ovary (both) (mg)	145.3	146.5	174.8	187.0	187.6	144.0	197.6	156.1	160.2	207.0
Spleen (g)	0.565	0.464	0.480	0.755	0.507	0.495	0.668	0.490	0.584	0.571

Organ weights (individuals) : females

group 6 :	1250 ppm				week 18					
	Animal no									
	151	152	153	154	155	156	157	158	159	160
Body (g)	254.1	301.6	281.3	339.2	329.7	291.9	329.6	338.6	323.9	299.8
Heart (g)	0.956	0.781	1.017	1.075	1.103	1.074	0.987	0.966	1.024	1.071
Liver (g)	8.683	10.79	9.467	10.58	12.24	9.654	13.23	12.79	10.94	10.52
Kidney (both) (g)	1.984	1.757	1.893	2.047	2.013	1.941	2.373	2.378	1.962	2.310

Organ weights (individuals) : females

group 6 : 1250 ppm week 18

	Animal no									
	151	152	153	154	155	156	157	158	159	160
Adrenal (both) (mg)	73.20	81.50	71.60	81.20	93.40	85.70	115.3	80.90	108.1	87.50
Thymus (mg)	391.9	306.4	371.9	210.8	313.4	292.5	299.6	260.1	419.6	264.4
Ovary (both) (mg)	143.0	142.3	135.7	152.7	207.8	158.2	237.4	157.7	205.6	160.7
Spleen (g)	0.566	0.445	0.512	0.479	0.553	0.543	0.673	0.691	0.619	0.693

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6.10.3. Organ to body weight ratios (individuals):  
 1. sacrifice

Organ to body weight ratios (individuals) : males

group 1 : 0 ppm week 14

	Animal no									
	1	2	3	4	5	6	7	8	9	10
Heart (o/oo)	3.407	2.675	3.426	3.143	2.857	3.026	3.017	2.715	3.083	3.063
Liver (o/oo)	42.04	39.00	45.15	42.14	40.87	36.71	39.74	37.56	40.07	39.60
Kidney (both) (o/oo)	6.431	6.217	6.519	6.667	6.352	6.508	6.130	5.821	6.845	6.238
Adrenal (both) (o/oo)	0.156	0.149	0.113	0.194	0.129	0.180	0.178	0.127	0.182	0.145
Thymus (o/oo)	0.909	1.436	1.111	1.071	1.116	1.318	1.313	1.250	1.112	1.353
Testis (both) (o/oo)	8.667	8.839	8.401	8.295	7.503	9.661	9.306	7.437	9.475	7.931
Spleen (o/oo)	1.488	1.509	1.747	1.652	1.966	1.732	1.724	1.868	1.784	1.766

Organ to body weight ratios (individuals) : males

group 2 : 25 ppm week 14

	Animal no									
	21	22	23	24	25	26	27	28	29	30
Heart (o/oo)	2.741	2.825	3.112	2.799	2.891	2.919	2.910	3.223	2.979	2.754
Liver (o/oo)	41.81	39.58	43.22	35.26	39.57	42.33	39.32	40.39	39.41	39.35



Organ to body weight ratios (individuals) : males

group 2 : 25 ppm week 14

	Animal no									
	21	22	23	24	25	26	27	28	29	30
Kidney (both) (o/oo)	6.453	6.519	6.252	5.661	6.271	6.810	6.805	6.691	6.019	6.715
Adrenal (both) (o/oo)	0.124	0.152	0.184	0.164	0.204	0.156	0.165	0.191	0.160	0.117
Thymus (o/oo)	1.070	0.934	1.252	1.156	0.721	1.081	0.711	1.108	0.990	1.000
Testis (both) (o/oo)	8.658	7.675	7.446	6.968	8.416	8.741	9.584	7.637	7.590	7.431
Spleen (o/oo)	1.641	1.660	1.573	1.768	1.578	1.440	1.693	1.671	1.852	1.556

Organ to body weight ratios (individuals) : males

group 3 : 50 ppm week 14

	Animal no									
	31	32	33	34	35	36	37	38	39	40
Heart (o/oo)	2.917	2.884	2.835	2.926	2.964	3.291	2.572	2.866	2.957	2.743
Liver (o/oo)	39.42	38.91	34.29	32.48	33.36	38.16	34.90	36.10	40.64	30.48
Kidney (both) (o/oo)	6.447	6.066	6.287	5.916	6.526	6.811	5.903	5.674	6.532	6.272
Adrenal (both) (o/oo)	0.138	0.152	0.166	0.147	0.188	0.160	0.139	0.174	0.149	0.127
Thymus (o/oo)	0.828	0.769	1.193	1.085	0.800	0.953	0.616	1.166	1.268	1.308
Testis (both) (o/oo)	8.848	6.586	9.625	9.010	8.724	8.486	4.364	7.699	8.337	8.414
Spleen (o/oo)	1.550	1.384	1.889	1.561	1.487	1.726	1.516	1.701	1.588	1.509

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Organ to body weight ratios (individuals) : males

group 4 : 250 ppm week 14

	Animal no									
	41	42	43	44	45	46	47	48	49	50
Heart (o/oo)	3.132	2.938	3.105	3.067	2.921	2.910	3.225	3.099	3.080	2.895
Liver (o/oo)	43.83	43.33	37.84	40.11	36.84	41.90	41.90	39.65	40.35	41.58
Kidney (both) (o/oo)	6.356	5.904	5.921	5.553	5.783	6.401	6.445	7.099	6.757	6.140
Adrenal (both) (o/oo)	0.162	0.145	0.177	0.141	0.175	0.153	0.148	0.164	0.122	0.164
Thymus (o/oo)	0.830	1.114	1.646	1.392	0.761	1.113	1.021	0.740	0.823	1.170
Testis (both) (o/oo)	8.142	7.910	8.802	7.945	8.050	8.971	9.282	10.17	8.150	7.722
Spleen (o/oo)	1.658	1.805	1.728	1.662	1.659	1.853	1.866	1.792	1.837	1.587

Organ to body weight ratios (individuals) : males

group 5 : 625 ppm week 14

	Animal no									
	51	52	53	54	55	56	57	58	59	60
Heart (o/oo)	3.039	2.673	2.672	2.648	2.982	3.154	3.068	2.951	2.789	2.671
Liver (o/oo)	40.89	41.29	33.57	38.35	42.61	40.51	44.98	44.24	41.43	37.53
Kidney (both) (o/oo)	6.395	6.247	6.579	5.553	6.016	6.397	7.027	6.775	6.268	6.213
Adrenal (both) (o/oo)	0.145	0.129	0.155	0.159	0.164	0.162	0.167	0.123	0.162	0.135
Thymus (o/oo)	1.087	0.913	0.718	1.414	1.158	0.988	0.971	0.742	0.970	1.013

Organ to body weight ratios (individuals) : males

group 5 : 625 ppm week 14

	Animal no									
	51	52	53	54	55	56	57	58	59	60
Testis (both) (o/oo)	8.332	6.751	7.418	7.584	7.684	8.313	10.09	7.143	8.024	8.663
Spleen (o/oo)	1.674	1.322	1.291	1.395	2.072	1.672	1.905	1.518	1.530	1.351

Organ to body weight ratios (individuals) : males

group 6 : 1250 ppm week 14

	Animal no									
	61	62	63	64	65	66	67	68	69	70
Heart (o/oo)	3.410	3.231	2.744	2.909	3.282	3.019	3.000	2.932	2.754	2.714
Liver (o/oo)	31.39	37.97	41.45	39.92	43.36	38.22	38.14	42.14	37.93	42.49
Kidney (both) (o/oo)	7.362	7.114	5.882	6.338	6.942	6.438	6.231	5.939	6.512	6.344
Adrenal (both) (o/oo)	0.174	0.167	0.138	0.114	0.173	0.178	0.151	0.138	0.145	0.155
Thymus (o/oo)	1.225	0.737	1.066	0.636	1.121	1.133	0.931	0.902	0.552	1.146
Testis (both) (o/oo)	8.917	6.090	8.011	8.207	8.104	7.739	7.379	7.405	8.337	8.074
Spleen (o/oo)	1.911	1.679	1.747	1.446	1.710	1.645	1.307	1.613	2.012	1.444

Test No.: 943127

Test Article: CGA 329351 tech.

## Organ to body weight ratios (individuals) : females

group 1 : 0 ppm

week 14

	Animal no									
	81	82	83	84	85	86	87	88	89	90
Heart (o/oo)	3.232	3.563	4.062	3.314	3.358	3.131	3.443	3.610	3.137	3.404
Liver (o/oo)	38.69	38.64	37.94	32.69	41.78	40.05	35.57	34.62	36.53	31.76
Kidney (both) (o/oo)	6.168	7.098	7.514	6.648	7.606	7.248	7.619	6.373	6.996	6.187
Adrenal (both) (o/oo)	0.312	0.374	0.407	0.279	0.250	0.293	0.327	0.317	0.293	0.285
Thymus (o/oo)	1.048	1.070	1.219	1.440	1.866	1.338	1.151	1.185	0.841	1.606
Ovary (both) (o/oo)	0.595	0.576	0.716	0.453	0.411	0.449	0.601	0.811	0.472	0.671
Spleen (o/oo)	1.964	2.149	2.207	1.724	2.094	1.700	1.787	1.855	1.786	1.956

## Organ to body weight ratios (individuals) : females

group 2 : 25 ppm

week 14

	Animal no									
	101	102	103	104	105	106	107	108	109	110
Heart (o/oo)	3.096	3.295	3.404	3.813	2.776	3.445	3.179	3.308	3.842	3.560
Liver (o/oo)	34.91	34.88	38.71	36.24	32.35	37.23	35.00	34.52	37.87	38.06
Kidney (both) (o/oo)	6.429	6.343	7.245	7.860	6.103	6.661	7.249	7.774	8.740	8.967
Adrenal (both) (o/oo)	0.376	0.319	0.348	0.316	0.263	0.378	0.283	0.277	0.342	0.342
Thymus (o/oo)	1.475	0.850	1.605	0.895	1.166	0.908	1.239	0.873	1.792	1.461

Organ to body weight ratios (individuals) : females

group 2 : 25 ppm week 14

	Animal no									
	101	102	103	104	105	106	107	108	109	110
Ovary (both) (o/oo)	0.564	0.427	0.692	0.614	0.483	0.700	0.471	0.625	0.621	0.602
Spleen (o/oo)	1.864	1.693	1.942	1.743	1.616	2.245	1.917	1.717	2.110	1.948

Organ to body weight ratios (individuals) : females

group 3 : 50 ppm week 14

	Animal no									
	111	112	113	114	115	116	117	118	119	120
Heart (o/oo)	3.407	2.860	3.503	2.993	3.396	3.202	3.047	3.665	3.335	3.214
Liver (o/oo)	39.92	37.19	37.98	33.73	37.75	36.41	30.53	37.65	32.20	36.51
Kidney (both) (o/oo)	7.587	6.332	7.419	6.338	7.737	5.613	6.767	7.870	7.117	7.866
Adrenal (both) (o/oo)	0.263	0.273	0.348	0.287	0.356	0.246	0.266	0.396	0.272	0.308
Thymus (o/oo)	1.470	0.922	1.431	0.973	1.683	1.043	1.147	1.309	1.266	0.977
Ovary (both) (o/oo)	0.594	0.436	0.685	0.573	0.642	0.516	0.518	0.790	0.536	0.530
Spleen (o/oo)	2.093	1.627	2.304	1.614	2.993	1.868	2.140	2.610	1.511	2.128

Organ to body weight ratios (individuals) : females

group 4 : 250 ppm week 14

	Animal no									
	121	122	123	124	125	126	127	128	129	130
Heart (o/oo)	3.214	3.102	3.622	2.966	3.754	3.462	3.067	2.954	3.297	3.453
Liver (o/oo)	44.72	34.98	39.12	33.44	42.85	33.34	39.42	34.91	39.41	40.15
Kidney (both) (o/oo)	7.453	6.206	7.115	6.479	7.702	7.257	7.080	6.518	7.145	7.023
Adrenal (both) (o/oo)	0.323	0.287	0.381	0.274	0.279	0.323	0.322	0.315	0.309	0.300
Thymus (o/oo)	1.096	1.078	1.074	1.275	1.267	0.936	1.044	0.840	0.992	0.848
Ovary (both) (o/oo)	0.406	0.520	0.723	0.527	0.712	0.520	0.516	0.485	0.694	0.769
Spleen (o/oo)	1.835	1.468	1.721	1.769	2.302	1.927	2.086	1.680	2.143	2.793

Organ to body weight ratios (individuals) : females

group 5 : 625 ppm week 14

	Animal no									
	131	132	133	134	135	136	137	138	139	140
Heart (o/oo)	3.291	3.652	3.308	3.282	3.454	3.449	3.332	3.051	3.398	3.146
Liver (o/oo)	42.65	40.08	38.22	41.37	40.32	40.23	42.47	33.29	40.06	35.13
Kidney (both) (o/oo)	7.030	7.207	7.476	7.539	8.467	7.475	7.345	7.586	8.361	6.469
Adrenal (both) (o/oo)	0.331	0.374	0.283	0.338	0.362	0.331	0.300	0.309	0.369	0.249
Thymus (o/oo)	1.355	1.468	0.957	1.369	1.254	1.263	1.343	1.473	1.197	1.265

Organ to body weight ratios (individuals) : females

group 5 : 625 ppm week 14

	Animal no									
	131	132	133	134	135	136	137	138	139	140
Ovary (both) (o/oo)	0.533	0.562	0.445	0.521	0.672	0.670	0.596	0.444	0.631	0.651
Spleen (o/oo)	2.292	1.950	2.152	1.906	2.316	2.070	1.659	1.409	1.971	1.612

Organ to body weight ratios (individuals) : females

group 6 : 1250 ppm week 14

	Animal no									
	141	142	143	144	145	146	147	148	149	150
Heart (o/oo)	3.744	3.227	3.790	3.292	3.483	3.671	3.109	3.267	3.427	3.628
Liver (o/oo)	41.60	38.38	38.54	37.91	38.06	40.90	36.21	36.90	40.48	39.39
Kidney (both) (o/oo)	8.158	7.869	7.377	6.832	7.163	8.050	6.797	6.507	8.185	7.952
Adrenal (both) (o/oo)	0.337	0.353	0.329	0.283	0.290	0.348	0.296	0.253	0.346	0.305
Thymus (o/oo)	1.030	1.390	0.928	1.370	0.931	1.292	1.583	1.464	1.185	1.542
Ovary (both) (o/oo)	0.522	0.645	0.548	0.482	0.504	0.696	0.582	0.582	0.540	0.568
Spleen (o/oo)	2.447	2.147	1.808	2.487	1.977	1.866	2.044	1.855	2.150	2.161

6.10.4. Organ to body weight ratios (individuals):  
 2. sacrifice (recovery)

Organ to body weight ratios (individuals) : males

group 1 : 0 ppm week 18

	Animal no									
	11	12	13	14	15	16	17	18	19	20
Heart (o/oo)	2.961	2.578	2.607	3.107	2.750	3.151	2.855	3.322	2.951	3.168
Liver (o/oo)	38.77	40.35	36.57	35.22	36.22	37.60	37.16	38.00	35.70	32.43
Kidney (both) (o/oo)	5.555	6.225	6.007	5.931	5.756	6.314	5.548	6.185	7.393	6.139
Adrenal (both) (o/oo)	0.236	0.142	0.112	0.091	0.143	0.180	0.151	0.119	0.164	0.153
Thymus (o/oo)	1.022	1.023	0.769	1.011	0.645	0.988	0.794	1.352	1.731	1.004
Testis (both) (o/oo)	7.404	6.933	7.451	7.115	7.617	8.244	6.709	7.938	6.258	6.986
Spleen (o/oo)	1.312	1.451	1.542	1.583	1.237	1.611	1.626	1.586	1.449	1.382

Organ to body weight ratios (individuals) : males

group 6 : 1250 ppm week 18

	Animal no									
	71	72	73	74	75	76	77	78	79	80
Heart (o/oo)	2.847	3.342	2.983	2.696	2.917	2.951	2.541	2.659	2.954	2.921
Liver (o/oo)	37.81	34.47	36.88	34.97	33.14	48.41	37.89	37.19	38.13	44.04



Organ to body weight ratios (individuals) : males

group 6 : 1250 ppm week 18

	Animal no									
	71	72	73	74	75	76	77	78	79	80
Kidney (both) (o/oo)	6.069	6.563	6.172	6.074	5.558	6.171	5.752	7.698	5.848	6.187
Adrenal (both) (o/oo)	0.110	0.141	0.092	0.151	0.166	0.103	0.154	0.163	0.098	0.135
Thymus (o/oo)	1.106	0.794	1.003	0.647	1.005	1.167	1.471	0.557	0.834	0.611
Testis (both) (o/oo)	7.589	9.352	7.087	8.301	8.003	8.423	9.278	7.101	7.358	8.064
Spleen (o/oo)	1.449	1.938	1.629	1.663	1.373	2.250	1.433	1.689	1.382	1.357

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Organ to body weight ratios (individuals) : females

group 1 : 0 ppm week 18

	Animal no									
	91	92	93	94	95	96	97	98	99	100
Heart (o/oo)	3.122	3.549	3.173	3.909	3.586	3.367	3.169	3.387	3.142	2.959
Liver (o/oo)	32.32	30.71	33.61	39.22	30.76	34.30	37.99	31.93	32.40	34.00
Kidney (both) (o/oo)	6.298	6.263	6.926	12.99	6.438	6.002	7.195	6.538	6.271	7.367
Adrenal (both) (o/oo)	0.265	0.228	0.319	0.345	0.265	0.278	0.360	0.341	0.342	0.343
Thymus (o/oo)	1.281	0.749	1.517	0.819	0.390	0.668	1.159	0.719	1.128	0.636
Ovary (both) (o/oo)	0.474	0.489	0.540	0.719	0.587	0.470	0.635	0.515	0.540	0.638
Spleen (o/oo)	1.844	1.547	1.484	2.899	1.584	1.616	2.149	1.616	1.966	1.758

Organ to body weight ratios (individuals) : females

group 6 : 1250 ppm week 18

	Animal no									
	151	152	153	154	155	156	157	158	159	160
Heart (o/oo)	3.763	2.588	3.616	3.168	3.346	3.681	2.995	2.854	3.162	3.573
Liver (o/oo)	34.17	35.78	33.65	31.19	37.13	33.07	40.15	37.78	33.78	35.10
Kidney (both) (o/oo)	7.807	5.824	6.730	6.036	6.105	6.651	7.200	7.023	6.056	7.705
Adrenal (both) (o/oo)	0.288	0.270	0.254	0.239	0.283	0.294	0.350	0.239	0.334	0.292
Thymus (o/oo)	1.542	1.016	1.322	0.621	0.950	1.002	0.909	0.768	1.295	0.882

Organ to body weight ratios (individuals) : females

group 6 : 1250 ppm week 18

	Animal no									
	151	152	153	154	155	156	157	158	159	160
Ovary (both) (o/oo)	0.563	0.472	0.482	0.450	0.630	0.542	0.720	0.466	0.635	0.536
Spleen (o/oo)	2.229	1.476	1.818	1.413	1.676	1.861	2.041	2.041	1.911	2.311

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**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	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Treatment ended in observation period, <u>selected</u>	20	10	10	10	10	20
Examined macroscopically						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

**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: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Lung alveolus : Foam cell +  
Renal tubule : Cast + bilateral  
Adrenal cortex : Fatty change + unilateral  
Thymic epithelium : Hyperplasia +

Male Nr. 2 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Mesenteric lymph node : Hypocellularity +  
Exocrine pancreas : Inflammatory cell infiltration +  
Renal tubule : Atrophy + unilateral  
Adrenal cortex : Fatty change ++ bilateral

Male Nr. 3 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Myocardium : Inflammation with fibrosis +  
Intrahepatic bile duct : Cholangiofibrosis +  
Renal tubule : Hyaline change + bilateral  
Urinary bladder : Precipitate ++  
Adenohypophysis : Developmental cyst  
Adrenal cortex : Fatty change + bilateral

Male Nr. 4 / Days on study: 93 / Scheduled sacrifice 1

Macro

A

Renal pelvis : Dilatation left

Micro

A

Renal pelvis : Dilatation ++ unilateral  
Epithelium of renal pelvis : Calcification + unilateral  
Epithelium of renal pelvis : Hyperplasia + unilateral  
Adrenal cortex : Fatty change + unilateral  
Adrenal medulla : One organ, no examination for technical reasons

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 0 ppm

Male Nr. 5 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Lung : Lymphocytic infiltration +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Urinary bladder : No examination for technical reasons  
Thyroid follicular epithelium : Hypertrophy +

Male Nr. 6 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Liver hepatocyte : Necrosis +  
Pancreas : Chronic inflammation +++  
Urinary bladder : Inflammatory oedema +

Male Nr. 7 / Days on study: 93 / Scheduled sacrifice 1

Macro

A Lung : Mottled

Micro

A Lung : Macroscopical change not observed

Male Nr. 8 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Hypertrophy +  
Urinary bladder : Precipitate ++  
Urinary bladder : Inflammatory oedema +

Male Nr. 9 / Days on study: 93 / Scheduled sacrifice 1

Macro

A Lung : Mottled

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 0 ppm

Micro

A Lung : Haemorrhage +++  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Urinary bladder : Precipitate +  
Urinary bladder : Oedema +

Male Nr. 10 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Exocrine pancreas : Necrosis + focal  
Adrenal cortex : Fatty change ++ bilateral

Male Nr. 11 / Days on study: 121 / Scheduled sacrifice 2

Macro

A Urinary bladder : Nodule (<.5 cm) one

Micro

A Urinary bladder : Precipitate +++

Male Nr. 12 / Days on study: 121 / Scheduled sacrifice 2

Macro

Adrenal gland : One organ, damaged during autopsy right

Micro

Organs and tissues as a whole : No changes observed

Male Nr. 13 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Inflammatory cell infiltration +  
Liver hepatocyte : Necrosis +

Male Nr. 14 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 0 ppm

Male Nr. 15 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Extramedullary haematopoiesis +

Male Nr. 16 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +

Male Nr. 17 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Male Nr. 18 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +  
Liver : Extramedullary haematopoiesis +  
Intrahepatic bile duct : Cholangiofibrosis +

Male Nr. 19 / Days on study: 121 / Scheduled sacrifice 2

Macro

Eye with optic nerve : One organ, damaged during autopsy  
right

Micro

Organs and tissues as a whole : No changes observed

Male Nr. 20 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed



**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES**

Exposure: 25 ppm

Male Nr. 21 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Urinary bladder : Precipitate +  
Adenohypophysis : Developmental cyst  
Thyroid gland : Squamous metaplasia +

Male Nr. 22 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Exocrine pancreas : Atrophy +  
Thymic epithelium : Hyperplasia +

Male Nr. 23 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis ++  
Lung alveolus : Foam cell +  
Liver hepatocyte : Necrosis +

Male Nr. 24 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Trachea : Lymphocytic infiltration +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Renal tubule : Calcification + unilateral

Male Nr. 25 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 25 ppm

Micro

Spleen : Haemosiderosis +  
Lung alveolus : Foam cell +  
Liver hepatocyte : Necrosis +  
Epididymis : Lymphocytic infiltration + unilateral

Male Nr. 26 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Myocardium : Inflammation with fibrosis +  
Adrenal cortex : Fatty change + bilateral  
Thymic epithelium : Hyperplasia +

Male Nr. 27 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Urinary bladder : Precipitate +++  
Adrenal cortex : Fatty change + bilateral

Male Nr. 28 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Renal tubule : Atrophy + unilateral  
Urinary bladder : Precipitate ++

Male Nr. 29 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung : Haemorrhage +  
Intrahepatic bile duct : Cholangiofibrosis +  
Adrenal cortex : Fatty change + bilateral

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES**

Exposure: 25 ppm

Male Nr. 30 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +

Spleen : Extramedullary haematopoiesis +

Lung : Haemorrhage +

Myocardium : Inflammation with fibrosis +

Liver : Lymphocytic infiltration +

Nonglandular stomach : Inflammatory cell infiltration +

Pituitary gland : Cholesterol granuloma +

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Test No.: 943127

Test Article: CGA 329351 tech.

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES**

Exposure: 50 ppm

Male Nr. 31 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Renal tubule : Atrophy + unilateral  
Urinary bladder : Precipitate ++  
Testis seminiferous tubule : Spermatic giant cell +  
unilateral  
Adrenal cortex : Fatty change ++ bilateral

Male Nr. 32 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Renal tubule : Cast + unilateral  
Adrenal cortex : Fatty change + bilateral

Male Nr. 33 / Days on study: 94 / Scheduled sacrifice 1

Macro

Brain : Damaged during autopsy

Micro

Spleen : Extramedullary haematopoiesis +  
Pituitary gland : Cholesterol granuloma +

Male Nr. 34 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Kidney : Lymphocytic infiltration + unilateral  
Urinary bladder : Inflammatory oedema +

Male Nr. 35 / Days on study: 94 / Scheduled sacrifice 1

Macro

A Thymus : Mottled

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 50 ppm

Micro

Bone marrow : Fatty atrophy +  
Trachea : Lymphocytic infiltration +  
Lung : Haemorrhage +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Adenohypophysis : Developmental cyst  
A Thymus : Haemorrhage +

Male Nr. 36 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Thymic epithelium : Hyperplasia +

Male Nr. 37 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver : Fatty change +  
Liver hepatocyte : Hypertrophy +  
Urinary bladder : Precipitate +++  
Testis : Tubular atrophy ++ bilateral  
Epididymis : Reduction of spermatozoa ++ bilateral

Male Nr. 38 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Extramedullary haematopoiesis +  
Lung : Haemosiderosis +  
Exocrine pancreas : Atrophy +  
Renal tubule : Cast + unilateral  
Adrenal cortex : Fatty change + bilateral  
Thymic epithelium : Hyperplasia +

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES**

Exposure: 50 ppm

Male Nr. 39 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +

Lung alveolus : Foam cell +

Myocardium : Inflammation with fibrosis +

Exocrine pancreas : Inflammatory cell infiltration +

Adrenal cortex : Fatty change ++ bilateral

Male Nr. 40 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Lung alveolus : Foam cell ++

Myocardium : Inflammation with fibrosis ++

Liver : Lymphocytic infiltration +

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Test No.: 943127

Test Article: CGA 329351 tech.

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES**

Exposure: 250 ppm

Male Nr. 41 / Days on study: 93 / Scheduled sacrifice 1Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +

Lung alveolus : Foam cell +

Liver : Lymphocytic infiltration +

Pancreas : Inflammatory cell infiltration +

Renal tubule : Cast + bilateral

Renal tubule : Atrophy + unilateral

Male Nr. 42 / Days on study: 93 / Scheduled sacrifice 1Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +

Spleen : Extramedullary haematopoiesis +

Lung : Haemorrhage +

Lung blood vessel : Calcification +

Pancreas : Inflammatory cell infiltration +

Renal tubule : Cast + unilateral

Adrenal cortex : Fatty change + unilateral

Male Nr. 43 / Days on study: 93 / Scheduled sacrifice 1Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +

Spleen : Extramedullary haematopoiesis +

Lung alveolus : Foam cell ++

Liver hepatocyte : Necrosis +

Liver hepatocyte : Hypertrophy +

Male Nr. 44 / Days on study: 93 / Scheduled sacrifice 1Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +

Spleen : Extramedullary haematopoiesis +

Axillary lymph node : Lymphoid hyperplasia +

Lung blood vessel : Calcification +

Myocardium : Inflammation with fibrosis ++

Liver : Lymphocytic infiltration +

Kidney : Lymphocytic infiltration + unilateral

Renal tubule : Atrophy + unilateral

Urinary bladder : Inflammatory cell infiltration +

Testis : Tubular atrophy + unilateral

Adrenal cortex : Fatty change + bilateral

Test No.: 943127

Test Article: CGA 329351 tech.

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES**

Exposure: 250 ppm

Male Nr. 45 / Days on study: 93 / Scheduled sacrifice 1Macro

A Liver: Mass up to 1 cm one

Micro

Spleen: Haemosiderosis +

Spleen: Extramedullary haematopoiesis +

Trachea: Mucous hypersecretion +

Lung: Osseous metaplasia +

Lung alveolus: Foam cell +

A Liver: Developmental malformation

Pancreas: Inflammatory cell infiltration +

Gastric gland: Dilatation +

Urinary bladder: Precipitate +++

Adrenal cortex: Fatty change + unilateral

Male Nr. 46 / Days on study: 93 / Scheduled sacrifice 1Macro

Body as a whole: No changes observed

Micro

Lung alveolus: Foam cell +

Large intestine: Parasite +

Male Nr. 47 / Days on study: 94 / Scheduled sacrifice 1Macro

Body as a whole: No changes observed

Micro

Lung alveolus: Foam cell +

Lung blood vessel: Calcification +

Myocardium: Inflammation with fibrosis +

Intrahepatic bile duct: Cholangiofibrosis +

Liver hepatocyte: Hypertrophy +

Renal tubule: Cast + unilateral

Urinary bladder: Precipitate ++

Adenohypophysis: Developmental cyst

Male Nr. 48 / Days on study: 94 / Scheduled sacrifice 1Macro

Body as a whole: No changes observed

Micro

Bone marrow: Fatty atrophy +

Male Nr. 49 / Days on study: 93 / Scheduled sacrifice 1Macro

Body as a whole: No changes observed





MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 625 ppm

Male Nr. 51 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Myocardium : Inflammation with fibrosis +  
Exocrine pancreas : Atrophy +  
Renal pelvis : Dilatation + unilateral  
Adenohypophysis : Developmental cyst

Male Nr. 52 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung : Haemorrhage +  
Lung alveolus : Foam cell +  
Pancreas : Inflammatory cell infiltration +  
Exocrine pancreas : Atrophy +  
Pituitary cell : Hypertrophy +  
Thyroid follicular epithelium : Hypertrophy +

Male Nr. 53 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Myocardium : Inflammation with fibrosis +  
Liver : Fatty change +  
Large intestine : Parasite +  
Urinary bladder : Precipitate +  
Urinary bladder : Inflammatory cell infiltration +  
Adrenal cortex : Fatty change + bilateral

Male Nr. 54 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver : Necrosis ++  
Exocrine pancreas : Atrophy ++

Test No.: 943127

Test Article: CGA 329351 tech.

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES**

Exposure: 625 ppm

Male Nr. 55 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Pituitary cell : Hypertrophy +

Male Nr. 56 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +  
Pancreas : Chronic inflammation ++  
Exocrine pancreas : Atrophy ++  
Renal tubule : Cast + bilateral  
Renal pelvis : Calculus + unilateral  
Renal pelvis : Dilatation + unilateral  
Epithelium of renal pelvis : Hyperplasia ++ unilateral  
Adrenal cortex : Fatty change + bilateral  
Thyroid follicular epithelium : Hypertrophy +  
Thymic epithelium : Hyperplasia +

Male Nr. 57 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Pituitary gland : Cholesterol granuloma +  
Thymus : Atrophy +

Male Nr. 58 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis ++  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Liver hepatocyte : Necrosis +  
Urinary bladder : Precipitate +

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES**

Exposure: 625 ppm

Male Nr. 59 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Cytoplasmic inclusion body +  
Optic nerve : Haemorrhage ++ unilateral  
Optic nerve : Demyelination ++ unilateral

Male Nr. 60 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Myocardium : Inflammation with fibrosis +  
Liver hepatocyte : Hypertrophy +  
Renal tubule : Hyaline change + bilateral  
Renal tubule : Atrophy + unilateral  
Urinary bladder : Precipitate +  
Epithelium of urinary bladder : Hyperplasia + focal  
Adrenal cortex : Fatty change ++ bilateral

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MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 1250 ppm

Male Nr. 61 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Cytoplasmic vacuolization +  
Thyroid gland : Squamous metaplasia +

Male Nr. 62 / Days on study: 93 / Scheduled sacrifice 1

Macro

A Testis : Small right

Micro

Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
A Testis : Tubular atrophy +++ unilateral  
Epididymis : Reduction of spermatozoa +++ unilateral  
Adrenal cortex : Fatty change + bilateral

Male Nr. 63 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Necrosis +

Male Nr. 64 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Lung : Haemorrhage ++  
Lung alveolus : Oedema +  
Lung alveolus : Foam cell +  
Adrenal cortex : Fatty change ++ bilateral

Male Nr. 65 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 1250 ppm

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Pancreas : Inflammatory cell infiltration +

Male Nr. 66 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Pancreas : Inflammatory cell infiltration +  
Urinary bladder : Precipitate +++  
Thyroid follicular epithelium : Hypertrophy +

Male Nr. 67 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Renal tubule : Cast + unilateral  
Adenohypophysis : Developmental cyst  
Adrenal cortex : Fatty change + bilateral

Male Nr. 68 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis ++  
Lung alveolus : Foam cell +  
Lung blood vessel : Calcification +  
Myocardium : Inflammation with fibrosis +  
Liver hepatocyte : Cytoplasmic inclusion body +  
Exocrine pancreas : Hyperplasia + focal  
Urinary bladder : No examination for technical reasons  
Adrenal cortex : Fatty change + bilateral  
Thyroid follicular epithelium : Hypertrophy +

Male Nr. 69 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 1250 ppm

Micro

Spleen : Extramedullary haematopoiesis +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Cytoplasmic inclusion body +  
Pancreas : No examination for technical reasons  
Small intestine peyer's patch : Calcification +  
Adrenal cortex : Fatty change ++ bilateral

Male Nr. 70 / Days on study: 93 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis ++  
Liver hepatocyte : Cytoplasmic inclusion body ++  
Exocrine pancreas : Atrophy +  
Testis seminiferous tubule : Impaction + unilateral  
Adrenal cortex : Fatty change + bilateral

Male Nr. 71 / Days on study: 121 / Scheduled sacrifice 2

Macro

Adrenal gland : One organ, damaged during autopsy right  
A Eye with optic nerve : One organ, not taken left

Micro

A Optic nerve : One organ, not taken  
A Eye : One organ, not taken

Male Nr. 72 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +  
Liver : Extramedullary haematopoiesis +

Male Nr. 73 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL MALES

Exposure: 1250 ppm

Male Nr. 74 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Male Nr. 75 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Fatty change +

Male Nr. 76 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +

Male Nr. 77 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +

Male Nr. 78 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +  
Liver hepatocyte : Necrosis +

Male Nr. 79 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +

Male Nr. 80 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Focus of cellular change +



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	6
Exposure : ppm	0	25	50	250	625	1250
Animals initially in study	20	10	10	10	10	20
Treatment ended in observation period, selected	20	10	10	10	10	20
Examined macroscopically						
S1	10	10	10	10	10	10
S2	10	0	0	0	0	10
Total	20	10	10	10	10	20
Examined microscopically	20	10	10	10	10	20

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. 81 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Lung blood vessel : Calcification +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Cast + unilateral

Female Nr. 82 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Mesenteric lymph node : Eosinophilic infiltration +  
Lung : Inflammatory cell infiltration +  
Lung alveolus : Foam cell +  
Exocrine pancreas : Hyperplasia +  
Uterus : Dilatation +  
Thymic epithelium : Hyperplasia +

Female Nr. 83 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Lung alveolus : Foam cell ++  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Adenohypophysis : Developmental cyst

Female Nr. 84 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Lung : Osseous metaplasia +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver : Fatty change +  
Kidney : Nephrocalcinosis + bilateral  
Urinary bladder : Inflammatory cell infiltration +  
Thyroid gland : Squamous metaplasia +

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 0 ppm

Female Nr. 85 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Exocrine pancreas : Atrophy ++  
Kidney : Nephrocalcinosis ++ bilateral  
Renal tubule : Cast + unilateral  
Renal tubule : Atrophy + unilateral

Female Nr. 86 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis ++  
Kidney : Lymphocytic infiltration + unilateral  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 87 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Trachea : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Renal pelvis : Dilatation + unilateral  
Adenohypophysis : Developmental cyst  
Thyroid gland : Squamous metaplasia +

Female Nr. 88 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 0 ppm

Female Nr. 89 / Days on study: 95 / Scheduled sacrifice 1

Macro

Spleen : Damaged during autopsy  
Thymus : Mottled

A

Micro

Spleen : Extramedullary haematopoiesis +  
Trachea : Mucous hypersecretion +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + unilateral  
Thymus : Haemorrhage +  
Thymic epithelium : Hyperplasia +

A

Female Nr. 90 / Days on study: 95 / Scheduled sacrifice 1

Macro

Uterus : Damaged during autopsy

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Pancreas : Inflammatory cell infiltration +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 91 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +

Female Nr. 92 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Fatty change +

Female Nr. 93 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Fatty change +

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES**

Exposure: 0 ppm

Female Nr. 94 / Days on study: 121 / Scheduled sacrifice 2

Macro

E Kidney : Scarring right  
B Renal pelvis : Calculus right  
D Urinary bladder : Thick  
C Urinary bladder : Calculus  
A Abdominal wall : Mass up to 1 cm one left

Micro

A Mammary gland : Carcinoma well-differentiated  
Liver : Lymphocytic infiltration +  
E Kidney : Chronic pyelonephritis +++ bilateral  
Kidney : Nephrocalcinosis + bilateral  
B Renal pelvis : Calculus +++ unilateral  
C Urinary bladder : Calculus +  
D Urinary bladder : Chronic inflammation ++  
D Epithelium of urinary bladder : Papillary hyperplasia +++

Female Nr. 95 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Female Nr. 96 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Female Nr. 97 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver portal tract : Eosinophilic infiltration +

Female Nr. 98 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +

Female Nr. 99 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES**

Exposure: 0 ppm

Micro

Liver : Lymphocytic infiltration +

Female Nr. 100 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

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MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 25 ppm

Female Nr. 101 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Lung alveolus : Foam cell +  
Kidney : Nephrocalcinosis + bilateral  
Uterus : Dilatation +  
Thymic epithelium : Hyperplasia +

Female Nr. 102 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Axillary lymph node : Chronic reactive hyperplasia +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Liver : Fatty change +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 103 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Kidney : Nephrocalcinosis + bilateral  
Thymic epithelium : Hyperplasia +

Female Nr. 104 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Lung alveolus : Foam cell +  
Myocardium : Inflammation with fibrosis +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + bilateral  
Adenohypophysis : Developmental cyst  
Thymic epithelium : Hyperplasia +

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES**

Exposure: 25 ppm

Female Nr. 105 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis ++  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver : Fatty change +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 106 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Cast + unilateral

Female Nr. 107 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell ++  
Lung blood vessel : Calcification +  
Liver : Lymphocytic infiltration +  
Liver : Fatty change +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral  
Thyroid gland : Squamous metaplasia +

Female Nr. 108 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung : Haemorrhage +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + unilateral  
Thymic epithelium : Hyperplasia +





MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 50 ppm

Female Nr. 111 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis ++  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Lung blood vessel : Calcification +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 112 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Trachea : Mucous hypersecretion +  
Myocardium : Inflammation with fibrosis +  
Kidney : Nephrocalcinosis + bilateral  
Uterus : Dilatation +  
Thymic epithelium : Hyperplasia +

Female Nr. 113 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Axillary lymph node : Lymphoid hyperplasia +  
Lung : Lymphocytic infiltration +  
Lung alveolus : Foam cell +  
Salivary gland : Cytoplasmic vacuolization + bilateral  
Pancreas : Lymphocytic infiltration +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral  
Adrenal cortex : Lymphocytic infiltration + bilateral

Female Nr. 114 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 50 ppm

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Lung alveolus : Foam cell +  
Lung blood vessel : Calcification +  
Liver : Lymphocytic infiltration +  
Large intestine : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 115 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis ++  
Spleen : Extramedullary haematopoiesis +  
Lung : Haemorrhage +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Necrosis +  
Kidney : Nephrocalcinosis ++ bilateral  
Renal tubule : Atrophy + bilateral  
Fallopian tube : Hyperplasia +

Female Nr. 116 / Days on study: 95 / Scheduled sacrifice 1

Macro

Pituitary gland : Damaged during autopsy

Micro

Bone marrow : Fatty atrophy +  
Spleen : Extramedullary haematopoiesis ++  
Lung alveolus : Foam cell +  
Liver hepatocyte : Hypertrophy +  
Kidney : Nephrocalcinosis + bilateral  
Thyroid gland : Accessory thymus

Female Nr. 117 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis ++ bilateral  
Renal tubule : Atrophy + bilateral

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 50 ppm

Female Nr. 118 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis ++  
Lung alveolus : Foam cell ++  
Liver hepatocyte : Hypertrophy +  
Kidney : Nephrocalcinosis + bilateral  
Thymic epithelium : Hyperplasia +

Female Nr. 119 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung : Osseous metaplasia +  
Stomach : No examination for technical reasons  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + unilateral  
Thymus : Atrophy +

Female Nr. 120 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Mesenteric lymph node : Lymphoid hyperplasia +  
Lung alveolus : Foam cell ++  
Lung blood vessel : Calcification +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 250 ppm

Female Nr. 121 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis ++ bilateral

Female Nr. 122 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Trachea : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Thymic epithelium : Hyperplasia +

Female Nr. 123 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Lung : Haemorrhage +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + bilateral  
Thymic epithelium : Hyperplasia +

Female Nr. 124 / Days on study: 94 / Scheduled sacrifice 1

Macro

A Thymus : Mottled

Micro

Spleen : Haemosiderosis ++  
Spleen : Extramedullary haematopoiesis +  
Lung : Lymphocytic infiltration +  
Lung alveolus : Foam cell +  
Liver : Fatty change +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + unilateral  
Thyroid gland : Squamous metaplasia +

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 250 ppm

A Thymus : Haemorrhage +

Female Nr. 125 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis ++  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Hypertrophy +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral  
Adenohypophysis : Developmental cyst  
Thymic epithelium : Hyperplasia +

Female Nr. 126 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Extramedullary haematopoiesis ++  
Mesenteric lymph node : Eosinophilic infiltration +  
Lung alveolus : Foam cell +  
Nonglandular stomach : Inflammatory cell infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + bilateral  
Uterus : Dilatation +  
Thyroid gland : Accessory thymus  
Thymic epithelium : Hyperplasia +

Female Nr. 127 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Cast + unilateral  
Thyroid gland : Squamous metaplasia +

Female Nr. 128 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 250 ppm

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Kidney : Nephrocalcinosis + bilateral  
Adrenal cortex : Osseous metaplasia ++ unilateral

Female Nr. 129 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Trachea : Mucous hypersecretion +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Intrahepatic bile duct : Cholangiofibrosis +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 130 / Days on study: 95 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis ++  
Thyroid gland : Squamous metaplasia ++  
Thymus : Atrophy +

Test No.: 943127

Test Article: CGA 329351 tech.

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 625 ppm

Female Nr. 131 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 132 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis ++  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Uterus : Dilatation +  
Thyroid gland : Accessory thymus  
Thymic epithelium : Hyperplasia +

Female Nr. 133 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung : Haemorrhage +  
Lung alveolus : Foam cell +  
Lung blood vessel : Calcification ++  
Liver : Lymphocytic infiltration +  
Liver : Necrosis +  
Liver hepatocyte : Hypertrophy +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + unilateral  
Adenohypophysis : Developmental cyst

Female Nr. 134 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed



**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES**

Exposure: 625 ppm

Micro

Spleen : Haemosiderosis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Thymic epithelium : Hyperplasia +

Female Nr. 135 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Liver hepatocyte : Hypertrophy +  
Kidney : Nephrocalcinosis + bilateral  
Thymic epithelium : Hyperplasia +

Female Nr. 136 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + unilateral

Female Nr. 137 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis ++  
Lung alveolus : Foam cell +  
Lung blood vessel : Calcification +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Hypertrophy +  
Kidney : Nephrocalcinosis + bilateral  
Thymic epithelium : Hyperplasia ++

Female Nr. 138 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 625 ppm

Micro

Spleen : Haemosiderosis +  
Lung blood vessel : Calcification +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Hypertrophy +  
Kidney : Nephrocalcinosis + bilateral  
Renal pelvis : Dilatation +++ unilateral  
Uterus : Dilatation +  
Thymic epithelium : Hyperplasia +

Female Nr. 139 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Liver hepatocyte : Hypertrophy +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 140 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis ++  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Fatty change +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral  
Thyroid gland : Squamous metaplasia +

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES**

Exposure: 1250 ppm

Female Nr. 141 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Mesenteric lymph node : Haemosiderosis +  
Trachea : Mucous hypersecretion +  
Lung alveolus : Foam cell +  
Kidney : Nephrocalcinosis + bilateral  
Urinary bladder : Inflammatory oedema +++

Female Nr. 142 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Lung alveolus : Foam cell +  
Kidney : Nephrocalcinosis + bilateral  
Uterus : Dilatation +  
Thyroid gland : Squamous metaplasia +

Female Nr. 143 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Hypertrophy +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Cast + unilateral  
Adenohypophysis : Developmental cyst

Female Nr. 144 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis ++  
Lung : Haemorrhage +  
Lung alveolus : Foam cell +  
Liver hepatocyte : Hypertrophy +  
Large intestine : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + unilateral

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES**

Exposure: 1250 ppm

Female Nr. 145 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Myocardium : Inflammation with fibrosis +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 146 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Lung alveolus : Foam cell +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Necrosis +  
Liver hepatocyte : Hypertrophy +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + unilateral  
Thyroid gland : Squamous metaplasia +  
Thymic epithelium : Hyperplasia +

Female Nr. 147 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Axillary lymph node : Chronic reactive hyperplasia +  
Liver : Fatty change +  
Exocrine pancreas : Atrophy +  
Epithelium of nonglandular stomach : Hyperkeratosis +  
Kidney : Nephrocalcinosis + bilateral  
Renal tubule : Atrophy + unilateral  
Uterus : Dilatation +

Female Nr. 148 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Test No.: 943127

Test Article: CGA 329351 tech.

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 1250 ppm

Micro

Bone marrow : Fatty atrophy +  
Spleen : Haemosiderosis +  
Liver hepatocyte : Hypertrophy +  
Exocrine pancreas : Atrophy +  
Nonglandular stomach : Chronic inflammation +  
Kidney : Nephrocalcinosis + bilateral

Female Nr. 149 / Days on study: 94 / Scheduled sacrifice 1

Macro

Body as a whole : No changes observed

Micro

Spleen : Haemosiderosis +  
Spleen : Extramedullary haematopoiesis +  
Liver : Lymphocytic infiltration +  
Kidney : Nephrocalcinosis + bilateral  
Thymic epithelium : Hyperplasia +

Female Nr. 150 / Days on study: 94 / Scheduled sacrifice 1

Macro

Thymus : Mottled

Micro

Spleen : Haemosiderosis ++  
Spleen : Extramedullary haematopoiesis +  
Lung : Osseous metaplasia +  
Myocardium : Inflammation with fibrosis +  
Liver : Lymphocytic infiltration +  
Liver hepatocyte : Hypertrophy +  
Exocrine pancreas : Atrophy +  
Kidney : Nephrocalcinosis + bilateral  
Thyroid follicular epithelium : Hypertrophy +  
A Thymus : Haemorrhage +

Female Nr. 151 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Female Nr. 152 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Test No.: 943127

Test Article: CGA 329351 tech.

MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES

Exposure: 1250 ppm

Female Nr. 153 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Female Nr. 154 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Female Nr. 155 / Days on study: 121 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Focus of cellular change +  
Liver hepatocyte : Hypertrophy +

Female Nr. 156 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Organs and tissues as a whole : No changes observed

Female Nr. 157 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +

Female Nr. 158 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +  
Intrahepatic bile duct : Cholangiofibrosis +

Female Nr. 159 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Lymphocytic infiltration +

**MACROSCOPICAL AND MICROSCOPICAL FINDINGS IN INDIVIDUAL FEMALES**

Exposure: 1250 ppm

Female Nr. 160 / Days on study: 122 / Scheduled sacrifice 2

Macro

Body as a whole : No changes observed

Micro

Liver : Fatty change +

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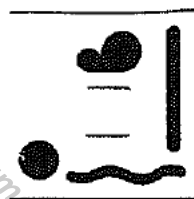
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**7. APPENDIX C: ANALYTICAL RESULTS**

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**Study Title:**

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

ANALYTICAL REPORT TO:

3-MONTH ORAL TOXICITY STUDY  
IN RATS

(ADMINISTRATION IN FOOD)

**Author:**

1.2.e Woo

**Study Completion Date:**

March 31, 1995

**Performing Laboratory:**

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

**Study Project No.:**

RCC PROJECT 384254  
CIBA-GEIGY PROJECT 943127

Page 1 of 20

**RCC**

Group

RCC PROJECT 384254  
CIBA-GEIGY PROJECT 943127  
CGA 329351 tech.

PROJECT STAFF

---

RESPONSIBLE FOR ANALYTICS:

5.12.e Woo

Date: *March 31, 1995*

MANAGING DIRECTOR:

5.12.e Woo

Date: *March 31, 1995*

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 CGA 329351 tech.

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2. Sample, nominal 25 ppm, diluted 20x
3. Sample, nominal 1250 ppm, diluted 100x

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## GENERAL INFORMATION

### GENERAL

RCC Project: 384254  
 CIBA-GEIGY Project: 943127  
 Sponsor: CIBA-GEIGY Limited  
 Short/Long-term Toxicology  
 4332 Stein / Switzerland  
 Study Director: Dr. rer. nat. [REDACTED]  
 Test Article: CGA 329351 tech.  
 Testing Facility: R C C  
 UMWELTCHEMIE AG  
 Department of Chemistry  
 CH-4452 Itingen / Switzerland

### PROJECT STAFF

Responsible for Analytics: [REDACTED]

### SCHEDULE

Dates of Analysis: see section 2.2  
 Study Completion Date: March 31, 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

RCC PROJECT 384254  
CIBA-GEIGY PROJECT 943127  
CGA 329351 tech.

**GOOD LABORATORY PRACTICE**

**STATEMENT OF COMPLIANCE**

PROJECT NUMBER: 384254  
 TEST ARTICLE: CGA 329351 tech.  
 RESPONSIBLE FOR ANALYTICS: 5.1.2.e.Woo  
 TITLE: Determination of Content, Homogeneity and Stability of CGA 329351 tech. in rodent feed.

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

Responsible for Analytics:

5.1.2.e.Woo

Date:

31.10.95

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## QUALITY ASSURANCE UNIT

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

### STATEMENT

PROJECT NUMBER: 384254

TEST ARTICLE: CGA 329351 tech.

RESPONSIBLE FOR ANALYTICS: S.1.2.e Woo

TITLE: Determination of Content, Homogeneity and Stability of CGA 329351 tech. in rodent 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
15-DEC-94	15-DEC-94
28/30-MAR-95	30-MAR-95

Manager, Quality Assurance Unit:

S.1.2.e Woo

Date:

April 04, 1995



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## GOOD LABORATORY PRACTICE

This study was performed in compliance with:

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

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## ABSTRACT

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

### Prepared on 18-OCT-94:

The test article concentrations in pelleted diet samples were found to be 97.1 %, 94.2 %, 91.1 %, 100.2 % and 97.1 % of the nominal concentrations for dose groups 2 (25 ppm), 3 (50 ppm), 4 (250 ppm), 5 (625 ppm) and 6 (1250 ppm), respectively. The homogeneity varied in the range from -3 % to +3 % of the mean concentrations.

CGA 329351 tech. was found to be stable in rodent feed at room temperature ( $22 \pm 2$  °C) over a period of 35 days.

### Prepared on 14-DEC-94:

The test article concentrations in pelleted diet samples were found to be 99.8 %, 105.7 %, 98.2 %, 99.1 % and 103.8 % of the nominal concentrations for dose groups 2 (25 ppm), 3 (50 ppm), 4 (250 ppm), 5 (625 ppm) and 6 (1250 ppm), respectively.

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## 1. INTRODUCTION

This report describes the analytical method used and the results obtained for content, homogeneity and stability of CGA 329351 tech. in rodent 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)

Company code No.: CGA 329351 tech.  
 Batch No.: OP.4  
 Purity: 97.1 %  
 Description: viscous liquid  
 Date of receipt: October 10, 1994  
 Storage conditions: room temperature  
 Stability: April 1998  
 Safety precautions: All personnel which was exposed to the test material during weighing, mixing or applying of the test substance wore dust masks, protective glasses and disposable plastic gloves.

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## 2.2. SAMPLES

---

- Shipment no.: 01
- Prepared by sponsor on: 18-OCT-94
- Received at RCC on: 21-OCT-94
- Dates of analysis: 28/29\*-DEC-94
- Shipment no.: 02
- Prepared by sponsor on: 18-OCT-94
- Received at RCC on: 22-NOV-94
- Dates of analysis: 28/29\*-DEC-94
- Shipment no.: 03
- Prepared by sponsor on: 14-DEC-94
- Received at RCC on: 16-DEC-94
- Dates of analysis: 28/29\*-DEC-94

- Was reinjected a day later

## 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 ( $22 \pm 2$  °C) at the sponsor's facility for 35 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.

## 2.4. ANALYTICAL PROCEDURE

---

### 2.4.1. Standard Solutions

First, a stock solution of the test article (see section 2.1) in methanol with a concentration from 1.0 mg/ml was prepared as follows: 50 mg of the test article were weighed into a 50 ml volumetric flask. Then, about 30 ml of methanol was added and these mixtures were dissolved by ultrasonic treatment. Next, the volumetric flasks were filled to volume with methanol. Finally, various standard solutions were prepared by respective dilution of these stock solutions with acetonitrile/bidistilled water (40:60) to yield concentrations in the range from 0.05 µg/ml to 100 µg/ml. The standard solutions in the concentration range from 0.05 µg/ml to 2 µg/ml were used to calibrate the HPLC.

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### 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 at 170 rpm. After 15 minutes of sedimentation, an aliquot was withdrawn from the supernatant and was further analyzed as described in sections 2.4.2.1 or 2.4.2.2. Finally, 50 $\mu$ l or 100  $\mu$ l aliquot was quantified by HPLC.

#### 2.4.2.1. Column Chromatography (0-1250 ppm)

N-hexane was filled into a chromatography column and 3 g of Florisil\* was added and allowed to sediment. A 10 ml (respectively 5 ml) aliquot of the supernatant derived from section 2.4.2 was transferred into a round bottom flask and rotary-evaporated to dryness under reduced pressure at 45 °C. The residue was dissolved in about 3 ml of acetone/n-hexane (1+20 v/v) by ultrasonic treatment and was further quantitatively transferred onto the column. The column was rinsed with 17 ml of acetone/n-hexane (1+20 v/v) and eluted with 40 ml of acetone/n-hexane (2+8 v/v) and collected in a 100 ml round bottom flask. The eluate was rotary-evaporated to dryness at 45 °C. The dry residue was dissolved in HPLC-eluent A (see section 2.4.4) by ultrasonic treatment. This sample solution was filtrated through a 0.45  $\mu$ m acrodisc filter before quantification by HPLC.

#### 2.4.2.2. Dilution (25 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  $\mu$ g/ml to 1000  $\mu$ g/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 or 2.4.2.2.

---

\* Florisil (Merck no. 12518) was dried overnight at 150 °C in a drying oven. After cooling to room temperature in a desiccator, 7 ml of bidistilled water was added to 100 g dried Florisil and homogenized for 2 to 3 hours.

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#### 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  $\mu$ m; 250 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  $\mu$ l or 100  $\mu$ l

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#### 2.4.5. Evaluation of Results

Injected samples were quantified by peak height with reference to the calibration curves. The latter were obtained by correlation of the 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.

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

where

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

a = y-axis intercept

b = slope

X = peak height of injected sample in counts

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

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

where

C = Concentration of CGA 329351 tech. in rodent 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 (%)

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### 3. RESULTS

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

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

#### Prepared on 18-OCT-94:

The test article concentrations in pelleted diet samples were found to be 97.1 %, 94.2 %, 91.1 %, 100.2 % and 97.1 of the nominal concentrations for dose groups 2 (25 ppm), 3 (50 ppm), 4 (250 ppm), 5 (625 ppm) and 6 (1250 ppm), respectively. The Homogeneity varied in the range from -3 % to +3 % of the mean concentrations.

CGA 329351 tech. was found to be stable in rodent feed at room temperature ( $22 \pm 2$  °C) over a period of 35 days.

#### Prepared on 14-DEC-94:

The test article concentrations in pelleted diet samples were found to be 99.8 %, 105.7 %, 98.2 %, 99.1 % and 103.8 of the nominal concentrations for dose groups 2 (25 ppm), 3 (50 ppm), 4 (250 ppm), 5 (625 ppm) and 6 (1250 ppm), respectively.

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.



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 CGA 329351 tech.

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Table 1: Example of a calibration curve

Standard ( $\mu\text{g/ml}$ )	Peak height (counts)	
	before samples	after samples
0.2	548	572
0.5	1380	1342
1	2742	2665
2	5541	5440

$$Y = 3.16 \text{ E-}3 + 3.65 \text{ E-}4 \cdot X \quad (R^2 = 1.00)$$

where

Y =  $\mu\text{g/ml}$  CGA 329351 tech. in injected sample

X = peak height of injected sample (in counts)

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 CIBA-GEIGY PROJECT 943127  
 CGA 329351 tech.

Table 2:

**TEST ARTICLE IN FEED  
 CONTENT, HOMOGENEITY AND STABILITY**

DATE OF PREPARATION: 18-OCT-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	29-DEC-94	0.000	---	---	---	---	---
Day 35			0.000	---	---			
GROUP 2	25	29-DEC-94	24.33	97.3	97.1	-3 / +3	25.0	104.4
Day 0			25.05	100.2				
Day 0			23.48	93.9				
Day 35			25.62	102.5	102.5			
GROUP 3	50	28-DEC-94	47.36	94.7	94.2	0 / +0	50.0	102.3
Day 0			47.01	94.0				
Day 0			47.01	94.0				
Day 35			51.14	102.3	102.3			
GROUP 4	250	28-DEC-94	229.1	91.6	91.1	-1 / +1	250	104.0
Day 0			225.6	90.2				
Day 0			229.0	91.6				
Day 35			237.2	94.9	94.9			
GROUP 5	625	28-DEC-94	620.0	99.2	100.2	-1 / +1	600	102.0
Day 0			626.8	100.3				
Day 0			631.4	101.0				
Day 35			638.8	102.2	102.2			
GROUP 6	1250	28-DEC-94	1221	97.6	97.1	-1 / +0	1000	102.3
Day 0			1217	97.3				
Day 0			1206	96.5				
Day 35			1229	98.3	98.3			

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

\* Stability test at room temperature (22 °C ± 2 °C) over a period of 35 days.

**TEST ARTICLE IN FEED  
 CONTENT**

DATE OF PREPARATION: 14-OEC-94

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	29-DEC-94	0.000	---	---	---	---	---
Group 2	25	29-DEC-94	24.95	99.8	---	---	25.0	104.4
Group 3	50	28-DEC-94	52.85	105.7	---	---	50.0	102.5
Group 4	250	28-DEC-94	245.5	98.2	---	---	250	104.0
Group 5	625	28-DEC-94	619.5	99.1	---	---	600	102.0
Group 6	1250	28-DEC-94	1298	103.8	---	---	1000	102.3

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CIBA-GEIGY PROJECT 943127  
CGA 329351 tech.

Figure 1: Typical Chromatograms:

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

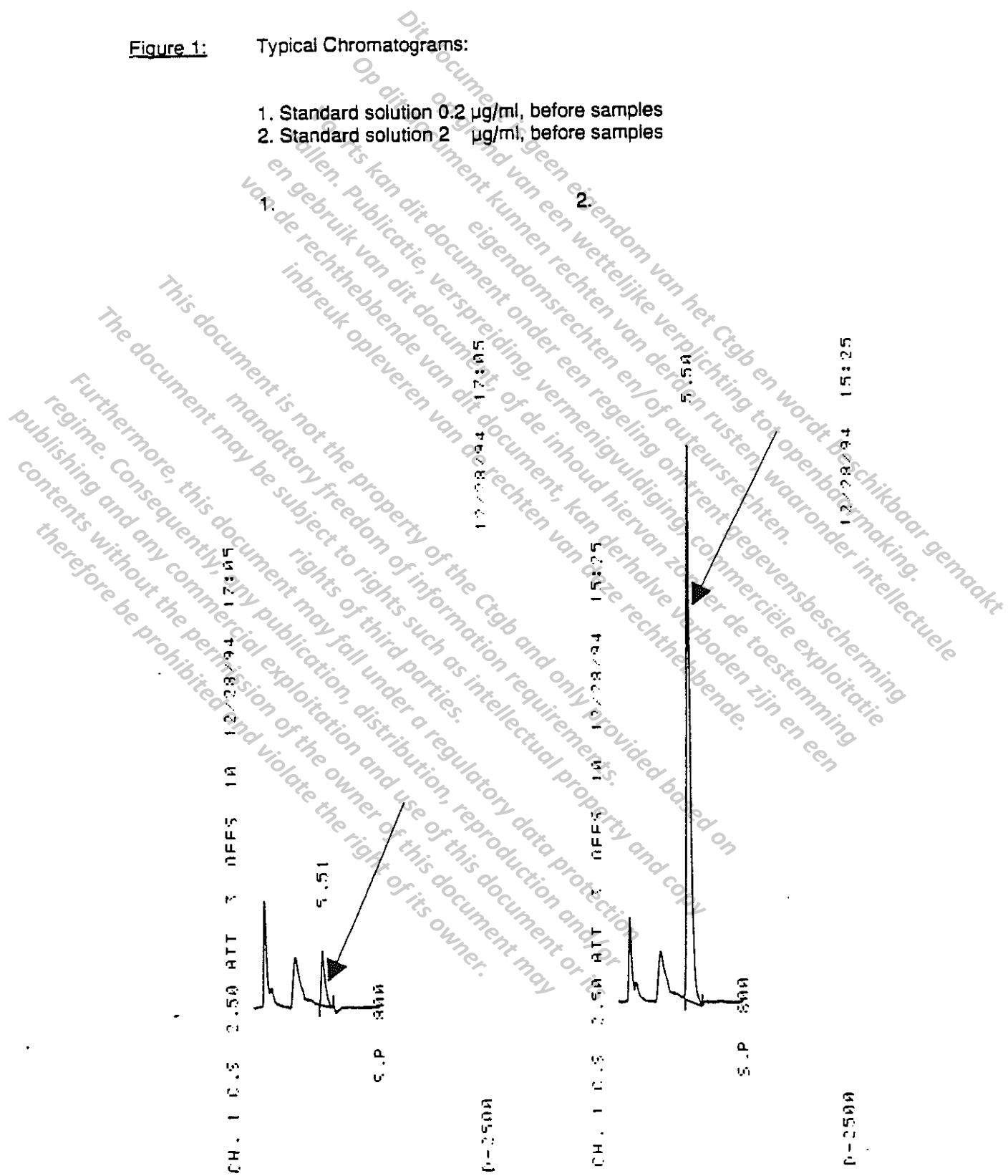
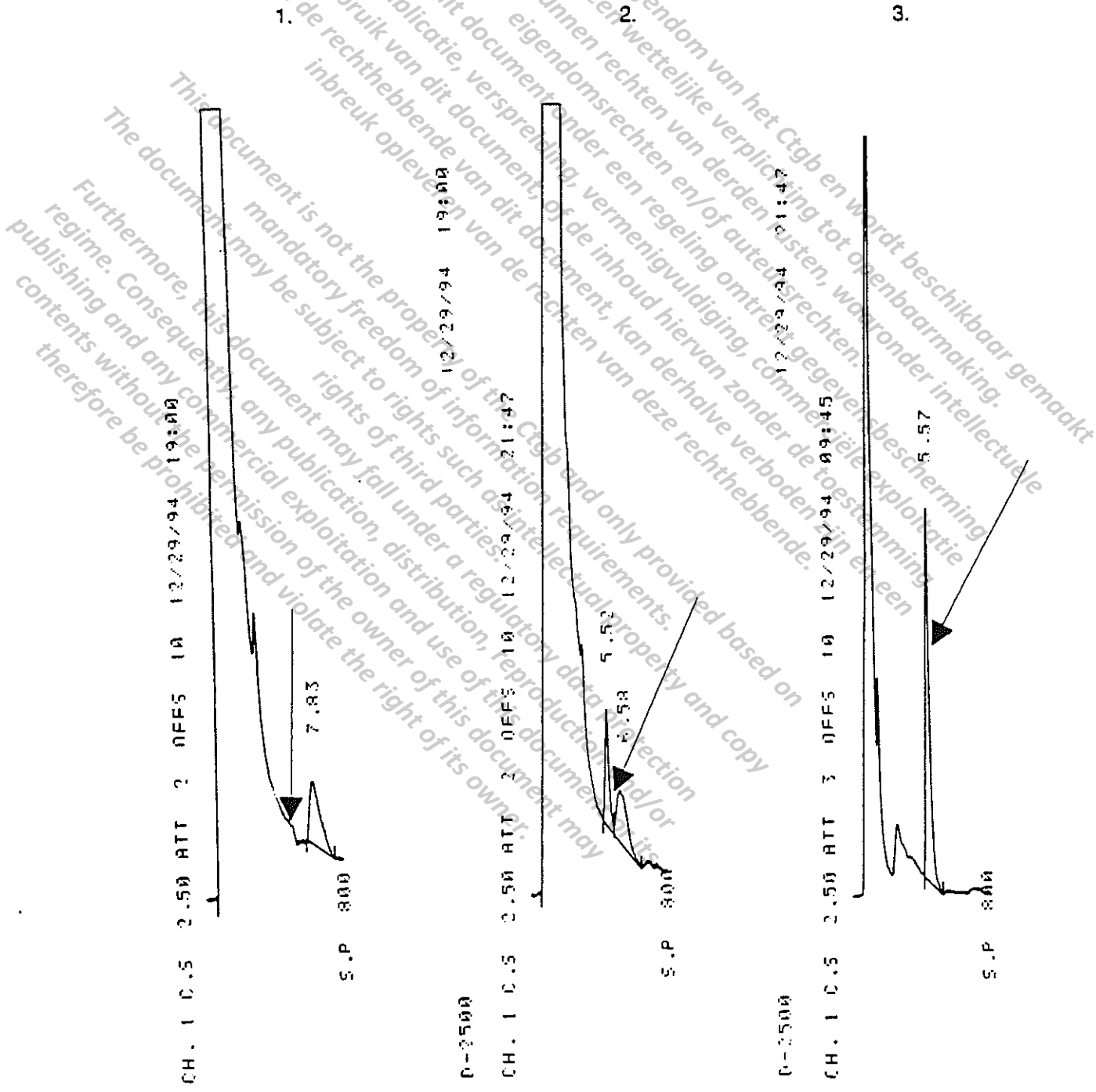


Figure 2: Typical Chromatograms:

1. Control sample
2. Sample, nominal 25 ppm, diluted 20x
3. Sample, nominal 1250 ppm, diluted 100x



**8. APPENDIX D: REFERENCE VALUES**

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**8.1. Reference values: Hematology**

HEMATOLOGY REFERENCE VALUES  
 UNTREATED MALE RATS Tif: RAIF (SPF)

Age : 17 - 24 weeks      Period : 17.04.91 - 31.01.94

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
RBC	M0002	T/l	480	7.830	8.460	9.070
Hb	M0002	mmol/l	480	8.900	9.400	9.900
Hct	M0002	l	480	0.421	0.448	0.477
MCV	M0002	fl	480	50.20	53.00	56.30
RDW	M0002	l	480	0.121	0.134	0.153
MCH	M0002	fmol	480	1.050	1.120	1.180
MCHC	M0002	mmol/l	480	20.19	21.00	21.96
HDW	M0002	mmol/l	480	1.400	1.610	2.290
Reti	M0001	l	20	0.009	0.013	0.020
	M0002	l	70	0.010	0.022	0.039
WBC	M0002	G/l	480	7.090	10.40	15.59
Neut	M0002	l	480	0.082	0.133	0.252
Eos	M0002	l	480	0.007	0.012	0.022
Baso	M0002	l	480	0.001	0.003	0.007
Lympho	M0002	l	480	0.652	0.779	0.855
Mono	M0002	l	480	0.023	0.040	0.064
Luc	M0002	l	480	0.011	0.026	0.043
Neut	M0002	G/l	140	0.930	1.545	2.830
Eos	M0002	G/l	140	0.070	0.130	0.250
Baso	M0002	G/l	140	0.020	0.040	0.090
Lympho	M0002	G/l	140	5.420	8.035	12.44
Mono	M0002	G/l	140	0.230	0.450	0.780
Luc	M0002	G/l	140	0.180	0.325	0.560
Plt	M0002	G/l	480	782.0	957.5	1128
PT(CS)	M0001	sec	480	29.06	37.72	50.23
MetHb	M0001	l	140	0.006	0.007	0.008

HEMATOLOGY REFERENCE VALUES  
 UNTREATED FEMALE RATS Tif: RAIf (SPF)

Age : 17 - 24 weeks      Period : 17.04.91 - 31.01.94

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
RBC	M0002	T/l	477	7.130	7.780	8.400
Hb	M0002	mmol/l	477	8.500	9.100	9.700
Hct	M0002	l	477	0.399	0.432	0.462
MCV	M0002	fl	477	51.80	55.70	59.00
RDW	M0002	l	477	0.112	0.125	0.145
MCH	M0002	fmol	477	1.110	1.170	1.240
MCHC	M0002	mmol/l	477	20.09	20.99	22.14
HDW	M0002	mmol/l	477	1.190	1.350	1.920
Reti	M0001	l	20	0.009	0.016	0.022
	M0002	l	49	0.010	0.020	0.033
	M0003	l	20	0.036	0.043	0.059
WBC	M0002	G/l	477	3.750	6.580	10.97
Neut	M0002	l	477	0.068	0.119	0.231
Eos	M0002	l	477	0.008	0.015	0.027
Baso	M0002	l	477	0.001	0.002	0.004
Lympho	M0002	l	477	0.666	0.793	0.870
Mono	M0002	l	477	0.022	0.039	0.064
Luc	M0002	l	477	0.010	0.023	0.045
Neut	M0002	G/l	139	0.510	0.860	1.620
Eos	M0002	G/l	139	0.050	0.110	0.220
Baso	M0002	G/l	139	0.010	0.020	0.050
Lympho	M0002	G/l	139	3.280	5.810	9.680
Mono	M0002	G/l	139	0.140	0.280	0.480
Luc	M0002	G/l	139	0.110	0.210	0.340
Plt	M0002	G/l	477	822.0	985.0	1153
PT(CS)	M0001	sec	477	22.13	28.99	35.47
Methb	M0001	l	139	0.006	0.007	0.009

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 Test Article: CGA 329351 tech.

### 8.2. Reference values: Blood chemistry

#### BLOOD CHEMISTRY REFERENCE VALUES UNTREATED MALE RATS Tif: RAIF (SPF)

Age : 17 - 24 weeks      Period : 17.04.91 - 31.01.94

PARAMETER	METHOD	UNIT	N	5%	MEDIAN	95%
Gluc	M0001	mmol/l	410	6.450	7.940	9.680
Urea	M0001	mmol/l	410	4.570	6.165	7.820
Creat-e	M0001	umol/l	410	44.70	63.80	80.90
Bili-tot	M0001	umol/l	410	1.770	2.500	3.430
Prot	M0001	g/l	410	64.17	67.76	72.37
Alb	M0001	g/l	410	35.17	37.23	39.38
Glob	M0001	g/l	410	27.50	30.40	35.20
A/G	M0001	l	410	1.050	1.230	1.360
Chol	M0001	mmol/l	410	1.320	1.750	2.450
Trigly	M0001	mmol/l	160	0.610	0.960	1.550
Phos-Lip	M0001	mmol/l	20	1.250	1.455	1.690
Na+	M0001	mmol/l	410	141.0	143.5	146.2
K+	M0001	mmol/l	410	3.190	3.550	4.030
Ca++	M0001	mmol/l	410	2.510	2.650	2.780
Cl-	M0001	mmol/l	410	95.90	99.80	102.5
PO4-in	M0001	mmol/l	410	1.240	1.560	2.000
ASAT (GOT)	M0001	U/l	410	42.50	56.50	88.30
ALAT (GPT)	M0001	U/l	410	19.40	32.30	52.40
ALP	M0001	U/l	410	62.00	95.70	143.5
GGT	M0001	U/l	390	0.000	0.000	0.000







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