

REPORT No. 1016118 Regulatory Documents

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Division: Vitamins & Fine Chemicals

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Title: AXN-DMS: 28-Day Range-Finding Oral Toxicity (Feeding) Study in the Wistar Rat
¹Study performed at RCC Ltd, Toxicology Division, CH-4452 Itingen, Switzerland; Study Number 853022

Summary

In this subacute toxicity (feeding) range-finding study, astaxanthin dimethyl disuccinate (AXN-DMS) was administered daily to SPF-bred Wistar rats of both sexes at target dose levels of 100, 500 and 1000 mg/kg body weight/day for a period of 28 days. A placebo control group was treated similarly with the placebo only and a control group was treated similarly with microgranulated standard rat maintenance diet only. The total dietary replacement was held constant for all test item-treated groups and for the placebo control group.

The groups comprised 5 animals per sex that were sacrificed after 28 days of treatment.

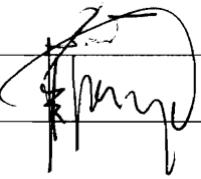
(Summary continued next page)

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Regulatory Document

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and 336 Pages

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Summary (continued)

Clinical signs, food consumption and body weights were recorded periodically during pretest and treatment periods.

At the end of the dosing period, blood samples were withdrawn for hematology and plasma chemistry analyses and for plasma level determination. All animals were killed, necropsied and examined post mortem. Histological examinations were performed on organs and tissues from all control and high dose animals, and all gross lesions from all animals.

No deaths or moribund animals were noted at any dose level. All animals survived until their scheduled day of necropsy.

Over the 28-day treatment period, the attained test item intakes deviated from the target doses of 100, 500 and 1000 mg/kg/day by +4.83%, +2.05% and +2.24% for males and +5.90%, +7.65% and +4.54% for females of the target dose levels, respectively.

Dark and red fecal discoloration was noted in all animals of the placebo group (dark) and of the test item-treated groups (red) from treatment week 1 until the end of the treatment week 4. Soft feces were noted in all animals of the placebo group and in all animals treated with 500 mg/kg/day from treatment week 3 until the end of the treatment week 4. In the animals treated with 1000 mg/kg/day, this finding was noted during the treatment week 4 only. Fecal discoloration and soft feces were considered to be typical passive effects noted after oral administration of a dyestuff, and are without toxicological relevance.

No test item-related changes in mean daily food consumption were noted at any dose level tested or in the placebo group.

No test item-related differences in mean body weight or mean body weight gain were noted at any dose level.

No test item-related changes were noted in the hematology parameters of test item-treated rats.

No test item-related changes were noted in the clinical biochemistry parameters of test item-treated rats.

Determinations of plasma and liver concentrations were performed in all animals on week 4 at scheduled necropsy (animals were fasted overnight). The results indicated that the test animals were adequately exposed to AXN-DMS under the conditions of the study. After AXN-DMS, treatment, dose-dependent concentrations of AXN and AXN isomers could be detected in plasma and liver samples of males and females. No AXN-DMS or isomers could be measured in plasma samples. In liver samples, small concentrations of AXN-DMS or isomers were measurable, which were up to 100 fold lower than the values of AXN and isomers.

No test item-related differences in the absolute or relative (organ-to-body, organ-to-brain) organ weights were noted at any dose level.

Under the conditions of this study, treatment with the test item AXN-DMS induced no macroscopic or microscopic test item-related changes.

According to the results of pathology the no observable effect level (NOEL) is above 1000 mg/kg/day.

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Assessment

Oral administration (feeding) of AXN-DMS to Wistar rats at target doses of 100, 500 and 1000 mg/kg/day, for 28 days resulted in no deaths, no test item-related changes of toxicological relevance, no changes in food consumption or body weight, no effects on hematology or clinical biochemistry, and no changes in absolute or relative organ weights. No macro- or microscopic changes were seen which were considered to be adverse.

Fecal discoloration was noted in all animals of the placebo group and of the test item-treated groups from treatment week 1 until the end of the treatment week 4. This was considered to be a non-adverse test item-related finding of no toxicological relevance.

The results of plasma and organ tissue (liver) indicated that the test animals were adequately exposed to AXN-DMS under the conditions of the study.

Based on the results of this study, similar dose levels could be used for a subsequent oral toxicity (feeding) study.

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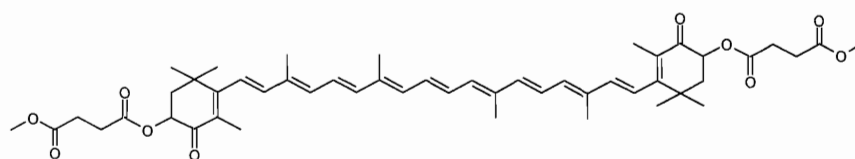
29-Jul-2004, Wolz E

Nomenclature and Structural Formula

Astaxanthin dimethyl disuccinate (AMN-DMS)

Succinic acid 4-{18-[4-{3-methoxycarbonyl-propionyloxy}-2,6,6-trimethyl-3-oxo-cyclohex-1-enyl]-3,7,12,16-tetramethyl-octadeca-1,3,5,7,9,11,13,15,17-nonaenyl}-3,5,5-trimethyl-2-oxo-cyclohex-3-enyl ester methyl ester

RO4381139-000-001



RCC Study Number 853022

AXN-DMS:

28-Day Range-Finding Oral Toxicity
(Feeding) Study in the Wistar Rat

Final Report (Part I of II)

Authors: W.H. Braun, PD Dr. A. Waldvogel,
Dr. J. Schierle, Dr V. Spitzer

Sponsor: DSM Nutritional Products
(registered as Roche Vitamins Ltd.)
Wurmisweg 576
CH-4303 Kaiseraugst / Switzerland

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REPORT

1 PREFACE

1.1 GENERAL

Title	AXN-DMS: 28-Day Range-Finding Oral Toxicity (Feeding) Study in the Wistar Rat
Sponsor	DSM Nutritional Products (registered as Roche Vitamins Ltd.) Wurmisweg 576 CH-4303 Kaiseraugst / Switzerland
Study Monitor	Dr. E. Wolz DSM Nutritional Products (registered as Roche Vitamins Ltd.) R&D Human Nutrition and Health Bldg. 205/316B P.O. Box 3255 CH-4002 Basel / Switzerland
Test Facilities	RCC Ltd Toxicology Operational Unit: Safety Assessment I a) CH-4452 Itingen / Switzerland b) CH – 4414 Füllinsdorf / Switzerland c) DSM Nutritional Products (registered as Roche Vitamins Ltd.) Wurmisweg 576 CH-4303 Kaiseraugst / Switzerland

1.2 RESPONSIBILITIES

Study Director	W. H. Braun (a)
Deputy Study Director	Dr. B. Damme (a)
Laboratory Coordinator	P. Althaus Ravenstijn (a)
Clinical Diagnostics	Dr. P. Gretener (b)
Necropsy/Histotechnology	Dr. K. Weber (a)
Study Pathologist	PD Dr. A. Waldvogel (a)
Analytical Chemistry (Biomatrices)	Dr. V. Spitzer (c)
Analytical Chemistry (Test item Preparations)	Dr. J. Schierle (c)

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1.3 SCHEDULE

Experimental Starting Date	10 March 2004
Experimental Completion Date	14 April 2004
Delivery of Animals	10 March 2004
Acclimatization/Pretest	10 to 16 March 2004
Administration/Treatment	17 March to 13 April 2004
Termination (Necropsy)	14 April 2004

1.4 ARCHIVING

RCC Ltd (CH-4452 Itingen / Switzerland) will retain the study plan, raw data, sample of test item(s), specimens (as long as the quality permits evaluation) and the final report of the present study for at least ten years. Wet tissue samples will be archived at RCC Ltd for a minimum of five years. Thereafter, in agreement with the Sponsor, these samples may be further archived at RCC Ltd or transferred to another GLP archive facility for the remainder of the prescribed period. No data will be discarded without the Sponsor's consent.

1.5 ANIMAL WELFARE

The in-life part of this study was performed in an AAALAC-approved laboratory in accordance with the Swiss Animal Protection Law under license no. 35.

1.6 ACCREDITATION

The test facility "RCC Ltd, Toxicology" is accredited according to ISO/IEC 17025 under accreditation number STS 085 by the Swiss Accreditation Service.


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1.7 SIGNATURES

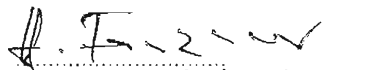
Study Director:

W.H. Braun


date: 29 July 2004

Management:

Dr. H. Fankhauser


date: 29 July 2004

The signatures of Dr. A. Waldvogel (Study Pathologist), Dr. V. Spitzer (Biomatrix analysis) and Dr. J. Schierle (Test item Preparations) are included in the relevant attached reports.

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2 SUMMARY

GENERAL

In this subacute toxicity (feeding) range-finding study, AXM-DMS was administered daily to SPF-bred Wistar rats of both sexes at target dose levels of 100, 500 and 1000 mg/kg body weight/day for a period of 28 days. A placebo control group was treated similarly with the placebo only and a control group was treated similarly with microgranulated standard rat maintenance diet only. The total dietary replacement was held constant for all test item-treated groups and for the placebo control group.

The groups comprised 5 animals per sex that were sacrificed after 28 days of treatment.

Clinical signs, food consumption and body weights were recorded periodically during pretest and treatment periods.

At the end of the dosing period, blood samples were withdrawn for hematology and plasma chemistry analyses and for plasma level determination. All animals were killed, necropsied and examined post mortem. Histological examinations were performed on organs and tissues from all control and high dose animals, and all gross lesions from all animals.

MORTALITY / VIABILITY

No deaths or moribund animals were noted at any dose level. All animals survived until their scheduled day of necropsy.

ATTAINED TEST ITEM INTAKE

Over the 28-day treatment period, the attained test item intakes deviated from the target doses of 100, 500 and 1000 mg/kg/day by +4.83%, +2.05% and +2.24% for males and +5.90%, +7.65% and +4.54% for females of the target dose levels, respectively.

CLINICAL SIGNS

Dark and red fecal discoloration was noted in all animals of the placebo group (dark) and of the test item-treated groups (red) from treatment week 1 until the end of the treatment week 4.

Soft feces were noted in all animals of the placebo group and in all animals treated with 500 mg/kg/day from treatment week 3 until the end of the treatment week 4. In the animals treated with 1000 mg/kg/day, this finding was noted during the treatment week 4 only.

Fecal discoloration and soft feces were considered to be typical passive effects noted after oral administration of a dyestuff, and are without toxicological relevance.

FOOD CONSUMPTION

No test item-related changes in mean daily food consumption were noted at any dose level tested or in the placebo group.

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BODY WEIGHT

No test item-related differences in mean body weight or mean body weight gain were noted at any dose level.

CLINICAL LABORATORY INVESTIGATIONS

Hematology

No test item-related changes were noted in the hematology parameters of test item-treated rats.

Clinical Biochemistry

No test item-related changes were noted in the clinical biochemistry parameters of test item-treated rats.

BLOOD AND TISSUE DETERMINATIONS

Determinations of plasma and liver concentrations were performed in all animals on week 4 at scheduled necropsy (animals were fasted overnight). The results indicated that the test animals were adequately exposed to AXN-DMS under the conditions of the study. After AXN-DMS treatment, dose-dependent concentrations of AXN and AXN isomers could be detected in plasma and liver samples of males and females. No AXN-DMS or isomers could be measured in plasma samples. In liver samples, small concentrations of AXN-DMS or isomers were measurable, which were up to 100 fold lower than the values of AXN and isomers.

ORGAN WEIGHTS

No test item-related differences in the absolute or relative (organ-to-body, organ-to-brain) organ weights were noted at any dose level.

MACROSCOPIC / MICROSCOPIC FINDINGS

Under the conditions of this study, treatment with the test item AXN-DMS induced no macroscopic or microscopic test item-related changes.

According to the results of pathology the no observable effect level (NOEL) is above 1000 mg/kg/day.

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3 ASSESSMENT

Oral administration (feeding) of AXN-DMS to Wistar rats at target doses of 100, 500 and 1000 mg/kg/day, for 28 days resulted in no deaths, no test item-related changes of toxicological relevance, no changes in food consumption or body weight, no effects on hematology or clinical biochemistry, and no changes in absolute or relative organ weights. No macro- or microscopic changes were seen which were considered to be adverse.

Fecal discoloration was noted in all animals of the placebo group and of the test item-treated groups from treatment week 1 until the end of the treatment week 4. This was considered to be a non-adverse test item-related finding of no toxicological relevance.

The results of plasma and organ tissue (liver) indicated that the test animals were adequately exposed to AXN-DMS under the conditions of the study.

Based on the results of this study, similar dose levels could be used for a subsequent oral toxicity (feeding) study.

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4 OBJECTIVE

4.1 PURPOSE AND RATIONALE

The purpose of this oral toxicity range-finding study was to assess the toxicological profile of AXN-DMS when administered daily to rats in the diet for a period of 28 days and to select appropriate doses for a subsequent oral toxicity (feeding) study.

This study should provide a rational basis for toxicological risk assessment in man. The results of this study should indicate potential target organs.

5 MATERIALS AND METHODS

5.1 TEST SYSTEM

Test system	Rat, HanBrl:WIST (SPF)
Rationale	Recognized by the international guidelines as the recommended test system.
Source	RCC Ltd Biotechnology & Animal Breeding Division CH-4414 Füllinsdorf / Switzerland
Group allocation	Group 1-5: 5 males and 5 females each
Total number of animals	25 males and 25 females
Age at delivery	Approximately 6 weeks
Body weight range at acclimatization	Males: 140.3 - 158.8 grams (mean 150.2 grams) Females: 116.5 - 132.2 grams (mean 124.1 grams)
Identification	Cage card and individual ear tattoo
Randomization	Computer-generated random algorithm
Acclimatization	Under test conditions after health examination. Only animals without any visible signs of illness were used for the study.

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5.2 ALLOCATION

Allocation and Target Dose Levels	Group 1* 0 mg/kg/day	Group 2** Placebo mg/kg/day	Group 3 100 mg/kg/day	Group 4 500 mg/kg/day	Group 5 1000 mg/kg/day
Males	1-5	6-10	11-15	16-20	21-25
Females	26-30	31-35	36-40	41-45	46-50

* - Control animals will be treated with control diet only.

** - Placebo diet

5.3 HUSBANDRY

Room number	131 (10 to 25 March 2004), 138 (25 to 31 March 2004), 138 (31 March 2004 until end of study)
Conditions	Standard Laboratory Conditions. Air-conditioned with 10-15 air changes per hour, and continuously monitored environment with a target range for temperature of 20 ± 3 °C and for relative humidity between 30-70 %. 12 hours fluorescent light / 12 hours dark, music during the light period.
Accommodation	Individually in Makrolon type-3 cages with wire mesh tops and standardized softwood bedding ('Lignocel' Schill AG, CH-4132 Muttenz/Switzerland).
Diet	Microgranulated standard Provimi Kliba 3433 (batch no. 6/04) rat maintenance diet (Provimi Kliba AG, CH- 4303 Kaiseraugst/ Switzerland) was available <i>ad libitum</i> . The feed batch was analyzed for contaminants (see Appendix II, pp. 170 - 172).
Water	Community tap-water from Itingen was available <i>ad libitum</i> in water bottles. Results of bacteriological assay, chemical and contaminant analyses of representative samples are attached to this report (see Appendix I, pp. 166 - 169). None of the contaminants analyzed in the water and diet is considered to have been present at a concentration which would have affected the validity of the results.

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5.4 TEST ITEM

Identity	Carophyll Stay Pink 15% CWS (RO4381139-000-001)
Name for report	AXN-DMS
Description	Beadlets
Batch number	B.2003.01.12/PC
Content (HPLC)	Astaxanthin dimethyl disuccinate: 163 g/kg Astaxanthin equivalent: 118 g/kg
Stability of test item	Stable under storage conditions
Retest date	09 December 2004
Storage conditions	Refrigerator (approx. 5°C) Protect from light; store under nitrogen or argon atmosphere
Safety precautions	Routine hygienic procedures (gloves, goggles, face mask)

The test item information was supplied by the sponsor.

5.5 FEED PREPARATION

The approximate start concentrations based on 15 g food consumption per 150 g animal were:

Test item	Group No.	Dietary concentration [ppm]*#	Daily Target dose AXN-equivalent (mg/kg body weight)	Dietary replacement [ppm]** Placebo + Test item
Control	Gr. 1	0	0	0
Placebo	Gr. 2	0	0	84700
AXN-DMS 15%CWS	Gr. 3	8470	100	84700
AXN-DMS 15%CWS	Gr. 4	42350	500	84700
AXN-DMS 15%CWS	Gr. 5	84700	1000	84700

*: ppm corresponds to mg beadlets per kg feed; corrected with a factor of 8.47 for AXN-DMS 15% CWS beadlets containing 118 g AXN-equivalent/kg and 163 g AXN-DMS/kg

** : Supplemented with placebo to a total amount equivalent to the dietary replacement of the high dose group

: JECFA: 1 mg/kg BW/day = 10ppm (young rats), = 20ppm (adult rats)

Fresh batches of the powdered feed for this study were prepared weekly, based upon the food consumption and body weights.

The adjustment to similar dietary replacement in all test item-treated groups and in the placebo control group was achieved by adding placebo to the required amount of test item up to a total amount equivalent to the dietary replacement of the high dose group.

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AXN-DMS and the placebo were weighed into a beaker on a tared Mettler balance and mixed. These mixtures were prepared using a homogenizer. Then the microgranulated feed was weighed into a beaker on a tared Mettler balance and added to the test item and placebo mixture. The dietary admixtures were prepared using a household mixer. The dietary admixtures were adjusted weekly to the mean food consumption and body weight of the animals to achieve the target dose levels.

Placebo control feed for the animals of group 2 was prepared similarly without the test item.

Control feed for the animals of group 1 was prepared similarly without the placebo and the test item.

The feed preparations were stored at room temperature (ca. 19-25°C) in disposable paper bags. After the new batches of feed were prepared any remaining feed from the preceding batch was discarded.

5.5.1 ANALYSIS OF DOSE FORMULATIONS

Content, stability and homogeneity of the test item were determined with the first diet preparation.

For assessment of content and homogeneity, an approximate 100 g sample was collected from each the top, middle and bottom of every dietary admixture (including controls and placebo) from the first diet preparation. Samples were collected on the day of preparation and retained frozen at nominal -20° C prior to dispatch to the sponsor for analysis.

For assessment of stability, a further sample (approximately 100 g) of every dietary admixture was collected. The samples were retained under the storage conditions outlined above for 14 days. After 14 days the samples were frozen at nominal -20° C prior to dispatch to the sponsor.

In treatment week 3, samples used for assessment of content, homogeneity and stability were sent to the sponsor as described below.

In addition, the achieved concentration of test item was analyzed in diets prepared for treatment week 4. A sample (approximately 100 g) was taken from the middle of each dietary admixture (including controls). Samples were taken on the day of preparation and retained frozen at nominal -20° C prior to dispatch to the Sponsor for analysis.

The samples were packed in dry ice and shipped together with a completed sample list (blank from VFHA) to DSM Nutritional Products.

The analyses of Astaxanthin dimethyl disuccinate were performed in the Analytical Laboratories of DSM Nutritional Products in the responsibility of the Analytical Investigator Dr. J. Schierle (VFHA).

The results are presented in Appendix IV.

See pp. 216 - 224

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5.6 VEHICLE AND CONTROL (PLACEBO) ITEMS

5.6.1 PLACEBO

Identity	Placebo Carophyll Stay Pink 15% CWS
Name for report	Placebo
Description	Beadlets
Batch number	B.2003.01.13/VN.002
Content (HPLC)	Astaxanthin dimethyl disuccinate: n.d. Astaxanthin equivalent: n.d.
Stability of test item	Stable under storage conditions
Retest date	22 December 2004
Storage conditions	Refrigerator (approx. 5°C) Protect from light; store under nitrogen or argon atmosphere
Safety precautions	Routine hygienic procedures (gloves, goggles, face mask)

The placebo information was supplied by the sponsor.

5.6.2 VEHICLE

Identity	Microgranulated standard Provimi Kliba 3433 rat maintenance diet
Batch number	6/04

5.7 TREATMENT

Method	Oral, by feeding
Rationale	Oral ingestion is a possible route of human exposure.
Daily target dose levels	Group 1: 0 mg/kg body weight (control diet) Group 2: Placebo mg/kg body weight (placebo) Group 3: 100 mg/kg body weight Group 4: 500 mg/kg body weight Group 5: 1000 mg/kg body weight Dose levels are expressed in terms of the test item as supplied.
Rationale for dose level selection	Based on previous studies with Astaxanthin in sponsor's file.
Frequency of administration	ad libitum
Duration of acclimatization period	7 days
Duration of treatment	28 days

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5.8 OBSERVATIONS

5.8.1 MORTALITY / VIABILITY

Observations for mortality/viability were recorded twice daily.

5.8.2 GENERAL CAGESIDE OBSERVATIONS (DAILY)

The animals were observed for clinical signs once before commencement of administration, three times on day 1 and twice daily on days 2-28 of the treatment period.

5.8.3 FOOD CONSUMPTION

The food consumption was recorded twice during the pretest period and from days 1-4, 4-7, 7-14, 14-21 and 21-28 of the treatment period, using an on-line electronic recording system consisting of a Mettler balance connected to the RCC computer.

5.8.4 BODY WEIGHTS

Body weights were recorded twice during pretest and from days 1-4, 4-7, 7-14, 14-21 and 21-28 of the treatment period, using an on-line electronic recording system consisting of a Mettler balance connected to the RCC computer.

5.9 CLINICAL LABORATORY INVESTIGATIONS

Blood sampling:
after 4 weeks

14 April 2004

Blood samples for hematology and clinical biochemistry were collected from all animals under light isoflurane anesthesia. The animals were fasted for approximately 18 hours before blood sampling but allowed access to water *ad libitum*. Blood samples were collected early in the working day to reduce biological variation caused by circadian rhythms. Blood samples were drawn from the retro-orbital plexus using a micro-hematocrit glass capillary tube.

The assays were performed at RCC Ltd (Füllinsdorf) under internal laboratory quality control conditions to assure reliable test results.

In the summary and individual tables the names of some parameters have been abbreviated. Any abbreviation has been defined in Appendix III.

Detailed methodology, abbreviations and general remarks are described in Appendix III.

Clinical laboratory data are expressed, with a few exceptions, in general accordance with the International System of Units (SI).

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5.9.1 HEMATOLOGY

The following hematology parameters were determined:

Erythrocyte count	Reticulocyte count
Hemoglobin	Reticulocyte maturity index
Hematocrit	Methemoglobin
Mean corpuscular volume	Total leukocyte count
Red cell volume distribution width	Differential leukocyte count
Mean corpuscular hemoglobin	Coagulation:
Mean corpuscular hemoglobin concentration	Thromboplastin time
Hemoglobin concentration distribution width	Activated partial thromboplastin time
Platelet (thrombocyte) count	

5.9.2 CLINICAL BIOCHEMISTRY

The following clinical biochemistry parameters were determined:

Glucose	Alkaline phosphatase
Urea	Gamma-glutamyl-transferase
Creatinine	Sodium
Bilirubin, total	Potassium
Cholesterol, total	Chloride
Triglycerides	Calcium
Phospholipids	Phosphorus inorganic
Aspartate aminotransferase	Protein, total
Alanine aminotransferase	Albumin
Lactate dehydrogenase	Globulin
Glutamate dehydrogenase	Albumin/Globulin ratio
Creatine kinase	

6 BLOOD AND TISSUE LEVEL DETERMINATIONS

The blood collection for plasma level determination in week 4 was performed prior to necropsy on the same occasion as blood collection for clinical laboratory investigations. Blood samples were collected by heart puncture from all animals. The samples were collected under light isoflurane anesthesia in EDTA tubes. The animals were fasted approximately 18 hours before blood collection but water was provided *ad libitum*. Plasma was prepared subsequently.

The blood samples were cooled prior to centrifugation between 2°C and 8°C. The samples were centrifuged as soon as it was practicable. The separated plasma was transferred to uniquely labeled clear polypropylene tubes and stored frozen (nominal -70°C) until dispatch to the Sponsor.

Liver samples were collected from all animals at necropsy. One section was retained for histopathology and the remaining part was rinsed in ice cold NaCl, dried by paper towel and frozen in liquid nitrogen. All samples were packed in dry ice and shipped together with the sample list to DSM Nutritional Products.

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The analyses of Astaxanthin dimethyl disuccinate and Astaxanthin in plasma and liver samples were performed in the Analytical Laboratories of DSM Nutritional Products in the responsibility of the Analytical Investigator Dr. V. Spitzer (VFHA).

The results are presented in Appendix V and VI.

See pp. 225 - 238

6.1 PATHOLOGY

6.1.1 NECROPSY

Sacrifice:

after 4 weeks

14 April 2004

All animals were weighed and necropsied. Descriptions of all macroscopic abnormalities were recorded.

All animals surviving to scheduled necropsy and all moribund animals were anesthetized by intraperitoneal injection of sodium pentobarbitone and killed by exsanguination.

Samples of the following tissues and organs were collected from all animals at necropsy and fixed in neutral phosphate buffered 4 % formaldehyde solution (unless otherwise indicated):

Adrenal glands

Aorta

Bone (sternum, femur including joint)

Bone marrow (femur)

Brain (3 levels)

Cecum

Colon

Duodenum

Epididymides (fixed in Bouin's solution)

Esophagus

Eyes with optic nerve (fixed in Davidson's solution)

Harderian gland (fixed in Davidson's solution)

Heart

Ileum, with Peyer's patches

Jejunum with Peyer's patches

Kidneys

Larynx

Lacrimal gland (exorbital)

Liver

Lungs (infused with formalin at necropsy)

Lymph nodes (mesenteric, mandibular)

Mammary gland area

Nasal cavity

Ovaries

Pancreas

Pituitary gland

Prostate gland

Rectum

Salivary glands (mandibular, sublingual)

Sciatic nerve

Seminal vesicles

Skeletal muscle

Skin

Spinal cord (cervical, midthoracic, lumbar)

Spleen

Stomach

Testes (fixed in Bouin's solution)

Thymus

Thyroid (incl. parathyroid gland)

Tongue

Trachea

Urinary bladder (infused with formalin at necropsy)

Uterus

Vagina

Gross lesions

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6.1.2 ABSOLUTE AND RELATIVE ORGAN WEIGHTS

The following organ weights were recorded on the scheduled dates of necropsy:

Brain	Thymus	Spleen	Ovaries
Heart	Kidneys	Testes	Thyroids w/parathyroids
Liver	Adrenals	Epididymides	

The organ to terminal body weight ratios as well as organ to brain weight ratios were determined.

The determination of the terminal body weight was performed immediately prior to necropsy.

6.1.3 HISTOTECHNIQUE

All organ and tissue samples, as defined under Histopathology (following), were processed, embedded and cut at an approximate thickness of 2 to 4 micrometers, and stained with hematoxylin and eosin.

6.1.4 HISTOPATHOLOGY

Slides of all organs and tissues listed in boldface type (see Necropsy, above) which were collected at scheduled sacrifice from the animals of control and high-dose groups were examined by a pathologist.

6.2 DATA COMPILATION

6.2.1 GENERAL

The following data were recorded on-line: food consumption, body weights, organ weights and macroscopic findings at necropsy and histopathology.

Clinical laboratory data were recorded on-line (Bayer Advia 120, Roche/Hitachi 917 Discrete Random-Access Analyzer) or on data sheets (STA-Analyzer, OSM3 Hemoximeter, diverse refractometers and light microscopes) and then transferred to the computer system.

Cageside clinical signs, were recorded on data sheets and transcribed for compilation and analysis into the computer system.

The computer-generated values which appear in the tables represent the rounded-off results of the raw data values or of calculations which used the exact raw data values.

Group means were calculated according to the definition of any mean value using the individual values per animal and the number of animals.

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6.3 DATA CALCULATION

6.3.1 FOOD CONSUMPTION

The food consumption was calculated per rat and per food consumption interval. It expresses the average food consumed per animal and per day over the food consumption interval.

$$FC = \frac{C}{AD}$$

where

FC is Food consumption in grams of food per animal and day;

C is measured food consumption in grams per cage over the consumption interval and

AD is total consumption days over all animals in the cage during the consumption interval.

6.3.2 RELATIVE FOOD CONSUMPTION

The relative food consumption was calculated according to the following formula:

$$RFC = \left[\frac{FC}{BW(i)} \right] \times 1000$$

where

BW(i) is the most ideal body weight in grams or the body weight (of the corresponding rats) recorded on the day most close to the middle of the food consumption interval. In cases of equal "closeness" of two body weight records the later one was chosen;

RFC is relative food consumption in grams of food per kg body weight and day, and

FC is food consumption in grams of food per animal and day.

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6.4 STATISTICAL ANALYSIS

The following statistical methods were used to analyze body weight, organ weights and ratios, as well as:

- The Dunnett-test (many to one t-test) based on a pooled variance estimate were applied if the variables could be assumed to follow a normal distribution for the comparison of the treated groups and the control groups for each sex.
- The Steel-test (many-one rank test) were applied instead of the Dunnett-test when the data can not be assumed to follow a normal distribution.
- Fisher's exact-test were applied to the macroscopic findings.

The following statistical methods were used for statistical analysis of clinical laboratory data:

- Quantitative data were analyzed by a one-way analysis of variance (ANOVA) when the variances are considered homogeneous according to Bartlett. Alternatively, if the variances are considered to be heterogenous ($p \leq 0.05$), a non-parametric Kruskal-Wallis test was used. Treated groups were compared to the control groups using Dunnett's test if the ANOVA was significant at the 5% level and by Dunn's test in the case of a significant Kruskal-Wallis test ($p \leq 0.05$).

References :

C.W. Dunnett: A Multiple Comparison Procedure for Comparing Several Treatments with a Control, J. Amer. Stat. Assoc. 50, 1096-1121 (1955).

S.C. Gad and C.S. Weil: Statistics and Experimental Design for Toxicologists. The Telford Press, Caldwell, New Jersey, 43-45 (1986).

W.H. Kruskal and W.A. Wallis: Use of ranks in one-criterion variance analysis. Journal of the American Statistical Association, 47, 583-621 (1952).

O.J. Dunn: Multiple comparisons using rank sums. Technometrics 6, 241-252 (1964).

R.G. Miller: Simultaneous Statistical Inference, Springer Verlag, New York (1981).

R.A. Fisher: Statistical Methods for Research Workers, Oliver and Boyd, Edinburgh (1950).

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AXN-DMS

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7 RESULTS

7.1 VIABILITY/MORTALITY

No deaths or moribund animals were noted at any dose level. All animals survived until their scheduled day of necropsy.

See pp. 83 - 92

7.2 ATTAINED TEST ITEM INTAKE

Over the 28-day treatment period, the attained test item intakes for mean target dose levels of 100, 500 and 1000 mg/kg/day were 104.83 mg/kg/day (+4.83%), 510.27 mg/kg/day (+2.05%) and 1022.42 (+2.24%) mg/kg/day for males and 105.90 mg/kg/day (+5.90%), 538.27 mg/kg/day (+7.65%) and 1045.38 mg/kg/day (+4.54%) for females.

7.3 OBSERVATIONS

7.3.1 GENERAL CAGESIDE OBSERVATIONS (DAILY)

Slightly dark feces were noted in all animals of the placebo group from treatment week 1 to 5 (=end of treatment week 4) and soft feces were noted in all animals of the placebo group from treatment week 3 to 5.

Slightly red feces were noted in all animals treated with 100 mg/kg/day from treatment week 1 to 5.

Moderately red feces were noted in all animals treated with 500 mg/kg/day from treatment week 1 to 5 and soft feces were noted in these animals from treatment week 3 to 5.

All animals treated with 1000 mg/kg/day had markedly red feces from treatment week 1 to 5 and soft feces were noted in these animals from treatment week 4 to 5.

Fecal discoloration and soft feces were considered to be typical passive effects noted after oral administration of a dyestuff, and are without toxicological relevance.

See pp. 36 - 45, 93 - 102

7.4 FOOD CONSUMPTION

No test item-related changes in mean daily food consumption were noted at any dose level tested. The placebo group compared favorably with the negative control.

Significantly increased mean food consumption was noted in males treated with 1000 mg/kg/day from treatment day 4 to 8 ($p < 0.05$) and in females treated with 500 mg/kg/day from treatment day 1 to 4 ($p < 0.05$) and from treatment day 22 to 28 ($p < 0.05$) when compared to the control group.

Significantly increased mean relative food consumption was noted in males treated with 100 mg/kg/day from treatment day 4 to 8 and from treatment day 22 to 28 (both: $p < 0.05$) and in males treated with 1000 mg/kg/day from treatment day 4 to 8 ($p < 0.01$) when compared to the control group. Females treated with 500 mg/kg/day had significantly increased mean relative food consumption from treatment day 1 to 4, 15 to 22 and 22 to 28 (all: $p < 0.05$) and females treated with 100 mg/kg/day and 1000 mg/kg/day had significantly increased mean relative

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food consumption from treatment day 15 to 22 (both: $p < 0.01$) when compared to the control group. Significantly increased mean relative food consumption was also noted in the females of the placebo group from treatment day 22 to 28 ($p < 0.05$) when compared to the control group.

See pp. 27 - 30, 46 - 57, 103 - 122

7.5 BODY WEIGHTS

No test item-related differences in mean body weight or mean body weight gain were noted at any dose level.

A significantly lower mean body weight was noted in the females of the placebo group on treatment day 15 ($p < 0.05$) when compared to the control group. In the absence of similar findings at other time points, this finding was considered to be incidental and not test item-related.

No significant differences in the mean body weight gain were noted at any dose level.

See pp. 31 - 34, 62 - 73, 123 - 142

7.6 CLINICAL LABORATORY INVESTIGATIONS

7.6.1 HEMATOLOGY

No test item-related changes were noted in the hematology parameters of test item-treated rats. The relative mean basophil counts of males and mean relative monocyte counts of females treated with the placebo were significantly lower ($p < 0.01$) than that of the controls or test item-treated rats. These findings were considered to be incidental.

See pp. 173 - 215

7.6.2 CLINICAL BIOCHEMISTRY

No test item-related changes were noted in the clinical biochemistry parameters of test item-treated rats.

When compared with the controls, plasma chloride levels were elevated in males treated with the placebo and all test item-treated males, although the changes were inverse to dose. In contrast, however, significantly elevated plasma chloride levels ($p < 0.05$) were noted in the placebo-treated females as well as the females treated with the test item at 1000 mg/kg/day. The differences remained within the ranges of the historical control data and were therefore considered to be incidental.

Albumin levels were elevated in males treated with 1000 mg/kg/day ($p < 0.05$) when compared with the controls. This value remained within the ranges of the historical control data and was considered incidental.

Alanine aminotransferase activity was significantly lower ($p < 0.05$) and creatine kinase was significantly lower ($p < 0.01$) in males treated with 500 mg/kg/day when compared with the controls. Lactate dehydrogenase levels were significantly elevated in females treated with 500 mg/kg/day ($p < 0.05$) when compared with the controls. These differences were not dose-related and considered to be of no toxicological relevance.

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Alanine aminotransferase activity was significantly elevated ($p < 0.01$) in females treated with the placebo. Females treated with the test item at 100 mg/kg/day showed no such trend, although they received the second highest compensatory dose of placebo, and therefore the finding in the placebo group was considered to be incidental.

Creatine kinase was significantly elevated ($p < 0.05$), inorganic phosphate was significantly lower ($p < 0.05$) and globulin was significantly lower ($p < 0.05$) in females treated with 1000 mg/kg/day, but all remained within the range of the historical control values and considered to be incidental.

See pp. 173 - 215

7.7 BLOOD AND TISSUE DETERMINATIONS

The objective of the study was to determine plasma and liver concentrations of astaxanthin (AXN), astaxanthin dimethyl disuccinate (AXN-DMS) and isomers following 28-day of oral (feed admix) administration of AXN-DMS in rats in terms of AXN-equivalent at doses of 100, 500 and 1000 mg /kg bw/day.

Determinations of *plasma* and *liver* concentrations were performed in all animals on week 4 at scheduled necropsy (animals were fasted overnight).

In *plasma* samples neither all-E-AXN-DMS nor 9Z-AXN-DMS were detected. Both sexes showed a dose-dependent but not dose-linear increase in plasma content of all-E-AXN, 9Z-AXN and 13Z-AXN whereas 13Z-AXN was the most prominent isomer followed by all-E-AXN and 9Z-AXN. At 1000 mg/kg the plasma content of all-E-AXN and 13Z-AXN was statistically significant higher in males compared to females.

There was a dose-dependent but not dose-linear increase of AXN isomers in *liver* samples of males and females: 13Z-AXN > all-E-AXN > 9Z-AXN. Small amounts of all-E-AXN-DMS and 13Z-AXN-DMS could be detected in both genders treated with 500 and 1000 mg/kg and females at 100 mg/kg, which were up to 100 fold lower than respective levels of AXN or AXN isomers.

It can be *concluded* that the test animals were adequately exposed to AXN-DMS under the conditions of the study. After AXN-DMS treatment dose-dependent concentrations of AXN and AXN isomers could be detected in plasma and liver samples of males and females. No AXN-DMS or isomers could be measured in plasma samples. In liver samples small concentrations of AXN-DMS or isomers were measurable, which were up to 100 fold lower than the values of AXN and isomers.

See pp. 225 - 238

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AXN-DMS

REPORT

7.8 PATHOLOGY

7.8.1 ORGAN WEIGHTS

No test item-related differences were noted at any dose level.

A significantly reduced mean absolute weight of the adrenals was noted in the females of the placebo group ($p < 0.05$) when compared to the control group.

A significant increase in the mean liver-to-body weight ratio ($p < 0.01$) and in the mean kidney-to-body weight ratio ($p < 0.05$) was noted in the males of the placebo group when compared to the control group.

In the absence of similar findings in the test item-treated animals, which have all identical dietary replacements, these findings were considered to be incidental and not a consequence of the dietary replacement.

No significant differences in the mean organ-to-brain weight ratios were noted at any dose level.

See pp. 76 - 81, 153 - 164

7.8.2 MACROSCOPIC FINDINGS

Discoloration of the caecum was noted in several males and females of both controls and test item-treated groups. Caecum discoloration was noted significantly more often in females treated with 1000 mg/kg/day when compared to the control group ($p < 0.05$).

Discoloration of the stomach, the kidneys, the pancreas, the thymus, the thyroid gland, the mandibular lymph nodes and the ovaries were noted in males and females of both test item-treated groups and control and placebo groups.

The other macroscopic findings noted include pelvic dilation, enlarged spleen, enlargement of the ovaries and watery cyst in ovaries and thickened thymus and foci in the thymus. These findings were noted in males and females of both test item-treated groups and control and placebo groups.

See pp. 74 - 75, 143 - 152

7.8.3 MICROSCOPIC FINDINGS

Numerous incidental microscopic findings were detected in various organs in this study. They commonly occur in laboratory rats of this strain and age. But neither their incidences nor their distribution or morphologic appearance indicated an association with treatment. The gastric glandular dilation of minimal severity observed most frequently in males treated with 1000 mg/kg/day reflects a physiologic condition and is of no toxicological relevance.

See pp. 239 - 333

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AXN-DMS

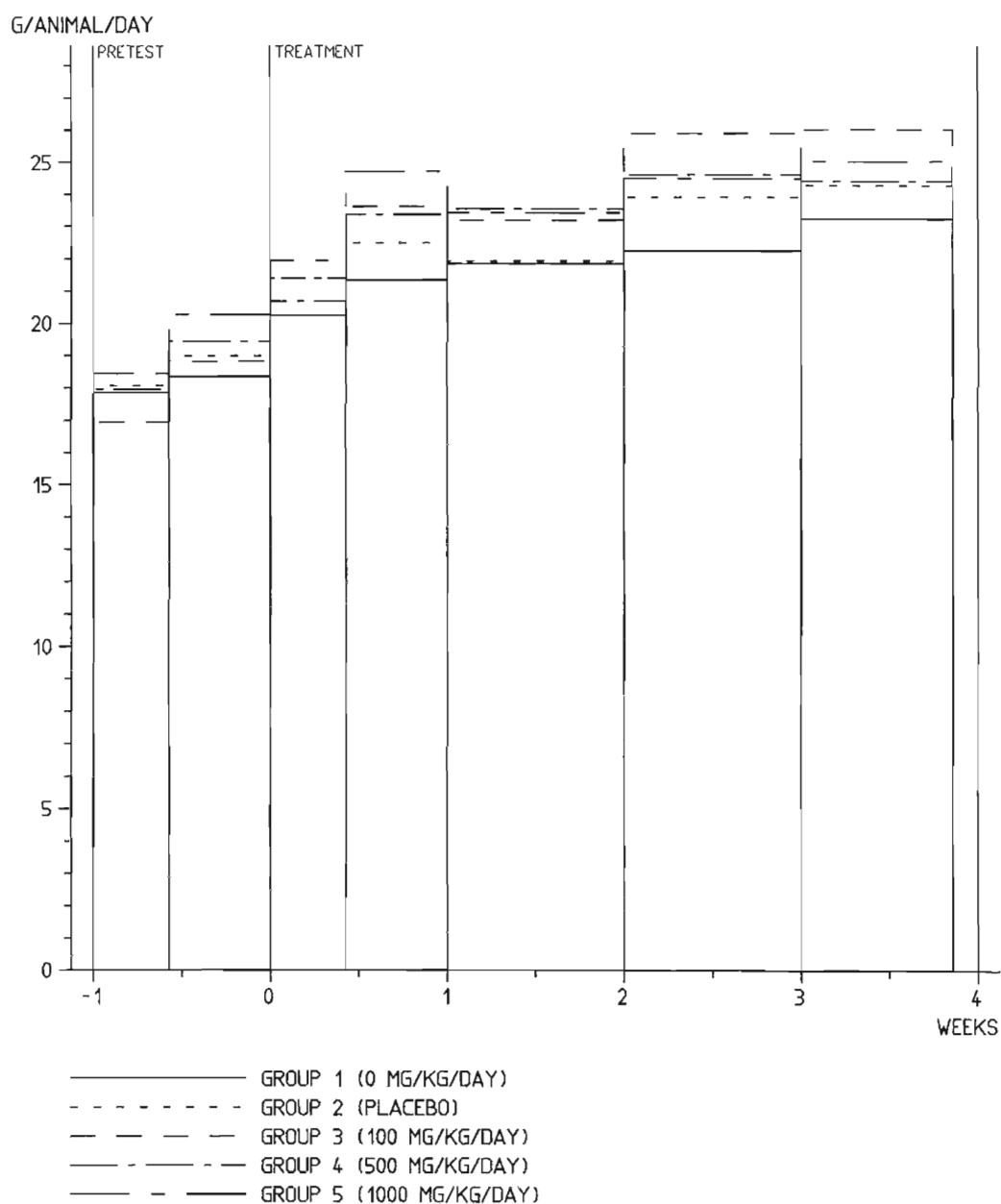
REPORT

8 FIGURES

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-SPLT - 1
22-APR-04

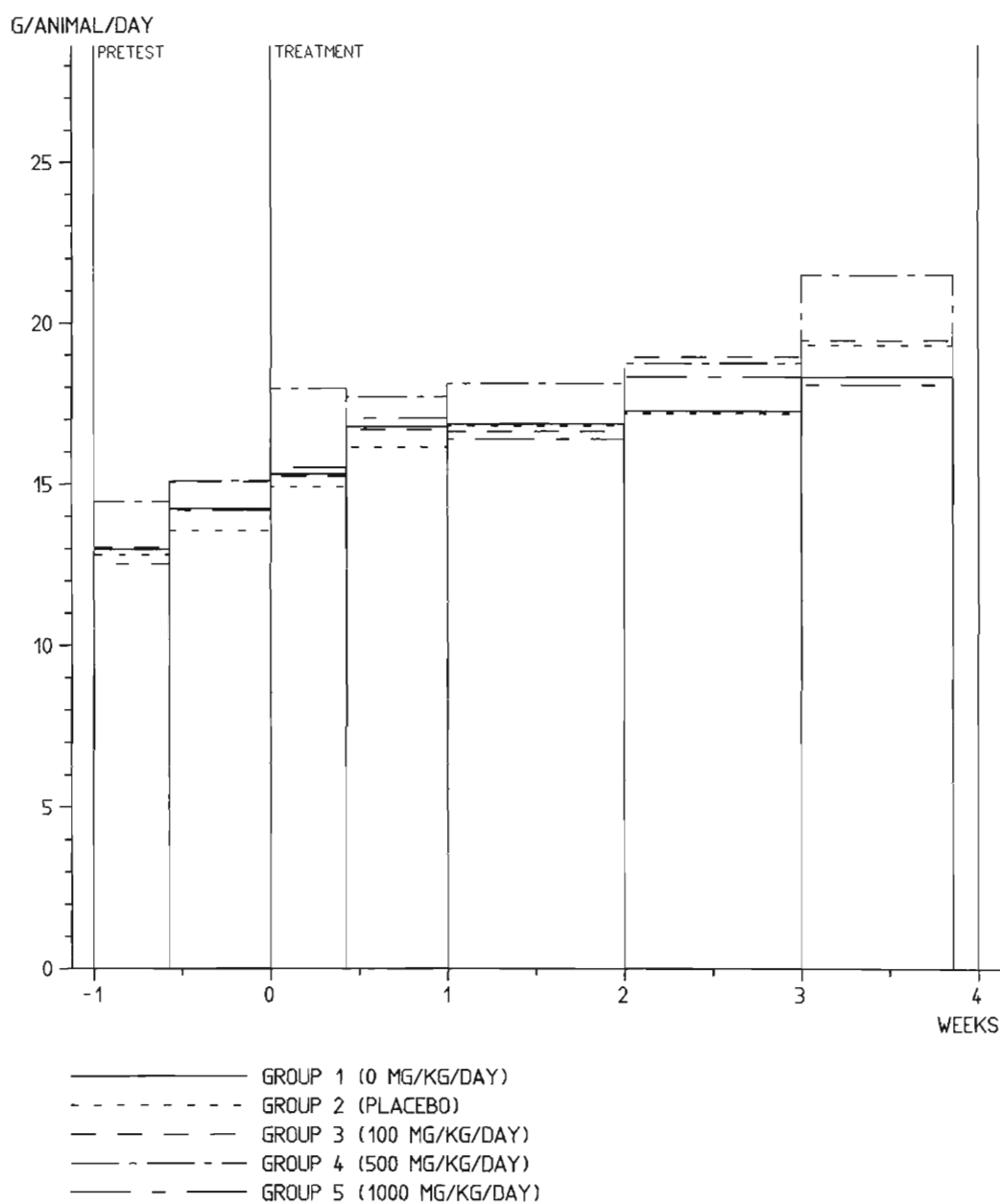
FOOD CONSUMPTION MALES



RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-SPLT - 2
22-APR-04

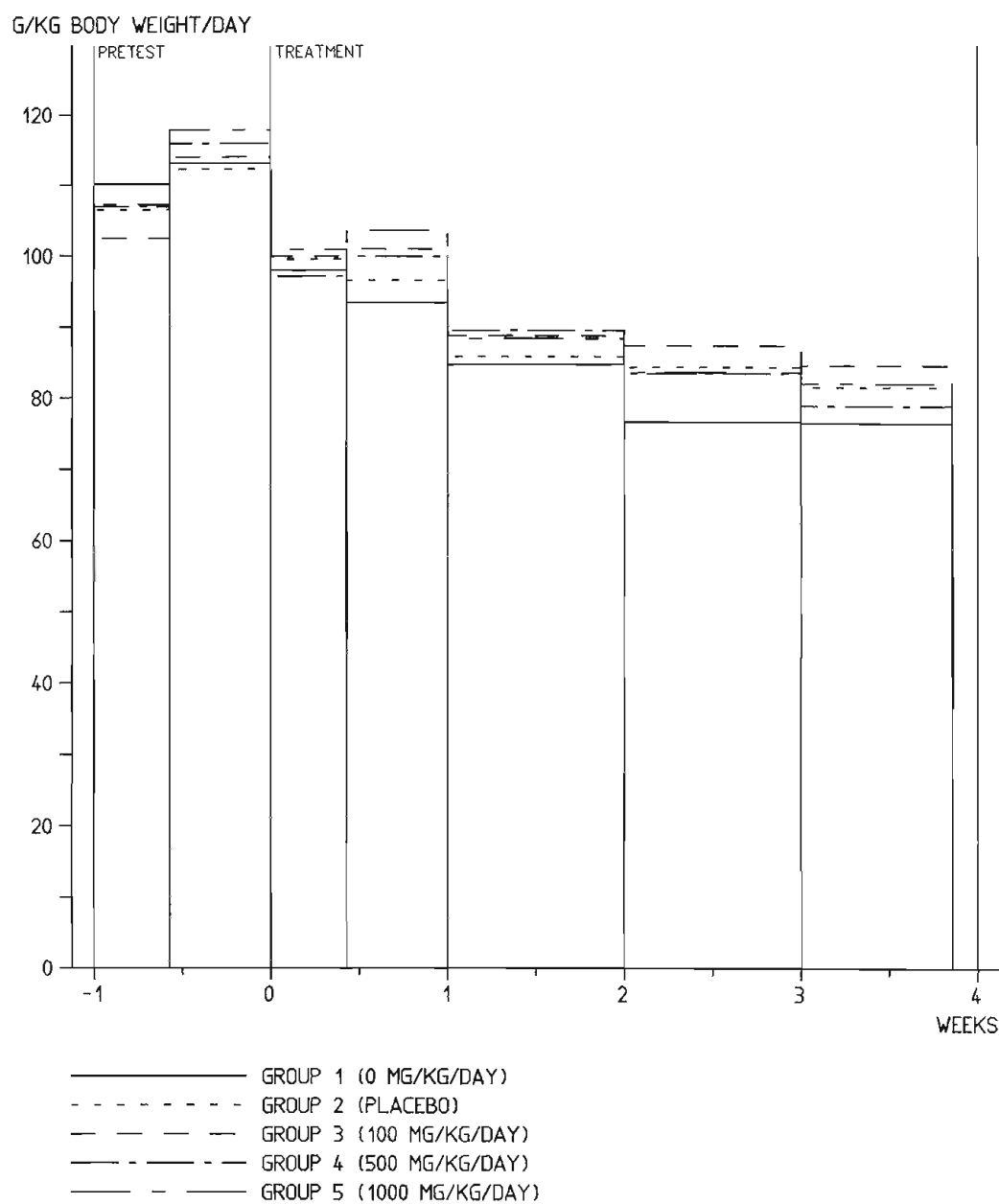
FOOD CONSUMPTION FEMALES



RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-SPLT - 1
22-APR-04

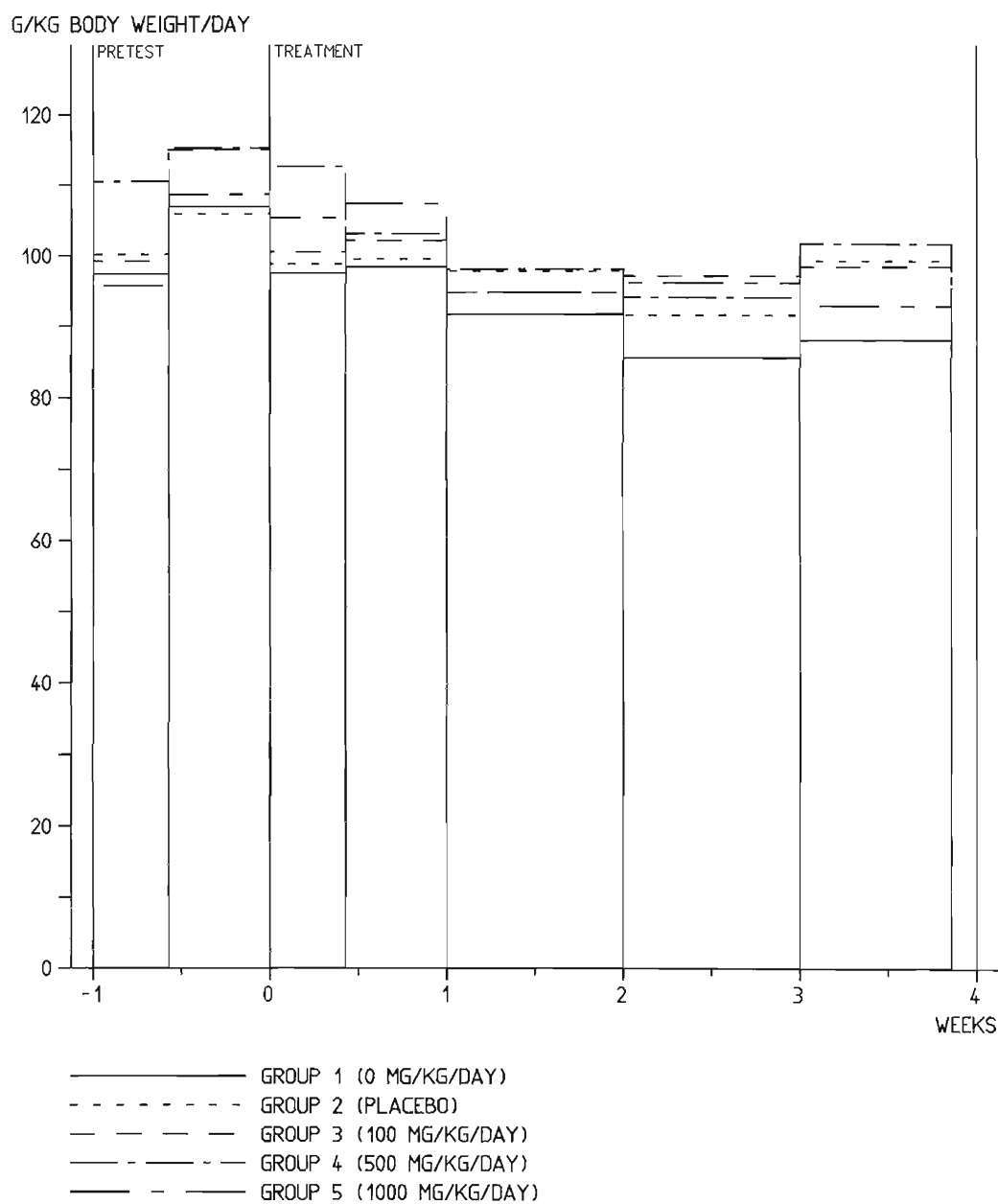
RELATIVE FOOD CONSUMPTION MALES



RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-SPLT - 2
22-APR-04

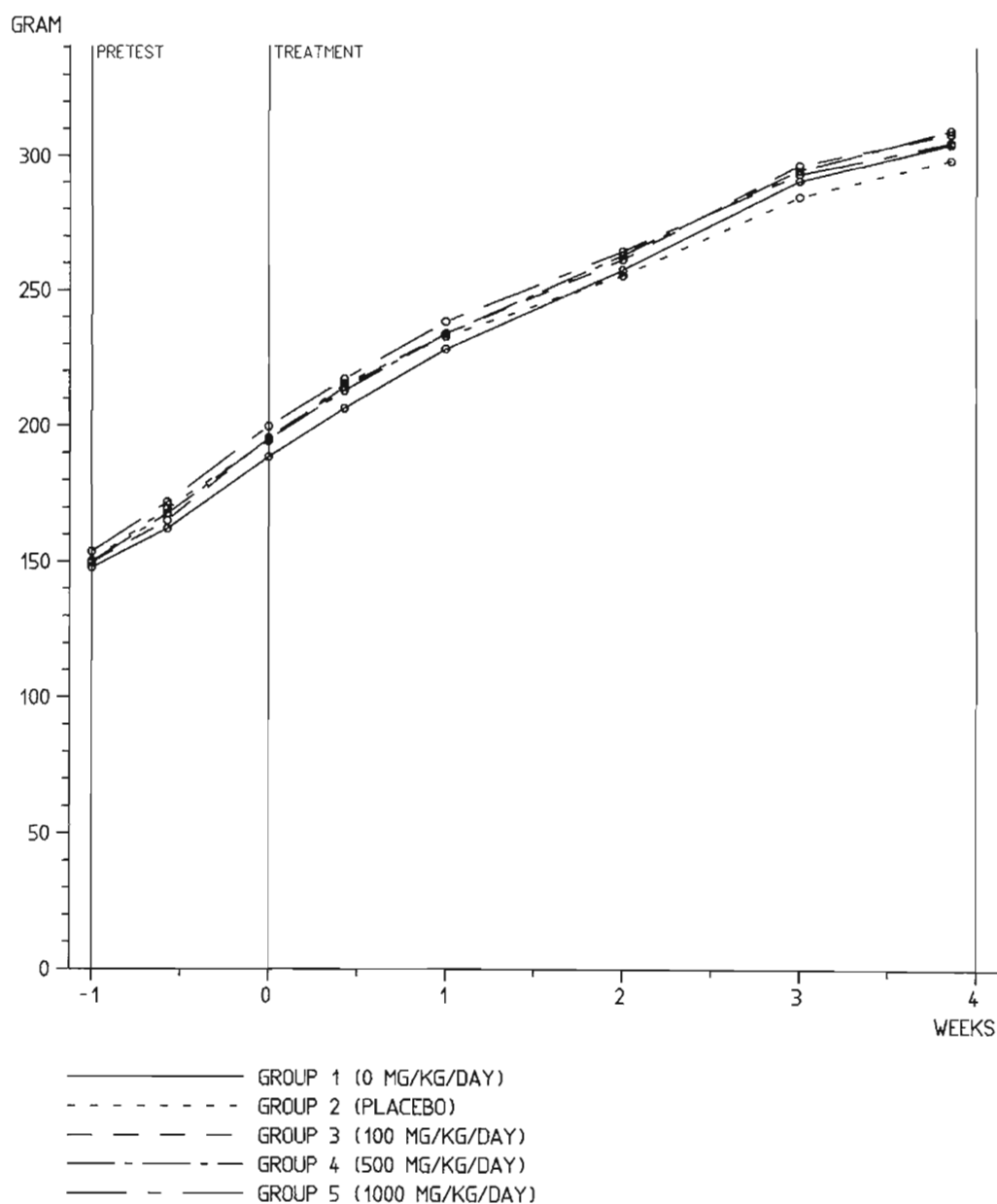
RELATIVE FOOD CONSUMPTION FEMALES



RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-SPLT - 1
22-APR-04

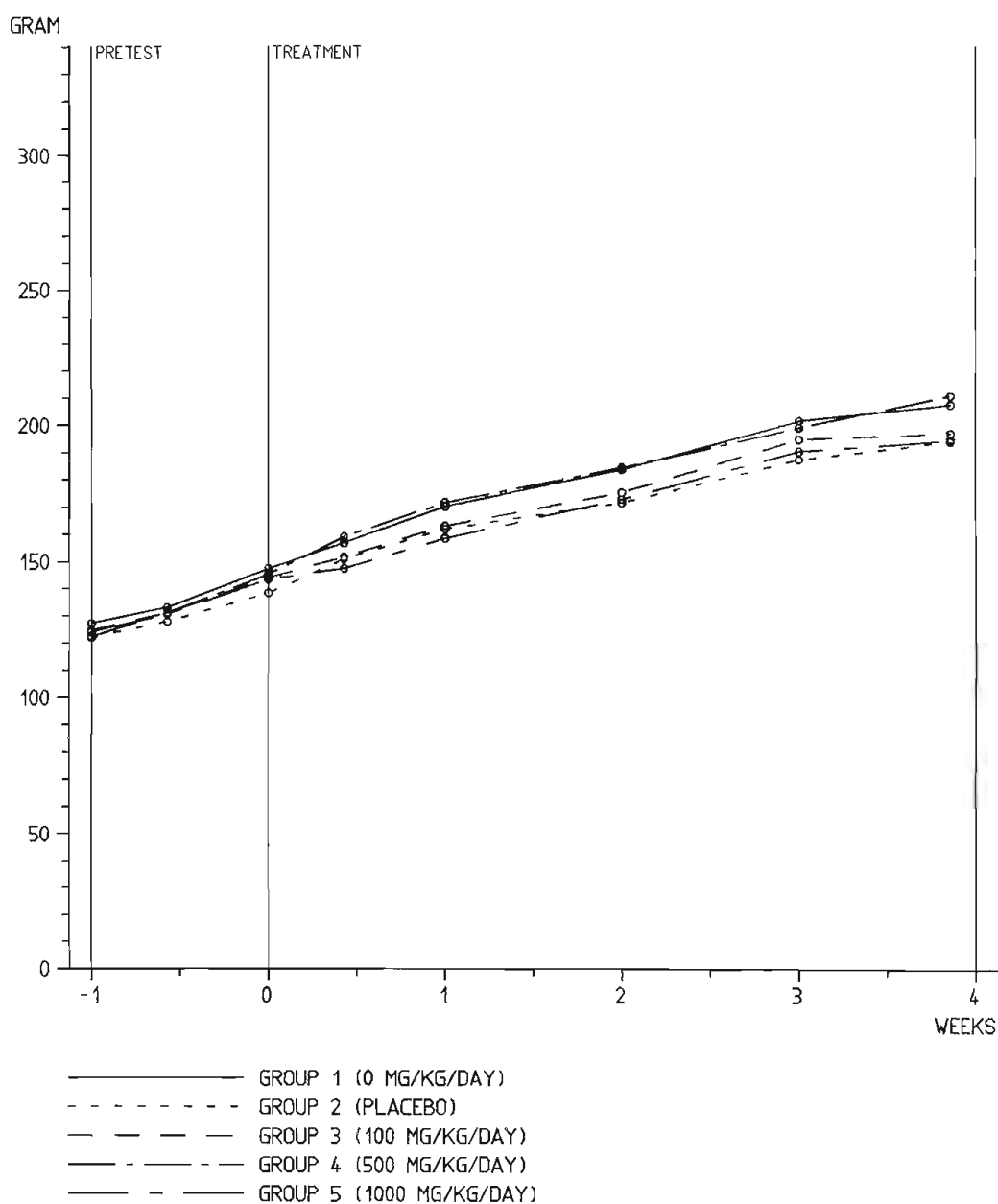
BODY WEIGHTS MALES



RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-SPLT - 2
22-APR-04

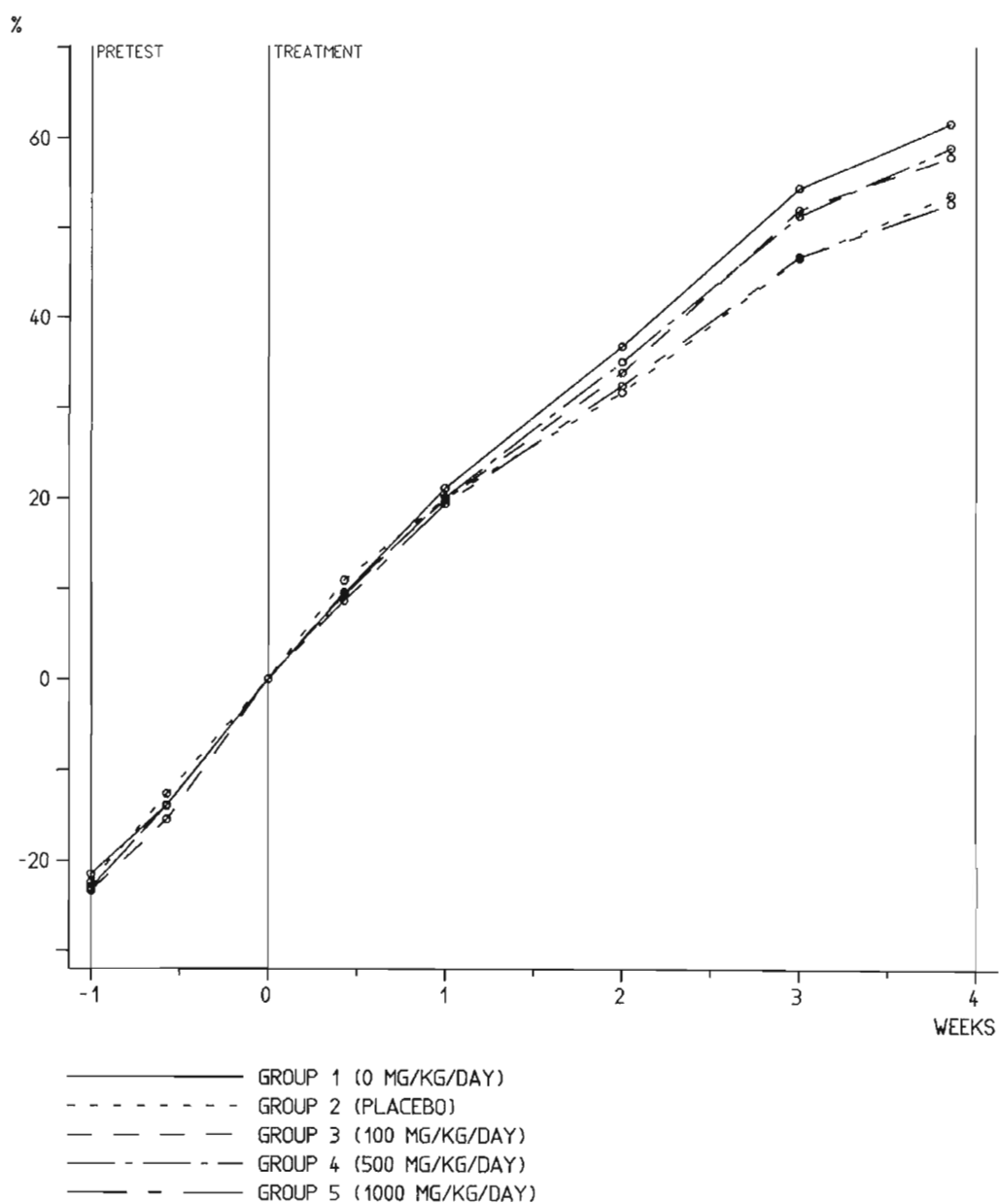
BODY WEIGHTS FEMALES



RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-SPLT - 1
22-APR-04

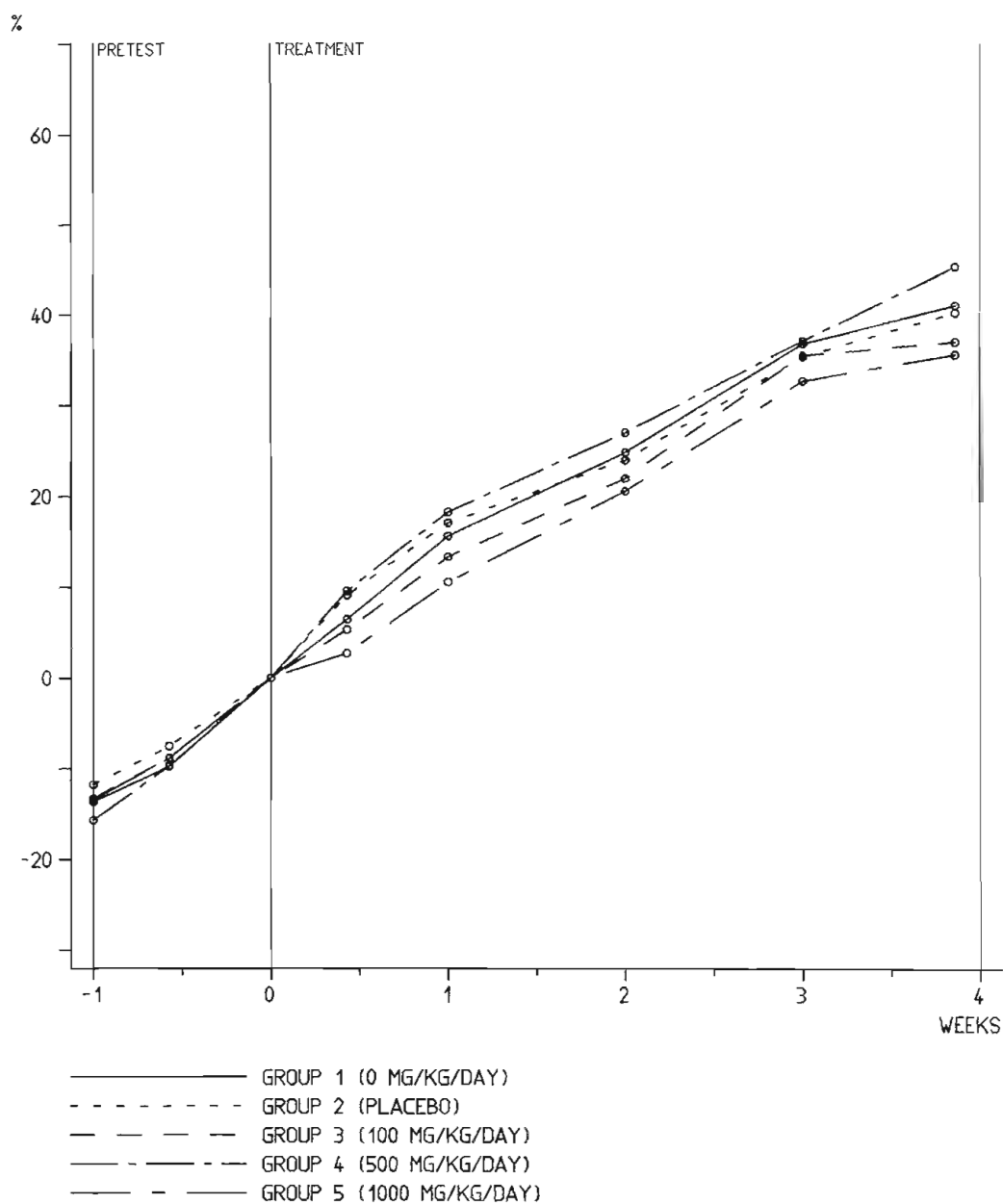
BODY WEIGHT GAIN MALES



RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-SPLT - 2
22-APR-04

BODY WEIGHT GAIN FEMALES



RCC STUDY NUMBER 853022
AXN-DMS

REPORT

9 SUMMARY TABLES

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 1
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)

MALES

GROUP 1 (0 MG/KG/DAY)

SIGN (MAX.GRADE)	PRETEST	TREATMENT
LOCATION	WEEKS: 1.....	1.....2.....3.....4.....5

NO CLINICAL SIGNS NOTED

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 2
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)

MALES

GROUP 2 (PLACEBO)

SIGN (MAX.GRADE) LOCATION	PRETEST					TREATMENT				
	WEEKS:	1.....				1.....	2.....	3.....	4.....	5
SECRETION / EXCRETION										

DARK FECES (1)	G:	111111111111111111111111			
	%:	AAAAAAAAAAAAAAAAAAAAAAAAAA			
SOFT FECES (1)	G:	1111111111			
	%:	AAAAAAAAAA			

G: Median value of the highest individual daily grades
%: Percent of affected animals (0 = less than 5%, 1 = between 5% and 15%,..., A = more than 95%)

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 3
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)

MALES

GROUP 3 (100 MG/KG/DAY)

[illegible]

G: Median value of the highest individual daily grades
%: Percent of affected animals (0 = less than 5%, 1 = between 5% and 15%, ..., A = more than 95%)

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 4
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)
MALES
GROUP 4 (500 MG/KG/DAY)

SIGN (MAX.GRADE) LOCATION	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
SECRETION / EXCRETION		
RED FECES (3)	G:122221111111112222222222
	%:AAAAAAAAAAAAAAAAAAAAAAAA
SOFT FECES (1)	G:1111111111
	%:AAAAAAAA

G: Median value of the highest individual daily grades
%: Percent of affected animals (0 = less than 5%, 1 = between 5% and 15%,..., A = more than 95%)

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 5
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)
MALES
GROUP 5 (1000 MG/KG/DAY)

SIGN (MAX.GRADE) LOCATION	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222233333333333
	%:AAAAAAAAAAAAAAAAAAAAAAAA
SOFT FECES (1)	G:111
	%:AAA

G: Median value of the highest individual daily grades
%: Percent of affected animals (0 = less than 5%, 1 = between 5% and 15%, ..., A = more than 95%)

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 6
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)
FEMALES
GROUP 1 (0 MG/KG/DAY)

SIGN (MAX.GRADE)	PRETEST	TREATMENT
LOCATION	WEEKS: 1.....	1.....2.....3.....4.....5

NO CLINICAL SIGNS NOTED

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 7
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)
FEMALES
GROUP 2 (PLACEBO)

SIGN (MAX.GRADE)	PRETEST	TREATMENT
LOCATION	WEEKS: 1.....	1.....2.....3.....4.....5
SECRETION / EXCRETION		

DARK FECES (1)	G: %:11111111111111111111AAAAAAAAAAAAAAAAAAAA
SOFT FECES (1)	G: %:1111111111AAAAAAAAA

G: Median value of the highest individual daily grades
%: Percent of affected animals (0 = less than 5%, 1 = between 5% and 15%, ..., A = more than 95%)

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 8
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)
FEMALES
GROUP 3 (100 MG/KG/DAY)

SIGN (MAX.GRADE)	PRETEST	TREATMENT
LOCATION	WEEKS: 1.....	1.....2.....3.....4.....5
SECRETION / EXCRETION		

RED FECES (3)	G:111111111111111111111111
	%:AAAAAAAAAAAAAAAAAAAAA

G: Median value of the highest individual daily grades
%: Percent of affected animals (0 = less than 5%, 1 = between 5% and 15%,..., A = more than 95%)

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 9
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)
FEMALES
GROUP 4 (500 MG/KG/DAY)

SIGN (MAX.GRADE) LOCATION	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
SECRETION / EXCRETION -----		
RED FECES (3)	G: %:122221111111112222222222AAAAAAAAAAAAAAAAAAAAAAAA
SOFT FECES (1)	G: %:1111111111AAAAAAAA

G: Median value of the highest individual daily grades
%: Percent of affected animals (0 = less than 5%, 1 = between 5% and 15%, ..., A = more than 95%)

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-SUM - 10
18-JUN-04

CLINICAL SIGNS, DAILY (SUMMARY)
FEMALES
GROUP 5 (1000 MG/KG/DAY)

SIGN (MAX.GRADE)	PRETEST	TREATMENT
LOCATION	WEEKS: 1.....	1.....2.....3.....4.....5
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222233333333333
	%:AAAAAAAAAAAAAAAAAAAAAAAA
SOFT FECES (1)	G:111
	%:AAA

G: Median value of the highest individual daily grades
%: Percent of affected animals (0 = less than 5%, 1 = between 5% and 15%, ..., A = more than 95%)

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-SUM - 1
22-APR-04

**FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES**

PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	17.9	18.1	16.9	17.9
WEEK 1	ST.DEV.	3.6	2.3	1.8	2.9
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	18.4			
	ST.DEV.	2.1			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	18.4	19.0	18.8	19.4
WEEKS 1/2	ST.DEV.	1.3	2.4	0.4	1.2
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	20.3			
	ST.DEV.	1.5			
	N	5			
MEAN OF MEANS OVER PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
	MEAN	18.1	18.5	17.9	18.7
GROUP 5 1000 MG/KG/DAY					
	MEAN	19.4			

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-SUM - 2
22-APR-04

**FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES**

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	20.2	21.4	21.4	20.7
WEEK 1	ST.DEV.	2.2	1.1	0.3	0.8
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	21.9			
	ST.DEV.	2.1			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	21.3	22.5	23.6	23.4
WEEKS 1/2	ST.DEV.	2.1	1.8	0.9	0.9
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	24.7 *			
	ST.DEV.	1.8			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 8-15	MEAN	21.8	21.9	23.2	23.5
WEEKS 2/3	ST.DEV.	1.8	1.8	0.5	0.5
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	23.4			
	ST.DEV.	2.4			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 15-22	MEAN	22.2	23.9	25.9	24.6
WEEKS 3/4	ST.DEV.	1.6	1.1	1.6	4.0
	N	5	5	5	5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

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FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES

TREATMENT		GROUP 5 1000 MG/KG/DAY			
		MEAN	24.5		
		ST.DEV.	2.4		
		N	5		
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS	22-28	MEAN	23.2	24.3	26.0
WEEK	4	ST.DEV.	1.4	1.8	24.4
		N	5	5	1.6
					5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	25.0		
		ST.DEV.	2.7		
		N	5		
MEAN OF MEANS OVER TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
		MEAN	21.8	22.8	24.0
					23.3
		GROUP 5 1000 MG/KG/DAY			
		MEAN	23.9		

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RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

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**FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES**

PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	13.0	12.8	13.0	14.5
WEEK 1	ST. DEV.	1.0	1.1	1.5	2.7
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	12.5			
	ST. DEV.	1.1			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	14.2	13.5	15.1	15.1
WEEKS 1/2	ST. DEV.	0.7	1.4	2.2	1.0
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	14.2			
	ST. DEV.	1.3			
	N	5			
MEAN OF MEANS OVER PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
	MEAN	13.6	13.2	14.0	14.8
		GROUP 5 1000 MG/KG/DAY			
	MEAN	13.4			

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CAROPHYLL STAY PINK 15% CWS

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FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	15.3	14.9	15.2	17.9 *
WEEK 1	ST.DEV.	0.9	1.2	1.6	1.9
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	15.5			
	ST.DEV.	0.7			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	16.8	16.1	16.7	17.7
WEEKS 1/2	ST.DEV.	1.3	1.2	2.3	1.3
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	17.0			
	ST.DEV.	1.4			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 8-15	MEAN	16.8	16.8	16.6	18.1
WEEKS 2/3	ST.DEV.	1.2	1.4	0.9	1.4
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	16.4			
	ST.DEV.	0.8			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 15-22	MEAN	17.2	17.1	18.9	18.7
WEEKS 3/4	ST.DEV.	1.1	1.3	1.1	1.3
	N	5	5	5	5

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CAROPHYLL STAY PINK 15% CWS

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FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES

TREATMENT		GROUP 5 1000 MG/KG/DAY			
		MEAN	18.3		
		ST.DEV.	1.5		
		N	5		
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS	22-28	MEAN	18.3	19.3	19.4
WEEK	4	ST.DEV.	1.2	2.2	2.1
		N	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	18.0		
		ST.DEV.	1.1		
		N	5		
MEAN OF MEANS OVER TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
		MEAN	16.9	16.8	17.4
					18.8
		GROUP 5 1000 MG/KG/DAY			
		MEAN	17.0		

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CAROPHYLL STAY PINK 15% CWS

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RELATIVE FOOD CONSUMPTION SUMMARY
(G/KG BODY WEIGHT/DAY)
MALES

PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	110	106	103	107
WEEK 1	ST.DEV.	22.0	10.6	8.7	16.6
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	107			
	ST.DEV.	11.0			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	113	112	114	116
WEEKS 1/2	ST.DEV.	6.0	15.5	3.6	7.2
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	118			
	ST.DEV.	7.8			
	N	5			
MEAN OF MEANS OVER PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
	MEAN	112	109	108	111
		GROUP 5 1000 MG/KG/DAY			
	MEAN	113			

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CAROPHYLL STAY PINK 15% CWS

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RELATIVE FOOD CONSUMPTION SUMMARY
(G/KG BODY WEIGHT/DAY)
MALES

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	98	100	100	97
WEEK 1	ST.DEV.	7.2	5.8	1.3	1.9
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	101			
	ST.DEV.	7.6			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	93	97	101 *	100
WEEKS 1/2	ST.DEV.	5.8	3.6	4.3	3.3
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	104 **			
	ST.DEV.	3.7			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 8-15	MEAN	85	86	89	89
WEEKS 2/3	ST.DEV.	4.6	1.7	3.6	3.6
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	88			
	ST.DEV.	4.6			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 15-22	MEAN	76	84	87	83
WEEKS 3/4	ST.DEV.	3.4	6.8	4.9	12.6
	N	5	5	5	5

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CAROPHYLL STAY PINK 15% CWS

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RELATIVE FOOD CONSUMPTION SUMMARY
(G/KG BODY WEIGHT/DAY)
MALES

TREATMENT		GROUP 5 1000 MG/KG/DAY				
		MEAN	83			
		ST. DEV.	5.4			
		N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY	
DAYS	22-28	MEAN	76	81	84 *	79
WEEK	4	ST. DEV.	2.5	3.2	6.6	3.1
		N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY				
		MEAN	82			
		ST. DEV.	3.2			
		N	5			
MEAN OF MEANS OVER TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY	
		MEAN	86	90	92	90
		GROUP 5 1000 MG/KG/DAY				
		MEAN	92			

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CAROPHYLL STAY PINK 15% CWS

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**RELATIVE FOOD CONSUMPTION SUMMARY
(G/KG BODY WEIGHT/DAY)
FEMALES**

PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	97	100	99	110
WEEK 1	ST.DEV.	5.2	8.9	8.1	21.8
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	96		
		ST.DEV.	6.6		
		N	5		
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	107	106	115	115
WEEKS 1/2	ST.DEV.	3.2	9.1	18.2	7.6
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	109		
		ST.DEV.	9.6		
		N	5		
MEAN OF MEANS OVER PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
MEAN		102	103	107	113
		GROUP 5 1000 MG/KG/DAY			
MEAN		102			

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CAROPHYLL STAY PINK 15% CWS

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RELATIVE FOOD CONSUMPTION SUMMARY
(G/KG BODY WEIGHT/DAY)
FEMALES

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	98	99	100	113 **
WEEK 1	ST.DEV.	6.0	8.6	7.3	8.6
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	105			
	ST.DEV.	2.8			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	98	100	102	103
WEEKS 1/2	ST.DEV.	6.7	5.6	11.2	6.8
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	107			
	ST.DEV.	4.3			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 8-15	MEAN	92	98	95	98
WEEKS 2/3	ST.DEV.	5.7	4.1	3.9	5.4
	N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY			
	MEAN	95			
	ST.DEV.	4.3			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 15-22	MEAN	85	92	97 **	94 *
WEEKS 3/4	ST.DEV.	5.0	4.0	2.5	5.5
	N	5	5	5	5

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CAROPHYLL STAY PINK 15% CWS

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RELATIVE FOOD CONSUMPTION SUMMARY
(G/KG BODY WEIGHT/DAY)
FEMALES

TREATMENT		GROUP 5 1000 MG/KG/DAY			
		MEAN	96 **		
		ST.DEV.	6.7		
		N	5		
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS	22-28	MEAN	88	99 *	98
WEEK	4	ST.DEV.	4.7	8.0	6.2
		N	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	93		
		ST.DEV.	5.4		
		N	5		
MEAN OF MEANS OVER TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
		MEAN	92	97	99
		GROUP 5 1000 MG/KG/DAY			
		MEAN	99		

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CAROPHYLL STAY PINK 15% CWS

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**TEST ITEM INTAKE SUMMARY
(MG SUBSTANCE/KG BODY WEIGHT/DAY)
MALES**

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	0.00	0.00	99.96	485.90
WEEK 1	ST.DEV.	0.00	0.00	1.31	9.27
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	1009.66			
	ST.DEV.	76.18			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	0.00	0.00	100.94	499.62
WEEKS 1/2	ST.DEV.	0.00	0.00	4.27	16.27
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	1035.63			
	ST.DEV.	37.16			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 8-15	MEAN	0.00	0.00	111.99	567.41
WEEKS 2/3	ST.DEV.	0.00	0.00	4.52	22.59
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	1067.89			
	ST.DEV.	55.54			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 15-22	MEAN	0.00	0.00	106.65	520.81
WEEKS 3/4	ST.DEV.	0.00	0.00	6.03	78.51
	N	5	5	5	5

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CAROPHYLL STAY PINK 15% CWS

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TEST ITEM INTAKE SUMMARY
(MG SUBSTANCE/KG BODY WEIGHT/DAY)
MALES

TREATMENT		GROUP 5 1000 MG/KG/DAY			
		MEAN	998.07		
		ST.DEV.	64.79		
		N	5		
		GROUP 1 0 MG/KG/DAY		GROUP 2 PLACEBO	
		GROUP 3 100 MG/KG/DAY		GROUP 4 500 MG/KG/DAY	
DAYS	22-28	MEAN	0.00	0.00	104.62
WEEK	4	ST.DEV.	0.00	0.00	8.23
		N	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	1000.83		
		ST.DEV.	39.11		
		N	5		
MEAN OF MEANS OVER TREATMENT		GROUP 1 0 MG/KG/DAY		GROUP 2 PLACEBO	
		GROUP 3 100 MG/KG/DAY		GROUP 4 500 MG/KG/DAY	
		MEAN	0.00	0.00	104.83
		GROUP 5 1000 MG/KG/DAY			
		MEAN	1022.42		

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CAROPHYLL STAY PINK 15% CWS

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TEST ITEM INTAKE SUMMARY
(MG SUBSTANCE/KG BODY WEIGHT/DAY)
FEMALES

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 1-4	MEAN	0.00	0.00	100.49	563.50
WEEK 1	ST. DEV.	0.00	0.00	7.26	43.04
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	1053.06			
	ST. DEV.	28.26			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 4-8	MEAN	0.00	0.00	102.12	515.39
WEEKS 1/2	ST. DEV.	0.00	0.00	11.20	33.98
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	1072.76			
	ST. DEV.	42.69			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 8-15	MEAN	0.00	0.00	107.36	533.69
WEEKS 2/3	ST. DEV.	0.00	0.00	4.43	29.37
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	1009.04			
	ST. DEV.	45.44			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAYS 15-22	MEAN	0.00	0.00	109.20	522.52
WEEKS 3/4	ST. DEV.	0.00	0.00	2.76	30.64
	N	5	5	5	5

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CAROPHYLL STAY PINK 15% CWS

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TEST ITEM INTAKE SUMMARY
(MG SUBSTANCE/KG BODY WEIGHT/DAY)
FEMALES

TREATMENT		GROUP 5 1000 MG/KG/DAY			
		MEAN	1051.00		
		ST.DEV.	72.96		
		N	5		
		GROUP 1 0 MG/KG/DAY		GROUP 2 PLACEBO	
		GROUP 3 100 MG/KG/DAY		GROUP 4 500 MG/KG/DAY	
DAYS	22-28	MEAN	0.00	0.00	110.34
WEEK	4	ST.DEV.	0.00	0.00	6.99
		N	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	1041.04		
		ST.DEV.	60.38		
		N	5		
MEAN OF MEANS OVER TREATMENT		GROUP 1 0 MG/KG/DAY		GROUP 2 PLACEBO	
		GROUP 3 100 MG/KG/DAY		GROUP 4 500 MG/KG/DAY	
		MEAN	0.00	0.00	105.90
		GROUP 5 1000 MG/KG/DAY			
		MEAN	1045.38		

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**BODY WEIGHTS (GRAM) SUMMARY
MALES**

PRETEST		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 1	MEAN	148	150	150	150
WEEK 1	ST. DEV.	5.6	6.3	6.3	4.9
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	154			
	ST. DEV.	2.3			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 4	MEAN	162	169	165	168
WEEK 1	ST. DEV.	6.4	11.3	8.2	3.7
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	172			
	ST. DEV.	3.0			
	N	5			

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CAROPHYLL STAY PINK 15% CWS

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**BODY WEIGHTS (GRAM) SUMMARY
MALES**

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 1	MEAN	188	194	195	195
WEEK 1	ST. DEV.	9.1	15.3	6.1	5.1
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	200			
	ST. DEV.	2.9			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 4	MEAN	206	215	214	213
WEEK 1	ST. DEV.	10.5	14.3	4.9	6.0
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	217			
	ST. DEV.	6.1			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 8	MEAN	228	233	234	234
WEEK 2	ST. DEV.	11.5	18.0	5.0	5.8
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	238			
	ST. DEV.	10.1			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 15	MEAN	258	255	261	263
WEEK 3	ST. DEV.	12.7	17.5	5.1	5.9
	N	5	5	5	5

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CAROPHYLL STAY PINK 15% CWS

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**BODY WEIGHTS (GRAM) SUMMARY
MALES**

TREATMENT		GROUP 5 1000 MG/KG/DAY				
		MEAN	264			
		ST. DEV.	14.6			
		N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY	
DAY	22	MEAN	291	285	297	295
WEEK	4	ST. DEV.	13.9	20.3	5.0	10.1
		N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY				
		MEAN	293			
		ST. DEV.	18.8			
		N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY	
DAY	28	MEAN	304	298	308	309
WEEK	4	ST. DEV.	16.5	26.6	5.1	9.2
		N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY				
		MEAN	305			
		ST. DEV.	25.3			
		N	5			

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-SUM - 4
22-APR-04

**BODY WEIGHTS (GRAM) SUMMARY
FEMALES**

PRETEST			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	1	MEAN	127	122	125	122
WEEK	1	ST.DEV.	4.5	4.1	5.5	3.1
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
			MEAN	124		
			ST.DEV.	3.9		
			N	5		
			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	4	MEAN	133	128	131	131
WEEK	1	ST.DEV.	4.8	4.0	7.3	6.1
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
			MEAN	131		
			ST.DEV.	3.7		
			N	5		

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-SUM - 5
22-APR-04

**BODY WEIGHTS (GRAM) SUMMARY
FEMALES**

TREATMENT			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	1	MEAN	147	138	144	145
WEEK	1	ST.DEV.	5.6	3.2	8.4	6.9
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
		MEAN	143			
		ST.DEV.	4.7			
		N	5			
			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	4	MEAN	157	151	151	159
WEEK	1	ST.DEV.	4.2	4.4	9.5	7.9
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
		MEAN	147			
		ST.DEV.	7.0			
		N	5			
			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	8	MEAN	170	162	163	172
WEEK	2	ST.DEV.	2.8	8.1	10.7	6.6
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
		MEAN	159			
		ST.DEV.	8.3			
		N	5			
			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	15	MEAN	184	171 *	175	184
WEEK	3	ST.DEV.	5.7	8.6	7.8	8.2
		N	5	5	5	5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-SUM - 6
22-APR-04

**BODY WEIGHTS (GRAM) SUMMARY
FEMALES**

TREATMENT		GROUP 5 1000 MG/KG/DAY			
		MEAN	173		
		ST.DEV.	5.3		
		N	5		
		GROUP 1 0 MG/KG/DAY		GROUP 2 PLACEBO	
		GROUP 3 100 MG/KG/DAY		GROUP 4 500 MG/KG/DAY	
DAY	22	MEAN	201	187	195
WEEK	4	ST.DEV.	3.1	11.3	9.0
		N	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	190		
		ST.DEV.	8.4		
		N	5		
		GROUP 1 0 MG/KG/DAY		GROUP 2 PLACEBO	
		GROUP 3 100 MG/KG/DAY		GROUP 4 500 MG/KG/DAY	
DAY	28	MEAN	208	194	197
WEEK	4	ST.DEV.	5.0	11.8	13.1
		N	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	194		
		ST.DEV.	7.9		
		N	5		

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-SUM - 1
22-APR-04

**BODY WEIGHT GAIN (%) SUMMARY
MALES**

PRETEST			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	1	MEAN	-21.5	-22.5	-23.4	-23.1
WEEK	1	ST.DEV.	3.1	4.7	1.1	1.7
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
			MEAN	-23.0		
			ST.DEV.	1.9		
			N	5		
			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	4	MEAN	-13.9	-12.7	-15.5	-13.9
WEEK	1	ST.DEV.	1.7	2.9	1.6	1.9
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
			MEAN	-13.9		
			ST.DEV.	0.8		
			N	5		

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-SUM - 2
22-APR-04

**BODY WEIGHT GAIN (%) SUMMARY
MALES**

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 1	MEAN	0.0	0.0	0.0	0.0
WEEK 1	ST. DEV.	0.0	0.0	0.0	0.0
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	0.0			
	ST. DEV.	0.0			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 4	MEAN	9.4	10.9	9.6	9.2
WEEK 1	ST. DEV.	1.1	2.0	1.2	0.9
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	8.6			
	ST. DEV.	1.9			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 8	MEAN	21.1	19.9	19.8	20.0
WEEK 2	ST. DEV.	2.9	3.9	1.5	1.7
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	19.3			
	ST. DEV.	4.1			
	N	5			
TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 15	MEAN	36.8	31.6	33.8	35.1
WEEK 3	ST. DEV.	5.6	3.9	3.5	1.6
	N	5	5	5	5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-SUM - 3
22-APR-04

**BODY WEIGHT GAIN (%) SUMMARY
MALES**

TREATMENT		GROUP 5 1000 MG/KG/DAY			
		MEAN	32.4		
		ST.DEV.	6.5		
		N	5		
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	22	MEAN	54.3	46.6	51.9
WEEK	4	ST.DEV.	6.8	4.6	5.5
		N	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	46.7		
		ST.DEV.	8.4		
		N	5		
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	28	MEAN	61.6	53.6	57.9
WEEK	4	ST.DEV.	7.9	5.0	5.7
		N	5	5	5
		GROUP 5 1000 MG/KG/DAY			
		MEAN	52.7		
		ST.DEV.	11.7		
		N	5		

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-SUM - 4
22-APR-04

**BODY WEIGHT GAIN (%) SUMMARY
FEMALES**

PRETEST			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	1	MEAN	-13.7	-11.7	-13.3	-15.7
WEEK	1	ST.DEV.	1.5	1.7	3.4	2.3
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
			MEAN	-13.4		
			ST.DEV.	3.1		
			N	5		
			GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY	4	MEAN	-9.7	-7.5	-8.8	-9.7
WEEK	1	ST.DEV.	0.5	1.4	1.9	1.6
		N	5	5	5	5
			GROUP 5 1000 MG/KG/DAY			
			MEAN	-8.9		
			ST.DEV.	1.5		
			N	5		

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-SUM - 5
22-APR-04

**BODY WEIGHT GAIN (%) SUMMARY
FEMALES**

TREATMENT		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 1	MEAN	0.0	0.0	0.0	0.0
WEEK 1	ST.DEV.	0.0	0.0	0.0	0.0
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	0.0			
	ST.DEV.	0.0			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 4	MEAN	6.4	9.1	5.3	9.6
WEEK 1	ST.DEV.	2.7	2.3	1.5	2.3
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	2.7			
	ST.DEV.	2.5			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 8	MEAN	15.6	17.1	13.3	18.2
WEEK 2	ST.DEV.	3.7	4.7	2.4	3.6
	N	5	5	5	5
GROUP 5 1000 MG/KG/DAY					
	MEAN	10.5			
	ST.DEV.	2.8			
	N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY
DAY 15	MEAN	24.8	23.9	21.9	27.0
WEEK 3	ST.DEV.	6.9	4.7	4.8	2.2
	N	5	5	5	5

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-SUM - 6
22-APR-04

**BODY WEIGHT GAIN (%) SUMMARY
FEMALES**

TREATMENT		GROUP 5 1000 MG/KG/DAY				
		MEAN	20.5			
		ST. DEV.	2.6			
		N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY	
DAY	22	MEAN	36.8	35.4	35.5	37.1
WEEK	4	ST. DEV.	3.6	7.2	5.2	4.3
		N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY				
		MEAN	32.7			
		ST. DEV.	2.7			
		N	5			
		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DAY	GROUP 4 500 MG/KG/DAY	
DAY	28	MEAN	41.1	40.3	37.0	45.4
WEEK	4	ST. DEV.	6.9	7.3	7.2	4.1
		N	5	5	5	5
		GROUP 5 1000 MG/KG/DAY				
		MEAN	35.6			
		ST. DEV.	2.7			
		N	5			

* / ** : Dunnett-Test based on pooled variance significant at 5% (*) or 1% (**) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-SUM - 1
22-APR-04

**MACROSCOPICAL FINDINGS SUMMARY
MALES**

	GROUP 1 0 MG/KG/DAY		GROUP 2 PLACEBO		GROUP 3 100 MG/KG/DA		GROUP 4 500 MG/KG/DA		GROUP 5 1000 MG/KG/D		
ANIMALS EXAMINED	5		5		5		5		5		
ANIMALS WITHOUT FINDINGS	4		4		2		2		3		
ANIMALS AFFECTED:											
CAECUM.....	1		0		0		3		1		
DISCOLORATION	20%		0%		0%		60%		20%		
PANCREAS.....	0		0		1		0		0		
DISCOLORATION	0%		0%		20%		0%		0%		
KIDNEYS.....	0		1		0		0		0		
DISCOLORATION	0%		20%		0%		0%		0%		
THYROID GLAND.....	0		1		0		0		0		
DISCOLORATION	0%		20%		0%		0%		0%		
SPLEEN.....	0		1		0		0		0		
ENLARGED	0%		20%		0%		0%		0%		
THYMUS.....	0		0		1		0		0		
FOCUS/FOCI	0%		0%		20%		0%		0%		
THICKENED	0		0		2		0		1		
	0%		0%		40%		0%		20%		

/ ## : Fisher's Exact Test based on counts significant at 5% (#) or 1% (##) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-SUM - 2
22-APR-04

**MACROSCOPICAL FINDINGS SUMMARY
FEMALES**

	GROUP 1 0 MG/KG/DAY		GROUP 2 PLACEBO		GROUP 3 100 MG/KG/DA		GROUP 4 500 MG/KG/DA		GROUP 5 1000 MG/KG/D	
ANIMALS EXAMINED	5		5		5		5		5	
ANIMALS WITHOUT FINDINGS	1		3		2		0		0	
ANIMALS AFFECTED:										
STOMACH.....										
DISCOLORATION	0	0%	0	0%	0	0%	1	20%	0	0%
CAECUM.....										
DISCOLORATION	1	20%	1	20%	0	0%	1	20%	5 #	100%
PANCREAS.....										
DISCOLORATION	3	60%	0	0%	0	0%	0	0%	1	20%
KIDNEYS.....										
PELVIC DILATION	0	0%	1	20%	1	20%	0	0%	1	20%
OVARIES.....										
DISCOLORATION	1	20%	0	0%	0	0%	1	20%	0	0%
ENLARGED	0	0%	0	0%	1	20%	0	0%	0	0%
WATERY CYST	0	0%	0	0%	0	0%	1	20%	0	0%
THYMUS.....										
DISCOLORATION	1	20%	0	0%	0	0%	0	0%	0	0%
THICKENED	0	0%	0	0%	1	20%	1	20%	0	0%
MANDIBULAR L.NODE.....										
DISCOLORATION	1	20%	0	0%	0	0%	0	0%	1	20%

/ ## : Fisher's Exact Test based on counts significant at 5% (#) or 1% (##) level

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-SUM - 1
22-APR-04

**ORGAN WEIGHTS (GRAM) SUMMARY
AFTER 4 WEEKS
MALES**

		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DA	GROUP 4 500 MG/KG/DA	GROUP 5 1000 MG/KG/D
BODY W.	MEAN	285.75	277.44	289.10	285.84	284.54
	ST.DEV.	14.63	24.12	3.12	9.71	24.81
	N	5	5	5	5	5
BRAIN	MEAN	1.85	1.93	1.92	1.92	1.90
	ST.DEV.	0.05	0.07	0.09	0.01	0.04
	N	5	5	5	5	5
HEART	MEAN	0.922	0.938	0.989	0.996	0.958
	ST.DEV.	0.065	0.126	0.073	0.069	0.078
	N	5	5	5	5	5
THYROIDS	MEAN	0.019	0.021	0.024	0.022	0.023
	ST.DEV.	0.006	0.006	0.003	0.001	0.003
	N	5	5	5	5	5
LIVER	MEAN	7.67	8.55	8.12	8.38	8.25
	ST.DEV.	0.55	1.20	0.41	0.40	0.68
	N	5	5	5	5	5
THYMUS	MEAN	0.42	0.45	0.52	0.45	0.50
	ST.DEV.	0.14	0.11	0.16	0.03	0.11
	N	5	5	5	5	5
KIDNEYS	MEAN	1.84	1.99	1.96	1.93	1.97
	ST.DEV.	0.17	0.20	0.06	0.17	0.13
	N	5	5	5	5	5
ADRENALS	MEAN	0.062	0.061	0.066	0.066	0.069
	ST.DEV.	0.010	0.006	0.006	0.003	0.007
	N	5	5	5	5	5
SPLEEN	MEAN	0.575	0.946	0.715	0.707	0.641
	ST.DEV.	0.095	0.610	0.088	0.044	0.084
	N	5	5	5	5	5
TESTES	MEAN	3.28	3.41	3.44	3.43	3.38
	ST.DEV.	0.28	0.27	0.28	0.13	0.16
	N	5	5	5	5	5
EPIDIDYMIDES	MEAN	0.961	0.997	1.003	0.954	1.000
	ST.DEV.	0.103	0.041	0.101	0.058	0.095
	N	5	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-SUM - 2
22-APR-04

**ORGAN/BODY WEIGHT RATIOS SUMMARY
AFTER 4 WEEKS
MALES**

		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DA	GROUP 4 500 MG/KG/DA	GROUP 5 1000 MG/KG/D
BODY W. (GRAM)	MEAN ST.DEV. N	285.75 14.63 5	277.44 24.12 5	289.10 3.12 5	285.84 9.71 5	284.54 24.81 5
BRAIN (%)	MEAN ST.DEV. N	0.65 0.02 5	0.70 0.05 5	0.66 0.03 5	0.67 0.02 5	0.67 0.04 5
HEART (%)	MEAN ST.DEV. N	0.323 0.010 5	0.337 0.027 5	0.342 0.024 5	0.348 0.022 5	0.337 0.018 5
THYROIDES (%)	MEAN ST.DEV. N	0.006 0.002 5	0.008 0.002 5	0.008 0.001 5	0.008 0.001 5	0.008 0.001 5
LIVER (%)	MEAN ST.DEV. N	2.68 0.10 5	3.07 ** 0.24 5	2.81 0.15 5	2.93 0.13 5	2.90 0.09 5
THYMUS (%)	MEAN ST.DEV. N	0.15 0.04 5	0.16 0.03 5	0.18 0.05 5	0.16 0.01 5	0.18 0.03 5
KIDNEYS (%)	MEAN ST.DEV. N	0.64 0.04 5	0.72 * 0.04 5	0.68 0.02 5	0.68 0.06 5	0.70 0.04 5
ADRENALS (%)	MEAN ST.DEV. N	0.022 0.004 5	0.022 0.002 5	0.023 0.002 5	0.023 0.002 5	0.025 0.004 5
SPLEEN (%)	MEAN ST.DEV. N	0.200 0.024 5	0.342 0.220 5	0.247 0.029 5	0.248 0.016 5	0.226 0.028 5
TESTES (%)	MEAN ST.DEV. N	1.15 0.12 5	1.24 0.15 5	1.19 0.09 5	1.20 0.06 5	1.19 0.08 5
EPIDIDYMIDES (%)	MEAN ST.DEV. N	0.336 0.032 5	0.361 0.032 5	0.347 0.035 5	0.334 0.018 5	0.353 0.038 5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-SUM - 3
22-APR-04

**ORGAN/BRAIN WEIGHT RATIOS SUMMARY
AFTER 4 WEEKS
MALES**

		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DA	GROUP 4 500 MG/KG/DA	GROUP 5 1000 MG/KG/D
BRAIN (GRAM)	MEAN ST. DEV. N	1.85 0.05 5	1.93 0.07 5	1.92 0.09 5	1.92 0.01 5	1.90 0.04 5
HEART (%)	MEAN ST. DEV. N	49.888 3.289 5	48.618 6.412 5	51.536 4.156 5	51.797 3.431 5	50.328 3.516 5
THYROIDES (%)	MEAN ST. DEV. N	1.003 0.303 5	1.105 0.296 5	1.258 0.173 5	1.161 0.064 5	1.206 0.159 5
LIVER (%)	MEAN ST. DEV. N	414.82 19.78 5	442.77 54.58 5	423.80 36.30 5	436.07 18.66 5	433.21 26.25 5
THYMUS (%)	MEAN ST. DEV. N	22.70 7.14 5	23.42 4.88 5	27.32 8.12 5	23.37 1.71 5	26.24 5.22 5
KIDNEYS (%)	MEAN ST. DEV. N	99.27 8.28 5	103.03 7.79 5	102.45 6.28 5	100.47 8.34 5	103.63 4.93 5
ADRENALS (%)	MEAN ST. DEV. N	3.329 0.535 5	3.154 0.200 5	3.413 0.252 5	3.434 0.179 5	3.633 0.411 5
SPLEEN (%)	MEAN ST. DEV. N	31.096 4.862 5	48.747 30.469 5	37.313 5.450 5	36.801 2.305 5	33.671 3.944 5
TESTES (%)	MEAN ST. DEV. N	177.46 16.45 5	176.92 14.31 5	178.91 12.51 5	178.17 6.52 5	177.51 5.93 5
EPIDIDYMIDES (%)	MEAN ST. DEV. N	52.056 5.851 5	51.786 3.329 5	52.296 5.699 5	49.607 2.799 5	52.523 4.382 5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-SUM - 4
22-APR-04

**ORGAN WEIGHTS (GRAM) SUMMARY
AFTER 4 WEEKS
FEMALES**

		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DA	GROUP 4 500 MG/KG/DA	GROUP 5 1000 MG/KG/D
BODY W.	MEAN	190.85	180.27	184.41	189.15	177.96
	ST.DEV.	4.08	12.31	11.24	6.07	7.29
	N	5	5	5	5	5
BRAIN	MEAN	1.83	1.81	1.80	1.79	1.84
	ST.DEV.	0.08	0.09	0.04	0.05	0.08
	N	5	5	5	5	5
HEART	MEAN	0.675	0.659	0.696	0.729	0.676
	ST.DEV.	0.063	0.074	0.075	0.090	0.054
	N	5	5	5	5	5
THYROIDES	MEAN	0.022	0.018	0.019	0.021	0.019
	ST.DEV.	0.005	0.003	0.003	0.003	0.002
	N	5	5	5	5	5
LIVER	MEAN	5.80	6.06	5.90	5.89	5.74
	ST.DEV.	0.20	0.81	0.74	0.65	0.37
	N	5	5	5	5	5
THYMUS	MEAN	0.44	0.43	0.44	0.44	0.42
	ST.DEV.	0.02	0.04	0.15	0.13	0.07
	N	5	5	5	5	5
KIDNEYS	MEAN	1.39	1.19	1.39	1.38	1.37
	ST.DEV.	0.06	0.26	0.15	0.11	0.06
	N	5	5	5	5	5
ADRENALS	MEAN	0.083	0.069 *	0.071	0.084	0.078
	ST.DEV.	0.009	0.008	0.006	0.007	0.007
	N	5	5	5	5	5
SPLEEN	MEAN	0.456	0.453	0.499	0.485	0.496
	ST.DEV.	0.046	0.069	0.053	0.067	0.110
	N	5	5	5	5	5
OVARIES	MEAN	0.113	0.101	0.108	0.147	0.102
	ST.DEV.	0.011	0.022	0.032	0.091	0.011
	N	5	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-SUM - 5
22-APR-04

**ORGAN/BODY WEIGHT RATIOS SUMMARY
AFTER 4 WEEKS
FEMALES**

		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DA	GROUP 4 500 MG/KG/DA	GROUP 5 1000 MG/KG/D
BODY W. (GRAM)	MEAN ST.DEV. N	190.85 4.08 5	180.27 12.31 5	184.41 11.24 5	189.15 6.07 5	177.96 7.29 5
BRAIN (%)	MEAN ST.DEV. N	0.96 0.05 5	1.01 0.08 5	0.98 0.04 5	0.95 0.02 5	1.03 0.04 5
HEART (%)	MEAN ST.DEV. N	0.354 0.035 5	0.365 0.027 5	0.377 0.024 5	0.385 0.041 5	0.381 0.040 5
THYROIDS (%)	MEAN ST.DEV. N	0.011 0.002 5	0.010 0.002 5	0.010 0.001 5	0.011 0.002 5	0.011 0.001 5
LIVER (%)	MEAN ST.DEV. N	3.04 0.05 5	3.35 0.24 5	3.19 0.24 5	3.11 0.31 5	3.23 0.26 5
THYMUS (%)	MEAN ST.DEV. N	0.23 0.01 5	0.24 0.03 5	0.24 0.07 5	0.23 0.06 5	0.23 0.03 5
KIDNEYS (%)	MEAN ST.DEV. N	0.73 0.04 5	0.67 0.16 5	0.75 0.07 5	0.73 0.05 5	0.77 0.06 5
ADRENALS (%)	MEAN ST.DEV. N	0.044 0.005 5	0.038 0.003 5	0.039 0.003 5	0.044 0.003 5	0.044 0.005 5
SPLEEN (%)	MEAN ST.DEV. N	0.239 0.024 5	0.251 0.032 5	0.271 0.023 5	0.256 0.036 5	0.277 0.052 5
OVARIES (%)	MEAN ST.DEV. N	0.059 0.005 5	0.056 0.010 5	0.059 0.017 5	0.078 0.049 5	0.057 0.007 5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-SUM - 6
22-APR-04

**ORGAN/BRAIN WEIGHT RATIOS SUMMARY
AFTER 4 WEEKS
FEMALES**

		GROUP 1 0 MG/KG/DAY	GROUP 2 PLACEBO	GROUP 3 100 MG/KG/DA	GROUP 4 500 MG/KG/DA	GROUP 5 1000 MG/KG/D
BRAIN (GRAM)	MEAN	1.83	1.81	1.80	1.79	1.84
	ST.DEV.	0.08	0.09	0.04	0.05	0.08
	N	5	5	5	5	5
HEART (%)	MEAN	36.840	36.668	38.698	40.761	36.953
	ST.DEV.	3.677	5.425	3.359	4.752	3.981
	N	5	5	5	5	5
THYROIDES (%)	MEAN	1.177	0.985	1.076	1.153	1.050
	ST.DEV.	0.231	0.185	0.126	0.196	0.089
	N	5	5	5	5	5
LIVER (%)	MEAN	316.65	336.48	328.27	329.68	313.16
	ST.DEV.	15.29	50.22	34.26	39.37	24.35
	N	5	5	5	5	5
THYMUS (%)	MEAN	23.80	23.80	24.40	24.77	22.79
	ST.DEV.	1.76	1.92	7.75	6.43	3.97
	N	5	5	5	5	5
KIDNEYS (%)	MEAN	75.74	65.47	77.29	77.08	74.91
	ST.DEV.	6.41	12.25	8.01	6.66	6.26
	N	5	5	5	5	5
ADRENALS (%)	MEAN	4.545	3.849	3.968	4.700	4.291
	ST.DEV.	0.509	0.464	0.288	0.389	0.519
	N	5	5	5	5	5
SPLEEN (%)	MEAN	24.941	25.062	27.797	27.115	26.860
	ST.DEV.	3.177	3.330	2.537	3.819	4.735
	N	5	5	5	5	5
OVARIES (%)	MEAN	6.184	5.617	5.995	8.310	5.559
	ST.DEV.	0.463	1.434	1.742	5.383	0.745
	N	5	5	5	5	5

*/**: Dunnett-test based on pooled variance sig. at 5% or 1% level.

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

10 INDIVIDUAL TABLES

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 1
22-APR-04

MORTALITY DATA

MALES

GROUP 1 (0 MG/KG/DAY)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
1	14-APR-04	17-MAR-04	13-APR-04
2	14-APR-04	17-MAR-04	13-APR-04
3	14-APR-04	17-MAR-04	13-APR-04
4	14-APR-04	17-MAR-04	13-APR-04
5	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 2
22-APR-04

MORTALITY DATA
MALES
GROUP 2 (PLACEBO)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
6	14-APR-04	17-MAR-04	13-APR-04
7	14-APR-04	17-MAR-04	13-APR-04
8	14-APR-04	17-MAR-04	13-APR-04
9	14-APR-04	17-MAR-04	13-APR-04
10	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 3
22-APR-04

MORTALITY DATA

MALES

GROUP 3 (100 MG/KG/DAY)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
11	14-APR-04	17-MAR-04	13-APR-04
12	14-APR-04	17-MAR-04	13-APR-04
13	14-APR-04	17-MAR-04	13-APR-04
14	14-APR-04	17-MAR-04	13-APR-04
15	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 4
22-APR-04

MORTALITY DATA

MALES

GROUP 4 (500 MG/KG/DAY)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
16	14-APR-04	17-MAR-04	13-APR-04
17	14-APR-04	17-MAR-04	13-APR-04
18	14-APR-04	17-MAR-04	13-APR-04
19	14-APR-04	17-MAR-04	13-APR-04
20	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 5
22-APR-04

MORTALITY DATA

MALES

GROUP 5 (1000 MG/KG/DAY)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
21	14-APR-04	17-MAR-04	13-APR-04
22	14-APR-04	17-MAR-04	13-APR-04
23	14-APR-04	17-MAR-04	13-APR-04
24	14-APR-04	17-MAR-04	13-APR-04
25	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 6
22-APR-04

MORTALITY DATA
FEMALES
GROUP 1 (0 MG/KG/DAY)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
26	14-APR-04	17-MAR-04	13-APR-04
27	14-APR-04	17-MAR-04	13-APR-04
28	14-APR-04	17-MAR-04	13-APR-04
29	14-APR-04	17-MAR-04	13-APR-04
30	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 7
22-APR-04

MORTALITY DATA
FEMALES
GROUP 2 (PLACEBO)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
31	14-APR-04	17-MAR-04	13-APR-04
32	14-APR-04	17-MAR-04	13-APR-04
33	14-APR-04	17-MAR-04	13-APR-04
34	14-APR-04	17-MAR-04	13-APR-04
35	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 8
22-APR-04

MORTALITY DATA
FEMALES
GROUP 3 (100 MG/KG/DAY)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
36	14-APR-04	17-MAR-04	13-APR-04
37	14-APR-04	17-MAR-04	13-APR-04
38	14-APR-04	17-MAR-04	13-APR-04
39	14-APR-04	17-MAR-04	13-APR-04
40	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 9
22-APR-04

MORTALITY DATA
FEMALES
GROUP 4 (500 MG/KG/DAY)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
41	14-APR-04	17-MAR-04	13-APR-04
42	14-APR-04	17-MAR-04	13-APR-04
43	14-APR-04	17-MAR-04	13-APR-04
44	14-APR-04	17-MAR-04	13-APR-04
45	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MORT-IND - 10
22-APR-04

MORTALITY DATA
FEMALES
GROUP 5 (1000 MG/KG/DAY)

ANIMAL	SCHEDULED NECROPSY	TREATMENT FROM	TO
46	14-APR-04	17-MAR-04	13-APR-04
47	14-APR-04	17-MAR-04	13-APR-04
48	14-APR-04	17-MAR-04	13-APR-04
49	14-APR-04	17-MAR-04	13-APR-04
50	14-APR-04	17-MAR-04	13-APR-04

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 1
18-JUN-04

CLINICAL SIGNS, DAILY
MALES
GROUP 1 (0 MG/KG/DAY)

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
<hr/>		
ANIMAL 1		

NO CLINICAL SIGNS NOTED		
ANIMAL 2		

NO CLINICAL SIGNS NOTED		
ANIMAL 3		

NO CLINICAL SIGNS NOTED		
ANIMAL 4		

NO CLINICAL SIGNS NOTED		
ANIMAL 5		

NO CLINICAL SIGNS NOTED		

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 2
18-JUN-04

CLINICAL SIGNS, DAILY
MALES
GROUP 2 (PLACEBO)

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
ANIMAL 6		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111
ANIMAL 7		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111
ANIMAL 8		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111
ANIMAL 9		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111
ANIMAL 10		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111

G: Highest daily grades

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 3
18-JUN-04

CLINICAL SIGNS, DAILY
MALES
GROUP 3 (100 MG/KG/DAY)

SIGN (MAX.GRADE) (LOCATION)	PRETEST		TREATMENT				
	WEEKS:	1.....	1.....	2.....	3.....	4.....	5
ANIMAL 11							

SECRETION / EXCRETION							
RED FECES (3)	G:	11111111111111111111111111111111			
ANIMAL 12							

SECRETION / EXCRETION							
RED FECES (3)	G:	11111111111111111111111111111111			
ANIMAL 13							

SECRETION / EXCRETION							
RED FECES (3)	G:	11111111111111111111111111111111			
ANIMAL 14							

SECRETION / EXCRETION							
RED FECES (3)	G:	11111111111111111111111111111111			
ANIMAL 15							

SECRETION / EXCRETION							
RED FECES (3)	G:	11111111111111111111111111111111			

G: Highest daily grades

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 4
18-JUN-04

CLINICAL SIGNS, DAILY
MALES
GROUP 4 (500 MG/KG/DAY)

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
ANIMAL 16		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111112222222222
SOFT FECES (1)	G:1111111111
ANIMAL 17		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111112222222222
SOFT FECES (1)	G:1111111111
ANIMAL 18		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111112222222222
SOFT FECES (1)	G:1111111111
ANIMAL 19		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111112222222222
SOFT FECES (1)	G:1111111111
ANIMAL 20		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111112222222222
SOFT FECES (1)	G:1111111111

G: Highest daily grades

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 5
18-JUN-04

**CLINICAL SIGNS, DAILY
MALES
GROUP 5 (1000 MG/KG/DAY)**

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
ANIMAL 21		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111
ANIMAL 22		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111
ANIMAL 23		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111
ANIMAL 24		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111
ANIMAL 25		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111

G: Highest daily grades

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 6
18-JUN-04

CLINICAL SIGNS, DAILY
FEMALES
GROUP 1 (0 MG/KG/DAY)

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
--------------------------------	--------------------------	--

ANIMAL 26		

NO CLINICAL SIGNS NOTED		
ANIMAL 27		

NO CLINICAL SIGNS NOTED		
ANIMAL 28		

NO CLINICAL SIGNS NOTED		
ANIMAL 29		

NO CLINICAL SIGNS NOTED		
ANIMAL 30		

NO CLINICAL SIGNS NOTED		

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 7
18-JUN-04

CLINICAL SIGNS, DAILY
FEMALES
GROUP 2 (PLACEBO)

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
ANIMAL 31		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111
ANIMAL 32		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111
ANIMAL 33		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111
ANIMAL 34		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111
ANIMAL 35		
SECRETION / EXCRETION		
DARK FECES (1)	G:11111111111111111111
SOFT FECES (1)	G:1111111111

G: Highest daily grades

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 8
18-JUN-04

CLINICAL SIGNS, DAILY
FEMALES
GROUP 3 (100 MG/KG/DAY)

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
<hr/>		
ANIMAL 36		

SECRETION / EXCRETION RED FECES (3)	G:11111111111111111111111111111111
ANIMAL 37		

SECRETION / EXCRETION RED FECES (3)	G:11111111111111111111111111111111
ANIMAL 38		

SECRETION / EXCRETION RED FECES (3)	G:11111111111111111111111111111111
ANIMAL 39		

SECRETION / EXCRETION RED FECES (3)	G:11111111111111111111111111111111
ANIMAL 40		

SECRETION / EXCRETION RED FECES (3)	G:11111111111111111111111111111111

G: Highest daily grades

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 9
18-JUN-04

**CLINICAL SIGNS, DAILY
FEMALES
GROUP 4 (500 MG/KG/DAY)**

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
ANIMAL 41		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111111222222222
SOFT FECES (1)	G:1111111111
ANIMAL 42		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111111222222222
SOFT FECES (1)	G:1111111111
ANIMAL 43		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111111222222222
SOFT FECES (1)	G:1111111111
ANIMAL 44		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111111222222222
SOFT FECES (1)	G:1111111111
ANIMAL 45		

SECRETION / EXCRETION		
RED FECES (3)	G:1222211111111222222222
SOFT FECES (1)	G:1111111111

G: Highest daily grades

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

SYM-IND - 10
18-JUN-04

**CLINICAL SIGNS, DAILY
FEMALES
GROUP 5 (1000 MG/KG/DAY)**

SIGN (MAX.GRADE) (LOCATION)	PRETEST WEEKS: 1.....	TREATMENT 1.....2.....3.....4.....5
ANIMAL 46		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111
ANIMAL 47		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111
ANIMAL 48		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111
ANIMAL 49		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111
ANIMAL 50		
SECRETION / EXCRETION		
RED FECES (3)	G:233331111222223333333333
SOFT FECES (1)	G:111

G: Highest daily grades

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 1
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 1 (0 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
1	15.2	18.1	18.4	19.1	20.1	21.1	21.7
2	15.4	16.3	17.4	19.0	20.0	20.9	22.3
3	18.5	19.7	21.9	22.8	22.4	22.0	23.6
4	16.3	18.6	21.6	22.6	24.0	24.8	25.4
5	23.9	19.1	21.9	23.1	22.7	22.4	23.2

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 2
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 2 (PLACEBO)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
6	19.8	20.1	21.9	23.5	22.1	22.3	24.7
7	16.6	21.3	22.8	23.7	22.7	25.3	25.0
8	15.2	15.1	19.8	19.3	18.9	23.5	21.2
9	20.9	20.3	21.1	23.0	22.8	24.2	24.3
10	17.9	18.1	21.3	22.9	23.2	24.1	26.1

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 3
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 3 (100 MG/KG/DAY)

	PRETEST		TREATMENT				
DAYS	1-4	4-8	1-4	4-8	8-15	15-22	22-28
WEEKS	1	1/2	1	1/2	2/3	3/4	4
ANIMAL							
11	14.7	18.6	21.3	24.9	24.1	24.8	26.8
12	17.9	19.1	21.6	23.1	22.8	26.1	24.5
13	18.4	18.9	21.1	23.4	23.0	25.7	24.6
14	15.3	18.2	21.1	22.6	23.0	24.3	25.2
15	18.4	19.3	21.7	24.0	23.0	28.4	29.0

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 4
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 4 (500 MG/KG/DAY)

	PRETEST		TREATMENT				
DAYS	1-4	4-8	1-4	4-8	8-15	15-22	22-28
WEEKS	1	1/2	1	1/2	2/3	3/4	4
ANIMAL							
16	16.6	20.9	20.9	23.0	23.9	26.1	23.6
17	16.8	19.0	20.5	23.6	23.7	26.3	25.9
18	23.1	20.1	20.7	24.4	24.0	27.3	24.0
19	16.4	19.5	21.8	23.6	22.8	25.9	26.2
20	16.8	17.7	19.5	22.1	23.2	17.4	22.3

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 5
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
MALES

GROUP 5 (1000 MG/KG/DAY)

	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
DAYS							
WEEKS	1	1/2	1	1/2	2/3	3/4	4
ANIMAL							
21	18.7	20.5	23.2	25.5	24.2	23.2	23.8
22	17.5	19.6	21.8	22.6	20.2	23.9	22.7
23	15.6	18.0	18.4	22.9	21.6	21.4	22.8
24	21.1	21.5	22.7	26.1	25.4	26.9	27.4
25	19.3	21.8	23.6	26.4	25.5	26.9	28.4

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 6
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 1 (0 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
26	13.4	14.7	14.1	15.3	15.9	16.8	17.2
27	11.7	13.1	14.8	15.5	16.0	16.2	17.5
28	14.3	14.8	16.2	18.4	18.6	18.9	19.6
29	12.5	14.0	15.1	17.3	16.0	16.7	17.6
30	13.0	14.5	16.3	17.3	17.6	17.4	19.7

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 7
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 2 (PLACEBO)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
31	14.1	13.5	14.7	15.6	15.2	16.3	17.2
32	13.5	15.8	14.6	16.1	17.8	17.6	19.2
33	11.9	13.4	16.1	18.0	18.5	19.2	22.8
34	13.1	13.3	15.8	16.1	16.3	16.6	19.7
35	11.4	11.8	13.2	14.7	16.0	15.9	17.5

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 8
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 3 (100 MG/KG/DAY)

	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
DAYS	1	1/2	1	1/2	2/3	3/4	4
WEEKS							
ANIMAL							
36	11.5	15.2	13.9	14.9	15.5	17.3	16.6
37	11.4	11.9	13.6	14.8	16.5	18.6	19.8
38	14.5	13.9	15.0	15.8	15.9	18.8	18.5
39	13.7	16.9	17.1	17.7	17.6	19.9	22.2
40	14.2	17.4	16.7	20.2	17.5	19.9	20.1

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 9
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 4 (500 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
41	14.9	16.0	20.5	18.7	19.7	19.2	23.0
42	12.9	14.9	18.6	18.0	17.9	18.1	20.5
43	12.6	14.8	18.3	19.1	19.2	20.9	24.1
44	13.0	13.7	15.7	16.1	16.6	17.6	19.8
45	18.9	16.1	16.6	16.5	17.0	17.8	19.9

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

FC-IND - 10
22-APR-04

FOOD CONSUMPTION (G/ANIMAL/DAY)
FEMALES

GROUP 5 (1000 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
46	12.7	12.6	14.4	15.6	15.5	16.1	16.5
47	12.2	16.0	15.4	15.5	16.9	17.8	18.6
48	11.7	13.4	15.8	18.7	15.7	18.1	17.5
49	11.6	14.1	15.5	17.3	17.5	19.7	18.3
50	14.4	14.8	16.4	17.8	16.2	19.8	19.3

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 1
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
MALES

GROUP 1 (0 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
1	97	116	93	89	83	76	76
2	98	103	89	87	78	72	73
3	107	114	99	95	84	74	75
4	100	114	101	95	88	80	78
5	149	119	107	102	90	80	80

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 2
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
MALES

GROUP 2 (PLACEBO)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
6	113	115	99	100	86	77	78
7	105	134	107	99	87	88	85
8	96	96	101	95	83	94	84
9	121	118	100	99	88	82	79
10	97	98	91	91	85	80	82

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 3
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
MALES

GROUP 3 (100 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4 1	4-8 1/2	1-4 1	4-8 1/2	8-15 2/3	15-22 3/4	22-28 4
11	91	114	100	107	95	86	89
12	102	108	98	96	86	89	80
13	113	116	100	101	87	85	78
14	99	118	102	99	90	82	81
15	108	113	100	102	87	95	94

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND ~ 4
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
MALES

GROUP 4 (500 MG/KG/DAY)

	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
DAYS	1	1/2	1	1/2	2/3	3/4	4
WEEKS							
ANIMAL							
16	98	124	97	98	91	91	78
17	104	118	99	103	92	88	82
18	136	119	98	104	92	92	77
19	97	115	98	97	83	84	82
20	99	104	94	97	89	61	75

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 5
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
MALES

GROUP 5 (1000 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4 1	4-8 1/2	1-4 1	4-8 1/2	8-15 2/3	15-22 3/4	22-28 4
21	106	116	106	105	92	81	80
22	102	115	102	101	83	89	82
23	93	107	88	99	84	76	78
24	122	124	104	107	92	88	86
25	113	127	104	106	91	85	83

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 6
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
FEMALES

GROUP 1 (0 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4 1	4-8 1/2	1-4 1	4-8 1/2	8-15 2/3	15-22 3/4	22-28 4
26	97	106	90	90	91	83	85
27	93	104	98	94	88	81	85
28	105	109	101	107	99	93	94
29	93	104	94	101	85	82	83
30	99	111	105	100	95	88	92

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 7
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
FEMALES

GROUP 2 (PLACEBO)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT					
	1-4 1	4-8 1/2	1-4 1	4-8 1/2	8-15 2/3	15-22 3/4	22-28 4	
31	112	107	99	100	93	88	92	
32	100	118	93	93	97	89	93	
33	96	108	106	107	104	98	111	
34	104	105	108	103	97	91	104	
35	89	92	88	95	98	93	96	

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 8
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
FEMALES

GROUP 3 (100 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4 1	4-8 1/2	1-4 1	4-8 1/2	8-15 2/3	15-22 3/4	22-28 4
36	94	124	99	99	92	94	89
37	89	93	93	96	100	98	105
38	102	98	95	94	90	98	97
39	101	124	104	100	96	96	103
40	110	135	111	122	96	100	97

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 9
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
FEMALES.

GROUP 4 (500 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
41	105	113	119	102	99	90	104
42	101	117	121	106	100	92	98
43	97	113	117	113	105	103	114
44	100	106	100	95	90	90	96
45	149	127	107	99	96	95	97

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

RFC-IND - 10
22-APR-04

RELATIVE FOOD CONSUMPTION
(G/KG BODY WEIGHT/DAY)
FEMALES

GROUP 5 (1000 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT				
	1-4	4-8	1-4	4-8	8-15	15-22	22-28
	1	1/2	1	1/2	2/3	3/4	4
46	99	99	103	103	93	88	88
47	95	124	108	104	99	98	99
48	90	103	102	112	92	90	86
49	89	109	108	111	99	104	96
50	105	108	106	107	90	100	95

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-TND - 1
22-APR-04

BODY WEIGHTS (GRAM)

MALES

GROUP 1 (0 MG/KG/DAY)

	PRETEST		TREATMENT						
DAYS	1	4	1	4	8	15	22	28	
WEEKS	1	1	1	1	2	3	4	4	
ANIMAL									
1	144	157	184	198	215	241	276	286	
2	148	158	177	195	219	255	288	304	
3	153	173	202	221	241	267	298	314	
4	154	163	193	213	238	273	311	326	
5	141	160	186	204	228	251	280	291	

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 2
22-APR-04

BODY WEIGHTS (GRAM)
MALES

GROUP 2 (PLACEBO)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT						
	1	4	1	4	8	15	22	28	
	1	1	1	1	2	3	4	4	
6	148	175	202	222	236	258	289	317	
7	143	159	190	213	240	260	288	295	
8	146	157	172	195	203	226	250	254	
9	154	172	194	211	234	260	294	309	
10	159	184	213	234	252	273	302	318	

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 3
22-APR-04

BODY WEIGHTS (GRAM)
MALES

GROUP 3 (100 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
11	150	163	193	214	232	254	289	300
12	156	176	203	220	242	264	295	308
13	147	162	194	211	231	266	302	313
14	140	155	187	207	228	257	298	310
15	154	171	199	217	236	265	299	309

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 4
22-APR-04

BODY WEIGHTS (GRAM)
MALES

GROUP 4 (500 MG/KG/DAY)

	PRETEST		TREATMENT						
DAYS	1	4	1	4	8	15	22	28	
WEEKS	1	1	1	1	2	3	4	4	
ANIMAL									
16	149	169	198	216	234	263	285	303	
17	142	161	189	208	230	258	299	315	
18	152	169	194	211	235	261	298	310	
19	155	169	201	222	243	273	307	321	
20	150	170	192	208	227	260	283	298	

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 5
22-APR-04

BODY WEIGHTS (GRAM)
MALES

GROUP 5 (1000 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
21	153	176	202	218	242	264	288	296
22	155	171	199	212	224	244	270	275
23	155	168	195	210	232	258	284	294
24	150	173	201	218	243	275	306	318
25	155	171	202	226	250	281	317	341

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 6
22-APR-04

BODY WEIGHTS (GRAM)
FEMALES

GROUP 1 (0 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
26	131	139	154	157	170	174	204	201
27	122	126	140	151	166	183	198	204
28	128	136	149	160	171	187	204	208
29	132	134	149	161	172	189	204	211
30	123	131	145	155	172	185	198	213

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 7
22-APR-04

**BODY WEIGHTS (GRAM)
FEMALES**

GROUP 2 (PLACEBO)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
31	117	126	136	148	157	163	186	187
32	127	134	144	158	173	183	199	207
33	120	124	136	152	168	178	197	206
34	124	127	139	146	156	169	183	188
35	123	129	136	150	155	164	171	182

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 8
22-APR-04

BODY WEIGHTS (GRAM)
FEMALES

GROUP 3 (100 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT						
	1	4	1	4	8	15	22	28	
	1	1	1	1	2	3	4	4	
36	120	123	134	140	150	170	185	185	
37	124	128	138	146	155	166	190	188	
38	132	141	152	157	168	176	192	190	
39	128	135	153	164	176	184	208	215	
40	119	129	143	150	166	181	199	206	

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 9
22-APR-04

BODY WEIGHTS (GRAM)
FEMALES

GROUP 4 (500 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
41	127	142	156	173	183	198	213	222
42	120	127	137	154	171	179	197	209
43	123	130	147	157	169	183	202	212
44	120	129	145	156	169	183	196	206
45	122	127	142	155	166	178	187	206

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BW-IND - 10
22-APR-04

BODY WEIGHTS (GRAM)
FEMALES

GROUP 5 (1000 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
46	119	128	140	141	152	167	182	188
47	125	129	138	142	150	170	182	189
48	121	130	146	154	167	171	200	203
49	127	130	144	144	156	176	189	190
50	128	137	150	155	167	180	197	203

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 1
22-APR-04

BODY WEIGHT GAIN (%)
MALES

GROUP 1 (0 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
1	-22.0	-15.0	0.0	7.4	16.5	30.8	49.6	55.2
2	-16.8	-11.1	0.0	10.0	23.2	43.6	62.4	71.3
3	-24.1	-14.2	0.0	9.6	19.6	32.6	47.8	55.9
4	-20.4	-15.5	0.0	10.2	23.5	41.6	61.0	69.1
5	-24.4	-13.8	0.0	9.8	22.4	35.2	50.8	56.6

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 2
22-APR-04

BODY WEIGHT GAIN (%)
MALES

GROUP 2 (PLACEBO)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
6	-26.5	-13.3	0.0	10.1	16.6	27.7	43.2	57.2
7	-24.5	-16.3	0.0	12.2	26.5	37.1	51.7	55.3
8	-15.0	-8.6	0.0	13.7	18.2	31.6	45.3	47.7
9	-20.8	-11.4	0.0	8.7	20.2	33.7	51.2	58.8
10	-25.5	-13.7	0.0	9.7	18.0	28.2	41.7	49.0

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 3
22-APR-04

BODY WEIGHT GAIN (%)
MALES

GROUP 3 (100 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT					
	1	4	1	4	8	15	22	28
	1	1	1	1	2	3	4	4
11	-22.4	-16.0	0.0	10.7	20.1	31.6	49.3	55.0
12	-23.2	-13.5	0.0	8.0	18.8	29.6	45.2	51.5
13	-24.0	-16.5	0.0	9.0	19.2	37.1	55.5	61.6
14	-25.0	-17.2	0.0	10.8	22.2	37.6	59.2	65.7
15	-22.3	-14.2	0.0	9.4	18.6	33.4	50.6	55.6

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 4
22-APR-04

BODY WEIGHT GAIN (%)
MALES

GROUP 4 (500 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
16	-25.2	-14.9	0.0	8.7	17.9	32.5	43.7	52.5
17	-24.5	-14.6	0.0	10.1	22.1	36.6	58.4	66.9
18	-21.5	-12.7	0.0	8.6	20.9	34.7	53.5	59.9
19	-22.8	-16.0	0.0	10.3	20.6	35.7	52.9	59.6
20	-21.4	-11.3	0.0	8.5	18.7	35.8	47.9	55.7

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 5
22-APR-04

BODY WEIGHT GAIN (%)
MALES

GROUP 5 (1000 MG/KG/DAY)

DAYS WEEKS ANIMAL	PRETEST		TREATMENT					
	1	4	1	4	8	15	22	28
	1	1	1	1	2	3	4	4
21	-24.2	-12.9	0.0	8.0	19.9	30.9	42.8	46.7
22	-22.1	-14.2	0.0	6.8	12.6	22.5	35.5	38.3
23	-20.3	-13.9	0.0	7.8	19.1	32.4	45.6	51.0
24	-25.3	-13.5	0.0	8.9	21.3	37.0	52.6	58.4
25	-23.3	-15.1	0.0	11.7	23.6	39.2	57.0	69.0

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 6
22-APR-04

BODY WEIGHT GAIN (%)
FEMALES

GROUP 1 (0 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
26	-15.1	-10.1	0.0	1.6	9.9	12.9	31.9	30.1
27	-12.6	-9.6	0.0	8.0	18.7	30.8	42.2	46.5
28	-14.2	-8.9	0.0	7.4	15.0	25.6	36.8	39.9
29	-11.6	-10.2	0.0	7.9	15.4	26.4	36.5	41.3
30	-14.8	-9.8	0.0	7.1	19.0	28.1	36.6	47.5

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 7
22-APR-04

BODY WEIGHT GAIN (%)
FEMALES

GROUP 2 (PLACEBO)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
31	-14.4	-7.7	0.0	9.0	15.4	20.1	36.8	37.1
32	-11.5	-6.5	0.0	9.8	20.2	27.2	38.3	44.0
33	-12.2	-9.1	0.0	11.5	23.5	30.5	44.4	51.3
34	-10.7	-8.6	0.0	5.3	12.3	21.8	32.1	35.7
35	-10.0	-5.8	0.0	9.9	14.0	20.1	25.2	33.2

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 8
22-APR-04

BODY WEIGHT GAIN (%)
FEMALES

GROUP 3 (100 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
36	-10.0	-8.1	0.0	4.6	12.1	26.9	38.3	38.7
37	-10.0	-7.6	0.0	6.0	12.1	19.8	37.8	36.0
38	-12.9	-6.9	0.0	3.5	10.7	15.8	26.3	25.3
39	-16.5	-11.4	0.0	7.4	15.3	20.5	36.1	40.9
40	-17.0	-10.1	0.0	4.9	16.2	26.6	38.9	44.2

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 9
22-APR-04

BODY WEIGHT GAIN (%)
FEMALES

GROUP 4 (500 MG/KG/DAY)

	PRETEST		TREATMENT					
DAYS	1	4	1	4	8	15	22	28
WEEKS	1	1	1	1	2	3	4	4
ANIMAL								
41	-18.2	-8.9	0.0	11.2	17.5	27.5	37.1	42.6
42	-12.5	-7.2	0.0	12.5	24.6	30.5	43.7	52.3
43	-16.1	-11.0	0.0	7.3	15.3	24.8	37.7	44.5
44	-17.5	-10.8	0.0	7.5	16.8	26.4	35.0	42.3
45	-14.2	-10.4	0.0	9.1	16.9	25.6	32.1	45.1

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

BWG-IND - 10
22-APR-04

BODY WEIGHT GAIN (%)
FEMALES

GROUP 5 (1000 MG/KG/DAY)

	PRETEST		TREATMENT					
	1	4	1	4	8	15	22	28
	1	1	1	1	2	3	4	4
DAYS								
WEEKS								
ANIMAL								
46	-14.8	-8.9	0.0	0.4	8.5	19.0	30.2	33.8
47	-9.2	-6.6	0.0	3.4	9.1	23.6	32.1	37.0
48	-17.2	-10.7	0.0	5.8	14.9	17.0	37.4	39.2
49	-11.6	-9.6	0.0	0.0	8.2	22.4	31.8	32.2
50	-14.2	-8.5	0.0	3.9	11.8	20.4	31.9	35.8

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 1
22-APR-04

MACROSCOPICAL FINDINGS
MALES
GROUP 1 (0 MG/KG/DAY)

ANIMAL 1 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM..... MUCOSA: DISCOLORATION, RED BROWN.

ANIMAL 2 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 3 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 4 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 5 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 2
22-APR-04

MACROSCOPICAL FINDINGS
MALES
GROUP 2 (PLACEBO)

ANIMAL 6 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 7 (SCHEDULED NECROPSY, 14-APR-2004)

KIDNEYS..... BOTH SIDES: DISCOLORATION, TAN.
THYROID GLAND..... BOTH SIDES: DISCOLORATION, TAN.
SPLEEN..... ENLARGED, D=50X15 MM.

ANIMAL 8 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 9 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 10 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 3
22-APR-04

MACROSCOPICAL FINDINGS
MALES
GROUP 3 (100 MG/KG/DAY)

ANIMAL 11 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 12 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 13 (SCHEDULED NECROPSY, 14-APR-2004)

THYMUS..... THICKENED.

ANIMAL 14 (SCHEDULED NECROPSY, 14-APR-2004)

THYMUS..... FOCUS/FOCI, ISOLATED, D=1 MM, DARK RED.

ANIMAL 15 (SCHEDULED NECROPSY, 14-APR-2004)

PANCREAS..... DISCOLORATION, RED BROWN.

THYMUS..... THICKENED.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 4
22-APR-04

MACROSCOPICAL FINDINGS
MALES
GROUP 4 (500 MG/KG/DAY)

ANIMAL 16 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM..... MUCOSA: DISCOLORATION, REDDISH.

ANIMAL 17 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 18 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM..... MUCOSA: DISCOLORATION, REDDISH.

ANIMAL 19 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 20 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM..... MUCOSA: DISCOLORATION, REDDISH.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 5
22-APR-04

MACROSCOPICAL FINDINGS
MALES
GROUP 5 (1000 MG/KG/DAY)

ANIMAL 21 (SCHEDULED NECROPSY, 14-APR-2004)

CARCUM..... MUCOSA: DISCOLORATION, REDDISH.

ANIMAL 22 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 23 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 24 (SCHEDULED NECROPSY, 14-APR-2004)

THYMUS..... THICKENED.

ANIMAL 25 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 6
22-APR-04

MACROSCOPICAL FINDINGS
FEMALES
GROUP 1 (0 MG/KG/DAY)

ANIMAL 26 (SCHEDULED NECROPSY, 14-APR-2004)

PANCREAS..... DISCOLORATION, DARK RED.

ANIMAL 27 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 28 (SCHEDULED NECROPSY, 14-APR-2004)

CARCINOM..... MUCOSA: DISCOLORATION, REDDISH.

PANCREAS..... DISCOLORATION, REDDISH.

ANIMAL 29 (SCHEDULED NECROPSY, 14-APR-2004)

THYMUS..... DISCOLORATION, DARK RED.

MANDIBULAR L.NODE... DISCOLORATION, DARK RED.

ANIMAL 30 (SCHEDULED NECROPSY, 14-APR-2004)

PANCREAS..... DISCOLORATION, DARK RED.

OVARIES..... BOTH SIDES: DISCOLORATION, DARK RED.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 7
22-APR-04

MACROSCOPICAL FINDINGS
FEMALES
GROUP 2 (PLACEBO)

ANIMAL 31 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM..... MUCOSA: DISCOLORATION, REDDISH.

ANIMAL 32 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 33 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 34 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 35 (SCHEDULED NECROPSY, 14-APR-2004)

KIDNEYS..... BOTH SIDES: PELVIC DILATION.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 8
22-APR-04

**MACROSCOPICAL FINDINGS
FEMALES
GROUP 3 (100 MG/KG/DAY)**

ANIMAL 36 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 37 (SCHEDULED NECROPSY, 14-APR-2004)

NO FINDINGS NOTED

ANIMAL 38 (SCHEDULED NECROPSY, 14-APR-2004)

KIDNEYS..... RIGHT SIDE: PELVIC DILATION.

ANIMAL 39 (SCHEDULED NECROPSY, 14-APR-2004)

THYMUS..... THICKENED.

ANIMAL 40 (SCHEDULED NECROPSY, 14-APR-2004)

OVARIES..... BOTH SIDES: ENLARGED.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 9
22-APR-04

MACROSCOPICAL FINDINGS
FEMALES
GROUP 4 (500 MG/KG/DAY)

ANIMAL 41 (SCHEDULED NECROPSY, 14-APR-2004)

THYMUS..... THICKENED.

ANIMAL 42 (SCHEDULED NECROPSY, 14-APR-2004)

OVARIES..... RIGHT SIDE: Watery cyst, D=6 mm.

ANIMAL 43 (SCHEDULED NECROPSY, 14-APR-2004)

STOMACH..... MUCOSA: DISCOLORATION, DARK RED.

ANIMAL 44 (SCHEDULED NECROPSY, 14-APR-2004)

OVARIES..... RIGHT SIDE: DISCOLORATION, REDDISH.

ANIMAL 45 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM..... MUCOSA: DISCOLORATION, REDDISH.

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

MAC-IND - 10
22-APR-04

**MACROSCOPICAL FINDINGS
FEMALES
GROUP 5 (1000 MG/KG/DAY)**

ANIMAL 46 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM.....	MUCOSA: DISCOLORATION, REDDISH.
KIDNEYS.....	BOTH SIDES: PELVIC DILATION.
MANDIBULAR L.NODE...	DISCOLORATION, DARK RED.

ANIMAL 47 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM.....	MUCOSA: DISCOLORATION, REDDISH.
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ANIMAL 48 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM.....	MUCOSA: DISCOLORATION, REDDISH.
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ANIMAL 49 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM.....	MUCOSA: DISCOLORATION, REDDISH.
PANCREAS.....	DISCOLORATION, DARK RED.

ANIMAL 50 (SCHEDULED NECROPSY, 14-APR-2004)

CAECUM.....	MUCOSA: DISCOLORATION, REDDISH.
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RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 1
22-APR-04

**ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
MALES**

GROUP 1 (0 MG/KG/DAY)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
1	269.89	1.77	0.876	0.016	6.87	0.29	1.78	0.054
2	287.46	1.90	0.886	0.016	8.11	0.42	1.93	0.060
3	290.84	1.84	0.969	0.028	7.86	0.53	1.86	0.066
4	306.64	1.88	1.012	0.016	8.15	0.58	2.03	0.052
5	273.92	1.85	0.867	0.017	7.37	0.28	1.58	0.076

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYD
1	0.504	3.26	0.924
2	0.552	2.93	0.822
3	0.664	3.12	1.092
4	0.684	3.42	1.025
5	0.472	3.65	0.944

GROUP 2 (PLACEBO)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
6	294.42	1.88	1.082	0.019	9.02	0.35	2.01	0.059
7	277.07	1.97	1.011	0.019	9.40	0.52	1.91	0.062
8	236.65	1.84	0.745	0.017	6.45	0.34	1.70	0.052
9	283.17	2.01	0.914	0.033	8.72	0.48	2.20	0.068
10	295.91	1.95	0.936	0.020	9.17	0.58	2.12	0.063

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYD
6	0.686	3.45	1.057
7	2.034	3.84	1.018
8	0.590	3.32	0.977
9	0.733	3.31	0.953
10	0.690	3.12	0.980

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
11	286.01	1.94	0.951	0.025	8.32	0.41	1.97	0.063
12	287.61	1.91	0.911	0.023	7.78	0.36	1.93	0.072
13	292.37	2.06	1.080	0.025	7.65	0.62	1.92	0.070
14	286.97	1.80	1.051	0.028	8.18	0.49	1.93	0.057
15	292.54	1.89	0.951	0.020	8.67	0.75	2.07	0.066

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 2
22-APR-04

**ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
MALES**

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYD
11	0.706	3.20	0.932
12	0.589	3.23	1.161
13	0.697	3.88	0.965
14	0.746	3.51	0.914
15	0.834	3.37	1.044

GROUP 4 (500 MG/KG/DAY)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
16	284.54	1.92	0.960	0.024	8.74	0.44	2.08	0.062
17	289.19	1.93	1.104	0.022	8.61	0.42	2.09	0.071
18	288.94	1.93	0.936	0.022	8.66	0.43	1.98	0.065
19	296.34	1.93	1.025	0.022	8.08	0.50	1.74	0.065
20	270.21	1.90	0.956	0.022	7.84	0.46	1.77	0.068

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYD
16	0.687	3.62	1.030
17	0.644	3.47	0.962
18	0.748	3.29	0.973
19	0.749	3.39	0.935
20	0.710	3.35	0.870

GROUP 5 (1000 MG/KG/DAY)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
21	277.15	1.88	0.897	0.020	7.75	0.47	1.81	0.065
22	257.77	1.85	0.946	0.025	7.69	0.46	1.89	0.076
23	268.47	1.89	0.894	0.021	7.84	0.43	1.99	0.071
24	300.44	1.95	0.968	0.027	9.00	0.69	2.05	0.075
25	318.89	1.94	1.085	0.022	8.99	0.45	2.13	0.059

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYD
21	0.560	3.24	0.999
22	0.641	3.18	0.865
23	0.604	3.52	1.085
24	0.781	3.43	1.093
25	0.620	3.53	0.959

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 3
22-APR-04

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

GROUP 1 (0 MG/KG/DAY)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
1	269.89	0.65	0.325	0.006	2.55	0.11	0.66	0.020
2	287.46	0.66	0.308	0.005	2.82	0.15	0.67	0.021
3	290.84	0.63	0.333	0.010	2.70	0.18	0.64	0.023
4	306.64	0.61	0.330	0.005	2.66	0.19	0.66	0.017
5	273.92	0.68	0.316	0.006	2.69	0.10	0.58	0.028

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYMI
1	0.187	1.21	0.342
2	0.192	1.02	0.286
3	0.228	1.07	0.375
4	0.223	1.12	0.334
5	0.172	1.33	0.345

GROUP 2 (PLACEBO)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
6	294.42	0.64	0.367	0.006	3.06	0.12	0.68	0.020
7	277.07	0.71	0.365	0.007	3.39	0.19	0.69	0.022
8	236.65	0.78	0.315	0.007	2.73	0.14	0.72	0.022
9	283.17	0.71	0.323	0.012	3.08	0.17	0.78	0.024
10	295.91	0.66	0.316	0.007	3.10	0.19	0.72	0.021

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYMI
6	0.233	1.17	0.359
7	0.734	1.39	0.367
8	0.249	1.40	0.413
9	0.259	1.17	0.337
10	0.233	1.05	0.331

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
11	286.01	0.68	0.333	0.009	2.91	0.14	0.69	0.022
12	287.61	0.67	0.317	0.008	2.70	0.12	0.67	0.025
13	292.37	0.71	0.369	0.009	2.62	0.21	0.66	0.024
14	286.97	0.63	0.366	0.010	2.85	0.17	0.67	0.020
15	292.54	0.65	0.325	0.007	2.96	0.25	0.71	0.023

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 4
22-APR-04

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYDYMID
11	0.247	1.12	0.326
12	0.205	1.12	0.404
13	0.239	1.33	0.330
14	0.260	1.22	0.318
15	0.285	1.15	0.357

GROUP 4 (500 MG/KG/DAY)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
16	284.54	0.68	0.337	0.009	3.07	0.15	0.73	0.022
17	289.19	0.67	0.382	0.007	2.98	0.15	0.72	0.024
18	288.94	0.67	0.324	0.008	3.00	0.15	0.68	0.023
19	296.34	0.65	0.346	0.007	2.73	0.17	0.59	0.022
20	270.21	0.70	0.354	0.008	2.90	0.17	0.66	0.025

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYDYMID
16	0.241	1.27	0.362
17	0.223	1.20	0.333
18	0.259	1.14	0.337
19	0.253	1.15	0.315
20	0.263	1.24	0.322

GROUP 5 (1000 MG/KG/DAY)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
21	277.15	0.68	0.324	0.007	2.80	0.17	0.65	0.023
22	257.77	0.72	0.367	0.010	2.98	0.18	0.73	0.030
23	268.47	0.71	0.333	0.008	2.92	0.16	0.74	0.026
24	300.44	0.65	0.322	0.009	2.99	0.23	0.68	0.025
25	318.89	0.61	0.340	0.007	2.82	0.14	0.67	0.018

ANIMAL NUMBER	SPLEEN	TESTES	EPIDIDYDYMID
21	0.202	1.17	0.360
22	0.249	1.23	0.335
23	0.225	1.31	0.404
24	0.260	1.14	0.364
25	0.194	1.11	0.301

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 5
22-APR-04

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

GROUP 1 (0 MG/KG/DAY)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
1	1.77	49.592	0.917	389.00	16.36	100.59	3.040	28.516
2	1.90	46.604	0.831	426.89	22.20	101.35	3.167	29.023
3	1.84	52.633	1.542	426.64	28.99	101.00	3.583	36.068
4	1.88	53.806	0.835	433.26	30.84	107.92	2.738	36.360
5	1.85	46.805	0.891	398.31	15.10	85.48	4.116	25.514
ANIMAL NUMBER	TESTES	EPIDIDYMI						
1	184.69	52.310						
2	153.88	43.243						
3	169.54	59.279						
4	181.94	54.476						
5	197.23	50.975						

GROUP 2 (PLACEBO)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
6	1.88	57.681	0.986	481.13	18.72	107.36	3.135	36.577
7	1.97	51.291	0.944	476.79	26.63	96.71	3.150	103.155
8	1.84	40.560	0.942	351.11	18.50	92.67	2.847	32.110
9	2.01	45.458	1.631	433.70	23.62	109.61	3.396	36.459
10	1.95	48.102	1.022	471.13	29.63	108.80	3.242	35.431
ANIMAL NUMBER	TESTES	EPIDIDYMI						
6	183.88	56.374						
7	195.04	51.651						
8	180.74	53.169						
9	164.69	47.402						
10	160.23	50.331						

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
11	1.94	49.054	1.279	429.20	21.37	101.66	3.249	36.403
12	1.91	47.619	1.181	406.42	18.69	100.71	3.784	30.800
13	2.06	52.386	1.222	370.78	29.86	93.35	3.385	33.822
14	1.80	58.278	1.536	453.66	27.22	106.96	3.133	41.384
15	1.89	50.344	1.070	458.95	39.47	109.58	3.516	44.154

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 6
22-APR-04

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
MALES

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	TESTES	EPIDIDYMI
11	164.83	48.053
12	168.91	60.675
13	188.13	46.809
14	194.47	50.660
15	178.20	55.285

GROUP 4 (500 MG/KG/DAY)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
16	1.92	49.886	1.268	454.08	22.86	108.21	3.212	35.716
17	1.93	57.164	1.114	446.09	21.82	108.21	3.667	33.332
18	1.93	48.472	1.134	448.21	22.09	102.28	3.371	38.707
19	1.93	53.069	1.119	418.69	25.98	90.17	3.362	38.793
20	1.90	50.396	1.171	413.29	24.10	93.49	3.560	37.459

ANIMAL NUMBER	TESTES	EPIDIDYMI
16	188.01	53.535
17	179.87	49.839
18	170.21	50.362
19	175.83	48.418
20	176.92	45.881

GROUP 5 (1000 MG/KG/DAY)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
21	1.88	47.716	1.063	412.21	25.22	96.24	3.461	29.792
22	1.85	51.232	1.359	416.21	25.04	102.42	4.121	34.714
23	1.89	47.195	1.093	413.81	22.59	104.80	3.737	31.892
24	1.95	49.565	1.398	460.61	35.33	104.93	3.815	39.995
25	1.94	55.931	1.118	463.18	22.99	109.79	3.030	31.959

ANIMAL NUMBER	TESTES	EPIDIDYMI
21	172.45	53.103
22	172.13	46.829
23	185.60	57.292
24	175.71	55.955
25	181.67	49.438

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 7
22-APR-04

**ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
FEMALES**

GROUP 1 (0 MG/KG/DAY)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
26	189.65	1.78	0.719	0.016	5.73	0.44	1.48	0.078
27	187.00	1.75	0.613	0.022	5.55	0.41	1.42	0.076
28	187.62	1.92	0.741	0.028	5.75	0.43	1.31	0.093
29	193.34	1.93	0.602	0.019	5.87	0.43	1.36	0.075
30	196.66	1.80	0.698	0.023	6.10	0.47	1.36	0.094

ANIMAL NUMBER	SPLEEN	OVARIES
26	0.534	0.115
27	0.425	0.096
28	0.436	0.125
29	0.425	0.114
30	0.459	0.117

GROUP 2 (PLACEBO)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
31	172.60	1.85	0.656	0.014	5.26	0.43	1.27	0.057
32	187.90	1.89	0.618	0.016	6.81	0.50	1.43	0.076
33	196.75	1.70	0.787	0.020	7.02	0.37	0.75	0.074
34	178.47	1.87	0.637	0.023	5.81	0.42	1.32	0.073
35	165.64	1.72	0.599	0.016	5.40	0.44	1.18	0.066

ANIMAL NUMBER	SPLEEN	OVARIES
31	0.372	0.110
32	0.522	0.091
33	0.454	0.136
34	0.520	0.085
35	0.397	0.083

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS
36	170.07	1.75	0.610	0.017	4.82	0.35	1.24	0.064
37	178.47	1.79	0.691	0.022	6.05	0.47	1.27	0.073
38	184.66	1.77	0.636	0.017	5.64	0.37	1.51	0.068
39	200.08	1.84	0.789	0.019	6.81	0.69	1.35	0.071
40	188.77	1.82	0.753	0.022	6.20	0.33	1.57	0.080

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 8
22-APR-04

**ORGAN WEIGHTS (GRAM)
AFTER 4 WEEKS
FEMALES**

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	SPLEEN	OVARIES
36	0.488	0.111
37	0.501	0.086
38	0.443	0.092
39	0.586	0.088
40	0.480	0.162

GROUP 4 (500 MG/KG/DAY)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
41	198.64	1.84	0.765	0.022	5.96	0.66	1.34	0.088
42	188.18	1.72	0.760	0.025	6.65	0.38	1.49	0.087
43	190.52	1.82	0.843	0.022	6.29	0.42	1.49	0.089
44	182.54	1.78	0.652	0.018	4.99	0.43	1.28	0.072
45	185.86	1.77	0.625	0.016	5.55	0.34	1.28	0.084

ANIMAL NUMBER	SPLEEN	OVARIES
41	0.467	0.087
42	0.458	0.305
43	0.512	0.147
44	0.403	0.093
45	0.582	0.104

GROUP 5 (1000 MG/KG/DAY)

ANIMAL NUMBER	BODY W.	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
46	171.41	1.82	0.643	0.019	5.55	0.32	1.41	0.082
47	171.09	1.78	0.770	0.021	6.26	0.42	1.45	0.087
48	184.78	1.76	0.675	0.017	5.68	0.49	1.37	0.080
49	176.06	1.84	0.649	0.017	5.28	0.38	1.34	0.075
50	186.45	1.97	0.646	0.022	5.94	0.48	1.28	0.069

ANIMAL NUMBER	SPLEEN	OVARIES
46	0.406	0.103
47	0.441	0.117
48	0.471	0.105
49	0.474	0.088
50	0.686	0.096

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 9
22-APR-04

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

GROUP 1 (0 MG/KG/DAY)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
26	189.65	0.94	0.379	0.008	3.02	0.23	0.78	0.041
27	187.00	0.94	0.328	0.012	2.97	0.22	0.76	0.041
28	187.62	1.02	0.395	0.015	3.06	0.23	0.70	0.049
29	193.34	1.00	0.312	0.010	3.04	0.22	0.70	0.039
30	196.66	0.92	0.355	0.012	3.10	0.24	0.69	0.048

ANIMAL
NUMBER

SPLEEN
OVARIES

26	0.282	0.061
27	0.227	0.051
28	0.232	0.067
29	0.220	0.059
30	0.234	0.059

GROUP 2 (PLACEBO)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
31	172.60	1.07	0.380	0.008	3.05	0.25	0.73	0.033
32	187.90	1.01	0.329	0.009	3.62	0.26	0.76	0.041
33	196.75	0.87	0.400	0.010	3.57	0.19	0.38	0.038
34	178.47	1.05	0.357	0.013	3.26	0.23	0.74	0.041
35	165.64	1.04	0.362	0.010	3.26	0.26	0.71	0.040

ANIMAL
NUMBER

SPLEEN
OVARIES

31	0.215	0.063
32	0.278	0.048
33	0.231	0.069
34	0.291	0.047
35	0.240	0.050

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
36	170.07	1.03	0.359	0.010	2.83	0.20	0.73	0.037
37	178.47	1.01	0.387	0.012	3.39	0.26	0.71	0.041
38	184.66	0.96	0.345	0.009	3.06	0.20	0.82	0.037
39	200.08	0.92	0.394	0.010	3.40	0.34	0.67	0.035
40	188.77	0.96	0.399	0.012	3.28	0.17	0.83	0.042

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 10
22-APR-04

ORGAN/BODY WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	SPLEEN	OVARIES
36	0.287	0.065
37	0.281	0.048
38	0.240	0.050
39	0.293	0.044
40	0.254	0.086

GROUP 4 (500 MG/KG/DAY)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
41	198.64	0.93	0.385	0.011	3.00	0.33	0.67	0.044
42	188.18	0.92	0.404	0.013	3.53	0.20	0.79	0.046
43	190.52	0.95	0.443	0.011	3.30	0.22	0.78	0.047
44	182.54	0.98	0.357	0.010	2.73	0.23	0.70	0.039
45	185.86	0.95	0.336	0.009	2.99	0.18	0.69	0.045

ANIMAL NUMBER	SPLEEN	OVARIES
41	0.235	0.044
42	0.243	0.162
43	0.269	0.077
44	0.221	0.051
45	0.313	0.056

GROUP 5 (1000 MG/KG/DAY)

ANIMAL NUMBER	BODY W. (GRAM)	BRAIN	HEART	THYROID	LIVER	THYMUS	KIDNEYS	ADRENALS
46	171.41	1.06	0.375	0.011	3.24	0.19	0.82	0.048
47	171.09	1.04	0.450	0.012	3.66	0.25	0.85	0.051
48	184.78	0.95	0.365	0.009	3.07	0.27	0.74	0.043
49	176.06	1.04	0.368	0.010	3.00	0.21	0.76	0.043
50	186.45	1.06	0.346	0.012	3.19	0.26	0.69	0.037

ANIMAL NUMBER	SPLEEN	OVARIES
46	0.237	0.060
47	0.258	0.068
48	0.255	0.057
49	0.269	0.050
50	0.368	0.051

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 11
22-APR-04

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

GROUP 1 (0 MG/KG/DAY)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
26	1.78	40.491	0.884	322.68	24.75	83.25	4.383	30.098
27	1.75	35.071	1.252	317.51	23.40	81.03	4.362	24.294
28	1.92	38.604	1.459	299.66	22.27	68.34	4.831	22.719
29	1.93	31.283	1.002	304.98	22.23	70.75	3.906	22.095
30	1.80	38.749	1.288	338.40	26.35	75.34	5.241	25.501
ANIMAL NUMBER	OVARIES							
26	6.501							
27	5.506							
28	6.536							
29	5.895							
30	6.485							

GROUP 2 (PLACEBO)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
31	1.85	35.526	0.780	284.83	23.28	68.58	3.100	20.153
32	1.89	32.700	0.867	360.01	26.22	75.41	4.031	27.617
33	1.70	46.188	1.156	412.17	21.88	44.12	4.361	26.624
34	1.87	34.050	1.203	310.91	22.25	70.47	3.925	27.799
35	1.72	34.876	0.920	314.50	25.38	68.78	3.830	23.117
ANIMAL NUMBER	OVARIES							
31	5.934							
32	4.808							
33	7.994							
34	4.529							
35	4.820							

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
36	1.75	34.972	0.951	276.23	19.81	70.91	3.650	27.931
37	1.79	38.498	1.209	336.92	26.09	70.48	4.084	27.918
38	1.77	35.923	0.966	318.74	20.90	85.52	3.857	24.997
39	1.84	42.773	1.047	369.22	37.19	73.08	3.845	31.775
40	1.82	41.322	1.208	340.26	18.01	86.47	4.403	26.366

RCC STUDY NUMBER 853022
CAROPHYLL STAY PINK 15% CWS

OW-IND - 12
22-APR-04

ORGAN/BRAIN WEIGHT RATIOS (%)
AFTER 4 WEEKS
FEMALES

GROUP 3 (100 MG/KG/DAY)

ANIMAL NUMBER	OVARIES
36	6.377
37	4.775
38	5.189
39	4.756
40	8.878

GROUP 4 (500 MG/KG/DAY)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
41	1.84	41.527	1.211	323.56	35.78	72.58	4.767	25.357
42	1.72	44.074	1.427	385.66	21.76	86.24	5.047	26.579
43	1.82	46.353	1.198	345.92	23.33	82.14	4.886	28.148
44	1.78	36.523	1.003	279.57	23.90	71.91	4.036	22.592
45	1.77	35.328	0.927	313.72	19.07	72.53	4.764	32.898

ANIMAL NUMBER	OVARIES
41	4.746
42	17.665
43	8.058
44	5.230
45	5.848

GROUP 5 (1000 MG/KG/DAY)

ANIMAL NUMBER	BRAIN (GRAM)	HEART	THYROIDS	LIVER	THYMUS	KIDNEYS	ADRENALS	SPLEEN
46	1.82	35.273	1.059	304.25	17.48	77.20	4.481	22.280
47	1.78	43.159	1.149	350.71	23.76	81.34	4.854	24.724
48	1.76	38.270	0.987	322.10	27.98	77.93	4.528	26.723
49	1.84	35.309	0.936	287.41	20.56	73.06	4.099	25.778
50	1.97	32.755	1.121	301.34	24.16	65.03	3.496	34.795

ANIMAL NUMBER	OVARIES
46	5.622
47	6.558
48	5.952
49	4.801
50	4.860

RCC Study Number 853022

AXN-DMS:

28-Day Range-Finding Oral Toxicity
(Feeding) Study in the Wistar Rat

Final Report (Part II of II)

Authors: W.H. Braun, PD Dr. A. Waldvogel,
Dr. J. Schierle, Dr V. Spitzer

Sponsor: DSM Nutritional Products
(registered as Roche Vitamins Ltd.)
Wurmisweg 576
CH-4303 Kaiseraugst / Switzerland

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

APPENDIX I:
DRINKING WATER ANALYSES

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

BACTERIOLOGICAL ASSAY OF DRINKING WATER, ITINGEN

Official Laboratory	Liestal, 28.01.2004
Basel-Landschaft	Ref.no. 200030332
Sampling point:	59.99 N Net water RCC Ltd, Itingen Room No. 10
Sampled on	28.01.2004
Sample:	
Time of sampling	7.40-8.40
Water temperature (°C)	12.6

BACTERIOLOGICAL TEST:


Aerobic mesophilic bacteria / ml	3
E.coli / 100 ml	0
Enterococci / 100 ml	0

ASSESSMENT

At the time of sampling, the tested bacteriological parameters met the requirements for drinking water according to article 275 of the "Eidg. Lebensmittelverordnung".

Willy Liestel, den 18.02.2004

Official Laboratory
The Official Chemist



(signed Dr. M. Jaggi)

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

CHEMICAL WATER ANALYSIS, ITINGEN

Official Laboratory	Liestal, 28.01.2004
Basel-Landschaft	Ref.no. 200030333
Sampling point:	59.99.N, Net water RCC Ltd, Itingen, Room no. 10
Sampled on:	28.01.2004
Time of sampling	7.40-8.40
Water temperature (°C)	12.6

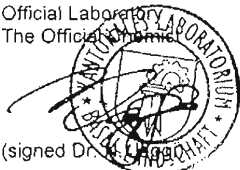
CHEMICAL TEST:

Appearance		clear, colourless
Odor		not remarkable
Taste		not remarkable
UV-absorption at 254 nm/100 cm		2.31
Conductivity		µS/cm 453.0
Oxygen demand	(KMnO ₄ cons.)	mg/l 3.1
Turbidity	FNU	0.484
Chloride	Cl ⁻	mg/l 3.8
Nitrate	NO ₃ ⁻	mg/l 10.5
Sulphate	SO ₄ ⁻	mg/l 17.9
Nitrite	NO ₂ ⁻	mg/l <0.005
Total hardness		fr.H° 27.6
Alkaline hardness		fr.H° 24.8
Non carbonate hardness		fr.H° 2.8
Calcium	Ca ⁺⁺	mg/l 106.7
Magnesium	Mg ⁺⁺	mg/l 2.2

ASSESSMENT:

At the time of sampling, the tested chemical parameters met the requirements for drinking water according to article 275 of the "Eidg. Lebensmittelverordnung".

4410 Liestal, den 19.02.2004

Official Laboratory
The Official Chemist

(signed Dr. J. L. L. L. L.)

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

CONTAMINANT ASSAY OF DRINKING WATER, ITINGEN

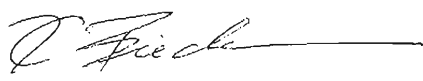
RCC Study No.: 852578
Date of Sampling: 28.01.2004
Sample: H₂O, RCC Ltd, Itingen, Room No. 10

PARAMETER	ASSAY LEVEL µg/l	LIMIT * µg/l
Lindane	< 0.05	0.1
Heptachlor	< 0.05	0.1
Malathion	< 0.05	0.1
DDT, total	< 0.05	0.1
Dieldrin	< 0.05	0.1
Cadmium	< 0.5	5
Arsenic	< 3	50
Lead	< 3	50
Mercury	< 1	1
Selenium	< 3	10
Copper	< 4	1500
PCBs (28, 52, 101, 138, 153, 180)	< 0.05	0.1
Nitrosamines, total (DMN, DEN, NPIP, NMORPH)	< 0.002	-----

< 0.05 = less than 0.05 microgram per liter

* Schweizer Lebensmittelbuch

February 12, 2004


signed K. Biedermann

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

APPENDIX II:

CHEMICAL ANALYSIS OF FEED

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

ANALYTICAL TEST REPORT

RCC Study 847194
12. February 2004

Prepared for

PROVIMI KLIBA AG
4303 Kaiseraugst

Attention of

Dr. Isler

Materials tested

KLIBA-NAFAG 3433
Batch 06/04 vom 29.01.04

Test performed

AAS, GC, GC-MS, HPLC

Test results

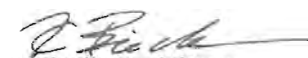
See attached Table 1

Submitted

E. Dettwiler

Issued by

K. Biedermann


.....
24. February 2004/zns

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

ATTACHMENT

RCC Study 847194
12. February 2004

Table 1 - Test Results

KLIBA-NAFAG 3433
Batch 06/04 vom 29.01.04

PARAMETER	ASSAY LEVEL mg/kg	LIMIT* mg/kg
Aflatoxins (B1, B2, G1, G2), total	< 0.001	0.005
Estrogens (DES, Hexestrol, Dienestrol), total	< 0.001	0.001
Lindane	< 0.005	0.02
Heptachlor	< 0.005	0.02
Malathion	< 0.5	2.5
DDT, total	< 0.025	0.100
Dieldrin	< 0.005	0.02
Cadmium	0.02	0.160
Arsenic	< 0.15	1.0
Lead	0.44	1.5
Mercury	< 0.05	0.1
Selenium	< 0.15	0.6
Copper	12	----
PCBs	< 0.025	0.05
Nitrosamines (DMN, DEN, NPIP, NMORPH), total	< 0.002	0.010

< 0.001 = less than 0.001 milligram per kilogram

* = USP EPA, Federal Register, Vol. 44, No. 91, May 9, 1979

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APPENDIX III:

CLINICAL LABORATORY INVESTIGATIONS

RCC Study Number 853022

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28-Day Range-Finding Oral Toxicity
(Feeding) Study in the Wistar Rat

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1.1 CLINICAL LABORATORY INVESTIGATIONS

Blood sampling: After 4 weeks: 14 April 2004

Blood samples for hematology and clinical chemistry were drawn from the retro-orbital plexus from all animals under light isoflurane anesthesia. The animals were fasted for approximately 18 hours before blood sampling but allowed access to water ad libitum. Blood samples were collected early in the working day to reduce biological variation caused by circadian rhythms.

In the summary and individual tables the names of some parameters have been abbreviated. Any abbreviation has been defined in this section. Clinical laboratory data are expressed, with a few exceptions, in general accordance with the International System of Units (SI).

Key to abbreviations of units:

l	liter	g	gram	m	milli (10^{-3})
mol	mole	kg	kilogram	μ	micro (10^{-6})
sec	second	T	tera (10^{12})	n	nano (10^{-9})
osm	osmol	G	giga (10^9)	p	pico (10^{-12})
U	Unit			f	femto (10^{-15})

General remarks:

n.d. = not determined, no value measured for this parameter

1.1.1 HEMATOLOGY

The following anticoagulants were used during blood collection:

Complete blood cell count	Di-potassium-EDTA
Methemoglobin	Lithium heparin
Coagulation	Sodium citrate, 3.2% (1 part anticoagulant to 9 parts blood)

Complete blood cell count			Method	
Parameter	Abbreviation	Unit	code	Instrumentation
Erythrocyte count	RBC	T/l	M01	Advia 120 ¹
Hemoglobin	Hb	mmol/l	M01	Advia 120
Hematocrit	Hct	rel.1	M01	Advia 120
Mean corpuscular volume	MCV	fl	M01	Advia 120
Red cell volume distribution width	RDW	rel.1	M01	Advia 120
Mean corpuscular hemoglobin	MCH	fmol	M01	Advia 120
Mean corpuscular hemoglobin concentration	MCHC	mmol/l	M01	Advia 120
Hemoglobin concentration distribution width	HDW	mmol/l	M01	Advia 120

¹ ADVIA 120 hematology system (Bayer)

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Complete blood cell count				Method	Instrumentation
Parameter	Abbreviation	Unit		code	
Reticulocyte count	Reti	relative rel.1	absolute G/l	M02	Advia 120
Reticulocyte maturity index	L Reti	rel.1		M01	Advia 120
(low, medium, high fluorescence)	M Reti	rel.1		M01	Advia 120
	H Reti	rel.1		M01	Advia 120
Leukocyte count, total	WBC	G/l		M01	Advia 120
Differential leukocyte count		relative	absolute		Advia 120
Neutrophils	Neut	rel.1	G/l	M01	Advia 120
Eosinophils	Eos	rel.1	G/l	M01	Advia 120
Basophils	Baso	rel.1	G/l	M01	Advia 120
Lymphocytes	Lympho	rel.1	G/l	M01	Advia 120
Monocytes	Mono	rel.1	G/l	M01	Advia 120
Large unstained cells	Luc	rel.1	G/l	M01	Advia 120
Platelet count	Plt	G/l		M01	Advia 120
Hemoglobin derivatives				Method	Instrumentation
Parameter	Abbreviation	Unit	Method	code	
Methemoglobin	MetHb	rel. 1	Spectrometry, results given as ratio of total hemoglobin	M01	OSM3 ²
Coagulation				Method	Instrumentation
Parameter	Abbreviation	Unit	Method	code	
Prothrombin time (=Thromboplastin time)	PT	rel. 1	Clotting assay, thromboplastin from rabbit brain tissue, results as ratio of normal activity	M01	STA ³
Activated partial thromboplastin time	PTT	sec	Clotting assay, cephalin from rabbit cerebral tissue, silica surface activator	M01	STA

² Hemoximeter OSM3

³ STA-compact analyzer (Roche Diagnostics)

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1.2 CLINICAL CHEMISTRY

Lithium heparin was used as anticoagulant during blood collection.

Parameter	Abbreviation	Unit	Method	Method code	Instrumentation
Glucose	Gluc	mmol/l	Hexokinase/G6P-DH	M01	Hitachi 917 ⁴
Urea	Urea	mmol/l	Urease/GLDH	M01	Hitachi 917
Creatinine	Creat	μmol/l	Enzymatic colorimetric test	M01	Hitachi 917
Bilirubin, total	Bili-tot	μmol/l	Reaction with 2,5-Dichlorophenyl-diazonium salt	M01	Hitachi 917
Cholesterol, total	Chol	mmol/l	Enzymatic, CHOD/PAP	M01	Hitachi 917
Triglycerides	Trigly	mmol/l	Glycerol-Kinase GPO/PAP method	M01	Hitachi 917
Phospholipids	Phos-Lip	mmol/l	Phospholipase- Cholinoxidase- Peroxidase-reaction	M01	Hitachi 917
Aspartate aminotransferase EC 2.6.1.1 ⁵	ASAT	U/l 37°C	MDH/NADH coupled reaction	M01	Hitachi 917
Alanine aminotransferase EC 2.6.1.2	ALAT	U/l 37°C	LDH/NADH coupled reaction	M01	Hitachi 917
Lactate dehydrogenase EC 1.1.1.27	LDH	U/l 37°C	NADH/LDH coupled reaction using pyruvate as substrate	M01	Hitachi 917
Glutamate dehydrogenase EC 1.4.1.3	GLDH	U/l 37°C	Standard method, optimized (DGKC)	M01	Hitachi 917
Alkaline phosphatase EC 3.1.3.1	AIP	U/l 37°C	p-Nitrophenyl-phosphate as substrate	M01	Hitachi 917
Gamma-glutamyl transferase EC 2.3.2.2	GGT	U/l 37°C	Substrate: L-gamma-glutamyl-3-carboxy-4-nitroanilide	M01	Hitachi 917
Creatine kinase EC 2.7.3.2	CK	U/l 37°C	HK/ATP and G6P-DH/NADPH coupled reaction method	M01	Hitachi 917
Sodium	Na+	mmol/l	Ion selective electrode	M01	Hitachi 917

⁴ Hitachi 917 analyzer, Roche Diagnostics

⁵ Identification of enzymes with EC-Number (Enzyme Commission) according to Enzyme Nomenclature, Recommendations (1972) of the IUPAC and IUB, Elsevier Scient. Publ. Comp., Amsterdam, 1973

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Parameter	Abbreviation	Unit	Method	Method code	Instrumentation
Potassium	K ⁺	mmol/l	Ion selective electrode	M01	Hitachi 917
Chloride	Cl ⁻	mmol/l	Ion selective electrode	M01	Hitachi 917
Calcium	Ca ⁺⁺	mmol/l	o-Cresolphthalein complexone method	M01	Hitachi 917
Phosphorus inorganic	PO ₄ -in	mmol/l	Phosphomolybdate reaction	M01	Hitachi 917
Protein, total	Prot	g/l	Biuret reaction	M01	Hitachi 917
Albumin	Alb	g/l	Bromocresol green method	M02	Hitachi 917
Globulin	Glob	g/l	Calculated value (Total protein minus Albumin)	M02	
Albumin/Globulin Ratio	A/G	rel.1	Calculated value (Albumin/Globulin)	M02	

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1.3 HEMATOLOGY (MEANS)

MALES

		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
RBC	T/l						
WEEK	5	MEAN	8.610 k	8.066	8.294	8.606	8.528
		S.D.	0.421	1.673	0.635	0.306	0.316
		N	5	5	5	5	5
Hb	mmol/l						
WEEK	5	MEAN	10.02 k	9.10	9.78	10.10	9.80
		S.D.	0.29	2.24	0.33	0.29	0.26
		N	5	5	5	5	5
Hct	rel. l						
WEEK	5	MEAN	0.4620 k	0.4300	0.4520	0.4660	0.4520
		S.D.	0.0192	0.0731	0.0148	0.0152	0.0148
		N	5	5	5	5	5
MCV	fl						
WEEK	5	MEAN	53.68 a	53.82	54.78	54.08	53.32
		S.D.	1.56	2.85	2.75	0.51	1.88
		N	5	5	5	5	5
PCV	rel. l						
WEEK	5	MEAN	0.1104 k	0.1342	0.1146	0.1168	0.1150
		S.D.	0.0043	0.0305	0.0043	0.0055	0.0116
		N	5	5	5	5	5
MCH	fmol						
WEEK	5	MEAN	1.164 a	1.114	1.184	1.174	1.148
		S.D.	0.039	0.074	0.068	0.025	0.036
		N	5	5	5	5	5
Statistical key: a=ANOVA k=Kruskal-Wallis							

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		Hematology (means)					
MALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
MCV		mmol/l					
WEEK	5	MEAN	21.716 k	20.790	21.606	21.686	21.564
		S.D.	0.311	2.089	0.213	0.350	0.403
		N	5	5	5	5	5
MCV		mmol/l					
WEEK	5	MEAN	1.466 k	1.632	1.428	1.462	1.552
		S.D.	0.040	0.241	0.050	0.077	0.172
		N	5	5	5	5	5
Pcti		rel. l					
WEEK	5	MEAN	0.0232 k	0.0776	0.0292	0.0254	0.0312
		S.D.	0.0013	0.1261	0.0115	0.0049	0.0150
		N	5	5	5	5	5
Pcti		G/l					
WEEK	5	MEAN	201.2 k	456.0	235.4	219.6	263.0
		S.D.	11.8	606.0	68.6	38.0	116.4
		N	5	5	5	5	5
L Pcti		rel. l					
WEEK	5	MEAN	0.4606 k	0.4542	0.4654	0.4710	0.4544
		S.D.	0.0167	0.1608	0.0766	0.0388	0.0377
		N	5	5	5	5	5
M Pcti		rel. l					
WEEK	5	MEAN	0.3944 k	0.3442	0.3884	0.3894	0.3890
		S.D.	0.0291	0.0725	0.0202	0.0179	0.0322
		N	5	5	5	5	5
Statistical key: k=Kruskal-Wallis							

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		Hematology (means)					
MALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
H Peti	rel. 1						
WEEK	5	MEAN	0.1450 k	0.2020	0.1458	0.1296	0.1568
		S.D.	0.0317	0.1969	0.0907	0.0266	0.0563
		N	5	5	5	5	5
WBC	G/l						
WEEK	5	MEAN	8.400 a	9.100	7.673	8.290	8.174
		S.D.	1.037	1.676	1.738	1.042	2.121
		N	5	5	4	4	5
Neut	rel. 1						
WEEK	5	MEAN	0.1312 a	0.1306	0.1203	0.0972	0.1298
		S.D.	0.0172	0.0695	0.0269	0.0276	0.0313
		N	5	5	4	4	5
Eos	rel. 1						
WEEK	5	MEAN	0.0098 a	0.0070	0.0088	0.0068	0.0096
		S.D.	0.0029	0.0042	0.0053	0.0013	0.0030
		N	5	5	4	4	5
Baso	rel. 1						
WEEK	5	MEAN	0.0028ad	0.0012**	0.0020	0.0022	0.0022
		S.D.	0.0004	0.0004	0.0008	0.0005	0.0004
		N	5	5	4	4	5
Lympho	rel. 1						
WEEK	5	MEAN	0.8312 a	0.8350	0.8455	0.8705	0.8302
		S.D.	0.0224	0.0740	0.0263	0.0263	0.0353
		N	5	5	4	4	5
Statistical key: a=ANOVA ad=ANOVA + Dunnett k=Kruskal-Wallis ** = p<0.01							

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		Hematology (means)					
MALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
Mono	rel. l						
WEEK	5	MEAN	0.0178 k	0.0554	0.0137	0.0153	0.0178
		S.D.	0.0038	0.0976	0.0050	0.0030	0.0041
		N	5	5	4	4	5
Luc	rel. l						
WEEK	5	MEAN	0.0074 a	0.0120	0.0095	0.0085	0.0102
		S.D.	0.0018	0.0062	0.0034	0.0029	0.0032
		N	5	5	4	4	5
Neut	G/l						
WEEK	5	MEAN	1.110 a	1.226	0.910	0.808	1.072
		S.D.	0.265	0.770	0.259	0.261	0.427
		N	5	5	4	4	5
Eos	G/l						
WEEK	5	MEAN	0.084 a	0.062	0.063	0.055	0.080
		S.D.	0.034	0.036	0.037	0.017	0.041
		N	5	5	4	4	5
Baso	G/l						
WEEK	5	MEAN	0.022 a	0.012	0.013	0.018	0.014
		S.D.	0.008	0.004	0.005	0.010	0.005
		N	5	5	4	4	5
Lympho	G/l						
WEEK	5	MEAN	6.970 a	7.554	6.510	7.218	6.778
		S.D.	0.723	1.308	1.570	0.937	1.697
		N	5	5	4	4	5
Statistical key:		a=ANOVA	k=Kruskal-Wallis				

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		Hematology (means)					
MALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
<hr/>							
Mono		G/l					
WEEK	5	MEAN	0.150 a	0.130	0.102	0.120	0.148
		S.D.	0.041	0.060	0.034	0.016	0.058
		N	5	5	4	4	5
Luc		G/l					
WEEK	5	MEAN	0.064 a	0.114	0.080	0.072	0.080
		S.D.	0.019	0.067	0.036	0.033	0.019
		N	5	5	4	4	5
Plt		G/l					
WEEK	5	MEAN	982.6kd	1247.8	913.6	959.4	1096.6
		S.D.	113.1	431.9	70.2	110.8	83.1
		N	5	5	5	5	5
Methb		rel. l					
WEEK	5	MEAN	0.0088 k	0.0100	0.0088	0.0090	0.0090
		S.D.	0.0004	0.0023	0.0008	0.0007	0.0007
		N	5	5	5	5	5
PT		rel. l					
WEEK	5	MEAN	0.834 a	0.878	0.848	0.830	0.854
		S.D.	0.034	0.057	0.034	0.029	0.059
		N	5	5	5	5	5
PTT		sec					
WEEK	5	MEAN	26.46 a	27.88	26.24	24.00	29.18
		S.D.	3.61	2.70	3.43	1.90	0.87
		N	5	5	5	5	5
<hr/>							
Statistical key:		a=ANOVA	k=Kruskal-Wallis	kd=Kruskal-Wallis + Dunn			

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		Hematology (means)					
FEMALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
RBC	T/l						
WEEK	5	MEAN	7.808 a	7.816	8.048	7.896	8.152
		S.D.	0.335	0.274	0.385	0.203	0.419
		N	5	5	5	5	5
Hb	mmol/l						
WEEK	5	MEAN	9.38 a	9.32	9.24	9.32	9.66
		S.D.	0.20	0.29	0.21	0.36	0.22
		N	5	5	5	5	5
Hct	rel. l						
WEEK	5	MEAN	0.4220 a	0.4180	0.4240	0.4200	0.4390
		S.D.	0.0192	0.0148	0.0114	0.0158	0.0124
		N	5	5	5	5	5
MCV	fL						
WEEK	5	MEAN	53.82 a	53.80	52.68	53.08	53.74
		S.D.	1.15	0.82	2.79	0.98	1.04
		N	5	5	5	5	5
RDW	rel. l						
WEEK	5	MEAN	0.1116 k	0.1088	0.1154	0.1070	0.1056
		S.D.	0.0092	0.0072	0.0181	0.0034	0.0057
		N	5	5	5	5	5
MCH	fmoL						
WEEK	5	MEAN	1.202 a	1.192	1.150	1.182	1.186
		S.D.	0.042	0.049	0.071	0.029	0.036
		N	5	5	5	5	5
Statistical key: a=ANOVA k=Kruskal-Wallis							

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		Hematology (means)					
FEMALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
MCHC	mmol/l						
WEEK 5		MEAN	22.332 a	22.160	21.854	22.250	22.070
		S.D.	0.545	0.619	0.555	0.251	0.328
		N	5	5	5	5	5
HDW	mmol/l						
WEEK 5		MEAN	1.370 a	1.366	1.340	1.366	1.330
		S.D.	0.039	0.096	0.116	0.036	0.075
		N	5	5	5	5	5
Peti	rel. l						
WEEK 5		MEAN	0.0236 a	0.0240	0.0240	0.0230	0.0240
		S.D.	0.0026	0.0035	0.0024	0.0025	0.0023
		N	5	5	5	5	5
Peti	G/l						
WEEK 5		MEAN	183.4 a	187.0	194.2	183.2	194.6
		S.D.	18.0	27.5	13.9	23.6	21.7
		N	5	5	5	5	5
L Peti	rel. l						
WEEK 5		MEAN	0.5230 a	0.4946	0.5402	0.4870	0.5134
		S.D.	0.0604	0.0696	0.0593	0.0328	0.0569
		N	5	5	5	5	5
M Peti	rel. l						
WEEK 5		MEAN	0.3916 a	0.3814	0.3744	0.3860	0.3702
		S.D.	0.0230	0.0234	0.0198	0.0175	0.0226
		N	5	5	5	5	5
Statistical key:		a=ANOVA					

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		Hematology (means)					
FEMALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
H Reti	rel. 1						
WEEK	5	MEAN	0.0852 a	0.1240	0.0852	0.1272	0.1170
		S.D.	0.0441	0.0506	0.0606	0.0377	0.0588
		N	5	5	5	5	5
WBC	G/l						
WEEK	5	MEAN	6.147ad	7.602	6.104	5.762	4.592
		S.D.	0.528	1.670	0.412	0.826	1.374
		N	3	5	5	5	5
Neut	rel. 1						
WEEK	5	MEAN	0.1307ad	0.0898	0.1284	0.0882	0.1492
		S.D.	0.0363	0.0290	0.0302	0.0275	0.0432
		N	3	5	5	5	5
Eos	rel. 1						
WEEK	5	MEAN	0.0707kd	0.0106	0.0098	0.0096	0.0204
		S.D.	0.1034	0.0059	0.0013	0.0036	0.0051
		N	3	5	5	5	5
Baso	rel. 1						
WEEK	5	MEAN	0.0020 k	0.0020	0.0016	0.0022	0.0020
		S.D.	0.0000	0.0000	0.0011	0.0008	0.0014
		N	3	5	5	5	5
Lympho	rel. 1						
WEEK	5	MEAN	0.8233ad	0.8792	0.8378	0.8802	0.8056
		S.D.	0.0391	0.0309	0.0306	0.0265	0.0474
		N	3	5	5	5	5
Statistical key: a=ANOVA ad=ANOVA + Dunnett k=Kruskal-Wallis kd=Kruskal-Wallis + Dunn							

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		Hematology (means)					
FEMALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
Mono		rel. l					
WEEK	5	MEAN	0.0170ad	0.0108**	0.0160	0.0130	0.0150
		S.D.	0.0017	0.0026	0.0019	0.0025	0.0021
		N	3	5	5	5	5
Luc		rel. l					
WEEK	5	MEAN	0.0130 a	0.0074	0.0066	0.0072	0.0080
		S.D.	0.0035	0.0021	0.0025	0.0026	0.0037
		N	3	5	5	5	5
Neut		G/l					
WEEK	5	MEAN	0.793 a	0.658	0.786	0.522	0.716
		S.D.	0.156	0.146	0.208	0.208	0.434
		N	3	5	5	5	5
Eos		G/l					
WEEK	5	MEAN	0.083 a	0.078	0.060	0.054	0.094
		S.D.	0.031	0.041	0.010	0.015	0.036
		N	3	5	5	5	5
Baso		G/l					
WEEK	5	MEAN	0.010 a	0.016	0.010	0.014	0.010
		S.D.	0.000	0.005	0.007	0.005	0.012
		N	3	5	5	5	5
Lympho		G/l					
WEEK	5	MEAN	5.070ad	6.710	5.110	5.060	3.664
		S.D.	0.639	1.622	0.318	0.645	0.905
		N	3	5	5	5	5
Statistical key: a=ANOVA ad=ANOVA + Dunnett ** = p<0.01							

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			Hematology (means)					
FEMALES								
			Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
Mono			G/l					
WEEK	5		MEAN	0.107 a	0.084	0.096	0.076	0.070
			S.D.	0.021	0.029	0.015	0.025	0.023
			N	3	5	5	5	5
Luc			G/l					
WEEK	5		MEAN	0.080 a	0.056	0.040	0.042	0.042
			S.D.	0.026	0.017	0.017	0.023	0.035
			N	3	5	5	5	5
Pit			G/l					
WEEK	5		MEAN	1077.0 a	1084.2	1021.4	976.8	929.0
			S.D.	110.1	83.5	85.2	86.4	168.5
			N	5	5	5	5	5
Methb			rel. 1					
WEEK	5		MEAN	0.0084 k	0.0088	0.0080	0.0076	0.0080
			S.D.	0.0005	0.0011	0.0009	0.0005	0.0007
			N	5	5	5	5	5
PT			rel. 1					
WEEK	5		MEAN	0.840 a	0.858	0.814	0.802	0.866
			S.D.	0.042	0.045	0.034	0.043	0.061
			N	5	5	5	5	5
PTT			sec					
WEEK	5		MEAN	23.04 a	22.80	22.98	22.24	20.38
			S.D.	3.47	1.89	2.24	4.09	2.60
			N	5	5	5	5	5
Statistical key:			a=ANOVA	k=Kruskal-Wallis				

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1.4 BLOOD CHEMISTRY (MEANS)

MALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
<hr/>							
Gluc	mmol/l						
WEEK	5	MEAN	4.538ad	5.502*	5.390	5.378	5.246
		S.D.	0.365	0.563	0.668	0.560	0.302
		N	5	5	5	5	5
Urea	mmol/l						
WEEK	5	MEAN	8.000 a	8.044	9.002	7.916	8.014
		S.D.	0.681	0.920	0.493	1.169	0.534
		N	5	5	5	5	5
Creat	μmol/l						
WEEK	5	MEAN	25.32 a	24.10	26.90	25.24	25.52
		S.D.	1.84	1.74	1.66	2.60	2.08
		N	5	5	5	5	5
Bili-tot	μmol/l						
WEEK	5	MEAN	1.904ad	1.478	2.054	2.078	2.366
		S.D.	0.259	0.300	0.508	0.555	0.305
		N	5	5	5	5	5
Chol	mmol/l						
WEEK	5	MEAN	1.792 a	2.076	1.780	1.974	2.312
		S.D.	0.223	0.321	0.144	0.234	0.446
		N	5	5	5	5	5
Trigly	mmol/l						
WEEK	5	MEAN	0.798 a	0.676	0.634	0.568	0.630
		S.D.	0.204	0.315	0.217	0.078	0.123
		N	5	5	5	5	5
<hr/>							
Statistical key:		a=ANOVA	ad=ANOVA + Dunnett	* = p<0.05			

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		Blood chemistry (means)					
MALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
Phos-Lip		mmol/l					
WEEK	5	MEAN	1.730 a	1.788	1.668	1.730	1.988
		S.D.	0.120	0.252	0.062	0.144	0.256
		N	5	5	5	5	5
ASAT		U/l					
WEEK	5	MEAN	67.32 a	61.48	66.52	57.98	60.74
		S.D.	11.99	6.45	4.55	5.03	6.21
		N	5	5	5	5	5
ALAT		U/l					
WEEK	5	MEAN	53.44kd	44.26	46.28	33.16*	36.86
		S.D.	12.93	10.27	12.99	3.34	3.94
		N	5	5	5	5	5
LDH		U/l					
WEEK	5	MEAN	150.90 a	155.36	139.42	113.90	125.30
		S.D.	38.26	49.03	16.14	10.89	24.48
		N	5	5	5	5	5
GLDH		U/l					
WEEK	5	MEAN	4.42 a	4.56	4.04	3.58	5.02
		S.D.	1.35	1.42	0.55	0.67	1.89
		N	5	5	5	5	5
ALP		U/l					
WEEK	5	MEAN	141.66 a	133.14	156.16	154.88	134.54
		S.D.	43.04	30.20	33.16	27.05	38.90
		N	5	5	5	5	5
Statistical key: a=ANOVA kd=Kruskal-Wallis + Dunn * = p<0.05							

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		Blood chemistry (means)					
MALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
GGT	U/l						
WEEK 5		MEAN	0.00 a	0.00	0.00	0.00	0.00
		S.D.	0.00	0.00	0.00	0.00	0.00
		N	5	5	5	5	5
CK	U/l						
WEEK 5		MEAN	220.32kd	181.52	155.54	132.20**	152.74
		S.D.	50.65	36.35	15.02	8.45	15.22
		N	5	5	5	5	5
Na+	mmol/l						
WEEK 5		MEAN	141.20 a	142.36	142.56	142.16	141.86
		S.D.	0.68	0.99	0.60	0.80	1.26
		N	5	5	5	5	5
K+	mmol/l						
WEEK 5		MEAN	3.676 a	3.838	3.908	3.996	3.798
		S.D.	0.215	0.309	0.315	0.324	0.317
		N	5	5	5	5	5
Cl-	mmol/l						
WEEK 5		MEAN	100.82ad	104.32**	104.26**	103.50*	102.08
		S.D.	1.92	2.04	1.73	0.82	0.54
		N	5	5	5	5	5
Ca++	mmol/l						
WEEK 5		MEAN	2.806 a	2.794	2.796	2.730	2.766
		S.D.	0.023	0.092	0.043	0.051	0.040
		N	5	5	5	5	5
Statistical key: a=ANOVA ad=ANOVA + Dunnett kd=Kruskal-Wallis + Dunn * = p<0.05 ** = p<0.01							

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		Blood chemistry (means)					
MALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
PO4-in	mmol/l						
WEEK	5	MEAN	2.314 a	2.164	2.238	2.356	2.228
		S.D.	0.075	0.220	0.161	0.189	0.205
		N	5	5	5	5	5
Prot	g/l						
WEEK	5	MEAN	64.530 a	64.618	63.346	64.166	65.258
		S.D.	1.797	2.206	1.369	1.600	1.342
		N	5	5	5	5	5
Alb	g/l						
WEEK	5	MEAN	41.008ad	41.394	41.674	42.490	43.828*
		S.D.	1.224	1.463	1.121	1.693	1.663
		N	5	5	5	5	5
Glob	g/l						
WEEK	5	MEAN	23.522 a	23.224	21.672	21.676	21.432
		S.D.	0.756	2.203	2.056	2.201	1.782
		N	5	5	5	5	5
A/G	rel. 1						
WEEK	5	MEAN	1.744 a	1.796	1.938	1.980	2.060
		S.D.	0.047	0.190	0.224	0.274	0.217
		N	5	5	5	5	5
Statistical key: a=ANOVA ad=ANOVA + Dunnett * = p<0.05							

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		Blood chemistry (means)					
FEMALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
Gluc	mmol/l						
WEEK	5	MEAN	5.044 a	6.036	5.516	5.238	4.704
		S.D.	0.650	1.008	0.905	0.635	0.186
		N	5	5	5	5	5
Urea	mmol/l						
WEEK	5	MEAN	8.312 a	7.436	7.808	7.286	7.986
		S.D.	1.391	1.490	1.288	0.831	0.710
		N	5	5	5	5	5
Creat	µmol/l						
WEEK	5	MEAN	29.46 a	26.66	27.30	28.22	28.26
		S.D.	2.20	2.48	2.47	0.94	2.61
		N	5	5	5	5	5
Bili.-tot	µmol/l						
WEEK	5	MEAN	1.874 a	1.780	1.678	1.768	1.932
		S.D.	0.327	0.275	0.334	0.260	0.539
		N	5	5	5	5	5
Chol	mmol/l						
WEEK	5	MEAN	1.580 a	1.658	1.458	1.596	1.706
		S.D.	0.311	0.417	0.410	0.434	0.326
		N	5	5	5	5	5
Trigly	mmol/l						
WEEK	5	MEAN	0.320 k	0.404	0.460	0.320	0.334
		S.D.	0.051	0.068	0.251	0.084	0.021
		N	5	5	5	5	5
Statistical key: a=ANOVA k=Kruskal-Wallis							

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		Blood chemistry (means)					
FEMALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
Phos-Lip		mmol/l					
WEEK	5	MEAN	1.744 a	1.740	1.610	1.638	1.674
		S.D.	0.282	0.283	0.357	0.307	0.201
		N	5	5	5	5	5
ASAT		U/l					
WEEK	5	MEAN	64.26 a	68.36	64.24	67.98	67.24
		S.D.	4.66	10.51	4.40	5.04	4.94
		N	5	5	5	5	5
ALAT		U/l					
WEEK	5	MEAN	34.28ad	53.18**	34.26	31.08	29.78
		S.D.	7.98	9.15	11.97	5.76	5.96
		N	5	5	5	5	5
LDH		U/l					
WEEK	5	MEAN	114.68kd	147.44	138.28	165.14*	144.82
		S.D.	7.05	36.35	16.45	35.76	15.43
		N	5	5	5	5	5
GLDH		U/l					
WEEK	5	MEAN	4.72 k	6.00	4.56	5.30	4.34
		S.D.	1.80	5.17	1.39	2.15	1.04
		N	5	5	5	5	5
ALP		U/l					
WEEK	5	MEAN	74.06 a	72.10	68.62	58.22	61.84
		S.D.	27.32	13.48	16.13	15.74	17.93
		N	5	5	5	5	5
Statistical key: a=ANOVA ad=ANOVA + Dunnett k=Kruskal-Wallis kd=Kruskal-Wallis + Dunn * = p<0.05 ** = p<0.01							

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		Blood chemistry (means)					
FEMALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
GGT		U/l					
WEEK	5	MEAN	0.00 a	0.00	0.00	0.00	0.00
		S.D.	0.00	0.00	0.00	0.00	0.00
		N	5	5	5	5	5
CK		U/l					
WEEK	5	MEAN	122.44kd	165.54	162.20	201.64	222.74*
		S.D.	4.11	37.44	50.18	68.64	88.92
		N	5	5	5	5	5
Na+		mmol/l					
WEEK	5	MEAN	141.18 a	142.26	142.60	141.18	141.64
		S.D.	0.75	0.93	0.76	1.21	0.51
		N	5	5	5	5	5
K+		mmol/l					
WEEK	5	MEAN	3.170 a	3.582	3.572	3.606	3.460
		S.D.	0.287	0.174	0.435	0.335	0.240
		N	5	5	5	5	5
Cl-		mmol/l					
WEEK	5	MEAN	102.72ad	104.48*	103.80	104.02	104.82*
		S.D.	1.08	1.10	0.82	1.31	0.66
		N	5	5	5	5	5
Ca++		mmol/l					
WEEK	5	MEAN	2.712ad	2.750	2.770	2.642	2.652
		S.D.	0.079	0.016	0.078	0.081	0.061
		N	5	5	5	5	5
Statistical key:		a=ANOVA	ad=ANOVA + Dunnett	kd=Kruskal-Wallis + Dunn	* = p<0.05		

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		Blood chemistry (means)					
FEMALES							
		Group Group Name Dose Level	Group 1 Control 0 mg/kg	Group 2 Placebo	Group 3 100 mg/kg	Group 4 500 mg/kg	Group 5 1000 mg/kg
PO4-in	mmol/l						
WEEK	5	MEAN	1.948ad	1.674	1.876	1.710	1.614*
		S.D.	0.125	0.215	0.211	0.175	0.160
		N	5	5	5	5	5
Prot	g/l						
WEEK	5	MEAN	67.542 a	64.688	66.674	64.914	63.912
		S.D.	1.964	2.283	1.686	1.899	2.193
		N	5	5	5	5	5
Alb	g/l						
WEEK	5	MEAN	46.614 a	44.234	45.712	45.644	45.602
		S.D.	2.451	1.047	1.302	1.988	1.994
		N	5	5	5	5	5
Glob	g/l						
WEEK	5	MEAN	20.928ad	20.454	20.962	19.270	18.308*
		S.D.	0.609	1.781	1.585	1.121	0.821
		N	5	5	5	5	5
A/G	rel. 1						
WEEK	5	MEAN	2.232 a	2.174	2.194	2.374	2.496
		S.D.	0.180	0.178	0.212	0.196	0.152
		N	5	5	5	5	5
Statistical key: a=ANOVA ad=ANOVA + Dunnett * = p<0.05							

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1.5 HEMATOLOGY (INDIVIDUALS)

WEEK 5

MALES

	RBC	Hb	Hct	MCV	RDW	MCH	MCHC	HDW	Reti	Reti	L Reti	M Reti
AN_NO	T/l	mmol/l	rel. l	fl	rel. l	fmol	mmol/l	mmol/l	rel. l	G/l	rel. l	rel. l
Group 1 Control (0 mg/kg)												
1 M	8.56	10.0	0.450	52.9	0.117	1.16	22.02	1.51	0.022	186	0.463	0.413
2 M	8.43	10.1	0.460	54.5	0.106	1.20	22.05	1.45	0.025	214	0.485	0.407
3 M	9.13	10.0	0.470	51.3	0.112	1.10	21.41	1.50	0.022	205	0.438	0.424
4 M	8.04	9.6	0.440	54.9	0.108	1.19	21.68	1.41	0.024	192	0.458	0.373
5 M	8.89	10.4	0.490	54.8	0.109	1.17	21.42	1.46	0.023	209	0.459	0.355
Group 2 Placebo												
6 M	8.81	10.0	0.450	51.3	0.123	1.13	22.05	1.78	0.025	216	0.469	0.408
7 M	5.09	5.1	0.300	58.1	0.186	0.99	17.08	1.95	0.303	1538	0.205	0.246
8 M	9.09	10.2	0.470	51.3	0.112	1.12	21.79	1.63	0.019	175	0.508	0.395
9 M	8.70	9.9	0.460	53.4	0.114	1.14	21.36	1.42	0.026	222	0.440	0.384
10 M	8.64	10.3	0.470	55.0	0.136	1.19	21.67	1.38	0.015	129	0.649	0.288
Group 3 (100 mg/kg)												
11 M	8.78	10.2	0.470	54.0	0.109	1.17	21.58	1.39	0.023	203	0.520	0.384
12 M	8.85	9.7	0.460	51.8	0.115	1.10	21.26	1.50	0.020	175	0.529	0.394
13 M	8.31	9.8	0.450	54.2	0.113	1.17	21.68	1.46	0.027	225	0.496	0.399
14 M	7.26	9.3	0.430	59.3	0.121	1.29	21.68	1.40	0.049	353	0.344	0.356
15 M	8.27	9.9	0.450	54.6	0.115	1.19	21.83	1.39	0.027	221	0.438	0.409
Group 4 (500 mg/kg)												
16 M	9.09	10.5	0.490	54.2	0.110	1.15	21.22	1.33	0.021	194	0.471	0.392
17 M	8.72	10.0	0.470	53.4	0.120	1.15	21.54	1.50	0.027	239	0.463	0.394
18 M	8.33	9.8	0.450	53.9	0.112	1.18	21.81	1.48	0.027	226	0.431	0.411
19 M	8.44	9.9	0.460	54.1	0.123	1.18	21.74	1.53	0.032	268	0.455	0.423
20 M	8.45	10.3	0.460	54.8	0.119	1.21	22.17	1.47	0.020	171	0.535	0.377
Group 5 (1000 mg/kg)												
21 M	8.46	9.9	0.450	52.8	0.108	1.17	22.11	1.61	0.025	209	0.490	0.378
22 M	8.08	9.7	0.450	56.2	0.135	1.20	21.41	1.79	0.058	471	0.408	0.345
23 M	8.96	10.2	0.470	53.0	0.107	1.13	21.40	1.33	0.023	204	0.496	0.396
24 M	8.53	9.5	0.430	51.0	0.115	1.11	21.82	1.57	0.025	217	0.433	0.392
25 M	8.61	9.7	0.460	53.6	0.110	1.13	21.08	1.46	0.025	214	0.445	0.434

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Hematology (individuals)												
WEEK	MALES											
	H Reti	WBC	Neut	Eos	Baso	Lympho	Mono	Luc	Neut	Eos	Baso	Lympho
AN_NO	rel. 1	G/l	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	G/l	G/l	G/l	G/l
Group 1 Control (0 mg/kg)												
1 M	0.124	10.24	0.151	0.014	0.003	0.805	0.019	0.008	1.54	0.14	0.03	8.24
2 M	0.108	7.85	0.133	0.011	0.003	0.825	0.023	0.006	1.04	0.09	0.02	6.48
3 M	0.139	8.01	0.140	0.009	0.003	0.820	0.019	0.009	1.12	0.07	0.03	6.57
4 M	0.169	8.12	0.127	0.009	0.003	0.843	0.014	0.005	1.03	0.07	0.02	6.84
5 M	0.185	7.78	0.105	0.006	0.002	0.863	0.014	0.009	0.82	0.05	0.01	6.72
Group 2 Placebo												
6 M	0.123	7.56	0.092	0.013	0.001	0.869	0.015	0.010	0.69	0.10	0.01	6.57
7 M	0.550	9.96	0.253	0.002	0.001	0.706	0.230	0.015	2.52	0.02	0.01	7.03
8 M	0.097	10.15	0.114	0.005	0.001	0.848	0.010	0.021	1.15	0.05	0.01	8.61
9 M	0.177	10.78	0.110	0.009	0.002	0.859	0.012	0.009	1.18	0.10	0.02	9.26
10 M	0.063	7.05	0.084	0.006	0.001	0.893	0.010	0.005	0.59	0.04	0.01	6.30
Group 3 (100 mg/kg)												
11 M	0.095	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
12 M	0.077	5.11	0.134	0.013	0.002	0.827	0.019	0.005	0.69	0.06	0.01	4.23
13 M	0.104	8.88	0.084	0.013	0.003	0.880	0.010	0.011	0.74	0.11	0.02	7.82
14 M	0.300	8.59	0.146	0.002	0.002	0.823	0.017	0.009	1.26	0.02	0.01	7.07
15 M	0.153	8.11	0.117	0.007	0.001	0.852	0.009	0.013	0.95	0.06	0.01	6.92
Group 4 (500 mg/kg)												
16 M	0.137	6.73	0.098	0.005	0.002	0.872	0.019	0.005	0.66	0.03	0.01	5.87
17 M	0.143	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
18 M	0.158	8.75	0.133	0.008	0.002	0.834	0.016	0.008	1.17	0.07	0.01	7.30
19 M	0.122	8.91	0.092	0.007	0.003	0.873	0.012	0.012	0.82	0.06	0.03	7.78
20 M	0.088	8.77	0.066	0.007	0.002	0.903	0.014	0.009	0.58	0.06	0.02	7.92
Group 5 (1000 mg/kg)												
21 M	0.132	7.91	0.097	0.007	0.002	0.872	0.011	0.010	0.77	0.06	0.01	6.90
22 M	0.247	5.57	0.158	0.010	0.003	0.794	0.020	0.015	0.88	0.05	0.02	4.42
23 M	0.108	6.90	0.095	0.012	0.002	0.864	0.017	0.010	0.65	0.08	0.01	5.96
24 M	0.175	9.56	0.155	0.006	0.002	0.811	0.021	0.006	1.48	0.06	0.01	7.75
25 M	0.122	10.93	0.144	0.013	0.002	0.810	0.020	0.010	1.58	0.15	0.02	8.86
n.d.=not determined												

n.d.=not determined

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Hematology (individuals)						
WEEK	MALES					
5	Mono	Luc	Plt	RetHb	PT	PTT
AN NO	G/l	G/l	G/l	rel. %	rel. %	sec
Group 1 Control (0 mg/kg)						
1 M	0.20	0.09	1160	0.009	0.86	24.3
2 M	0.18	0.05	873	0.009	0.82	29.4
3 M	0.15	0.07	933	0.009	0.78	31.2
4 M	0.11	0.04	923	0.009	0.86	23.0
5 M	0.11	0.07	1024	0.008	0.85	24.4
Group 2 Placebo						
6 M	0.11	0.08	1019	0.009	0.88	31.3
7 M	0.23	0.15	2014	0.014	0.83	27.0
8 M	0.11	0.21	986	0.009	0.83	30.1
9 M	0.13	0.09	1105	0.008	0.88	25.0
10 M	0.07	0.04	1115	0.010	0.97	26.0
Group 3 (100 mg/kg)						
11 M	n.d.	n.d.	812	0.009	0.88	23.4
12 M	0.10	0.03	919	0.009	0.80	29.7
13 M	0.09	0.10	908	0.008	0.83	21.8
14 M	0.15	0.08	1010	0.010	0.88	28.3
15 M	0.07	0.11	919	0.008	0.85	28.0
Group 4 (500 mg/kg)						
16 M	0.12	0.03	802	0.010	0.83	25.7
17 M	n.d.	n.d.	1026	0.008	0.81	23.6
18 M	0.14	0.07	1083	0.009	0.81	25.2
19 M	0.10	0.11	988	0.009	0.88	24.6
20 M	0.12	0.08	888	0.009	0.82	20.9
Group 5 (1000 mg/kg)						
21 M	0.09	0.08	1198	0.010	0.89	29.8
22 M	0.11	0.08	1058	0.008	0.89	29.1
23 M	0.12	0.07	1174	0.009	0.79	28.4
24 M	0.20	0.06	1030	0.009	0.79	30.3
25 M	0.22	0.11	1023	0.009	0.91	28.3

n.d.=not determined

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Hematology (individuals)												
WEEK	FEMALES											
AN_NO	RBC	Hb	Hct	MCV	RDW	MCH	MCHC	RDW	Reti	Reti	L Reti	M Reti
	T/l	mmol/l	rel. l	fl	rel. l	fmol	mmol/l	mmol/l	rel. l	G/l	rel. l	rel. l
Group 1 Control (0 mg/kg)												
26 F	8.39	9.6	0.450	53.2	0.112	1.14	21.46	1.34	0.022	187	0.585	0.359
27 F	7.68	9.2	0.410	53.7	0.105	1.20	22.27	1.36	0.024	181	0.555	0.396
28 F	7.73	9.2	0.400	52.3	0.110	1.19	22.84	1.40	0.026	200	0.540	0.398
29 F	7.71	9.6	0.430	54.8	0.127	1.25	22.74	1.42	0.020	154	0.508	0.383
30 F	7.53	9.3	0.420	55.1	0.104	1.23	22.35	1.33	0.026	195	0.427	0.422
Group 2 Placebo												
31 F	7.81	9.4	0.420	53.7	0.103	1.20	22.39	1.35	0.019	145	0.599	0.344
32 F	7.56	9.5	0.410	54.9	0.121	1.26	22.92	1.52	0.029	219	0.429	0.390
33 F	7.65	8.8	0.400	52.8	0.108	1.15	21.80	1.27	0.024	185	0.449	0.388
34 F	7.79	9.5	0.420	54.3	0.108	1.21	22.38	1.38	0.024	184	0.530	0.378
35 F	8.27	9.4	0.440	53.3	0.104	1.14	21.31	1.31	0.024	202	0.466	0.407
Group 3 (100 mg/kg)												
36 F	7.62	9.4	0.410	54.0	0.147	1.23	22.84	1.53	0.025	194	0.586	0.356
37 F	8.20	9.1	0.420	51.2	0.104	1.11	21.71	1.36	0.022	184	0.533	0.408
38 F	8.63	9.0	0.420	48.5	0.114	1.05	21.55	1.31	0.021	182	0.586	0.369
39 F	7.86	9.2	0.430	54.5	0.106	1.17	21.54	1.24	0.025	194	0.554	0.373
40 F	7.93	9.5	0.440	55.2	0.106	1.19	21.63	1.26	0.027	217	0.442	0.366
Group 4 (500 mg/kg)												
41 F	7.94	9.7	0.440	54.8	0.109	1.22	22.20	1.38	0.024	191	0.467	0.398
42 F	7.96	9.2	0.420	52.5	0.112	1.15	21.98	1.41	0.027	218	0.450	0.392
43 F	7.61	8.8	0.400	52.7	0.104	1.16	22.06	1.32	0.021	157	0.482	0.355
44 F	7.81	9.3	0.410	52.9	0.105	1.20	22.58	1.34	0.021	167	0.535	0.392
45 F	8.16	9.6	0.430	52.5	0.105	1.18	22.43	1.38	0.022	183	0.501	0.393
Group 5 (1000 mg/kg)												
46 F	8.70	9.9	0.450	52.2	0.104	1.14	21.80	1.26	0.025	220	0.581	0.367
47 F	7.57	9.3	0.420	55.0	0.112	1.23	22.36	1.39	0.024	184	0.430	0.371
48 F	8.36	9.7	0.450	53.5	0.102	1.16	21.64	1.24	0.020	164	0.543	0.366
49 F	8.02	9.7	0.440	54.3	0.099	1.21	22.32	1.36	0.025	197	0.504	0.342
50 F	8.11	9.7	0.435	53.7	0.111	1.19	22.23	1.40	0.026	208	0.509	0.405

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Hematology (individuals)												
WEEK	FEMALES											
	H Reti	WBC	Neut	Eos	Baso	Lympho	Mono	Luc	Neut	Eos	Baso	Lympho
AN_NO	rel. 1	G/l	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	rel. 1	G/l	G/l	G/l	G/l
Group 1 Control (0 mg/kg)												
26 F	0.056	6.21	0.104	0.008	0.002	0.853	0.016	0.017	0.65	0.05	0.01	5.29
27 F	0.048	6.64	0.116	0.014	0.002	0.838	0.019	0.011	0.77	0.09	0.01	5.57
28 F	0.061	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
29 F	0.110	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
30 F	0.151	5.59	0.172	0.190	0.002	0.779	0.016	0.011	0.96	0.11	0.01	4.35
Group 2 Placebo												
31 F	0.058	6.90	0.080	0.020	0.002	0.879	0.008	0.011	0.55	0.14	0.01	6.06
32 F	0.181	5.48	0.137	0.011	0.002	0.829	0.014	0.007	0.75	0.06	0.01	4.54
33 F	0.163	8.70	0.097	0.005	0.002	0.879	0.010	0.007	0.85	0.04	0.02	7.65
34 F	0.091	9.78	0.066	0.011	0.002	0.902	0.013	0.006	0.65	0.10	0.02	8.82
35 F	0.127	7.15	0.069	0.006	0.002	0.907	0.009	0.006	0.49	0.05	0.02	6.48
Group 3 (100 mg/kg)												
36 F	0.058	5.90	0.080	0.010	0.002	0.886	0.017	0.005	0.47	0.06	0.01	5.22
37 F	0.059	6.21	0.135	0.011	0.002	0.833	0.014	0.006	0.84	0.07	0.01	5.18
38 F	0.044	6.58	0.160	0.008	0.003	0.802	0.017	0.011	1.05	0.05	0.02	5.28
39 F	0.073	6.32	0.123	0.011	0.001	0.841	0.018	0.005	0.78	0.07	0.01	5.32
40 F	0.192	5.51	0.144	0.009	0.000	0.827	0.014	0.006	0.79	0.05	0.00	4.55
Group 4 (500 mg/kg)												
41 F	0.135	5.01	0.069	0.010	0.002	0.901	0.014	0.004	0.35	0.05	0.01	4.52
42 F	0.158	6.47	0.129	0.006	0.003	0.842	0.011	0.010	0.83	0.04	0.02	5.44
43 F	0.164	5.48	0.101	0.012	0.001	0.867	0.011	0.008	0.56	0.07	0.01	4.75
44 F	0.074	5.05	0.060	0.014	0.002	0.907	0.012	0.005	0.31	0.07	0.01	4.58
45 F	0.105	6.80	0.082	0.006	0.003	0.884	0.017	0.009	0.56	0.04	0.02	6.01
Group 5 (1000 mg/kg)												
46 F	0.053	3.60	0.161	0.024	0.001	0.797	0.013	0.004	0.58	0.09	0.00	2.87
47 F	0.199	3.36	0.139	0.016	0.001	0.819	0.018	0.006	0.47	0.05	0.00	2.75
48 F	0.091	4.60	0.113	0.027	0.003	0.837	0.013	0.008	0.52	0.12	0.01	3.85
49 F	0.155	4.56	0.115	0.015	0.001	0.847	0.015	0.008	0.52	0.07	0.01	3.87
50 F	0.087	6.84	0.218	0.020	0.004	0.728	0.016	0.014	1.49	0.14	0.03	4.98
n.d.=not determined												

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Hematology (individuals)						
WEEK						
5						
AN_NO	Mono	Luc	Plt	Methb	PT	PTT
	G/l	G/l	G/l	rel. 1	rel. 1	sec
Group 1 Control (0 mg/kg)						
26 F	0.10	0.11	1131	0.008	0.88	20.9
27 F	0.13	0.07	1018	0.009	0.83	26.6
28 F	n.d.	n.d.	962	0.008	0.78	27.0
29 F	n.d.	n.d.	1033	0.009	0.83	21.0
30 F	0.09	0.06	1241	0.008	0.88	19.7
Group 2 Placebo						
31 F	0.06	0.08	1185	0.009	0.86	19.5
32 F	0.08	0.04	1047	0.009	0.89	23.6
33 F	0.09	0.06	1115	0.010	0.78	24.1
34 F	0.13	0.06	1111	0.009	0.89	23.0
35 F	0.06	0.04	963	0.007	0.87	23.8
Group 3 (100 mg/kg)						
36 F	0.10	0.03	929	0.008	0.79	22.0
37 F	0.08	0.04	960	0.008	0.82	25.4
38 F	0.11	0.07	1082	0.008	0.84	24.0
39 F	0.11	0.03	1002	0.008	0.85	23.9
40 F	0.08	0.03	1134	0.008	0.77	19.6
Group 4 (500 mg/kg)						
41 F	0.07	0.02	924	0.007	0.84	19.1
42 F	0.07	0.07	1037	0.008	0.81	16.9
43 F	0.06	0.04	993	0.008	0.73	24.5
44 F	0.06	0.02	1072	0.007	0.80	26.8
45 F	0.12	0.06	858	0.008	0.83	23.9
Group 5 (1000 mg/kg)						
46 F	0.05	0.01	919	0.008	0.96	18.5
47 F	0.06	0.02	889	0.009	0.86	20.7
48 F	0.06	0.04	1216	0.008	0.80	24.7
49 F	0.07	0.04	837	0.008	0.83	19.7
50 F	0.11	0.10	784	0.007	0.88	18.3
n.d.=not determined						

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1.6 BLOOD CHEMISTRY (INDIVIDUALS)

WEEK	5	MALES											
		Gluc	Urea	Creat	Bili-tot	Chol	Trigly	Phos-Lip	ASAT	ALAT	LDH	GLDH	ALP
AN_NO		mmol/l	mmol/l	μmol/l	μmol/l	mmol/l	mmol/l	mmol/l	U/l	U/l	U/l	U/l	U/l
Group 1 Control (0 mg/kg)													
1 M	4.33	8.09	26.1	2.06	1.85	0.93	1.79	63.6	65.1	167.8	3.6	209.6	
2 M	4.23	7.56	23.2	1.73	1.93	0.78	1.82	56.0	33.1	107.8	4.0	101.4	
3 M	4.46	8.76	26.7	1.99	1.51	0.90	1.52	67.3	55.7	131.6	3.6	111.4	
4 M	5.16	7.09	23.5	1.55	1.62	0.93	1.75	62.2	49.8	139.7	4.1	154.2	
5 M	4.51	8.50	27.1	2.19	2.05	0.45	1.77	87.5	63.5	207.6	6.8	131.7	
Group 2 Placebo													
6 M	4.83	7.59	24.6	1.50	2.47	1.03	2.04	63.8	43.1	239.2	4.6	139.3	
7 M	5.08	7.27	26.2	0.99	2.16	0.80	2.00	59.7	47.0	132.7	2.9	79.8	
8 M	6.25	9.63	24.4	1.79	1.58	0.30	1.43	71.5	58.8	119.6	6.8	152.3	
9 M	5.77	7.87	21.4	1.48	2.12	0.39	1.66	55.3	30.2	127.3	4.0	148.7	
10 M	5.58	7.86	23.9	1.63	2.05	0.86	1.81	57.1	42.2	158.0	4.5	145.6	
Group 3 (100 mg/kg)													
11 M	5.69	8.89	28.1	1.19	1.63	0.76	1.68	69.9	57.0	166.0	4.2	208.6	
12 M	5.24	9.28	24.1	2.13	1.66	0.82	1.59	58.6	39.1	132.4	3.6	118.4	
13 M	4.37	8.76	27.2	2.17	1.99	0.30	1.64	68.7	31.0	139.6	4.2	150.2	
14 M	6.18	8.40	28.2	2.25	1.81	0.53	1.67	68.5	42.0	122.8	4.8	160.4	
15 M	5.47	9.68	26.9	2.53	1.81	0.76	1.76	66.9	62.3	136.3	3.4	143.2	
Group 4 (500 mg/kg)													
16 M	6.26	7.79	23.3	1.94	1.71	0.65	1.58	53.5	32.8	122.9	4.0	155.5	
17 M	5.30	7.03	23.0	1.26	1.89	0.54	1.72	59.5	35.9	128.0	2.9	181.6	
18 M	5.00	7.35	26.5	2.40	2.35	0.52	1.93	57.6	30.2	106.9	4.2	180.8	
19 M	4.82	7.46	29.2	2.05	1.94	0.48	1.61	65.7	29.7	103.0	4.0	136.1	
20 M	5.51	9.95	24.2	2.74	1.98	0.65	1.81	53.6	37.2	108.7	2.8	120.4	
Group 5 (1000 mg/kg)													
21 M	5.51	7.58	26.8	2.12	1.98	0.59	1.81	71.3	40.8	102.4	4.2	131.0	
22 M	4.78	8.42	22.3	2.43	3.01	0.84	2.38	56.9	31.0	146.1	4.4	80.9	
23 M	5.47	7.91	26.5	2.05	1.88	0.63	1.74	59.6	36.0	155.4	3.0	159.1	
24 M	5.12	7.46	24.6	2.41	2.28	0.53	1.92	60.3	36.3	102.9	5.5	182.7	
25 M	5.35	8.70	27.4	2.82	2.41	0.56	2.09	55.6	40.2	119.7	8.0	119.0	

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Blood chemistry (individuals)											
WEEK											MALES
AN_NO	GST	CK	Na+	K+	Cl-	Ca++	PO4-in	Prot	Alb	Glob	A/G
	U/l	U/l	mmol/l	mmol/l	mmol/l	mmol/l	mmol/l	g/l	g/l	g/l	rel. 1
Group 1 Control (0 mg/kg)											
1 M	0.0	247.5	140.4	3.67	97.6	2.81	2.22	66.42	42.16	24.26	1.74
2 M	0.0	146.8	141.6	3.73	100.5	2.77	2.40	64.22	40.17	24.05	1.67
3 M	0.0	269.0	141.2	3.69	101.8	2.80	2.32	62.91	40.34	22.57	1.79
4 M	0.0	189.6	140.7	3.77	102.0	2.82	2.26	62.73	39.87	22.86	1.74
5 M	0.0	248.7	142.1	3.32	102.2	2.83	2.37	66.37	42.50	23.87	1.78
Group 2 Placebo											
6 M	0.0	226.3	141.6	3.76	100.7	2.93	2.38	67.41	40.73	26.68	1.53
7 M	0.0	136.0	141.6	4.35	105.0	2.76	2.18	61.50	39.69	21.81	1.82
8 M	0.0	154.1	142.5	3.68	105.0	2.74	1.94	63.60	41.78	21.82	1.91
9 M	0.0	201.1	142.1	3.66	105.2	2.70	2.38	65.33	41.14	24.19	1.70
10 M	0.0	190.1	144.0	3.54	105.7	2.84	1.94	65.25	43.63	21.62	2.02
Group 3 (100 mg/kg)											
11 M	0.0	170.7	142.0	4.22	105.2	2.85	2.09	63.05	40.41	22.64	1.78
12 M	0.0	132.6	142.5	3.88	104.7	2.83	2.14	65.50	40.82	24.68	1.66
13 M	0.0	167.3	143.4	4.22	105.3	2.75	2.19	62.76	41.58	21.18	1.96
14 M	0.0	153.6	142.0	3.72	104.9	2.76	2.50	61.81	42.43	19.38	2.19
15 M	0.0	153.5	142.9	3.50	101.2	2.79	2.27	63.61	43.13	20.48	2.11
Group 4 (500 mg/kg)											
16 M	0.0	138.5	142.8	4.39	104.6	2.78	2.33	62.92	44.39	18.53	2.40
17 M	0.0	137.9	141.9	3.68	103.9	2.75	2.12	65.22	40.73	24.49	1.66
18 M	0.0	129.3	142.4	3.70	102.8	2.65	2.65	62.41	40.69	21.72	1.87
19 M	0.0	136.7	142.8	3.94	103.6	2.76	2.34	64.00	43.05	20.95	2.05
20 M	0.0	118.6	140.9	4.27	102.6	2.71	2.34	66.28	43.59	22.69	1.92
Group 5 (1000 mg/kg)											
21 M	0.0	179.3	142.1	3.39	101.3	2.78	2.03	63.35	42.34	21.01	2.02
22 M	0.0	142.6	143.8	3.67	102.5	2.74	2.06	66.08	44.57	21.51	2.07
23 M	0.0	150.0	141.2	4.11	102.2	2.73	2.17	64.34	44.30	20.04	2.21
24 M	0.0	143.0	141.8	3.69	102.6	2.75	2.50	66.39	41.96	24.43	1.72
25 M	0.0	148.8	140.4	4.13	101.8	2.83	2.38	66.13	45.97	20.17	2.28

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Blood chemistry (individuals)												
WEEK	FEMALES											
5	Gluc	Urea	Creat	Bili-tot	Chol	Trigly	Phos-Lip	ASAT	ALAT	LDH	GLDH	ALP
AN_NO	mmol/l	mmol/l	μmol/l	μmol/l	mmol/l	mmol/l	mmol/l	U/l	U/l	U/l	U/l	U/l
Group 1 Control (0 mg/kg)												
26 F	4.29	6.84	27.2	2.28	1.52	0.28	1.74	63.0	46.0	109.4	7.9	75.5
27 F	5.56	8.61	27.6	1.92	1.42	0.26	1.58	61.2	34.6	114.1	3.6	52.4
28 F	4.75	7.90	31.7	2.03	1.20	0.34	1.41	69.6	24.1	114.6	4.1	58.3
29 F	4.75	10.53	31.8	1.73	1.75	0.39	1.83	68.6	30.9	108.9	3.7	120.5
30 F	5.87	7.68	29.0	1.41	2.01	0.33	2.16	58.9	35.8	126.4	4.3	63.6
Group 2 Placebo												
31 F	4.79	9.06	24.3	1.62	1.33	0.40	1.47	71.5	46.5	160.0	15.2	66.0
32 F	6.14	8.04	30.3	1.48	2.11	0.34	1.94	66.5	50.4	201.4	3.7	92.4
33 F	7.58	6.43	25.2	1.73	1.17	0.52	1.46	55.4	47.9	110.7	2.9	61.6
34 F	5.97	8.26	25.4	2.20	1.64	0.38	1.73	84.0	69.1	118.0	4.0	79.2
35 F	5.70	5.39	28.1	1.87	2.04	0.38	2.10	64.4	52.0	147.1	4.2	61.3
Group 3 (100 mg/kg)												
36 F	5.20	6.71	25.2	1.33	1.61	0.32	1.63	60.3	21.9	115.7	3.6	87.4
37 F	7.01	9.54	30.1	1.54	1.68	0.47	1.75	61.9	45.2	161.4	2.9	78.4
38 F	5.09	8.54	25.8	1.45	1.87	0.86	2.05	66.5	46.0	136.5	5.7	47.2
39 F	5.63	7.82	29.9	2.02	1.31	0.46	1.55	61.6	36.5	143.0	6.2	57.7
40 F	4.65	6.43	25.5	2.05	0.82	0.19	1.07	70.9	21.7	134.8	4.4	72.4
Group 4 (500 mg/kg)												
41 F	4.60	6.00	28.3	2.00	2.09	0.37	2.05	66.6	28.7	210.3	3.5	63.3
42 F	5.37	8.13	27.3	1.45	1.23	0.27	1.40	72.3	39.9	172.7	8.8	44.2
43 F	5.71	7.84	27.4	1.60	1.30	0.29	1.48	60.9	24.4	132.5	4.6	56.4
44 F	4.56	7.43	28.5	1.73	1.31	0.23	1.38	66.7	32.7	125.5	3.8	44.8
45 F	5.95	7.03	29.6	2.06	2.05	0.44	1.88	73.4	29.7	184.7	5.8	82.4
Group 5 (1000 mg/kg)												
46 F	4.79	8.44	27.2	1.31	1.35	0.36	1.48	68.4	21.3	129.4	5.8	53.5
47 F	4.96	7.56	26.9	2.12	1.78	0.32	1.79	66.6	27.0	141.0	4.4	92.7
48 F	4.58	7.75	30.2	2.53	1.51	0.31	1.63	60.5	35.8	152.4	3.0	61.8
49 F	4.71	7.21	25.3	1.42	1.68	0.33	1.51	66.4	29.9	133.7	4.7	48.2
50 F	4.48	8.97	31.7	2.28	2.21	0.35	1.96	74.3	34.9	167.6	3.8	53.0

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Blood chemistry (individuals)											
WEEK	5										
FEMALES											
	GGT	CK	Na+	K+	Cl-	Ca++	PO4-in	Prot	Alb	Glob	A/G
AN_NO	U/l	U/l	mmol/l	mmol/l	mmol/l	mmol/l	mmol/l	g/l	g/l	g/l	rel. 1
Group 1 Control (0 mg/kg)											
26 F	0.0	121.3	141.7	3.13	101.7	2.83	2.02	70.07	50.03	20.04	2.50
27 F	0.0	123.2	140.2	3.51	101.9	2.74	2.05	66.89	45.18	21.71	2.08
28 F	0.0	127.0	141.1	2.97	102.4	2.67	2.02	66.25	45.28	20.97	2.16
29 F	0.0	124.6	142.1	2.83	104.3	2.62	1.90	65.41	44.25	21.16	2.09
30 F	0.0	116.1	140.8	3.41	103.3	2.70	1.75	69.09	48.33	20.76	2.33
Group 2 Placebo											
31 F	0.0	212.3	142.9	3.62	104.0	2.74	1.90	64.99	43.75	21.24	2.06
32 F	0.0	173.7	142.3	3.35	104.5	2.77	1.61	68.27	45.05	23.22	1.94
33 F	0.0	107.8	141.9	3.59	104.5	2.73	1.44	64.70	45.38	19.32	2.35
34 F	0.0	164.2	140.9	3.83	103.2	2.76	1.90	62.33	42.76	19.57	2.18
35 F	0.0	169.7	143.3	3.52	106.2	2.75	1.52	63.15	44.23	18.92	2.34
Group 3 (100 mg/kg)											
36 F	0.0	119.9	141.3	3.93	104.1	2.80	1.88	68.06	46.71	21.35	2.19
37 F	0.0	157.8	143.2	3.60	104.3	2.78	1.61	65.33	44.39	20.94	2.12
38 F	0.0	245.4	142.6	3.83	104.7	2.85	1.77	66.43	44.19	22.24	1.99
39 F	0.0	162.3	143.0	3.67	102.7	2.78	2.18	68.72	46.72	22.00	2.12
40 F	0.0	125.6	142.9	2.83	103.2	2.64	1.94	64.83	46.55	18.28	2.55
Group 4 (500 mg/kg)											
41 F	0.0	194.2	142.6	3.84	104.1	2.65	1.62	67.44	48.29	19.15	2.52
42 F	0.0	313.4	140.4	3.27	104.7	2.53	1.53	62.21	43.02	19.19	2.24
43 F	0.0	156.8	140.3	3.23	104.3	2.60	1.75	64.46	46.46	18.00	2.58
44 F	0.0	136.4	142.4	3.73	105.2	2.69	1.66	64.83	45.90	18.93	2.42
45 F	0.0	207.4	140.2	3.96	101.8	2.74	1.99	65.63	44.55	21.08	2.11
Group 5 (1000 mg/kg)											
46 F	0.0	134.4	142.3	3.39	104.6	2.62	1.40	63.65	46.25	17.40	2.66
47 F	0.0	173.7	141.5	3.28	105.6	2.62	1.59	61.84	44.40	17.43	2.55
48 F	0.0	367.0	141.4	3.49	104.7	2.76	1.84	67.55	48.78	18.78	2.60
49 F	0.0	202.2	142.0	3.86	105.3	2.63	1.67	62.66	43.79	18.87	2.32
50 F	0.0	236.4	141.0	3.28	103.9	2.63	1.57	63.85	44.79	19.06	2.35

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1.7 REFERENCE VALUES - HEMATOLOGY

SPECIES	RAT										
STRAIN	HanSpr:WIST(SPF)										
SUPPLIER	ROC Ltd.										
STUDY TYPE	[ALL]										
DOSE ROUTE	[ALL]										
DATES:	[ALL]										
PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES				RANGE OF STUDY MEANS		
					N	5%	MEDIAN	95%	N	MIN	MAX
RBC	T/L	M01	9 TO 12	864	869	7.71	8.35	9.02	95	7.65	9.07
Hb	mmol/l	M01	9 TO 12	864	869	9.2	9.9	10.4	95	8.8	10.4
Hct	rel. l	M01	9 TO 12	864	869	0.43	0.47	0.50	95	0.44	0.50
MCV	fl	M01	9 TO 12	864	869	52.5	56.0	59.7	95	52.0	60.5
PCW	rel. l	M01	9 TO 12	864	869	0.103	0.112	0.150	95	0.104	0.140
MCH	fmol	M01	9 TO 12	864	869	1.11	1.17	1.26	95	1.08	1.26
MCHC	mmol/l	M01	9 TO 12	864	869	19.81	20.91	22.59	95	18.81	22.81
HDW	mmol/l	M01	9 TO 12	864	869	1.22	1.46	1.69	95	1.23	1.84
Reti	rel. l	M02	9 TO 12	556	556	0.020	0.026	0.036	64	0.022	0.051
Reti	G/l	M02	9 TO 12	556	556	171.	219.	293.	64	183.	409.
L Reti	rel. l	M01	9 TO 12	556	556	0.302	0.416	0.520	64	0.281	0.517
M Reti	rel. l	M01	9 TO 12	556	556	0.251	0.360	0.406	64	0.233	0.409
H Reti	rel. l	M01	9 TO 12	556	556	0.101	0.223	0.447	64	0.109	0.484
WBC	G/l	M01	9 TO 12	864	869	4.93	7.22	10.51	95	4.99	12.53
Neut	rel. l	M01	9 TO 12	858	863	0.086	0.144	0.243	94	0.085	0.210
Eos	rel. l	M01	9 TO 12	858	863	0.007	0.012	0.025	94	0.008	0.038
Baso	rel. l	M01	9 TO 12	858	863	0.001	0.003	0.011	94	0.002	0.020
Lympho	rel. l	M01	9 TO 12	858	863	0.708	0.807	0.872	94	0.730	0.873

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Reference values - Hematology											
SPECIES	RAT										MALE
STRAIN	HarBr1:WIST(SPF)										
SUPPLIER	RCC Ltd.										
STUDY TYPE	[ALL]										
DOSE ROUTE	[ALL]										
DATES:	[ALL]										
PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES				RANGE OF STUDY MEANS		
					N	5%	MEDIAN	95%	N	MIN	MAX
Mono	rel. 1	M01	9 TO 12	858	863	0.012	0.021	0.041	94	0.014	0.043
Luc	rel. 1	M01	9 TO 12	858	863	0.003	0.007	0.022	94	0.003	0.034
Neut	G/l	M01	9 TO 12	858	863	0.59	1.04	1.75	94	0.59	2.50
Eos	G/l	M01	9 TO 12	858	863	0.05	0.09	0.18	94	0.05	0.19
Baso	G/l	M01	9 TO 12	858	863	0.01	0.02	0.09	94	0.01	0.19
Lympho	G/l	M01	9 TO 12	858	863	3.80	5.77	8.69	94	3.82	9.44
Mono	G/l	M01	9 TO 12	858	863	0.08	0.15	0.35	94	0.08	0.39
Luc	G/l	M01	9 TO 12	858	863	0.02	0.05	0.20	94	0.02	0.32
Plt	G/l	M01	9 TO 12	864	869	782.	977.	1191.	95	809.	1189.
PT	rel. 1	M01	9 TO 12	745	750	0.69	0.84	1.00	83	0.40	1.18
PTT	sec	M01	9 TO 12	572	577	14.6	17.8	20.4	64	14.4	20.4
Methb	rel. 1	M01	9 TO 12	473	473	0.006	0.008	0.010	55	0.004	0.011

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Reference values - Hematology

SPECIES	RAT											FEMALE
STRAIN	HarBrl:WIST(SPF)											
SUPPLIER	RCC Ltd.											
STUDY TYPE	[ALL]											
DOSE ROUTE	[ALL]											
DATES:	[ALL]											
PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES				RANGE OF STUDY MEANS			
					N	5%	MEDIAN	95%	N	MIN	MAX	
RBC	T/l	M01	9 TO 12	819	824	7.28	7.95	8.60	88	7.26	8.52	
Hb	mmol/l	M01	9 TO 12	819	824	8.7	9.4	10.0	88	8.5	10.1	
Hct	rel. l	M01	9 TO 12	819	824	0.41	0.44	0.47	88	0.41	0.47	
MCV	fl	M01	9 TO 12	819	824	52.0	55.6	59.3	88	51.6	60.4	
RDW	rel. l	M01	9 TO 12	819	824	0.098	0.106	0.153	88	0.095	0.143	
MCH	fmol	M01	9 TO 12	819	824	1.11	1.18	1.25	88	1.12	1.24	
MCHC	mmol/l	M01	9 TO 12	819	824	19.96	21.21	22.81	88	19.77	23.15	
MCW	mmol/l	M01	9 TO 12	819	824	1.14	1.31	1.50	88	1.15	1.47	
Reti	rel. l	M02	9 TO 12	547	547	0.021	0.029	0.038	63	0.024	0.051	
Reti	G/l	M02	9 TO 12	547	547	172.	225.	295.	63	186.	366.	
L Reti	rel. l	M01	9 TO 12	547	547	0.296	0.412	0.527	63	0.284	0.525	
M Reti	rel. l	M01	9 TO 12	547	547	0.231	0.324	0.386	63	0.220	0.388	
H Reti	rel. l	M01	9 TO 12	547	547	0.117	0.263	0.462	63	0.106	0.496	
WBC	G/l	M01	9 TO 12	819	824	3.19	5.00	7.65	88	2.67	7.65	
Neut	rel. l	M01	9 TO 12	814	819	0.082	0.157	0.285	87	0.092	0.225	
Eos	rel. l	M01	9 TO 12	814	819	0.008	0.014	0.026	87	0.007	0.028	
Baso	rel. l	M01	9 TO 12	814	819	0.001	0.002	0.008	87	0.001	0.014	
Lympho	rel. l	M01	9 TO 12	814	819	0.664	0.793	0.877	87	0.689	0.873	

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Reference values - Hematology

SPECIES	RAT											FEMALE
STRAIN	HarBr1:WIST(SPF)											
SUPPLIER	RCC Ltd.											
STUDY TYPE	[ALL]											
DOSE ROUTE	[ALL]											
DATES:	[ALL]											
PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES				RANGE OF STUDY MEANS			
					N	5%	MEDIAN	95%	N	MIN	MAX	
Mono	rel. l	M01	9 TO 12	814	819	0.011	0.020	0.039	87	0.013	0.041	
Luc	rel. l	M01	9 TO 12	814	819	0.003	0.007	0.019	87	0.003	0.032	
Neut	G/l	M01	9 TO 12	814	819	0.43	0.80	1.51	87	0.46	1.24	
Eos	G/l	M01	9 TO 12	814	819	0.03	0.07	0.14	87	0.04	0.15	
Baso	G/l	M01	9 TO 12	814	819	0.00	0.01	0.05	87	0.00	0.10	
Lympho	G/l	M01	9 TO 12	814	819	2.36	3.92	6.12	87	1.96	6.52	
Mono	G/l	M01	9 TO 12	814	819	0.05	0.10	0.22	87	0.05	0.23	
Luc	G/l	M01	9 TO 12	814	819	0.01	0.03	0.11	87	0.01	0.18	
Plt	G/l	M01	9 TO 12	819	824	819.	1034.	1274.	88	819.	1218.	
PT	rel. l	M01	9 TO 12	740	745	0.84	0.96	1.26	82	0.80	1.33	
PTT	sec	M01	9 TO 12	569	574	14.6	17.8	20.6	63	14.9	21.7	
Methb	rel. l	M01	9 TO 12	478	478	0.005	0.008	0.010	55	0.003	0.010	

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1.8 REFERENCE VALUES - BLOOD CHEMISTRY

SPECIES	RAT	MALE									
STRAIN	HarBr1:WIST(SPF)										
SUPPLIER	RCC Ltd.										
STUDY TYPE	[ALL]										
DOSE ROUTE	[ALL]										
DATES:	[ALL]										
PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES				RANGE OF STUDY MEANS		
					N	5%	MEDIAN	95%	N	MIN	MAX
Gluc	mmol/l	M01	9 TO 12	850	855	3.80	5.52	9.40	91	3.48	9.24
Urea	mmol/l	M01	9 TO 12	850	855	4.76	6.07	8.28	91	4.98	9.40
Creat	μmol/l	M01	9 TO 12	825	830	18.0	22.8	28.8	86	18.8	31.5
Bili-tot	μmol/l	M01	9 TO 12	825	830	0.83	1.33	1.98	86	0.93	1.95
Prot	g/l	M01	9 TO 12	850	855	61.68	65.96	69.67	91	60.62	69.57
Alb	g/l	M02	9 TO 12	501	506	38.80	41.58	44.88	57	39.14	44.09
Glob	g/l	M02	9 TO 12	501	506	21.25	24.20	27.04	57	21.77	26.32
A/G	rel. 1	M02	9 TO 12	501	506	1.51	1.72	2.00	57	1.54	1.93
Chol	mmol/l	M01	9 TO 12	850	855	1.13	1.61	2.23	91	1.23	2.25
Trigly	mmol/l	M01	9 TO 12	735	740	0.26	0.56	1.26	77	0.31	1.47
Phos-Lip	mmol/l	M01	9 TO 12	620	625	1.24	1.58	1.99	62	1.29	2.07
Na+	mmol/l	M01	9 TO 12	849	854	139.3	142.8	147.4	91	138.9	147.7
K+	mmol/l	M01	9 TO 12	850	855	3.21	3.71	4.37	91	3.26	5.13
Ca++	mmol/l	M01	9 TO 12	825	830	2.61	2.78	2.96	86	2.59	3.01
Cl-	mmol/l	M01	9 TO 12	830	835	95.9	100.4	106.1	87	95.3	107.3
PO4-in	mmol/l	M01	9 TO 12	830	835	1.94	2.31	2.69	87	1.91	2.87
ASAT	U/l	M01	9 TO 12	850	855	62.0	74.4	98.0	91	60.5	99.7
ALAT	U/l	M01	9 TO 12	850	855	21.0	28.6	50.9	91	19.4	65.7

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Reference values - Blood chemistry

SPECIES	RAT											MALE
STRAIN	HanBr1:WIST(SPF)											
SUPPLIER	RCC Ltd.											
STUDY TYPE	[ALL]											
DOSE ROUTE	[ALL]											
DATES:	[ALL]											
PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES				RANGE OF STUDY MEANS			
					N	5%	MEDIAN	95%	N	MIN	MAX	
ALP	U/l	M01	9 TO 12	850	855	80.8	115.2	178.6	91	78.7	178.6	
GGT	U/l	M01	9 TO 12	705	710	0.0	0.0	0.0	76	0.0	0.9	
GLDH	U/l	M01	9 TO 12	284	284	4.6	6.3	9.3	32	4.4	9.5	
CK	U/l	M01	9 TO 12	557	562	117.4	168.4	318.5	61	138.6	287.8	
LDH	U/l	M01	9 TO 12	542	547	85.2	128.8	226.4	60	81.1	246.8	

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Reference values - Blood chemistry

SPECIES	RAT	FEMALE									
STRAIN	HarBr1:WIST(SPF)										
SUPPLIER	RCC Ltd.										
STUDY TYPE	[ALL]										
DOSE ROUTE	[ALL]										
DATES:	[ALL]										
PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES				RANGE OF STUDY MEANS		
					N	5%	MEDIAN	95%	N	MIN	MAX
Gluc	mmol/l	M01	9 TO 12	813	818	3.76	5.34	8.84	84	3.16	9.07
Urea	mmol/l	M01	9 TO 12	813	818	5.49	7.01	9.21	84	5.81	9.99
Creat	μmol/l	M01	9 TO 12	813	818	20.9	25.8	32.7	84	21.6	36.0
Bili-tot	μmol/l	M01	9 TO 12	813	818	1.04	1.59	2.32	84	1.21	2.32
Prot	g/l	M01	9 TO 12	813	818	61.84	66.56	71.44	84	61.20	70.48
Alb	g/l	M02	9 TO 12	498	503	41.46	45.13	49.32	56	42.34	47.69
Glob	g/l	M02	9 TO 12	498	503	18.75	21.65	24.41	56	19.59	23.89
A/G	rel. 1	M02	9 TO 12	498	503	1.80	2.08	2.45	56	1.86	2.33
Chol	mmol/l	M01	9 TO 12	813	818	0.97	1.44	2.04	84	1.01	1.89
Trigly	mmol/l	M01	9 TO 12	724	729	0.19	0.30	0.56	75	0.22	0.99
Phos-Lip	mmol/l	M01	9 TO 12	623	628	1.17	1.58	2.03	62	1.20	2.08
Na+	mmol/l	M01	9 TO 12	810	815	139.2	142.4	147.6	84	138.4	148.7
K+	mmol/l	M01	9 TO 12	813	818	2.81	3.42	4.04	84	2.74	4.11
Ca++	mmol/l	M01	9 TO 12	813	818	2.57	2.74	2.92	84	2.57	2.90
Cl-	mmol/l	M01	9 TO 12	813	818	97.8	102.8	108.4	84	97.3	109.3
PO4-in	mmol/l	M01	9 TO 12	813	818	1.40	1.91	2.29	84	1.45	2.36
ASAT	U/l	M01	9 TO 12	813	818	59.3	70.4	89.2	84	60.4	80.8
ALAT	U/l	M01	9 TO 12	813	818	15.4	21.0	37.9	84	15.4	49.8

RCC STUDY NUMBER 853022
AXN-DMS

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Reference values - Blood chemistry											
SPECIES	RAT										FEMALE
STRAIN	HanBr1.WIST(SPF)										
SUPPLIER	RCC Ltd.										
STUDY TYPE	[ALL]										
DOSE ROUTE	[ALL]										
DATES:	[ALL]										
PARAMETER	UNIT	METHOD	ANIMAL AGE IN WEEKS	NO. OF ANIMALS	PERCENTILES OF INDIV. VALUES				RANGE OF STUDY MEANS		
					N	5%	MEDIAN	95%	N	MIN	MAX
ALP	U/l	M01	9 TO 12	813	818	34.8	55.8	97.2	84	34.7	92.2
GGT	U/l	M01	9 TO 12	669	674	0.0	0.0	0.0	69	0.0	0.3
GLDH	U/l	M01	9 TO 12	284	284	4.1	5.7	11.9	32	4.6	10.1
CK	U/l	M01	9 TO 12	554	559	94.9	141.5	262.5	60	116.1	422.1
LDH	U/l	M01	9 TO 12	539	544	79.1	125.7	210.8	59	79.8	276.2

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

APPENDIX IV:

ANALYSIS OF DOSE FORMULATIONS

VFHA Food and Feed Analytic

NON-GLP

Analytical Report
RCC Study No. 853022
Ro 04381139-000-001

Analytical Report

on the Achieved Concentration, Homogeneity and Stability of AXN-DMS in Feed Admixtures

Study Title AXN-DMS: 28-Day Range-Finding Oral Toxicity (Feeding)
Study in the Wistar Rat

Study Head: W.H. Braun
RCC Ltd. Toxicology
CH-4452 Ittingen, Switzerland

Sponsor: J. Bausch
DSM Nutritional Products (registered as Roche Vitamins Ltd.)
VFHS, P.O. Box 3255, CH-4002 Basel, Switzerland, Switzerland

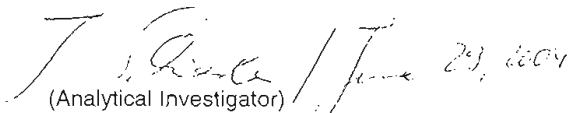
Study Monitor: E. Wolz
DSM Nutritional Products, (registered as Roche Vitamins Ltd.)
VFHS, P.O. Box 3255, CH-4002 Basel, Switzerland

Test Site: DSM Nutritional Products (registered as Roche Vitamins Ltd.)
R&D – Human Nutrition and Health – Analytics, VFHA
Wurmisweg 576, CH-4303 Kaiseraugst, Switzerland

Analytical Investigator: J. Schierle
DSM Nutritional Products, (registered as Roche Vitamins Ltd.)
VFHA, P.O. Box 3255, CH-4002 Basel, Switzerland

Report to: *Study Head:* ☒
(copies) *Study Monitor:* ☒
Analytical Investigator: ☒

No of Pages: 8

Signature/Date: 
(Analytical Investigator) / June 29, 2004

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VFHA Food and Feed Analytic

NON-GLP

Analytical Report
RCC Study No. 853022
Ro 04381139-000-001

Test item: Carophyll Stay Pink 15% CWS (Ro 04381139-000-001)

Test system: Rat, HanBrl:WIST(SPF)

Sample material: Feed Admixtures

Deviation from Protocol -

Storage conditions: After receipt at VFHA the samples were stored in the sample registration and the analytical laboratory at freezer temperature of nominal -20 °C. Before the analysis, the samples were thawed at 5 ± 3 °C (refrigerator).

Theme No.: 6276

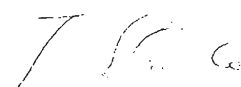
Analysis required: Astaxanthin dimethyl disuccinate (AXN-DMS)

Analytical Method: AMS-101/01

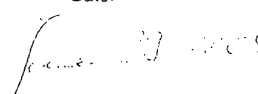
Deviations from Method -

Analyst: Mrs. N. Faccin

Approval of Results:


(Dr. J. Schierle)

Date:



VFHA Food and Feed Analytic

NON-GLP

Analytical Report
RCC Study No. 853022
Ro 04381139-000-001

Results

Table 1: Analysis of AXN-DMS in Diet Admixtures of Control Groups
- Achieved Concentration and Homogeneity in preparations of weeks 1 and 4

Sample ID	Vela ID LAB_ORD009854 _00..	Nominal Content (mg/kg)	Analysed Content (mg/kg)	Deviation from Nominal Content (%) ^a
Gr. 1, M + F, W 1 - top	01	0	nd	0
Gr. 1, M + F, W 1 - middle	02	0	nd	0
Gr. 1, M + F, W 1 - bottom	03	0	nd	0
Gr. 2, M, W 1 - top	04	0	nd	0
Gr. 2, M, W 1 - middle	05	0	nd	0
Gr. 2, W 1 - bottom	06	0	nd	0
Gr. 2, F, W 1 - top	07	0	nd	0
Gr. 2, F, W 1 - middle	08	0	nd	0
Gr. 2, F, W 1 - bottom	09	0	nd	0
Gr. 1, M + F, W 4 - top	46	0	nd	0
Gr. 1, M + F, W 4 - middle	47	0	nd	0
Gr. 1, M + F, W 4 - bottom	48	0	nd	0
Gr. 2, M, W 4 - top	49	0	nd	0
Gr. 2, M, W 4 - middle	50	0	nd	0
Gr. 2, W 4 - bottom	51	0	nd	0
Gr. 2, F, W 4 - top	52	0	nd	0
Gr. 2, F, W 4 - middle	53	0	nd	0
Gr. 2, F, W 4 - bottom	54	0	nd	0

Gr. = group; M = males; F = females; W = week of preparation; nd = below detection limit of approx. 0.5 mg AXN-DMS/kg
^a nominal content = 100%

VFHA Food and Feed Analytic

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Analytical Report
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Table 2a: Analysis of AXN-DMS In Diet Admixtures of groups 3, 4, and 5 -
Achieved Concentration and Homogeneity in week 1 preparations

Sample ID	Vela ID LAB_ORD009854 _00..	Nominal Content (g/kg)	Analysed Content (g/kg)	Deviation from Nominal Content (%) ^a
Gr. 3, M, W 1, top	10	1.38	1.69	22.5
Gr. 3, M, W 1, middle	11	1.38	1.69	22.5
Gr. 3, M, W 1, bottom	12	1.38	1.62	17.4
		Average:	1.67 g/kg	20.8
		CV:	2.4 %	
Gr. 3, F, W 1, top	13	1.38	1.39	0.7
Gr. 3, F, W 1, middle	14	1.38	1.51	9.4
Gr. 3, F, W 1, bottom	15	1.38	1.72	24.6
		Average:	1.54 g/kg	11.6
		CV:	10.8 %	
Gr. 4, M, W 1, top	16	6.90	8.33	20.7
Gr. 4, M, W 1, middle	17	6.90	8.23	19.3
Gr. 4, M, W 1, bottom	18	6.90	8.30	20.3
		Average:	8.29 g/kg	20.1
		CV:	0.6 %	
Gr. 4, F, W 1, top	19	6.90	8.16	18.3
Gr. 4, F, W 1, middle	20	6.90	8.30	20.3
Gr. 4, F, W 1, bottom	21	6.90	9.40	36.2
		Average:	8.62 g/kg	24.9
		CV:	7.9 %	
Gr. 5, M, W 1, top	22	13.8	14.9	8.0
Gr. 5, M, W 1, middle	23	13.8	17.3	25.4
Gr. 5, M, W 1, bottom	24	13.8	16.3	18.1
		Average:	16.2 g/kg	17.1
		CV:	7.5 %	
Gr. 5, F, W 1, top	25	13.8	19.8	43.5
Gr. 5, F, W 1, middle	26	13.8	15.3	10.9
Gr. 5, F, W 1, bottom	27	13.8	11.5	-16.7
		Average:	15.5 g/kg	12.6
		CV:	26.7 %	

Gr. = group; M = males; F = females; W = week of preparation, ^a nominal content = 100%, CV = coefficient of variation

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Ro 04381139-000-001

**Table 2b: Analysis of AXN-DMS in Diet Admixtures of groups 3, 4, and 5 -
Achieved Concentration and Homogeneity in week 4 preparations**

Sample ID	Vela ID LAB_ORD009854 _00..	Nominal Content (g/kg)	Analysed Content (g/kg)	Deviation from Nominal Content (%) ^a
Gr. 3, M, W 4, top	55	1.71	2.21	29.2
Gr. 3, M, W 4, middle	56	1.71	1.89	10.5
Gr. 3, M, W 4, bottom	57	1.71	2.04	19.3
		Average:	2.05 g/kg	19.7
		CV:	7.8 %	
Gr. 3, F, W 4, top	58	1.55	1.78	14.8
Gr. 3, F, W 4, middle	59	1.55	1.68	8.4
Gr. 3, F, W 4, bottom	60	1.55	1.90	22.6
		Average:	1.79 g/kg	15.3
		CV:	6.2 %	
Gr. 4, M, W 4, top	61	8.37	8.67	3.6
Gr. 4, M, W 4, middle	62	8.37	9.52	13.7
Gr. 4, M, W 4, bottom	63	8.37	9.84	17.6
		Average:	9.34 g/kg	11.6
		CV:	6.5 %	
Gr. 4, F, W 4, top	64	7.56	9.06	19.8
Gr. 4, F, W 4, middle	65	7.56	8.79	16.3
Gr. 4, F, W 4, bottom	66	7.56	8.70	15.1
		Average:	8.85 g/kg	17.1
		CV:	2.1 %	
Gr. 5, M, W 4, top	67	16.9	16.9	0.0
Gr. 5, M, W 4, middle	68	16.9	19.6	16.0
Gr. 5, M, W 4, bottom	69	16.9	19.4	14.8
		Average:	18.6 g/kg	10.3
		CV:	8.1 %	
Gr. 5, F, W 4, top	70	15.5	13.5	-12.9
Gr. 5, F, W 4, middle	71	15.5	17.7	14.2
Gr. 5, F, W 4, bottom	72	15.5	15.9	2.6
		Average:	15.7 g/kg	1.3
		CV:	13.4 %	

Gr. = group; M = males; F = females; W = week of preparation, ^a nominal content = 100%, CV = coefficient of variation

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VFHA Food and Feed Analytic

NON-GLP

Analytical Report
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Table 3a: Analysis of AXN-DMS in Diet Admixtures of week 1 preparation
– Stability at refrigerator temperature (approx. 5°C) for 7 days

Sample ID	Vela ID LAB_ORD009854 _00..	Analysed Content (g/kg)	Deviation from Initial Content (%) ^a
Gr. 1, M + F, Initial content ^b	(01, 02, 03)	nd	-
Gr. 2, M, Initial content ^b	(04, 05, 06)	nd	-
Gr. 2, F, Initial content ^b	(07, 08, 09)	nd	-
Gr. 3, M, Initial content ^b	(10,11,12)	1.67	-
Gr. 3, F, Initial content ^b	(13,14,15)	1.54	-
Gr. 4, M, Initial content ^b	(16,17,18)	8.29	-
Gr. 4, F, Initial content ^b	(19,20,21)	8.62	-
Gr. 5, M, Initial content ^b	(22,23,24)	16.2	-
Gr. 5, F, Initial content ^b	(25,26,27)	15.5	-
Gr. 1, M + F, 7 days	28	nd	0
Gr. 2, M, 7 days	29	nd	0
Gr. 2, F, 7 days	30	nd	0
Gr. 3, M, 7 days	31	1.17	-29.8
Gr. 3, F, 7 days	32	1.16	-24.7
Gr. 4, M, 7 days	33	8.98	8.4
Gr. 4, F, 7 days	34	9.25	7.3
Gr. 5, M, 7 days	35	18.8	16.3
Gr. 5, F, 7 days	36	18.7	20.4
Mean Deviation from Initial Content for Groups 3, 4 and 5:			- 0.4

Gr. = group; M = males; F = females; nd = below detection limit of approx. 0.5 mg AXN-DMS/kg

^a Initial content = 100%;

^b Initial Content = Average of samples which were taken for assessment of achieved concentration and homogeneity (Table 1 and Tables 2a,b)

VFHA Food and Feed Analytic

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**Table 3b: Analysis of AXN-DMS in Diet Admixtures of week 1 preparation
– Stability at refrigerator temperature (approx. 5°C) for 14 days**

Sample ID	Vela ID LAB_ORD009854 _00..	Analysed Content (g/kg)	Deviation from Initial Content (%) ^a
Gr. 1, M + F, Initial content ^b	(01, 02, 03)	nd	-
Gr. 2, M, Initial content ^b	(04, 05, 06)	nd	-
Gr. 2, F, Initial content ^b	(07, 08, 09)	nd	-
Gr. 3, M, Initial content ^b	(10,11,12)	1.67	-
Gr. 3, F, Initial content ^b	(13,14,15)	1.54	-
Gr. 4, M, Initial content ^b	(16,17,18)	8.29	-
Gr. 4, F, Initial content ^b	(19,20,21)	8.62	-
Gr. 5, M, Initial content ^b	(22,23,24)	16.2	-
Gr. 5, F, Initial content ^b	(25,26,27)	15.5	-
Gr. 1, M + F, 14 days	37	nd	0
Gr. 2, M, 14 days	38	nd	0
Gr. 2, F, 14 days	39	nd	0
Gr. 3, M, 14 days	40	1.16	-30.4
Gr. 3, F, 14 days	41	1.35	-12.3
Gr. 4, M, 14 days	42	8.83	6.6
Gr. 4, F, 14 days	43	8.08	-6.3
Gr. 5, M, 14 days	44	19.0	17.5
Gr. 5, F, 14 days	45	16.5	6.2
Mean Deviation from Initial Content for Groups 3, 4 and 5:			- 3.1

Gr. = group; M = males; F = females; nd = below detection limit of approx. 0.5 mg AXN-DMS/kg

^a Initial content = 100%;

^b Initial Content = Average of samples which were taken for assessment of achieved concentration and homogeneity (Table 1 and Tables 2a,b)

Free astaxanthin was detected besides AXN-DMS in 16 of the 51 analysed diet admixtures of group 3, 4, and 5. The levels were in a range of 0.1 - 0.2% of the respective AXN-DMS contents. Free astaxanthin was not detected in diets of the control groups 1 and 2.

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NON-GLP

Analytical Report
RCC Study No. 853022
Ro 04381139-000-001

Summary


- 1) **Absence of AXN-DMS in control samples:** AXN-DMS could not be detected in the diet admixtures of the control groups 1 and 2 (basic diets and placebo, Tables 1 and 3a,b). The detection limit of the analytical method was approx. 0.5 mg AXN-DMS /kg diet.
- 2) **Achieved concentration:** The AXN-DMS levels found in samples of groups 3, 4 and 5 deviated from the respective nominal contents in a range of -16.7 to +43.5% (table 2a and 2b). Most of the individual deviations clearly exceed the statistical variation due to the analytical method (the coefficient of variation is $\pm 10\%$ for samples with a nominal AXN-DMS content below 10 g/kg, and $\pm 5\%$ for samples with a nominal AXN-DMS content equal or above 10 g/kg). Therefore, the found contents can be regarded as not well corresponding to the target levels.
- 3) **Homogeneity:** The AXN-DMS contents measured in samples taken from the top, middle and bottom of the diet admixtures of groups 3 and 5, showed coefficients of variation ranging from 0.6% to 26.7% (tables 2a-c). For five treatment groups (Gr. 3, F, W1; Gr. 5, M, W1; Gr. 5, F, W1; Gr. 5, M, W4 and Gr. 5, F, W4) the coefficients of variation exceeded the statistical variation of the method (see above) so that the test item cannot be regarded as being homogeneously distributed in all diets.
- 4) **Stability:** As shown in tables 3a and 3b, the AXN-DMS contents determined in samples stored at refrigerator temperature for 7 and 14 days deviated from the initial contents in a range of -30.4% (Gr.3, M, 14 days) to +20.4% (Gr.5, F, 7 days). The deviation found for the diets of groups 3, 4, and 5 averaged on -0.4% for storage over 7 days and on -3.1% for storage over 14 days. As this decrease is within the statistical variation of the method (see above) there is no indication for an instability of the test item in diets stored for 7 and 14 weeks in the refrigerator.

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

APPENDIX V:

ANALYSIS OF TEST ITEM IN PLASMA AND LIVER

DSM 	VFHA	Biochemical Analytics
	<i>Bioanalytical Phase Report</i>	<i>NON-GLP</i>
	1 of 5	


DRAFT

**Bioanalytical Phase Report on the determination of Astaxanthin
and Astaxanthindimethyldisuccinate in Rat Plasma and Liver**

Study title:

**“AXN-DMS: 28-Day Range-Finding Oral Toxicity (Feeding) Study in
the Wistar Rat”**

Study-ID:	RCC Study N°853022
Roche Internal ID:	STUDY__000924
Purpose of this bioanalytical phase:	Analytical determination of the concentration of Astaxanthin and Astaxanthindimethyldisuccinate in rat plasma and liver
Test item:	AXN-DMS
Compound analyzed:	all-E-Astaxanthin and cis-isomers all-E-Astaxanthindimethyldisuccinate and cis isomer
Sponsor:	DSM Nutritional Products Research & Development – VFHS P.O. Box 3255, CH-4002 Basle, Switzerland
Study director:	W.H. Braun RCC Ltd CH-4452 Itingen, Switzerland Fax +41 (0)61 971 77 25
Principal Investigator:	Dr. Volker Spitzer, DSM Nutritional Products, Human Nutrition and Health, VFHA, Biochemical Analytical Laboratories, P.O. Box 3255, Bldg. 205/7, CH-4002 Basle, Switzerland
Technicians:	Nathalie Decker Ramanzina, Karin Volz, DSM Nutritional Products, Human Nutrition and Health, VFHA, Biochemical Analytical Laboratories, P.O. Box 3255, Bldg. 205/8, CH-4002 Basle, Switzerland

DSM 	VFHA	Biochemical Analytics
	<i>Bioanalytical Phase Report</i>	<i>NON-GLP</i>
	2 of 5	

Test Site: DSM Nutritional Products (registered as Roche Vitamins Ltd.), formerly Roche Vitamins Ltd., Human Nutrition and Health, VFHA, P.O. Box 3255, CH-4002 Basle, Switzerland

Test site management: Dr. Christian Fizet, DSM Nutritional Products, Human Nutrition & Health, VFHA, Bldg. 205/202, CH-4070 Basle, Switzerland

Theme No.: Internal 6276

Experimental starting and completion dates: Start: 13.05.2004
End: 22.06.2004

Abstract of the Methods: An aliquot of the sample is first diluted with water, then the proteins are precipitated with ethanol and finally the extraction is done with a n-hexane/chloroforme 20 % (v/v) mixture. After centrifugation an aliquot of the clear supernatant is dried under nitrogen at room temperature. The dried residue is quantitatively redissolved in the mobile phase (n-heptane/acetone 12% (v/v)). An aliquot of the resulting solution is injected into a normal phase HPLC-system. Astaxanthin and Astaxanthindimethyldisuccinate are detected and quantified at a wavelength of 470 nm.
An aliquot of minced liver and acetone are homogenised with a Polytron. After centrifugation, the organic phase undergoes a solid phase extraction (C8- BondElut, elution with n-heptane/acetone 12% (v/v)). An aliquot of the resulting solution is injected into a normal phase HPLC-system. Astaxanthin and Astaxanthindimethyldisuccinate are detected and quantified at a wavelength of 470 nm

Reporting: According to the VFHA SOP (VFHA-008,) a copy of th|s phase study report was handed over to the study director. This report was an appendix to the main report.
Only the analytical results of single determinations were reported. No statistical analysis will be performed. See Results and Discussion.

Archiving: All original documents including the raw data will be retained in the archives of VFHA for at least 10 years.

Guidelines: This was a NON-GLP study

Results and Discussion

Astaxanthin, Astaxanthindimethyldisuccinate and some isomeres have been analysed in all samples and the results are summarized in Table 1 for Plasma and Table 2 for Liver.

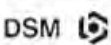
	VFHA	Biochemical Analytics
	Bioanalytical Phase Report	NON-GLP
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Table 1: Quantification of Astaxanthin, Astaxanthindimethyldisuccinate and isomers in Plasma

Sample Name	all-E-Astaxanthin ug/l	9Z-Astaxanthin ug/l	13Z-Astaxanthin ug/l	all-E-Astaxanthin dimethyldisuccinate ug/l	13Z-Astaxanthin dimethyldisuccinate ug/l
M1 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M2 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M3 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M4 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M5 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M6 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M7 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M8 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M9 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M10 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
M11 Plasma	16	Lod*	48	Lod*	Lod*
M12 Plasma	16	Lod*	63	Lod*	Lod*
M13 Plasma	21	Lod*	79	Lod*	Lod*
M14 Plasma	16	Lod*	53	Lod*	Lod*
M15 Plasma	17	Lod*	66	Lod*	Lod*
M16 Plasma	59	Liq*	218	Lod*	Lod*
M17 Plasma	21	Lod*	95	Lod*	Lod*
M18 Plasma	61	Liq*	203	Lod*	Lod*
M19 Plasma	33	Lod*	154	Lod*	Lod*
M20 Plasma	99	6	340	Lod*	Lod*
M21 Plasma	108	Liq*	670	Lod*	Lod*
M22 Plasma	169	10	818	Lod*	Lod*
M23 Plasma	101	6	428	Lod*	Lod*
M24 Plasma	130	8	800	Lod*	Lod*
M25 Plasma	90	Liq*	410	Lod*	Lod*
F26 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F27 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F28 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F29 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F30 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F31 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F32 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F33 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F34 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F35 Plasma	Lod*	Lod*	Lod*	Lod*	Lod*
F36 Plasma	7	Lod*	25	Lod*	Lod*
F37 Plasma	20	Lod*	70	Lod*	Lod*
F38 Plasma	24	Lod*	75	Lod*	Lod*
F39 Plasma	24	Lod*	58	Lod*	Lod*
F40 Plasma	16	Lod*	27	Lod*	Lod*
F41 Plasma	15	Lod*	69	Lod*	Lod*
F42 Plasma	44	Liq*	167	Lod*	Lod*
F43 Plasma	46	Liq*	123	Lod*	Lod*
F44 Plasma	9	Lod*	50	Lod*	Lod*
F45 Plasma	37	Lod*	217	Lod*	Lod*
F46 Plasma	35	Lod*	197	Lod*	Lod*
F47 Plasma	71	Liq*	246	Lod*	Lod*
F48 Plasma	65	Liq*	343	Liq*	Lod*
F49 Plasma	73	Liq*	296	Lod*	Lod*
F50 Plasma	108	7	473	Lod*	Lod*

	Lod	Liq
Astaxanthin	2 ug/l	5 ug/l
Astaxanthindimethyldisuccinate	4 ug/l	14 ug/l

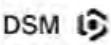

	VFHA		Biochemical Analytics
	Bioanalytical Phase Report		NON-GLP
	4 of 5		

Table 2: Table 1: Quantification of Astaxanthin, Astaxanthindimethydisuccinate and isomers in Liver

Sample Name	all-E-Astaxanthin ug/kg	9Z-Astaxanthin ug/kg	13Z-Astaxanthin ug/kg	all-E-Astaxanthin- dimethydisuccinate ug/kg	13Z-Astaxanthin- dimethydisuccinate ug/kg
M1 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M2 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M3 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M4 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M5 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M6 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M7 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M8 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M9 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M10 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
M11 Liver	97	Lod*	126	Liq*	Lod*
M12 Liver	85	Lod*	195	Liq*	Lod*
M13 Liver	95	Liq*	259	Liq*	Lod*
M14 Liver	110	Liq*	144	Liq*	Lod*
M15 Liver	79	Liq*	197	Liq*	Lod*
M16 Liver	222	Liq*	703	44	Lod*
M17 Liver	173	Liq*	322	33	Lod*
M18 Liver	251	15	446	61	Lod*
M19 Liver	219	Liq*	646	39	Lod*
M20 Liver	200	10	572	31	Lod*
M21 Liver	723	35	1825	75	Lod*
M22 Liver	1085	62	2297	87	Lod*
M23 Liver	586	27	1584	52	Lod*
M24 Liver	314	17	1130	45	Lod*
M25 Liver	467	32	1251	49	Lod*
F26 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F27 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F28 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F29 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F30 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F31 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F32 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F33 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F34 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F35 Liver	Lod*	Lod*	Lod*	Lod*	Lod*
F36 Liver	97	Liq*	161	Liq*	Lod*
F37 Liver	362	Liq*	247	Liq*	Lod*
F38 Liver	333	Liq*	273	Liq*	Lod*
F39 Liver	292	Liq*	241	29	Lod*
F40 Liver	193	Liq*	297	Liq*	Lod*
F41 Liver	161	Liq*	246	Liq*	Lod*
F42 Liver	542	23	985	56	Lod*
F43 Liver	688	37	823	76	Lod*
F44 Liver	154	Liq*	250	Liq*	Lod*
F45 Liver	201	12	455	26	Lod*
F46 Liver	633	18	1458	62	Lod*
F47 Liver	600	24	1134	52	Lod*
F48 Liver	1348	42	2893	66	Lod*
F49 Liver	515	21	1127	38	Lod*
F50 Liver	758	31	1434	46	Lod*

	Lod	Liq
Astaxanthin	3 ug/kg	10 ug/kg
Astaxanthindimethydisuccinate	8 ug/kg	25 ug/kg

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Approval of the results

Principal
Investigator: Date:
(Dr. Volker Spitzer)

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

APPENDIX VI:

DATA EVALUATION OF TEST ITEM IN PLASMA AND LIVER

DSM Nutritional Products

R&D Human Nutrition and Health



**AXN-DMS:
28-Day Range-Finding Oral Toxicity (Feeding) Study
in the Wistar Rat**

Plasma and Liver Concentration Determinations

**Data Evaluation
(not audited)**

Sponsor	DSM Nutritional Products (registered as Roche Vitamins Ltd.) R&D Human Nutrition and Health Nutrition Safety (VFHS) CH-4303 Kaiseraugst Switzerland
Testing Facility	RCC Ltd CH-4452 Itingen Switzerland Project No.: 853022
Data Evaluation	E. Wolz, VFHS W. Cohn, VFHS
Date	02-Jul-2004
No. of Pages	7

1. Summary

The objective of the study was to determine plasma and liver concentrations of astaxanthin (AXN), astaxanthin dimethyl disuccinate (AXN-DMS) and isomers following 28-day of oral (feed admix) administration of AXN-DMS in rats in terms of AXN-equivalent at doses of 0, 100, and 500 mg/kg bw/day.

Determinations of *plasma* and *liver* concentrations were performed in all animals on week 4 at scheduled necropsy (animals were fasted overnight).

In *plasma* samples neither all-E-AXN-DMS nor 9Z-AXN-DMS were detected. Both sexes showed a dose-dependent but not dose-linear increase in plasma content of all-E-AXN, 9Z-AXN and 13Z-AXN whereas 13Z-AXN was the most prominent isomer followed by all-E-AXN and 9Z-AXN. At 1000 mg/kg the plasma content of all-E-AXN and 13Z-AXN was statistically significant higher in males compared to females.

There was a dose-dependent but not dose-linear increase of AXN isomers in *liver* samples of males and females: 13Z-AXN > all-E-AXN > 9Z-AXN. Small amounts of all-E-AXN-DMS and 13Z-AXN-DMS could be detected in both genders treated with 500 and 1000 mg/kg and females at 100 mg/kg, which were up to 100 fold lower than respective levels of AXN or AXN isomers.

It can be *concluded* that the test animals were adequately exposed to AXN-DMS under the conditions of the study. After AXN-DMS treatment dose-dependent concentrations of AXN and AXN isomers could be detected in plasma and liver samples of males and females. No AXN-DMS or isomers could be measured in plasma samples. In liver samples small concentrations of AXN-DMS or isomers were measurable, which were up to 100 fold lower than the values of AXN and isomers.

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2. Summary Tables and Figures

2.1. Plasma concentrations of AXN, AXN-DMS and isomers

Week 4 (n=5)

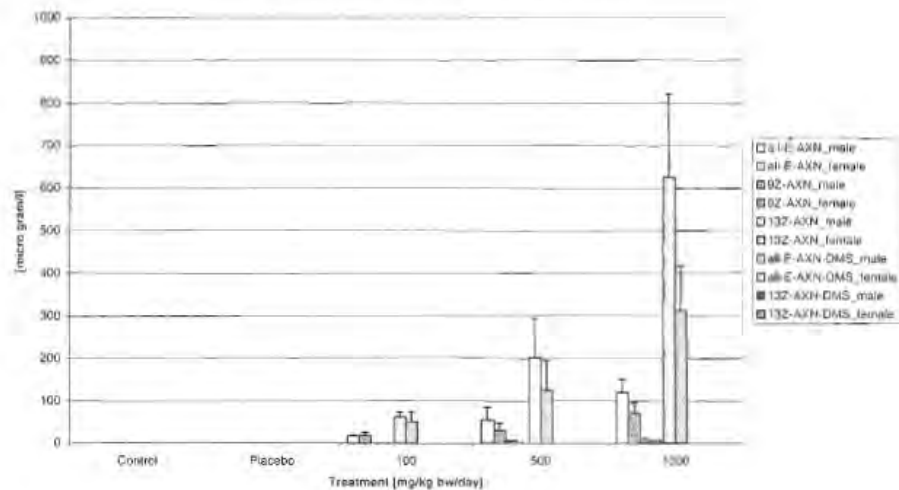
Group	Dose (mg/kg/day)	all-E-Astaxanthin				9Z-Astaxanthin				13Z-Astaxanthin			
		Male mean [µg/l]	SD	Female mean [µg/l]	SD	Male mean [µg/l]	SD	Female mean [µg/l]	SD	Male mean [µg/l]	SD	Female mean [µg/l]	SD
1	Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	Placebo	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
3	100	17.2	2.2	16.2	7.1	6.8	0.0	0.0	0.0	61.6	12.1	51.0	29.1
4	500	84.6	30.1	30.2	17.1	6.0	0.0	0.0	0.0	202.0	90.0	126.3	88.6
5	1000	119.0	31.7	79.4	26.0	5.0	2.0	7.0	0.0	655.2	196.8	311.0	105.4

Note: All values below the limit of quantification (5 µg/L) and below the limit of detection (2 µg/L) are set to zero (0.0)

Group	Dose (mg/kg/day)	all-E-Astaxanthin dimethyl disuccinate				13Z-Astaxanthin dimethyl disuccinate			
		Male mean [µg/l]	SD	Female mean [µg/l]	SD	Male mean [µg/l]	SD	Female mean [µg/l]	SD
1	Control	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	Placebo	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
3	100	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
4	500	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
5	1000	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Note: All values below the limit of quantification (14 µg/L) and below the limit of detection (4 µg/L) are set to zero (0.0)

Plasma contents of AXN, AXN-DMS and isomers



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2.2. Liver concentrations of AXN, AXN-DMS and isomers

Week 4 (n=5)

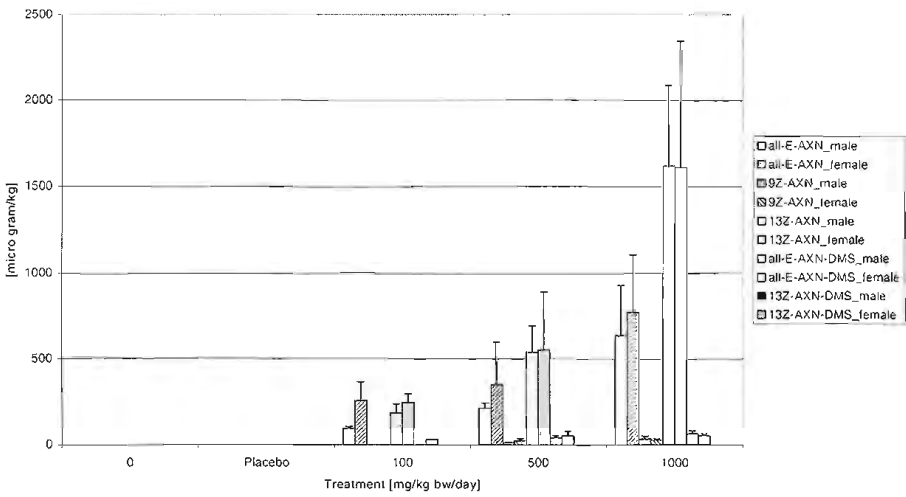
Group	Dose (mg/kg/day)	all-E-Astaxanthin				9Z-Astaxanthin				13Z-Astaxanthin			
		Male mean [µg/kg]	SD	Female mean [µg/kg]	SD	Male mean [µg/kg]	SD	Female mean [µg/kg]	SD	Male mean [µg/kg]	SD	Female mean [µg/kg]	SD
1	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	Placebo	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
3	100	93.2	11.9	255.4	109.2	0.0	0.0	0.0	0.0	184.2	52.2	243.8	51.4
4	500	213.0	28.9	349.2	248.7	12.5	3.5	24.0	12.5	537.8	154.2	551.8	337.3
5	1000	635.0	293.2	770.8	334.3	34.6	16.8	27.2	9.6	1617.4	458.5	1609.2	734.9

Note: All values below the limit of quantification (10 µg/kg) and below the limit of detection (3 µg/kg) are set to zero (0.0)

Group	Dose (mg/kg/day)	all-E-Astaxanthin dimethyl disuccinate				13Z-Astaxanthin dimethyl disuccinate			
		Male mean [µg/kg]	SD	Female mean [µg/kg]	SD	Male mean [µg/kg]	SD	Female mean [µg/kg]	SD
1	0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	Placebo	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
3	100	0.0	0.0	29.0	0.0	0.0	0.0	0.0	0.0
4	500	41.6	12.0	52.7	25.2	0.0	0.0	0.0	0.0
5	1000	61.6	18.4	52.8	11.5	0.0	0.0	0.0	0.0

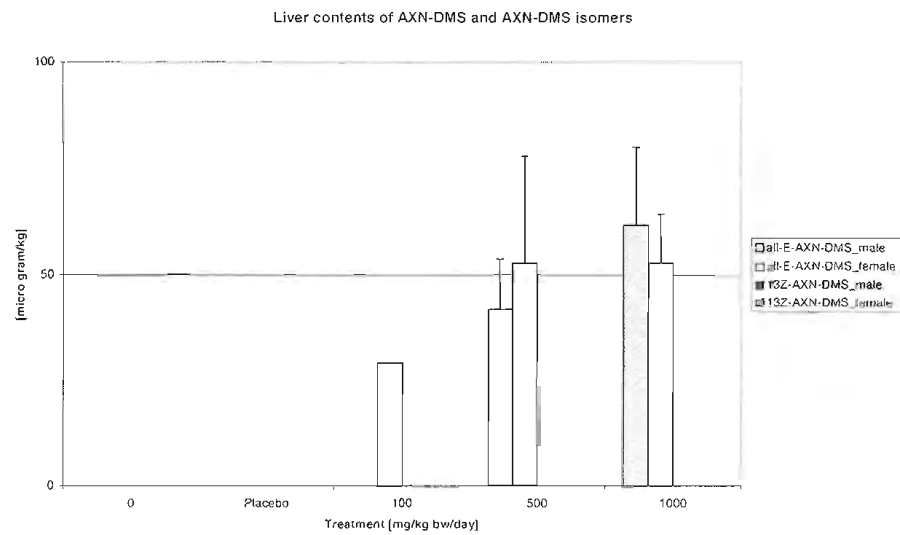
Note: All values below the limit of quantification (25 µg/kg) and below the limit of detection (8 µg/kg) are set to zero (0.0)

Liver contents of AXN, AXN-DMS and isomers



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3. Summary Tables and Figures

3.1. Plasma concentrations

Group	mg/kgbw	Sample Name	Description	Result	Units	Result	Units	Result	Units	dimethylsuccinyl Result	Units	dimethylsuccinyl Result	Units
Group 1	0	M1 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		M2 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		M3 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		M4 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		M5 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
Group 2	Placeto	M6 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		M7 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		M8 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		M9 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		M10 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
Group 3	100	M11 Plasma	RCC 853022	18	µg/l	LOD	µg/l	85	µg/l	LOD	µg/l	LOD	µg/l
		M12 Plasma	RCC 853022	16	µg/l	LOD	µg/l	83	µg/l	LOD	µg/l	LOD	µg/l
		M13 Plasma	RCC 853022	21	µg/l	LOD	µg/l	79	µg/l	LOD	µg/l	LOD	µg/l
		M14 Plasma	RCC 853022	16	µg/l	LOD	µg/l	53	µg/l	LOD	µg/l	LOD	µg/l
		M15 Plasma	RCC 853022	17	µg/l	LOD	µg/l	66	µg/l	LOD	µg/l	LOD	µg/l
Group 4	500	M16 Plasma	RCC 853022	59	µg/l	LOD	µg/l	219	µg/l	LOD	µg/l	LOD	µg/l
		M17 Plasma	RCC 853022	21	µg/l	LOD	µg/l	95	µg/l	LOD	µg/l	LOD	µg/l
		M18 Plasma	RCC 853022	51	µg/l	LOD	µg/l	203	µg/l	LOD	µg/l	LOD	µg/l
		M19 Plasma	RCC 853022	33	µg/l	LOD	µg/l	154	µg/l	LOD	µg/l	LOD	µg/l
		M20 Plasma	RCC 853022	89	µg/l	LOD	µg/l	349	µg/l	LOD	µg/l	LOD	µg/l
Group 5	1000	M21 Plasma	RCC 853022	108	µg/l	LOD	µg/l	870	µg/l	LOD	µg/l	LOD	µg/l
		M22 Plasma	RCC 853022	169	µg/l	LOD	µg/l	818	µg/l	LOD	µg/l	LOD	µg/l
		M23 Plasma	RCC 853022	101	µg/l	LOD	µg/l	428	µg/l	LOD	µg/l	LOD	µg/l
		M24 Plasma	RCC 853022	130	µg/l	LOD	µg/l	800	µg/l	LOD	µg/l	LOD	µg/l
		M25 Plasma	RCC 853022	90	µg/l	LOD	µg/l	410	µg/l	LOD	µg/l	LOD	µg/l
Group 6	3	F26 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		F27 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		F28 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		F29 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		F30 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
Group 7	Placeto	F31 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		F32 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		F33 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		F34 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
		F35 Plasma	RCC 853022	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l	LOD	µg/l
Group 8	100	F36 Plasma	RCC 853022	7	µg/l	LOD	µg/l	25	µg/l	LOD	µg/l	LOD	µg/l
		F37 Plasma	RCC 853022	20	µg/l	LOD	µg/l	70	µg/l	LOD	µg/l	LOD	µg/l
		F38 Plasma	RCC 853022	24	µg/l	LOD	µg/l	75	µg/l	LOD	µg/l	LOD	µg/l
		F39 Plasma	RCC 853022	24	µg/l	LOD	µg/l	58	µg/l	LOD	µg/l	LOD	µg/l
		F40 Plasma	RCC 853022	19	µg/l	LOD	µg/l	27	µg/l	LOD	µg/l	LOD	µg/l
Group 9	500	F41 Plasma	RCC 853022	19	µg/l	LOD	µg/l	59	µg/l	LOD	µg/l	LOD	µg/l
		F42 Plasma	RCC 853022	44	µg/l	LOD	µg/l	197	µg/l	LOD	µg/l	LOD	µg/l
		F43 Plasma	RCC 853022	46	µg/l	LOD	µg/l	123	µg/l	LOD	µg/l	LOD	µg/l
		F44 Plasma	RCC 853022	9	µg/l	LOD	µg/l	50	µg/l	LOD	µg/l	LOD	µg/l
		F45 Plasma	RCC 853022	27	µg/l	LOD	µg/l	277	µg/l	LOD	µg/l	LOD	µg/l
Group 10	1000	F46 Plasma	RCC 853022	29	µg/l	LOD	µg/l	187	µg/l	LOD	µg/l	LOD	µg/l
		F47 Plasma	RCC 853022	71	µg/l	LOD	µg/l	348	µg/l	LOD	µg/l	LOD	µg/l
		F48 Plasma	RCC 853022	86	µg/l	LOD	µg/l	343	µg/l	LOD	µg/l	LOD	µg/l
		F49 Plasma	RCC 853022	73	µg/l	LOD	µg/l	296	µg/l	LOD	µg/l	LOD	µg/l
		F50 Plasma	RCC 853022	106	µg/l	LOD	µg/l	473	µg/l	LOD	µg/l	LOD	µg/l

LOD
LOD

Adaptation:
7 µg/l
5 µg/l

Accepted/denied/used/ret.
+ µg/l
- µg/l

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3.2. Liver concentrations

Group	Sample Name	Description	all-E-Astaxanthin		9Z-Astaxanthin		13Z-Astaxanthin		all-E-Astaxanthin- dimethyldiacetate		13Z-Astaxanthin- dimethyldiacetate	
			Result	Units	Result	Units	Result	Units	Result	Units	Result	Units
Group 1	M1 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M2 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M3 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M4 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
Group 2	M5 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M6 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M7 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M8 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
Group 3	M9 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M10 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M11 Liver	RCC 853022	97	µg/kg	LOD	µg/kg	128	µg/kg	LOD	µg/kg	LOD	µg/kg
	M12 Liver	RCC 853022	85	µg/kg	LOD	µg/kg	199	µg/kg	LOD	µg/kg	LOD	µg/kg
Group 4	M13 Liver	RCC 853022	26	µg/kg	LOD	µg/kg	258	µg/kg	LOD	µg/kg	LOD	µg/kg
	M14 Liver	RCC 853022	110	µg/kg	LOD	µg/kg	144	µg/kg	LOD	µg/kg	LOD	µg/kg
	M15 Liver	RCC 853022	78	µg/kg	LOD	µg/kg	197	µg/kg	LOD	µg/kg	LOD	µg/kg
	M16 Liver	RCC 853022	222	µg/kg	LOD	µg/kg	703	µg/kg	84	µg/kg	LOD	µg/kg
Group 5	M17 Liver	RCC 853022	173	µg/kg	LOD	µg/kg	322	µg/kg	33	µg/kg	LOD	µg/kg
	M18 Liver	RCC 853022	251	µg/kg	15	µg/kg	846	µg/kg	81	µg/kg	LOD	µg/kg
	M19 Liver	RCC 853022	219	µg/kg	LOD	µg/kg	846	µg/kg	39	µg/kg	LOD	µg/kg
	M20 Liver	RCC 853022	200	µg/kg	10	µg/kg	572	µg/kg	31	µg/kg	LOD	µg/kg
Group 6	M21 Liver	RCC 853022	723	µg/kg	36	µg/kg	1825	µg/kg	75	µg/kg	LOD	µg/kg
	M22 Liver	RCC 853022	1089	µg/kg	62	µg/kg	2297	µg/kg	81	µg/kg	LOD	µg/kg
	M23 Liver	RCC 853022	586	µg/kg	37	µg/kg	1384	µg/kg	52	µg/kg	LOD	µg/kg
	M24 Liver	RCC 853022	314	µg/kg	27	µg/kg	1135	µg/kg	49	µg/kg	LOD	µg/kg
Group 7	M25 Liver	RCC 853022	467	µg/kg	32	µg/kg	1053	µg/kg	43	µg/kg	LOD	µg/kg
	M26 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M27 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M28 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
Group 8	M29 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M30 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M31 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M32 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
Group 9	M33 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M34 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M35 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
	M36 Liver	RCC 853022	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg	LOD	µg/kg
Group 10	M37 Liver	RCC 853022	97	µg/kg	LOD	µg/kg	163	µg/kg	LOD	µg/kg	LOD	µg/kg
	M38 Liver	RCC 853022	382	µg/kg	LOD	µg/kg	243	µg/kg	LOD	µg/kg	LOD	µg/kg
	M39 Liver	RCC 853022	333	µg/kg	LOD	µg/kg	273	µg/kg	LOD	µg/kg	LOD	µg/kg
	M40 Liver	RCC 853022	232	µg/kg	LOD	µg/kg	241	µg/kg	24	µg/kg	LOD	µg/kg
Group 11	M41 Liver	RCC 853022	193	µg/kg	LOD	µg/kg	297	µg/kg	LOD	µg/kg	LOD	µg/kg
	M42 Liver	RCC 853022	181	µg/kg	LOD	µg/kg	286	µg/kg	LOD	µg/kg	LOD	µg/kg
	M43 Liver	RCC 853022	542	µg/kg	23	µg/kg	955	µg/kg	58	µg/kg	LOD	µg/kg
	M44 Liver	RCC 853022	688	µg/kg	27	µg/kg	920	µg/kg	76	µg/kg	LOD	µg/kg
Group 12	M45 Liver	RCC 853022	154	µg/kg	LOD	µg/kg	250	µg/kg	LOD	µg/kg	LOD	µg/kg
	M46 Liver	RCC 853022	201	µg/kg	17	µg/kg	455	µg/kg	26	µg/kg	LOD	µg/kg
	M47 Liver	RCC 853022	633	µg/kg	18	µg/kg	1458	µg/kg	82	µg/kg	LOD	µg/kg
	M48 Liver	RCC 853022	800	µg/kg	24	µg/kg	1134	µg/kg	52	µg/kg	LOD	µg/kg
Group 13	M49 Liver	RCC 853022	1349	µg/kg	42	µg/kg	2893	µg/kg	86	µg/kg	LOD	µg/kg
	M50 Liver	RCC 853022	515	µg/kg	21	µg/kg	1127	µg/kg	36	µg/kg	LOD	µg/kg
	M51 Liver	RCC 853022	758	µg/kg	31	µg/kg	1434	µg/kg	46	µg/kg	LOD	µg/kg

LOD
LOD

Astaxanthin
3 µg/kg
10 µg/kg

Astaxanthindimethyldiacetate
8 µg/kg
25 µg/kg

End of Evaluation

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

APPENDIX VII:
PATHOLOGY REPORT

PATHOLOGY REPORT		RCC STUDY NUMBER 853022	
TEST ITEM	: AXN-DMS	PATH. NO	: 91003 WLA
TEST SYSTEM	: Rat, HanBrl:WIST (SPF)	DATE	: 22-JUN-04
STUDY TYPE	: 28-day range-finding oral toxicity (feeding) study	SPONSOR	: DSM Nutritional Products

Prepared by:

PD Dr. A. Waldvogel
Veterinary Pathologist

PATHOLOGY REPORT		PAGE: 2	
PRINCIPAL SECTION		RCC STUDY NUMBER 853022	
TEST ITEM	: AXN-DMS	PATH. NO.	: 91003 WLA
TEST SYSTEM	: Rat, 28-day range-finding oral toxicity (feeding) study	DATE	: 22-JUN-04
SPONSOR	: DSM Nutritional Products		

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¹ Animal organ finding table

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PRINCIPAL SECTION

RCC STUDY NUMBER 853022

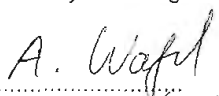
TEST ITEM	: AXN-DMS	PATH. NO.	: 91003 WLA
TEST SYSTEM	: Rat, 28-day range-finding oral toxicity (feeding) study	DATE	: 22-JUN-04
SPONSOR	: DSM Nutritional Products		

AUTHENTICATION


I, the undersigned hereby declare that the histopathology data (Principal Section and Tables) in this report were compiled by me, and that they accurately reflect the primary data records.

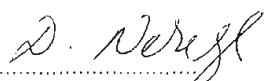
Prepared by:

PD Dr. A. Waldvogel
Veterinary Pathologist


date: 22.6.04

Cross-checked by:

 Dr. Ph. Schaetti
Toxicologic Pathologist


date: 22.6.04

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PRINCIPAL SECTION

RCC STUDY NUMBER 853022

TEST ITEM	: AXN-DMS	PATH. NO.	: 91003 WLA
TEST SYSTEM	: Rat, 28-day range-finding oral toxicity (feeding) study	DATE	: 22-JUN-04
SPONSOR	: DSM Nutritional Products		

SUMMARY

In this sub acute toxicity (feeding) range-finding study, AXN-DMS was administered daily to SPF-bred Wistar rats of both sexes at dose levels of 100, 500 and 1000 mg/kg/day for a period of 28 days (groups 3, 4 and 5, respectively). A placebo control group was treated similarly with the placebo only (group 2) and a control group (group 1) was treated similarly with microgranulated standard rat maintenance diet only.

The groups comprised 5 animals per sex that were sacrificed after 28 days of treatment.

At the end of the dosing period, all animals were sacrificed, necropsied and examined post mortem. Histological examinations were performed on organs and tissues selected in the study plan from all control and high dose animals, and gross lesions from all animals.

There were no premature deaths, all animals survived the scheduled study period.

At necropsy, performed at the end of treatment period, no test item-related macroscopic findings were recorded.

Under the conditions of this study, treatment with the test item AXN-DMS induced no macroscopic or microscopic test item-related changes.

According to the results of pathology the no observable effect level (NOEL) is above 1000 mg/kg/day.

PATHOLOGY REPORT

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PRINCIPAL SECTION

RCC STUDY NUMBER 853022

TEST ITEM	: AXN-DMS	PATH. NO.	: 91003 WLA
TEST SYSTEM	: Rat, 28-day range-finding oral toxicity (feeding) study	DATE	: 22-JUN-04
SPONSOR	: DSM Nutritional Products		

MATERIALS AND METHODS

Group Allocation

Allocation	Group 1*	Group 2**	Group 3	Group 4	Group 5
and	0	Placebo	100	500	1000
Target Dose Levels	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day
Males	1-5	6-10	11-15	16-20	21-25
Females	26-30	31-35	36-40	41-45	46-50

* - Control animals were treated with control diet only.

** - Placebo diet

Necropsy

Sacrifice:

after 4 weeks, on 14 April 2004

All animals were weighed and necropsied at the end of the treatment period at RCC Ltd., Itingen, Switzerland. The animals were anesthetized by intraperitoneal injection of sodium pentobarbitone and killed by exsanguination. Descriptions of all macroscopic abnormalities were recorded.

The liver was collected from all animals at necropsy. A part was kept for histopathology. The remaining part was rinsed in ice cold NaCl, dried by paper towel and frozen in liquid nitrogen. They were packed in dry ice and shipped together with the sample list to DSM Nutritional Products.

Samples of the following organs and tissues were collected from all animals at necropsy and fixed in neutral phosphate buffered 4 % formaldehyde solution (unless otherwise indicated):

Adrenal glands

Aorta
Bone (sternum, femur including joint)
Bone marrow (femur)
Brain (3 levels)
Cecum
Colon
Duodenum
Epididymides (fixed in Bouin's solution)
Esophagus
Eyes with optic nerve (fixed in Davidson's solution)
Harderian gland (fixed in Davidson's

Ovaries

Pancreas
Pituitary gland
Prostate gland
Rectum
Salivary glands (mandibular, sublingual)
Sciatic nerve
Seminal vesicles
Skeletal muscle
Skin
Spinal cord (cervical, midthoracic, lumbar)

PATHOLOGY REPORT

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PRINCIPAL SECTION

RCC STUDY NUMBER 853022

TEST ITEM	: AXN-DMS	PATH. NO.	: 91003 WLA
TEST SYSTEM	: Rat, 28-day range-finding oral toxicity (feeding) study	DATE	: 22-JUN-04
SPONSOR	: DSM Nutritional Products		

solution)	Spleen
Heart	Stomach
Ileum, with Peyer's patches	Testes (fixed in Bouin's solution)
Jejunum with Peyer's patches	Thymus
Kidneys	Thyroid (incl. parathyroid gland)
Larynx	Tongue
Lacrimal gland (exorbital)	Trachea
Liver	Urinary bladder (infused with formalin at necropsy)
Lungs (infused with formalin at necropsy)	Uterus
Lymph nodes (mesenteric, mandibular)	Vagina
Mammary gland area	Gross lesions
Nasal cavity	

Histopathology

Histological preparation of the tissues was performed at RCC Ltd., Itingen, Switzerland. All organ and tissue samples to be examined by the study pathologist were processed, embedded and cut at an approximate thickness of 2 to 4 micrometers and stained with hematoxylin and eosin. Slides of all organs and tissues listed in boldface type (see Necropsy, above) were prepared from all animals of control and high-dose groups (group 1 and 5, respectively), and from organs with gross lesions from all animals, and examined by the study pathologist by light microscopy.

Data Compilation

The animal data and necropsy findings were recorded on TEC-TOX Release 7.0, RCC Ltd, and were transferred electronically via transfer file into the PathData System V6.2.

The microscopic findings were recorded during histopathologic examination by the pathologist and entered directly into the PathData System. The slides were evaluated in April and May 2004.

Histological changes were described, wherever possible, according to distribution, severity and morphologic character. Severity scores were assigned as given under "Explanation of Codes and Symbols". In paired organs, findings occurred sometimes bilaterally and were of different degrees of severity. When this occurred, the higher degree was recorded and comment was made which indicated the severity of the lesion in the contra lateral organ.

All microscopic findings are listed in the "TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS" (= AOFT, animal organ finding table), along with an explanation of the codes and symbols used. Computer-generated incidence tables derived from these data are also presented as well as the complete narrative of the both macroscopic and microscopic findings.

Data Cross Checking

Selected sections were reviewed by Dr. Ph. Schaetti, Pathology Unit, RCC Ltd, Itingen / Switzerland).

The assessment of the study pathologist and reviewing pathologist compared favorably.

PATHOLOGY REPORT

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PRINCIPAL SECTION

RCC STUDY NUMBER 853022

TEST ITEM	: AXN-DMS	PATH. NO.	: 91003 WLA
TEST SYSTEM	: Rat, 28-day range-finding oral toxicity (feeding) study	DATE	: 22-JUN-04
SPONSOR	: DSM Nutritional Products		

RESULTS

Mortality

There were no premature deaths. All animals on study survived the scheduled study period.

Organ weights

There were no differences indicating an effect of the test item. A few statistically significant deviations in average organ weights at the end of treatment period were considered to be incidental and of no toxicological relevance.

Macroscopic Findings

At the end of the treatment period no test item-related gross lesions were observed. The macroscopic findings recorded were considered to be within the range of normal background lesions, which may be seen in rats of this strain and age in oral toxicity studies and were considered incidental, reflecting the usual individual variability.

Microscopic Findings

Numerous incidental microscopic findings were detected in various organs in this study. They commonly occur in laboratory rats of this strain and age. But neither their incidences nor their distribution or morphologic appearance indicated an association with treatment. The gastric glandular dilation of minimal severity observed most frequently in group 5 male animals reflects a physiologic condition and is of no toxicological relevance.

The detailed incidence data for all organs as well as tables of selected changes including their severity appear in "SUMMARY INCIDENCE OF GRADINGS" and "NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS".

CONCLUSIONS

Under the conditions of this experiment, the test item AXN-DMS produced no morphological evidence of adverse effects.

According to the results of pathology the no observable effect level (NOEL) is above 1000 mg/kg body weight/day.

PATHOLOGY REPORT PAGE : 8
SUMMARY TABLES RCC : 853022

TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

SEX :						MALE
DOSE GROUP:	01	02	03	04	05	
NO.ANIMALS:	5	5	5	5	5	
CEREBRUM :	5	-	-	-	5	
- Neuron.Fix.Artefacts:	5	-	-	-	5	
CEREBELLUM :	5	-	-	-	5	
- Neuron.Fix.Artefacts:	3	-	-	-	2	
MEDULLA OBLONGATA :	5	-	-	-	5	
- Neuron.Fix.Artefacts:	2	-	-	-	2	
PONS :	5	-	-	-	5	
- Neuropil Vacuolation:	2	-	-	-	1	
- Neuron.Fix.Artefacts:	1	-	-	-	-	
SCIATIC NERVE :	5	-	-	-	5	
- Inf. mast cells :	4	-	-	-	5	
HEART :	5	-	-	-	5	
- Lymphoid c infiltr :	1	-	-	-	-	
- Granuloma :	1	-	-	-	2	
- Myocardial Fibrosis :	-	-	-	-	1	
TRACHEA :	5	-	-	-	5	
- Inclusion:Cytoplasm.:	4	-	-	-	4	
- Lymphoid C.Infiltr. :	2	-	-	-	1	
- Glandular Ectasia :	-	-	-	-	1	
LUNGS :	5	-	-	-	5	
- Alveol.Histiocytosis:	2	-	-	-	1	
- Granuloma :	1	-	-	-	1	
- Mixed Cell Infiltr. :	-	-	-	-	1	
- Lymphoid Hyperplasia:	-	-	-	-	2	

PATHOLOGY REPORT PAGE : 9
SUMMARY TABLES RCC : 853022

TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

SEX :						MALE
DOSE GROUP:	01	02	03	04	05	
NO. ANIMALS:	5	5	5	5	5	
STOMACH :	5	-	-	-	5	
- Inclusion:Cytoplasm.:	4	-	-	-	3	
- Granulocytic Infiltr:	5	-	-	-	5	
- Inflammation :	1	-	-	-	-	
- Glandular Dilatation :	-	-	-	-	5	
- Fibrosis :	-	-	-	-	1	
- Lymphoid C.Infiltr. :	-	-	-	-	1	
DUODENUM :	5	-	-	-	5	
- Granulocytic Infiltr:	1	-	-	-	-	
JEJUNUM :	5	-	-	-	5	
- Autolysis :	2	-	-	-	1	
PEYERS PATCHES JEJ. :	5	-	-	-	5	
- Mineralization :	-	-	-	-	1	
ILEUM :	5	-	-	-	5	
- Autolysis :	1	-	-	-	4	
CECUM :	5	-	-	3	5	
- Autolysis :	1	-	-	2	2	
- Mucosal Hyperplasia :	-	-	-	-	1	
- Mixed cell infiltran:	-	-	-	-	1	
- crypt with bacteria :	-	-	-	-	2	
COLON :	5	-	-	-	5	
- Autolysis :	3	-	-	-	1	
LIVER :	5	-	-	-	5	
- Lymphoid C.Infiltr. :	2	-	-	-	1	
- Granuloma :	5	-	-	-	5	
- Vacuolation:Periport:	2	-	-	-	-	

PATHOLOGY REPORT
SUMMARY TABLES

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TEST ARTICLE : AXN-DMS
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING)
SPONSOR : DSM NUTRITIONAL PRODUCTS

PATHOL. NO.: 91003 WLA
DATE : 22-JUN-04
PathData®System V6.2a2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

SEX :						MALE
DOSE GROUP:	01	02	03	04	05	
NO.ANIMALS:	5	5	5	5	5	
KIDNEYS :	5	1	-	-	5	
- Hyaline Casts :	4	-	-	-	3	
- Urothelial vesicles :	2	-	-	-	-	
- Hyaline Droplets :	4	1	-	-	5	
- Mononuclear Infiltr.:	1	1	-	-	1	
- Tubular Basophilia :	2	-	-	-	1	
- Tubul.Simple Dilat. :	-	1	-	-	2	
- Granular Casts :	-	1	-	-	-	
- Apoptosis :	-	1	-	-	-	
URINARY BLADDER :	5	-	-	-	5	
- Autolysis :	2	-	-	-	-	
TESTES :	5	-	-	-	5	
- Spermat.Giant Cells :	-	-	-	-	1	
EPIDIDYMIDES :	5	-	-	-	5	
- Mixed Cell Infiltr. :	2	-	-	-	1	
THYROID GLAND :	5	1	-	-	5	
- Lymphoid C.Infiltr. :	-	-	-	-	1	
ADRENAL CORTICES :	5	-	-	-	5	
- Diffuse Fatty Change:	5	-	-	-	5	
SPLEEN :	5	1	-	-	5	
- Erythroid Hyperpl. :	2	1	-	-	3	
- Hemosiderin Deposits:	2	-	-	-	3	
- Megakaryoc.Hyperpl. :	1	1	-	-	-	
- Lymphoid Depletion :	-	1	-	-	-	
- Myeloid Hyperplasia :	-	1	-	-	-	
BONE MARROW, FEMUR :	5	-	-	-	5	
- Adipocyte infiltrate:	2	-	-	-	4	
THYMUS :	5	-	3	-	5	
- Hemorrhage :	-	-	1	-	-	

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SUMMARY TABLES	RCC :	853022

TEST ARTICLE : AXN-DMS	PATHOL. NO. : 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

SEX :						MALE
DOSE GROUP:	01	02	03	04	05	
NO.ANIMALS:	5	5	5	5	5	
MESENT. LYMPH NODE :	5	-	-	-	5	
- Lymphoid Depletion :	-	-	-	-	1	
- Mast Cell Hyperpl. :	-	-	-	-	2	

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 12
RCC : 853022

TEST ARTICLE : AXN-DMS
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING)
SPONSOR : DSM NUTRITIONAL PRODUCTS

PATHOL. NO.: 91003 WLA
DATE : 22-JUN-04
PathData®System V6.2a2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

SEX :						FEMALE
DOSE GROUP:	01	02	03	04	05	
NO.ANIMALS:	5	5	5	5	5	
CEREBRUM :	5	-	-	-	5	
- Neuron.Fix.Artefacts:	5	-	-	-	5	
CEREBELLUM :	5	-	-	-	5	
- Neuron.Fix.Artefacts:	5	-	-	-	5	
- Edema :	-	-	-	-	1	
MEDULLA OBLONGATA :	5	-	-	-	5	
- Neuron.Fix.Artefacts:	1	-	-	-	1	
PONS :	5	-	-	-	5	
- Neuron.Fix.Artefacts:	-	-	-	-	1	
SCIATIC NERVE :	5	-	-	-	5	
- Inf. mast cells :	5	-	-	-	5	
HEART :	5	-	-	-	5	
- Lymphoid c infiltr :	-	-	-	-	1	
- Myocardial Fibrosis :	1	-	-	-	-	
TRACHEA :	5	-	-	-	5	
- Inclusion:Cytoplasm.:	4	-	-	-	1	
- Lymphoid C.Infiltr. :	1	-	-	-	1	
- Glandular Ectasia :	-	-	-	-	1	
STOMACH :	5	-	-	1	5	
- Inclusion:Cytoplasm.:	3	-	-	1	3	
- Granulocytic Infiltr:	4	-	-	-	5	
- Glandular Dilation :	3	-	-	1	5	
- Lymphoid C.Infiltr. :	1	-	-	-	-	
- Epithel.Vacuolizat. :	1	-	-	-	-	
DUODENUM :	5	-	-	-	5	
- Granulocytic Infiltr:	2	-	-	-	-	
- Autolysis :	2	-	-	-	4	

PATHOLOGY REPORT
SUMMARY TABLES

PAGE : 13
RCC : 853022

TEST ARTICLE : AXN-DMS
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING)
SPONSOR : DSM NUTRITIONAL PRODUCTS

PATHOL. NO.: 91003 WLA
DATE : 22-JUN-04
PathData®System V6.2a2

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

	SEX :						FEMALE
	DOSE GROUP:	01	02	03	04	05	
	NO. ANIMALS:	5	5	5	5	5	
JEJUNUM	:	5	-	-	-	5	
- Autolysis	:	4	-	-	-	2	
PEYERS PATCHES JEJ.	:	4	-	-	-	5	
- Mineralization	:	-	-	-	-	3	
ILEUM	:	5	-	-	-	5	
- Autolysis	:	5	-	-	-	2	
CECUM	:	5	1	-	1	5	
- Autolysis	:	4	1	-	1	2	
COLON	:	5	-	-	-	5	
- Autolysis	:	2	-	-	-	1	
RECTUM	:	5	-	-	-	5	
- Glandular dilation	:	1	-	-	-	-	
LIVER	:	5	-	-	-	5	
- Lymphoid C. Infiltr.	:	2	-	-	-	2	
- Granuloma	:	5	-	-	-	4	
- Vacuolation: Periportal	:	1	-	-	-	-	
- Bile Duct Hyperpl.	:	4	-	-	-	3	
- Vacuolation, diffuse	:	-	-	-	-	3	
KIDNEYS	:	5	1	1	-	5	
- Urothelial vesicles	:	1	-	-	-	-	
- Tubular Basophilia	:	2	1	-	-	4	
- Tubul. Simple Dilat.	:	2	1	1	-	5	
- Mineraliz: Interstit.	:	2	-	-	-	4	
- Basophilia, diffuse	:	3	-	-	-	-	
- Granular Casts	:	1	1	1	-	5	
- Hyperplasia, Urothel.	:	1	-	-	-	-	
- Pelvic Dilation	:	-	1	1	-	1	

PATHOLOGY REPORT PAGE : 14
SUMMARY TABLES RCC : 853022

TEST ARTICLE : AXN-DMS **PATHOL. NO.:** 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) **DATE** : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS *PathData®System V6.2a2*

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

	SEX :						FEMALE
	DOSE GROUP:	01	02	03	04	05	
	NO.ANIMALS:	5	5	5	5	5	
URINARY BLADDER	:	5	-	-	-	5	
- Autolysis	:	2	-	-	-	1	
- Vacuolation u	:	-	-	-	-	1	
OVARIES	:	5	-	1	2	5	
- Cyst salpinx	:	-	-	-	1	-	
UTERUS	:	5	-	-	-	5	
- Cycle:Diestrus	:	1	-	-	-	1	
- Cycle:Metestrus	:	4	-	-	-	4	
VAGINA	:	5	-	-	-	5	
- Cycle:Diestrus	:	1	-	-	-	2	
- Cycle:Metestrus	:	4	-	-	-	2	
- Cycle:Estrus	:	-	-	-	-	1	
ADRENAL CORTICES	:	5	-	-	-	5	
- Focal Fatty Change	:	3	-	-	-	1	
SPLEEN	:	5	-	-	-	5	
- Hemosiderin Deposits:	:	4	-	-	-	5	
- Lymphoid Depletion	:	1	-	-	-	-	
- Congestion	:	-	-	-	-	1	
BONE MARROW, FEMUR	:	5	-	-	-	5	
- Adipocyte infiltrate:	:	2	-	-	-	1	
THYMUS	:	5	-	1	1	5	
- Hemorrhage	:	1	-	-	1	1	
MESENT. LYMPH NODE	:	5	-	-	-	5	
- Lymphoid Depletion	:	1	-	-	-	1	
- Mast Cell Hyperpl.	:	1	-	-	-	1	
- Granulocytic Infiltr:	:	-	-	-	-	1	
MANDIB. LYMPH NODE	:	5	-	-	-	5	
- Hemorrhage	:	-	-	-	-	1	

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

CORRELATION TABLE: NECROPSY - MICROSCOPY	DOSE GROUP 01, MALE
--	---------------------

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
----------------------	-----------------------------------

ANIMAL NO: 1

CECUM

- 01: MUCOSA: DISCOLORATION, RED BROWN.	- Nothing abnormal discovered.
--	--------------------------------

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<hr/>			
TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2
<hr/>			
CORRELATION TABLE: NECROPSY - MICROSCOPY			DOSE GROUP 01, FEMALE

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
----------------------	-----------------------------------

	ANIMAL NO:	26
	
PANCREAS		
- 01: DISCOLORATION, DARK RED.	-	Nothing abnormal discovered.
.....		
	ANIMAL NO:	28
	
CECUM		
- 01: MUCOSA: DISCOLORATION, REDDISH.	-	Nothing abnormal discovered.
PANCREAS		
- 01: DISCOLORATION, REDDISH.	-	Nothing abnormal discovered.
.....		
	ANIMAL NO:	29
	
THYMUS		
- 01: DISCOLORATION, DARK RED.	-	Hemorrhage, multifocal, grade 1.
MANDIBULAR LYMPH NODE		
- 01: DISCOLORATION, DARK RED.	-	Nothing abnormal discovered.
.....		
	ANIMAL NO:	30
	
PANCREAS		
- 01: DISCOLORATION, DARK RED.	-	Nothing abnormal discovered.
OVARIES		
- 01: BOTH SIDES: DISCOLORATION, DARK RED.	-	No corresponding finding.
.....		

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

CORRELATION TABLE: NECROPSY - MICROSCOPY	DOSE GROUP 02, MALE
--	---------------------

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 7

KIDNEYS	
- 01: BOTH SIDES: DISCOLORATION, TAN.	- No corresponding finding.
THYROID GLAND (BOTH LOBES)	
- 01: BOTH SIDES: DISCOLORATION, TAN.	- No corresponding finding.
SPLEEN	
- 01: ENLARGED, D=50X15 MM.	- Myeloid hyperplasia, grade 4.
.....	

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

CORRELATION TABLE: NECROPSY - MICROSCOPY	DOSE GROUP 02, FEMALE
--	-----------------------

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
----------------------	-----------------------------------

ANIMAL NO: 31

CECUM

- 01: MUCOSA: DISCOLORATION, REDDISH.	- Nothing abnormal discovered.
--	--------------------------------

ANIMAL NO: 35

KIDNEYS

- 01: BOTH SIDES: PELVIC DILATION.	- Pelvic dilation, bilateral, grade 3.
------------------------------------	---

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
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SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2
<hr/>			
CORRELATION TABLE: NECROPSY - MICROSCOPY		DOSE GROUP 03, MALE	
<hr/>			
NECROPSY OBSERVATION		CORRESPONDING MICROSCOPIC FINDING	
<hr/>			
		ANIMAL NO:	13
		
THYMUS			
- 01: THICKENED.		- Nothing abnormal discovered.	
.....			
		ANIMAL NO:	14
		
THYMUS			
- 01: FOCUS/FOCI, ISOLATED, D=1 MM, DARK RED.		- Hemorrhage, multifocal, grade 1.	
.....			
		ANIMAL NO:	15
		
PANCREAS			
- 01: DISCOLORATION, RED BROWN.		- Nothing abnormal discovered.	
THYMUS			
- 01: THICKENED.		- Nothing abnormal discovered.	
.....			

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

CORRELATION TABLE: NECROPSY - MICROSCOPY	DOSE GROUP 03, FEMALE
--	-----------------------

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
	ANIMAL NO: 38

KIDNEYS	
- 01: RIGHT SIDE: PELVIC DILATION.	- Pelvic dilation, unilateral, grade 2.
.....
	ANIMAL NO: 39

THYMUS	
- 01: THICKENED.	- Nothing abnormal discovered.
.....
	ANIMAL NO: 40

OVARIES	
- 01: BOTH SIDES: ENLARGED.	- Nothing abnormal discovered.
.....

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TEST ARTICLE : AXN-DMS		PATHOL. NO.: 91003 WLA		
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING)		DATE : 22-JUN-04		
SPONSOR : DSM NUTRITIONAL PRODUCTS		PathData®System V6.2a2		
CORRELATION TABLE: NECROPSY - MICROSCOPY		DOSE GROUP 04, MALE		
NECROPSY OBSERVATION		CORRESPONDING MICROSCOPIC FINDING		
		ANIMAL NO: 16		
CECUM			
- 01: MUCOSA: DISCOLORATION, REDDISH.		- Nothing abnormal discovered.		
.....				
		ANIMAL NO: 18		
CECUM			
- 01: MUCOSA: DISCOLORATION, REDDISH.		- Nothing abnormal discovered.		
.....				
		ANIMAL NO: 20		
CECUM			
- 01: MUCOSA: DISCOLORATION, REDDISH.		- Nothing abnormal discovered.		
.....				

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TEST ARTICLE : AXN-DMS	PATHOL. NO. : 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2

CORRELATION TABLE: NECROPSY - MICROSCOPY	DOSE GROUP 04, FEMALE
--	-----------------------

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
----------------------	-----------------------------------

ANIMAL NO: 41

THYMUS

- 01: THICKENED.

- Nothing abnormal discovered.

ANIMAL NO: 42

OVARIES

- 01: RIGHT SIDE: WATERY CYST, D=6
MM.

- Cystic dilation of salpinx,
bilateral, grade 2.

ANIMAL NO: 43

STOMACH

- 01: MUCOSA: DISCOLORATION, DARK
RED.

- No corresponding finding.

ANIMAL NO: 44

OVARIES

- 01: RIGHT SIDE: DISCOLORATION,
REDDISH.

- Nothing abnormal discovered.

ANIMAL NO: 45

CECUM

- 01: MUCOSA: DISCOLORATION,
REDDISH.

- Nothing abnormal discovered.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

CORRELATION TABLE: NECROPSY - MICROSCOPY	DOSE GROUP 05, MALE
--	---------------------

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
----------------------	-----------------------------------

ANIMAL NO: 21

CECUM

- 01: MUCOSA: DISCOLORATION, REDDISH.	- Nothing abnormal discovered.
--	--------------------------------

ANIMAL NO: 24

THYMUS

- 01: THICKENED.	- Nothing abnormal discovered.
------------------	--------------------------------

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
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SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

CORRELATION TABLE: NECROPSY - MICROSCOPY	DOSE GROUP 05, FEMALE
--	-----------------------

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
----------------------	-----------------------------------

ANIMAL NO: 46

CECUM

- 01: MUCOSA: DISCOLORATION,
REDDISH.

- Nothing abnormal discovered.

KIDNEYS

- 01: BOTH SIDES: PELVIC DILATION.

- Pelvic dilation, bilateral,
grade 3.

MANDIBULAR LYMPH NODE

- 01: DISCOLORATION, DARK RED.

- Hemorrhage, focal, bilateral,
grade 2.

ANIMAL NO: 47

CECUM

- 01: MUCOSA: DISCOLORATION,
REDDISH.

- Nothing abnormal discovered.

ANIMAL NO: 48

CECUM

- 01: MUCOSA: DISCOLORATION,
REDDISH.

- Nothing abnormal discovered.

ANIMAL NO: 49

CECUM

- 01: MUCOSA: DISCOLORATION,
REDDISH.

- Nothing abnormal discovered.

PANCREAS

- 01: DISCOLORATION, DARK RED.

- Nothing abnormal discovered.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

CORRELATION TABLE: NECROPSY - MICROSCOPY	DOSE GROUP 05, FEMALE
--	-----------------------

NECROPSY OBSERVATION	CORRESPONDING MICROSCOPIC FINDING
----------------------	-----------------------------------

ANIMAL NO: 50

CECUM

- 01: MUCOSA: DISCOLORATION, REDDISH.	- Nothing abnormal discovered.
--	--------------------------------

.....

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

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

CODES AND SYMBOLS USED AT ORGAN LEVEL:

G = Gross observation checked off histologically
* = Comment in text of individual animal data
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
- = Organ examined, no pathologic findings noted (AOFT only)

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / few / small
GRADE 3 = Moderate / moderate number / moderate size
GRADE 4 = Marked / many / large
P = Finding present, severity not scored
(= Finding unilateral in paired organs
* = Comment in text of individual animal data

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TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 MG/KG/DAY

ANIMAL NUMBER :

	1	2	3	4	5	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
CEREBRUM	+	+	+	+	+	+	+	+	+	+
- Neuron.Fix.Artefacts	3.	2.	2.	2.	3.	3.	2.	3.	3.	3.
CEREBELLUM	+	-	-	+	+	+	+	+	+	+
- Neuron.Fix.Artefacts	3.	.	.	2.	3.	2.	1.	3.	1.	3.
MEDULLA OBLONGATA	-	-	-	+	+	+	-	-	-	-
- Neuron.Fix.Artefacts	.	.	.	1.	1.	1.
PONS	+	-	+	+	-	-	-	-	-	-
- Neuropil Vacuolation	1.	.	1.
- Neuron.Fix.Artefacts	.	.	.	1.
SPINAL CORD, CERVIC.	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, THORAC.	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, LUMBAR	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	+	+	-	+	+	+	+	+	+	+
- Inf. mast cells	1.	1.	.	1.	1.	1.	1.	1.	1.	1.
HEART	-	-	+	+	-	-	+	-	-	-
- Lymphoid c infiltr	.	.	1.
- Granuloma	.	.	.	1.
- Myocardial Fibrosis	1.	.	.	.
TRACHEA	+	+	+	+	+	-	+	+	+	+
- Inclusion:Cytoplasm.	1.	1.	.	1.	1.	.	1.	1.	1.	1.
- Lymphoid C.Infiltr.	.	.	1.	1.	.	.	.	1.	.	.
LUNGS	+	+	-	-	-	-	-	-	-	-
- Alveol.Histiocytosis	1.	1.
- Granuloma	1.

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 MG/KG/DAY

ANIMAL NUMBER :

	1	2	3	4	5	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
STOMACH	+	+	+	+	+	+	+	+	+	+
- Inclusion: Cytoplasm.	1.	1.	1.	1.	.	1.	.	.	2.	1.
- Granulocytic Infiltr.	2.	1.	1.	1.	1.	1.	.	1.	1.	1.
- Inflammation	1.
- Glandular Dilatation	1.	1.	1.	.	.
- Lymphoid C. Infiltr.	1.
- Epithel. Vacuolizat.	1.	.
DUODENUM	-	+	-	-	-	+	+	-	+	-
- Granulocytic Infiltr.	.	1.	.	.	.	1.	1.	.	.	.
- Autolysis	1.	.	1.	.
JEJUNUM	+	-	-	-	+	+	-	+	+	+
- Autolysis	2.	.	.	.	1.	2.	.	2.	1.	1.
PEYERS PATCHES JEJ.	-	-	-	-	-	-	0	-	-	-
ILEUM	+	-	-	-	-	+	+	+	+	+
- Autolysis	2.	2.	3.	1.	2.	3.
PEYERS PATCHES ILE	0	-	-	-	-	-	-	-	-	-
CECUM	-G	-	-	+	-	+	-	+G	+	+
- Autolysis	.	.	.	3.	.	3.	.	1.	2.	3.
COLON	+	+	-	+	-	-	-	+	+	-
- Autolysis	2.	3.	.	1.	.	.	.	2.	2.	.
RECTUM	-	-	-	-	-	-	-	-	-	+
- Glandular dilatation	P.
LIVER	+	+	+	+	+	+	+	+	+	+
- Lymphoid C. Infiltr.	1.	.	1.	1.	.	1.
- Granuloma	1.	2.	1.	1.	2.	1.	2.	1.	1.	1.
- Vacuolation: Periport	.	1.	.	1.	2*	.
- Bile Duct Hyperpl.	1.	.	1.	1.	1.
PANCREAS	-G	.	-G	.	-G

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 MG/KG/DAY

ANIMAL NUMBER :

	1	2	3	4	5	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
KIDNEYS	+	+	+	+	+	+	+	+	+	-
- Hyaline Casts	1.	.	1.	1.	(1.
- Urothelial vesicles	(1.	(1.	1.	.
- Hyaline Droplets	.	1.	2.	2*	1.
- Mononuclear Infiltr.	.	(1.
- Tubular Basophilia	.	.	(1.	(1.	.	(1.	(1.	.	.	.
- Tubul.Simple Dilat.	1.	1.	.
- Mineraliz:Interstit.	(1.	1.	.	.	.
- Basophilia, diffuse	1.	1.	1.	.
- Granular Casts	1.	.
- Hyperplasia, Urothel	(1.	.	.
.....										
URINARY BLADDER	+	-	-	-	+	-	+	-	-	+
- Autolysis	1.	.	.	.	1.	.	1.	.	.	1.
.....										
TESTES	-	-	-	-	-					
.....										
EPIDIDYMIDES	-	+	-	+	-					
- Mixed Cell Infiltr.	.	(1.	.	(1.	.					
.....										
PROSTATE GLAND	-	-	-	-	-					
.....										
SEMINAL VESICLES	-	-	-	-	-					
.....										
OVARIES						-	-	-	-	-G
.....										
UTERUS						+	+	+	+	+
- Cycle:Diestrus						P.
- Cycle:Metestrus						.	P.	P.	P.	P.
.....										
VAGINA						+	+	+	+	+
- Cycle:Diestrus						P.
- Cycle:Metestrus						.	P.	P.	P.	P.
.....										
THYROID GLAND	-	-	-	-	-	-	-	-*	-	-
.....										
PARATHYROID GLANDS	0	-*	-*	-	0	-*	-*	-*	-*	-*
.....										

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SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, 0 MG/KG/DAY

ANIMAL NUMBER :

	1	2	3	4	5	26	27	28	29	30
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
ADRENAL CORTICES	+	+	+	+	+	-	+	+	-	+
- Diffuse Fatty Change	1.	2.	1.	2.	2.
- Focal Fatty Change	1.	1.	.	1.
ADRENAL MEDULLAS	-	-	-	-	-	-	-	-	-*	-
SPLEEN	+	+	+	-	-	-	+	+	+	+
- Erythroid Hyperpl.	1.	1.
- Hemosiderin Deposits	1.	1.	1.	2.	1.	1.
- Megakaryoc.Hyperpl.	.	.	1.
- Lymphoid Depletion	1.
BONE MARROW, FEMUR	-	-	+	-	+	+	-	-	+	-
- Adipocyte infiltrate	.	.	1.	.	2.	3.	.	.	2.	.
THYMUS	-	-	-	-	-	-	-	-	+G	-
- Hemorrhage	1.	.
MESENT. LYMPH NODE	-	-	-	-	-	-	-	+	-	+
- Lymphoid Depletion	1.	.	.
- Mast Cell Hyperpl.	1.
MANDIB. LYMPH NODE	-	-	-	-	-	-	-	-	-G	-

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SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, PLACEBO

ANIMAL NUMBER :

	6	7	8	9	10	31	32	33	34	35
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
CECUM						+G				
- Autolysis						2.				
KIDNEYS		+G								+G
- Hyaline Droplets		1.								.
- Mononuclear Infiltr.		1.								.
- Tubular Basophilia		.								1.
- Tubul.Simple Dilat.		1.								1.
- Granular Casts		1.								1.
- Pelvic Dilation		.								3*
- Apoptosis		1.								.
THYROID GLAND		-G								
SPLEEN		+G								
- Erythroid Hyperpl.		2.								
- Megakaryoc.Hyperpl.		1.								
- Lymphoid Depletion		1.								
- Myeloid Hyperplasia		4.								

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SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 03, 100 MG/KG/DAY

ANIMAL NUMBER :

	11	12	13	14	15	36	37	38	39	40
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
PANCREAS					-G					
KIDNEYS								+G		
- Tubul.Simple Dilat.								1.		
- Granular Casts								1.		
- Pelvic Dilation								(2.		
OVARIES										-G
THYMUS			-G	+G	-G				-G	
- Hemorrhage				1.						

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
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SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 04, 500 MG/KG/DAY

ANIMAL NUMBER :

	16	17	18	19	20	41	42	43	44	45
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
STOMACH								+G		
- Inclusion:Cytoplasm.								1.		
- Glandular Dilation								1.		
CECUM	+G		+G		-G					+G
- Autolysis	1.		1.		.					2.
OVARIES							+G		-G	
- Cyst salpinx							2.		.	
THYMUS						+G				
- Hemorrhage						1.				

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 MG/KG/DAY

ANIMAL NUMBER :

	21	22	23	24	25	46	47	48	49	50
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
CEREBRUM	+	+	+	+	+	+	+	+	+	+
- Neuron.Fix.Artefacts	3.	2.	1.	2.	1.	2.	3.	2.	2.	3.
CEREBELLUM	+	+	-	-	-	+	+	+	+	+
- Neuron.Fix.Artefacts	2.	2.	.	.	.	1.	2.	2.	1.	2.
- Edema	1.
MEDULLA OBLONGATA	+	+	-	-	-	-	-	+	-	-
- Neuron.Fix.Artefacts	1.	1.	1.	.	.
PONS	+	-	-	-	-	-	-	+	-	-
- Neuropil Vacuolation	1.
- Neuron.Fix.Artefacts	1.	.	.
SPINAL CORD, CERVIC.	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, THORAC.	-	-	-	-	-	-	-	-	-	-
SPINAL CORD, LUMBAR	-	-	-	-	-	-	-	-	-	-
SCIATIC NERVE	+	+	+	+	+	+	+	+	+	+
- Inf. mast cells	1.	1.	1.	2.	1.	1.	1.	1.	1.	1.
HEART	-	+	-	+	+	+	-	-	-	-
- Lymphoid c infiltr	1.
- Granuloma	.	1.	.	.	1.
- Myocardial Fibrosis	.	.	.	1.
TRACHEA	+	+	-	+	+	+	-	-	-	+
- Inclusion:Cytoplasm.	1.	2.	.	1.	1.	1.
- Lymphoid C.Infiltr.	1.	1.
- Glandular Ectasia	.	.	.	1.	2.
LUNGS	+	+	+	+	+	-	-	-	-	-
- Alveol.Histiocytosis	.	1.
- Granuloma	.	.	.	1.
- Mixed Cell Infiltr.	1.
- Lymphoid Hyperplasia	.	.	1.	.	1.

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INDIVIDUAL ANIMAL DATA RCC : 853022

TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 MG/KG/DAY

ANIMAL NUMBER :

	21	22	23	24	25	46	47	48	49	50
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
STOMACH	+	+	+	+	+	+	+	+	+	+
- Inclusion:Cytoplasm.	1.	.	1.	.	1.	.	1.	1.	1.	.
- Granulocytic Infiltr	1.	1.	1.	1.	1.	1.	1.	1.	1.	1.
- Glandular Dilatation	2.	3.	1.	3.	2.	2.	1.	1.	1.	2.
- Fibrosis	.	.	.	1.
- Lymphoid C.Infiltr.	.	.	.	1.
DUODENUM	-	-	-	-	-	-	+	+	+	+
- Autolysis	1.	1.	1.	1.
JEJUNUM	+	-	-	-	-	-	-	+	-	+
- Autolysis	1.	2.	.	1.
PEYERS PATCHES JEJ.	-	-	+	-	-	+	-	-	+	+
- Mineralization	.	.	1.	.	.	1.	.	.	1.	1.
ILEUM	+	-	+	+	+	-	+	-	-	+
- Autolysis	2.	.	2.	2.	1.	.	3.	.	.	2.
PEYERS PATHCHES ILE	-	-	-	-	-	-	-	-	-	-
CECUM	+G	+	+	-	+	-G	-G	-G	+G	+G
- Autolysis	1.	.	.	.	2.	.	.	.	3.	1.
- Mucosal Hyperplasia	.	2.
- Mixed cell infiltran	.	1.
- crypt with bacteria	.	3.	1.
COLON	-	-	-	-	+	-	-	-	-	+
- Autolysis	3.	3.
RECTUM	-	-	-	-	-	-	-	-	-	-
LIVER	+	+	+	+	+	+	+	+	+	+
- Lymphoid C.Infiltr.	2.	.	.	.	1.	1.
- Granuloma	1.	1.	1.	1.	1.	1.	.	1.	1.	1.
- Bile Duct Hyperpl.	1.	1.	.	1.	.
- Vacuolation, diffuse	1.	.	1.	1*
PANCREAS	-G	.

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<hr/>			
TEST ARTICLE : AXN-DMS	PATHOL. NO.:	91003 WLA	
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04	
SPONSOR : DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2	

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 MG/KG/DAY

ANIMAL NUMBER :

	21	22	23	24	25	46	47	48	49	50
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
KIDNEYS	+	+	+	+	+	+G	+	+	+	+
- Hyaline Casts	2*	.	.	2.	1.
- Hyaline Droplets	3.	2.	3*	3.	1.
- Mononuclear Infiltr.	(1.
- Tubular Basophilia	1.	1.	1.	1.	(1.	.
- Tubul.Simple Dilat.	.	.	.	1.	1.	(1.	(2.	(1.	2.	1.
- Mineraliz:Interstit.	1.	1.	1.	1.	.
- Granular Casts	1.	2*	(1.	1.	(1.
- Pelvic Dilation	3.
.....										
URINARY BLADDER	-	-	-	-	-	+	+	-	-	-
- Autolysis	1.
- Vacuolation u	1.	.	.	.
.....										
TESTES	-	-	-	-	+					
- Spermat.Giant Cells	(1.					
.....										
EPIDIDYIMIDES	-	-	-	-	+					
- Mixed Cell Infiltr.	(1.					
.....										
PROSTATE GLAND	-	-	-	-	-					
.....										
SEMINAL VESICLES	-	-	-	-	-					
.....										
OVARIES						-	-	-	-	-
.....										
UTERUS						+	+	+	+	+
- Cycle:Diestrus						.	.	P.	.	.
- Cycle:Metestrus						P.	P.	.	P.	P.
.....										
VAGINA						+	+	+	+	+
- Cycle:Diestrus						.	.	P.	P.	.
- Cycle:Metestrus						.	P.	.	.	P.
- Cycle:Estrus						P.
.....										
THYROID GLAND	-	-	-	+	-	-	-	-	-	-
- Lymphoid C.Infiltr.	.	.	.	(1.
.....										
PARATHYROID GLANDS	-	0	-*	-*	-*	-*	-	-*	-	-
.....										

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 05, 1000 MG/KG/DAY

ANIMAL NUMBER :	21	22	23	24	25	46	47	48	49	50
	MK0	MK0	MK0	MK0	MK0	FK0	FK0	FK0	FK0	FK0
ADRENAL CORTICES	+	+	+	+	+	-	-	-	+	-
- Diffuse Fatty Change	1.	2.	3.	1.	2.
- Focal Fatty Change	1.	.
ADRENAL MEDULLAS	-	-	-	-	-	-	-	-	-	-
SPLEEN	+	+	+	-	+	+	+	+	+	+
- Erythroid Hyperpl.	1.	1.	.	.	1.
- Hemosiderin Deposits	1.	1.	1.	.	.	1.	1.	1.	1*	1.
- Congestion	1.
BONE MARROW, FEMUR	+	-	+	+	+	-	+	-	-	-
- Adipocyte infiltrate	1.	.	3.	2.	1.	.	2.	.	.	.
THYMUS	-	-	-	-G	-	-	-	-	-	+
- Hemorrhage	1.
MESENT. LYMPH NODE	+	-	+	-	-	+	-	-	+	-
- Lymphoid Depletion	2.	1.
- Mast Cell Hyperpl.	1.	.	1.	.	.	1.
- Granulocytic Infiltr	1.	.
MANDIB. LYMPH NODE	-	-	-	-	-	+G	-	-	-	-
- Hemorrhage	2.

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

ANIMAL HEADING DATA
DOSE GROUP : 01, 0 MG/KG/DAY

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST AND LAST DAY UNDER TEST	DATE OF NECROPSY
1	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
2	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
3	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
4	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
5	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
26	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
27	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
28	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
29	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
30	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY
	MALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 1
.....	

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, RED BROWN.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 3
PONS:
-Vacuolation of neuropil, focal, grade 1
SCIATIC NERVE:
-Infiltration mast cells, multifocal, bilateral, grade 1
TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1
LUNGS:
-Alveolar histiocytosis, multifocal, grade 1
-Granuloma, single, grade 1
STOMACH:
-Cytoplasmic inclusion, hyaline, grade 1
-Granulocytic Infiltration, multifocal, grade 2
JEJUNUM:
-Autolysis, grade 2
ILEUM:
-Autolysis, grade 2
PEYER'S PATCHES IEUM:
Tissue not present for histologic examination
CECUM:
Nothing abnormal discovered corresponding to necropsy observation no.01.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY

CONT./FF. ANIMAL NO. : 1

.....

COLON:
-Autolysis, grade 2

LIVER:
-Lymphoid cell infiltration, multifocal, grade 1
-Granuloma, single, grade 1

KIDNEYS:
-Hyaline casts, bilateral, grade 1
-Urothelial vesicles, superficial, pelvis, unilateral, grade 1

URINARY BLADDER:
-Autolysis, loss of urothelium, grade 1

PARATHYROID GLANDS:
Tissue not present for histologic examination

ADRENAL CORTICES:
-Diffuse fatty change, zona fasciculata & reticularis, bilateral, grade 1

SPLEEN:
-Erythroid hyperplasia, grade 1
-Hemosiderin deposits, focal, within macrophages, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28

* ANIMAL NO. :	2
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* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2
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TEXT OF GROSS AND MICROSCOPIC FINDINGS			
DOSE GROUP	: 01, 0 MG/KG/DAY		MALE

CONT./FF. ANIMAL NO. : 2

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 2
SCIATIC NERVE:
-Infiltration mast cells, multifocal, bilateral, grade 1
TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1
LUNGS:
-Alveolar histiocytosis, multifocal, grade 1
STOMACH:
-Cytoplasmic inclusion, hyaline, grade 1
-Granulocytic Infiltration, multifocal, grade 1
DUODENUM:
-Granulocytic Infiltration, multifocal, grade 1
COLON:
-Autolysis, grade 3
LIVER:
-Granuloma, multiple, grade 2
-Periportal vacuolation, fine droplet, multifocal, grade 1
KIDNEYS:
-Urothelial vesicles, superficial, pelvis, unilateral, grade 1
-Hyaline droplets, proximal convoluted tubules, bilateral, grade 1
-Mononuclear infiltration, focal, unilateral, grade 1
EPIDIDYMIDES:
-Mixed cell infiltration, focal, unilateral, grade 1
PARATHYROID GLANDS:
only one side on section
ADRENAL CORTICES:
-Diffuse fatty change, zona fasciculata & reticularis, bilateral, grade 2
SPLEEN:
-Erythroid hyperplasia, grade 1
-Hemosiderin deposits, focal, within macrophages, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY

CONT./FF. ANIMAL NO. : 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28

* ANIMAL NO. :	3
----------------	---

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

CEREBRUM:

-Neuronal fixation artefacts, grade 2

PONS:

-Vacuolation of neuropil, focal, grade 1

HEART:

-Mononuclear infiltration, grade 1

TRACHEA:

-Lymphoid cell infiltration, focal, grade 1

STOMACH:

-Cytoplasmic inclusion, hyaline, grade 1

-Granulocytic Infiltration, multifocal, grade 1

LIVER:

-Lymphoid cell infiltration, multifocal, grade 1

-Granuloma, multiple, grade 1

KIDNEYS:

-Hyaline casts, bilateral, grade 1

-Hyaline droplets, proximal convoluted tubules, bilateral, grade 2

-Tubular basophilia, focal, unilateral, grade 1

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY
	MALE

CONT./FF. ANIMAL NO. : 3

PARATHYROID GLANDS:

Only one side on section

ADRENAL CORTICES:

-Diffuse fatty change, zona fasciculata & reticularis, bilateral,
grade 1

SPLEEN:

-Megakaryocytic hyperplasia, diffuse, grade 1

BONE MARROW (FEMUR):

-Adipocyte infiltration, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0

DAYS ON TEST : 28

* ANIMAL NO. : 4

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

CEREBRUM:

-Neuronal fixation artefacts, grade 2

CEREBELLUM:

-Neuronal fixation artefacts, grade 2

MEDULLA OBLONGATA:

-Neuronal fixation artefacts, grade 1

PONS:

-Neuronal fixation artefacts, grade 1

SCIATIC NERVE:

-Infiltration mast cells, multifocal, bilateral, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY

CONT./FF. ANIMAL NO. : 4

.....

HEART:

-Granuloma, single, grade 1

TRACHEA:

-Cytoplasmic inclusion, eosinophilic, grade 1

-Lymphoid cell infiltration, focal, grade 1

STOMACH:

-Cytoplasmic inclusion, hyaline, grade 1

-Granulocytic Infiltration, multifocal, grade 1

CECUM:

-Autolysis, grade 3

COLON:

-Autolysis, grade 1

LIVER:

-Granuloma, multiple, grade 1

-Periportal vacuolation, grade 1

KIDNEYS:

-Hyaline casts, bilateral, grade 1

-Hyaline droplets, proximal convoluted tubules, bilateral,
grade 2

contralateral kidney grade 1

-Tubular basophilia, focal, unilateral, grade 1

EPIDIDYMIDES:

-Mixed cell infiltration, focal, unilateral, grade 1

ADRENAL CORTICES:

-Diffuse fatty change, zona fasciculata & reticularis, bilateral,
grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY
	MALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO. :	5

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 3
MEDULLA OBLONGATA:
-Neuronal fixation artefacts, grade 1
SCIATIC NERVE:
-Infiltration mast cells, focal, bilateral, grade 1
TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1
STOMACH:
-Granulocytic Infiltration, multifocal, grade 1
-Inflammation, focal, granulocytic, mucosa, grade 1
JEJUNUM:
-Autolysis, grade 1
LIVER:
-Granuloma, multiple, grade 2
KIDNEYS:
-Hyaline casts, unilateral, grade 1
-Hyaline droplets, proximal convoluted tubules, bilateral, grade 1
URINARY BLADDER:
-Autolysis, loss of urothelium, grade 1
PARATHYROID GLANDS:
Tissue not present for histologic examination
ADRENAL CORTICES:
-Diffuse fatty change, zona fasciculata & reticularis, bilateral, grade 2

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
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SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY
	MALE

CONT./FF. ANIMAL NO. : 5

.....

BONE MARROW (FEMUR) :
-Adipocyte infiltration, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
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SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO.	: 26

* NECROPSY FINDINGS

PANCREAS:
01: DISCOLORATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 2
MEDULLA OBLONGATA:
-Neuronal fixation artefacts, grade 1
SCIATIC NERVE:
-Infiltration mast cells, focal, bilateral, grade 1
STOMACH:
-Cytoplasmic inclusion, hyaline, grade 1
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 1
-Lymphoid cell infiltration, focal, grade 1
DUODENUM:
-Granulocytic Infiltration, multifocal, grade 1
JEJUNUM:
-Autolysis, grade 2
ILEUM:
-Autolysis, grade 2
CECUM:
-Autolysis, grade 3
LIVER:
-Granuloma, multiple, grade 1
-Bile duct hyperplasia, focal, grade 1
PANCREAS:
Nothing abnormal discovered corresponding to necropsy observation no.01.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY

CONT./FF. ANIMAL NO. : 26

KIDNEYS:

- Tubular basophilia, focal, unilateral, grade 1
- Interstitial mineralization, focal, unilateral, grade 1

UTERUS (INCLUDING CERVIX):

- Diestrus phase of the estrous cycle

VAGINA:

- Diestrus phase of the estrous cycle

PARATHYROID GLANDS:

- One side missing on section

BONE MARROW (FEMUR):

- Adipocyte infiltration, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0

DAYS ON TEST : 28

* ANIMAL NO. : 27

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

CEREBRUM:

- Neuronal fixation artefacts, grade 2

CEREBELLUM:

- Neuronal fixation artefacts, grade 1

SCIATIC NERVE:

- Infiltration mast cells, focal, bilateral, grade 1

HEART:

- Myocardial fibrosis, focal, grade 1

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY
	FEMALE

CONT./FF. ANIMAL NO. : 27

.....

TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1

STOMACH:
-Mucosal gland dilation, focal, grade 1

DUODENUM:
-Granulocytic Infiltration, multifocal, grade 1
-Autolysis, grade 1

PEYER'S PATCHES, JEJUNUM:
Tissue not present for histologic examination

ILEUM:
-Autolysis, grade 3

LIVER:
-Granuloma, multiple, grade 2

KIDNEYS:
-Tubular basophilia, focal, unilateral, grade 1
-Interstitial mineralization, multifocal, bilateral, grade 1
-Basophilia, diffuse, inner cortex, bilateral, grade 1

URINARY BLADDER:
-Autolysis, loss of urothelium, grade 1

UTERUS (INCLUDING CERVIX):
-Metestrus phase of the estrous cycle

VAGINA:
-Metestrus phase of the estrous cycle

PARATHYROID GLANDS:
One side missing on section

ADRENAL CORTICES:
-Focal fatty change, multiple, bilateral, grade 1

SPLEEN:
-Hemosiderin deposits, multifocal, within macrophages, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY
	FEMALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO. :	28

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
PANCREAS:
01: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 3
SCIATIC NERVE:
-Infiltration mast cells, multifocal, bilateral, grade 1
TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1
-Lymphoid cell infiltration, focal, grade 1
STOMACH:
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 1
JEJUNUM:
-Autolysis, grade 2
ILEUM:
-Autolysis, grade 1
CECUM:
Nothing abnormal discovered corresponding to necropsy observation no.01.
-Autolysis, grade 1
COLON:
-Autolysis, grade 2
LIVER:
-Lymphoid cell infiltration, focal, grade 1
-Granuloma, multiple, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
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SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY
	FEMALE

CONT./FF. ANIMAL NO. : 28

.....

-Bile duct hyperplasia, focal, grade 1

PANCREAS:

Nothing abnormal discovered corresponding to necropsy observation no.01.

KIDNEYS:

-Tubular simple dilation, multifocal, papillary, bilateral, grade 1

-Basophilia, diffuse, inner cortex, bilateral, grade 1

-Hyperplasia, Urothel, calix, unilateral, grade 1

UTERUS (INCLUDING CERVIX):

-Metestrus phase of the estrous cycle

VAGINA:

-Metestrus phase of the estrous cycle

THYROID GLAND (BOTH LOBES):

Only one lobe on section

PARATHYROID GLANDS:

One side missing on section

ADRENAL CORTICES:

-Focal fatty change, multiple, bilateral, grade 1

SPLEEN:

-Hemosiderin deposits, multifocal, within macrophages, grade 2

MESENTERIC LYMPH NODE:

-Lymphoid depletion, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO. :	29

* NECROPSY FINDINGS

THYMUS:
01: DISCOLORATION, DARK RED.
MANDIBULAR LYMPH NODE:
01: DISCOLORATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 1
SCIATIC NERVE:
-Infiltration mast cells, focal, bilateral, grade 1
TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1
STOMACH:
-Cytoplasmic inclusion, hyaline, grade 2
-Granulocytic Infiltration, multifocal, grade 1
-Epithelial vacuolization, focal, grade 1
DUODENUM:
-Autolysis, grade 1
JEJUNUM:
-Autolysis, grade 1
ILEUM:
-Autolysis, grade 2
CECUM:
-Autolysis, grade 2
COLON:
-Autolysis, grade 2
LIVER:
-Granuloma, multiple, grade 1
-Periportal vacuolation, fine droplet, grade 2

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
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SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY

CONT./FF. ANIMAL NO. : 29

.....

One focus medium size vacuoles, remaining lobules small size vacuoles

-Bile duct hyperplasia, multifocal, grade 1

KIDNEYS:

-Urothelial vesicles, superficial, pelvis, bilateral, grade 1

-Tubular simple dilation, multifocal, papilla, bilateral, grade 1

-Basophilia, diffuse, inner cortex, bilateral, grade 1

-Intratubular granular casts, bilateral, grade 1

UTERUS (INCLUDING CERVIX):

-Metestrus phase of the estrous cycle

VAGINA:

-Metestrus phase of the estrous cycle

PARATHYROID GLANDS:

One side missing on section

ADRENAL MEDULLAS:

medulla of only one adrenal on section

SPLEEN:

-Hemosiderin deposits, focal, within macrophages, grade 1

BONE MARROW (FEMUR):

-Adipocyte infiltration, grade 2

THYMUS:

dark red colour due to hemorrhage

-Hemorrhage, multifocal, grade 1

This finding corresponds to necropsy observation no: 01.

MANDIBULAR LYMPH NODE:

Nothing abnormal discovered corresponding to necropsy observation no.01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 01, 0 MG/KG/DAY

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO.:	30

* NECROPSY FINDINGS

PANCREAS:
01: DISCOLORATION, DARK RED.
OVARIES:
01: BOTH SIDES: DISCOLORATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 3
SCIATIC NERVE:
-Infiltration mast cells, multifocal, bilateral, grade 1
TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1
STOMACH:
-Cytoplasmic inclusion, hyaline, grade 1
-Granulocytic Infiltration, multifocal, grade 1
JEJUNUM:
-Autolysis, grade 1
ILEUM:
-Autolysis, grade 3
CECUM:
-Autolysis, grade 3
RECTUM:
-Glandular dilation, single
LIVER:
-Lymphoid cell infiltration, multifocal, grade 1
-Granuloma, multiple, grade 1
-Bile duct hyperplasia, multifocal, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2
<hr/>			
TEXT OF GROSS AND MICROSCOPIC FINDINGS			
DOSE GROUP	:	01, 0 MG/KG/DAY	FEMALE

CONT./FF. ANIMAL NO. : 30

.....

PANCREAS:

Nothing abnormal discovered corresponding to necropsy observation no.01.

URINARY BLADDER:

-Autolysis, loss of urothelium, grade 1

OVARIES:

No microscopic finding corresponding to necropsy observation no. 01.

UTERUS (INCLUDING CERVIX):

-Metestrus phase of the estrous cycle

VAGINA:

-Metestrus phase of the estrous cycle

PARATHYROID GLANDS:

Only one side on section

ADRENAL CORTICES:

-Focal fatty change, solitary, bilateral, grade 1

SPLEEN:

-Hemosiderin deposits, focal, within macrophages, grade 1

-Lymphoid depletion, grade 1

MESENTERIC LYMPH NODE:

-Mast cell hyperplasia, medullary, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

.....

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

ANIMAL HEADING DATA
DOSE GROUP : 02, PLACEBO

ANIMAL NUMBER	SEX M/F	DEFINED AND STATE OF NECROPSY	FINAL K0	TEST DAYS	FIRST AND DAY UNDER TEST	LAST 13-APR-04	DATE OF NECROPSY
6	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
7	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
8	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
9	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
10	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
31	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
32	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
33	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
34	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
35	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 02, PLACEBO
	MALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 6

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 7

* NECROPSY FINDINGS

KIDNEYS:
01: BOTH SIDES: DISCOLORATION, TAN.
THYROID GLAND (BOTH LOBES):
01: BOTH SIDES: DISCOLORATION, TAN.
SPLEEN:
01: ENLARGED, D=50X15 MM.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:
No microscopic finding corresponding to necropsy observation no. 01.
-Hyaline droplets, proximal convoluted tubules, bilateral, grade 1
-Mononuclear infiltration, focal, bilateral, grade 1
-Tubular simple dilation, multifocal, bilateral, grade 1
-Intratubular granular casts, bilateral, grade 1

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 02, PLACEBO
	MALE

CONT./FF. ANIMAL NO. : 7

.....

-Apoptosis, tubular epithelia, bilateral, grade 1
THYROID GLAND (BOTH LOBES):
Organ examined, no pathologic findings noted
No microscopic finding corresponding to necropsy observation no. 01.
SPLEEN:
-Erythroid hyperplasia, grade 2
-Megakaryocytic hyperplasia, diffuse, grade 1
-Lymphoid depletion, grade 1
-Myeloid hyperplasia, grade 4
This finding corresponds to necropsy observation no: 01.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 8

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 02, PLACEBO
	MALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. :
	9

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. :
	10

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 02, PLACEBO
	FEMALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 31
.....	

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CECUM:
Nothing abnormal discovered corresponding to necropsy obser-
vation no.01.
-Autolysis, grade 2

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 32
.....	

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 02, PLACEBO
	FEMALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 33
.....	

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 34
.....	

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP : 02, PLACEBO	FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 35
.....

* NECROPSY FINDINGS

KIDNEYS:
01: BOTH SIDES: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:
-Tubular basophilia, focal, bilateral, grade 1
-Tubular simple dilation, multifocal, bilateral, grade 1
-Intratubular granular casts, bilateral, grade 1
-Pelvic dilation, bilateral, grade 3
controlateral side grade 2
This finding corresponds to necropsy observation no: 01.

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

ANIMAL HEADING DATA
DOSE GROUP : 03, 100 MG/KG/DAY

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST AND LAST DAY UNDER TEST	DATE OF NECROPSY
11	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
12	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
13	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
14	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
15	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
36	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
37	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
38	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
39	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
40	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04

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TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 03, 100 MG/KG/DAY MALE

```
* STATE AT NECROPSY: K0
DAYS ON TEST      :      28                      * ANIMAL NO. :      11
.....
```

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

```
* STATE AT NECROPSY: K0
DAYS ON TEST      :      28                      * ANIMAL NO. :      12
.....
```

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 03, 100 MG/KG/DAY
	MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 13
.....

* NECROPSY FINDINGS

THYMUS:
01: THICKENED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
Organ examined, no pathologic findings noted
Nothing abnormal discovered corresponding to necropsy obser-
vation no.01.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 14
.....

* NECROPSY FINDINGS

THYMUS:
01: FOCUS/FOCI, ISOLATED, D=1 MM, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
-Hemorrhage, multifocal, grade 1
This finding corresponds to necropsy observation no: 01.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 03, 100 MG/KG/DAY
	MALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 15

.....

* NECROPSY FINDINGS

PANCREAS:
01: DISCOLORATION, RED BROWN.
THYMUS:
01: THICKENED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

PANCREAS:
Nothing abnormal discovered corresponding to necropsy obser-
vation no.01.
THYMUS:
Nothing abnormal discovered corresponding to necropsy obser-
vation no.01.
NO MICROSCOPIC FINDINGS NOTED.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 03, 100 MG/KG/DAY FEMALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO. :	36

.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO. :	37

.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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INDIVIDUAL ANIMAL DATA	RCC	:	853022

TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 03, 100 MG/KG/DAY FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 38
.....

* NECROPSY FINDINGS

KIDNEYS:
01: RIGHT SIDE: PELVIC DILATION.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:
-Tubular simple dilation, multifocal, bilateral, grade 1
-Intratubular granular casts, bilateral, grade 1
-Pelvic dilation, unilateral, grade 2
This finding corresponds to necropsy observation no: 01.

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 39
.....

* NECROPSY FINDINGS

THYMUS:
01: THICKENED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
Organ examined, no pathologic findings noted
Nothing abnormal discovered corresponding to necropsy observation no.01.

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INDIVIDUAL ANIMAL DATA		RCC	:	853022

TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP	:	03, 100 MG/KG/DAY	FEMALE
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* STATE AT NECROPSY: K0

DAYS ON TEST	:	28	* ANIMAL NO. :	40
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* NECROPSY FINDINGS

OVARIES:

01: BOTH SIDES: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

OVARIES:

Organ examined, no pathologic findings noted

Nothing abnormal discovered corresponding to necropsy observation no.01.

PATHOLOGY REPORT PAGE : 70
INDIVIDUAL ANIMAL DATA RCC : 853022

TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

ANIMAL HEADING DATA
DOSE GROUP : 04, 500 MG/KG/DAY

ANIMAL NUMBER	SEX M/F	DEFINED AND STATE OF NECROPSY	FINAL K0	TEST DAYS	FIRST AND DAY UNDER TEST	LAST 13-APR-04	DATE OF NECROPSY
16	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
17	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
18	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
19	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
20	M	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
41	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
42	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
43	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
44	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04
45	F	K0	K0	28	17-MAR-04	13-APR-04	14-APR-04

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 04, 500 MG/KG/DAY
	MALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28

* ANIMAL NO. :	16
----------------	----

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CECUM:
Nothing abnormal discovered corresponding to necropsy obser-
vation no.01.
-Autolysis, focal, grade 1

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28

* ANIMAL NO. :	17
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* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS		
DOSE GROUP	:	04, 500 MG/KG/DAY
		MALE

* STATE AT NECROPSY: K0		
DAYS ON TEST	:	28
		* ANIMAL NO. : 18
.....		

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CECUM:
Nothing abnormal discovered corresponding to necropsy observation no.01.
-Autolysis, focal, grade 1

* STATE AT NECROPSY: K0		
DAYS ON TEST	:	28
		* ANIMAL NO. : 19
.....		

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 04, 500 MG/KG/DAY
	MALE

* STATE AT NECROPSY: K0

DAYS ON TEST	:	28	* ANIMAL NO. :	20
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* NECROPSY FINDINGS

CECUM:

01: MUCOSA: DISCOLORATION, REDDISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CECUM:

Organ examined, no pathologic findings noted

Nothing abnormal discovered corresponding to necropsy observation no.01.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 04, 500 MG/KG/DAY
	FEMALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 41

* NECROPSY FINDINGS

THYMUS:
01: THICKENED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

THYMUS:
Nothing abnormal discovered corresponding to necropsy observation no.01.
-Hemorrhage, focal, grade 1

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 42

* NECROPSY FINDINGS

OVARIES:
01: RIGHT SIDE: WATERY CYST, D=6 MM.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

OVARIES:
-Cystic dilation of salpinx, bilateral, grade 2
This finding corresponds to necropsy observation no: 01.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 04, 500 MG/KG/DAY FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 43
.....

* NECROPSY FINDINGS

STOMACH:
01: MUCOSA: DISCOLORATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

STOMACH:
No microscopic finding corresponding to necropsy observation no. 01.
-Cytoplasmic inclusion, eosinophilic, grade 1
-Mucosal gland dilation, multifocal, grade 1

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 44
.....

* NECROPSY FINDINGS

OVARIES:
01: RIGHT SIDE: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

OVARIES:
Organ examined, no pathologic findings noted
Nothing abnormal discovered corresponding to necropsy observation no.01.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP : 04, 500 MG/KG/DAY	FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 45
.....

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CECUM:
Nothing abnormal discovered corresponding to necropsy obser-
vation no.01.
-Autolysis, grade 2

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INDIVIDUAL ANIMAL DATA RCC : 853022

TEST ARTICLE : AXN-DMS PATHOL. NO.: 91003 WLA
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING) DATE : 22-JUN-04
SPONSOR : DSM NUTRITIONAL PRODUCTS PathData®System V6.2a2

ANIMAL HEADING DATA
DOSE GROUP : 05, 1000 MG/KG/DAY

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY	TEST DAYS	FIRST AND LAST DAY UNDER TEST	DATE OF NECROPSY
21	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
22	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
23	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
24	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
25	M	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
46	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
47	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
48	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
49	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04
50	F	K0 K0	28	17-MAR-04 13-APR-04	14-APR-04

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	MALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 21

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 2
MEDULLA OBLONGATA:
-Neuronal fixation artefacts, grade 1
PONS:
-Vacuolation of neuropil, focal, grade 1
SCIATIC NERVE:
-Infiltration mast cells, multifocal, bilateral, grade 1
TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1
-Lymphoid cell infiltration, focal, grade 1
LUNGS:
-Mixed cell infiltration, focal, grade 1
STOMACH:
-Cytoplasmic inclusion, hyaline, grade 1
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 2
JEJUNUM:
-Autolysis, grade 1
ILEUM:
-Autolysis, grade 2
CECUM:
Nothing abnormal discovered corresponding to necropsy observation no.01.
-Autolysis, focal, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	MALE

CONT./FF. ANIMAL NO. : 21

.....

LIVER:
-Granuloma, multiple, grade 1

KIDNEYS:
-Hyaline casts, bilateral, grade 2
 controlateral kidney: grade 1
-Hyaline droplets, proximal convoluted tubules, bilateral,
 grade 3
-Mononuclear infiltration, focal, unilateral, grade 1

ADRENAL CORTICES:
-Diffuse fatty change, zona fasciculata & reticularis, bilateral,
 grade 1

SPLEEN:
-Erythroid hyperplasia, grade 1
-Hemosiderin deposits, focal, within macrophages, grade 1

BONE MARROW (FEMUR):
-Adipocyte infiltration, grade 1

MESENTERIC LYMPH NODE:
-Lymphoid depletion, grade 2
-Mast cell hyperplasia, medullary, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 22

.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	MALE

CONT./FF. ANIMAL NO. : 22

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 2

CEREBELLUM:
-Neuronal fixation artefacts, grade 2

MEDULLA OBLONGATA:
-Neuronal fixation artefacts, grade 1

SCIATIC NERVE:
-Infiltration mast cells, focal, bilateral, grade 1

HEART:
-Granuloma, single, grade 1

TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 2

LUNGS:
-Alveolar histiocytosis, multifocal, grade 1

STOMACH:
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 3

CECUM:
-Mucosal hyperplasia, focal, grade 2
-Mixed cell infiltration, submucosa below hyperplasia, grade 1
-crypt, intraluminal bacteria, grade 3

LIVER:
-Granuloma, multiple, grade 1

KIDNEYS:
-Hyaline droplets, proximal convoluted tubules, bilateral, grade 2

PARATHYROID GLANDS:
Tissue not present for histologic examination

ADRENAL CORTICES:
-Diffuse fatty change, zona fasciculata, bilateral, grade 2

SPLEEN:
-Erythroid hyperplasia, grade 1
-Hemosiderin deposits, multifocal, within macrophages, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	MALE

CONT./FF. ANIMAL NO. : 22

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO.	: 23

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

CEREBRUM:

-Neuronal fixation artefacts, grade 1

SCIATIC NERVE:

-Infiltration mast cells, multifocal, bilateral, grade 1

LUNGS:

-Lymphoid hyperplasia, peribronchiolar, grade 1

STOMACH:

-Cytoplasmic inclusion, hyaline, grade 1

-Granulocytic Infiltration, multifocal, grade 1

-Mucosal gland dilation, multifocal, grade 1

PEYER'S PATCHES, JEJUNUM:

-Mineralization, focal, grade 1

ILEUM:

-Autolysis, grade 2

CECUM:

-crypt, intraluminal bacteri, grade 1

LIVER:

-Granuloma, multiple, grade 1

KIDNEYS:

-Hyaline droplets, proximal convoluted tubules, bilateral, grade 3

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	MALE

CONT./FF. ANIMAL NO. : 23

.....

 controlateral kidney: grade 2

PARATHYROID GLANDS:

 One side missing on section

ADRENAL CORTICES:

 -Diffuse fatty change, zona fasciculata & reticularis, bilateral,
 grade 3

SPLEEN:

 -Hemosiderin deposits, focal, within macrophages, grade 1

BONE MARROW (FEMUR):

 -Adipocyte infiltration, grade 3

MESENTERIC LYMPH NODE:

 -Mast cell hyperplasia, medullary, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0		
DAYS ON TEST	:	28
		* ANIMAL NO. : 24

* NECROPSY FINDINGS

THYMUS:

 01: THICKENED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:

 -Neuronal fixation artefacts, grade 2

SCIATIC NERVE:

 -Infiltration mast cells, multifocal, bilateral, grade 2

HEART:

 -Myocardial fibrosis, focal, base of septum, grade 1

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY

CONT./FF. ANIMAL NO. : 24

TRACHEA:

- Cytoplasmic inclusion, eosinophilic, grade 1
- Glandular ectasia, grade 1

LUNGS:

- Granuloma, single, grade 1

STOMACH:

- Granulocytic Infiltration, multifocal, grade 1
- Mucosal gland dilation, multifocal, grade 3
- Fibrosis, focal, grade 1
- Lymphoid cell infiltration, focal, grade 1

ILEUM:

- Autolysis, grade 2

LIVER:

- Granuloma, multiple, grade 1

KIDNEYS:

- Hyaline casts, bilateral, grade 2
- Hyaline droplets, proximal convoluted tubules, bilateral, grade 3
- Tubular simple dilation, diffuse in renal papilla, bilateral, grade 1

THYROID GLAND (BOTH LOBES):

- Lymphoid cell infiltration, focal, unilateral, grade 1

PARATHYROID GLANDS:

- One side missing on section

ADRENAL CORTICES:

- Diffuse fatty change, zona fasciculata & reticularis, bilateral, grade 1

BONE MARROW (FEMUR):

- Adipocyte infiltration, grade 2

THYMUS:

- Nothing abnormal discovered corresponding to necropsy observation no.01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	MALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
* ANIMAL NO.:	25

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 1

SCIATIC NERVE:
-Infiltration mast cells, multifocal, bilateral, grade 1

HEART:
-Granuloma, single, grade 1

TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1

LUNGS:
-Lymphoid hyperplasia, peribronchiolar, grade 1

STOMACH:
-Cytoplasmic inclusion, hyaline, grade 1
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 2

ILEUM:
-Autolysis, grade 1

CECUM:
-Autolysis, grade 2

COLON:
-Autolysis, grade 3

LIVER:
-Lymphoid cell infiltration,portal, grade 2
-Granuloma, single, grade 1

KIDNEYS:
-Hyaline casts, bilateral, grade 1
-Hyaline droplets, proximal convoluted tubules, bilateral, grade 1
-Tubular basophilia, focal, bilateral, grade 1
-Tubular simple dilation, diffuse, papilla, bilateral, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	MALE

CONT./FF. ANIMAL NO. : 25

.....

TESTES:

-Multinucleated spermatid giant cells, focal, unilateral,
grade 1

EPIDIDYMIDES:

-Mixed cell infiltration, focal, unilateral, grade 1

PARATHYROID GLANDS:

One side missing on section

ADRENAL CORTICES:

-Diffuse fatty change, zona fasciculata & reticularis, bilateral,
grade 2

SPLEEN:

-Erythroid hyperplasia, grade 1

BONE MARROW (FEMUR):

-Adipocyte infiltration, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	FEMALE

* STATE AT NECROPSY: K0	
DAYS ON TEST	: 28
	* ANIMAL NO. : 46

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* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
KIDNEYS:
01: BOTH SIDES: PELVIC DILATION.
MANDIBULAR LYMPH NODE:
01: DISCOLORATION, DARK RED.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 2
CEREBELLUM:
-Neuronal fixation artefacts, grade 1
-Edema, white matter vacuolation, grade 1
SCIATIC NERVE:
-Infiltration mast cells, focal, bilateral, grade 1
HEART:
-Mononuclear infiltration, focal, grade 1
TRACHEA:
-Cytoplasmic inclusion, eosinophilic, grade 1
STOMACH:
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 2
PEYER'S PATCHES, JEJUNUM:
-Mineralization, focal, grade 1
CECUM:
Nothing abnormal discovered corresponding to necropsy observation no.01.
LIVER:
-Granuloma, single, grade 1
-Bile duct hyperplasia, multifocal, grade 1

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY FEMALE

CONT./FF. ANIMAL NO. : 46

KIDNEYS:

- Pelvic dilation
- Tubular basophilia, focal, bilateral, grade 1
- Tubular simple dilation, multifocal, papilla, unilateral, grade 1
- Interstitial mineralization, multifocal, bilateral, grade 1
- Intratubular granular casts, bilateral, grade 1
- Pelvic dilation, bilateral, grade 3
- This finding corresponds to necropsy observation no: 01.

URINARY BLADDER:

- Autolysis, loss of urothelium, grade 1

UTERUS (INCLUDING CERVIX):

- Metestrus phase of the estrous cycle

VAGINA:

- Estrus phase of the estrous cycle

PARATHYROID GLANDS:

- Only one side on section

SPLEEN:

- Hemosiderin deposits, multifocal, within macrophages, grade 1

MESENTERIC LYMPH NODE:

- Lymphoid depletion, grade 1
- Mast cell hyperplasia, medullary, grade 1

MANDIBULAR LYMPH NODE:

- Hemorrhage, focal, bilateral, grade 2
- This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY
	FEMALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 28 * ANIMAL NO. : 47
.....

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 2
SCIATIC NERVE:
-Infiltration mast cells, multifocal, bilateral, grade 1
STOMACH:
-Cytoplasmic inclusion, hyaline, grade 1
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 1
DUODENUM:
-Autolysis, grade 1
ILEUM:
-Autolysis, grade 3
CECUM:
Nothing abnormal discovered corresponding to necropsy observation no.01.
LIVER:
-Bile duct hyperplasia, multifocal, grade 1
-Vacuolation, diffuse, small vacuoles, grade 1
KIDNEYS:
-Tubular basophilia, focal, bilateral, grade 1
-Tubular simple dilation, multifocal, unilateral, grade 2
-Interstitial mineralization, multifocal, bilateral, grade 1
-Intratubular granular casts, bilateral, grade 2
controlateral kidney: grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2
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TEXT OF GROSS AND MICROSCOPIC FINDINGS			
DOSE GROUP	:	05, 1000 MG/KG/DAY	FEMALE

CONT./FF. ANIMAL NO. : 47

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URINARY BLADDER:
-Vacuolation, urothelial, grade 1
UTERUS (INCLUDING CERVIX):
-Metestrus phase of the estrous cycle
VAGINA:
-Metestrus phase of the estrous cycle
SPLEEN:
-Hemosiderin deposits, focal, within macrophages, grade 1
BONE MARROW (FEMUR):
-Adipocyte infiltration, grade 2
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

.....

* STATE AT NECROPSY: K0		
DAYS ON TEST	:	28
		* ANIMAL NO. : 48

.....

* NECROPSY FINDINGS

CECUM:
01: MUCOSA: DISCOLORATION, REDDISH.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 2
CEREBELLUM:
-Neuronal fixation artefacts, grade 2
MEDULLA OBLONGATA:
-Neuronal fixation artefacts, grade 1
PONS:
-Neuronal fixation artefacts, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2
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TEXT OF GROSS AND MICROSCOPIC FINDINGS			
DOSE GROUP	:	05, 1000 MG/KG/DAY	FEMALE

CONT./FF. ANIMAL NO. : 48

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SCIATIC NERVE:
-Infiltration mast cells, bilateral, grade 1

STOMACH:
-Cytoplasmic inclusion, hyaline, grade 1
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 1

DUODENUM:
-Autolysis, grade 1

JEJUNUM:
-Autolysis, grade 2

CECUM:
Nothing abnormal discovered corresponding to necropsy observation no.01.

LIVER:
-Granuloma, single, grade 1

KIDNEYS:
-Tubular basophilia, focal, bilateral, grade 1
-Tubular simple dilation, multifocal, papilla, unilateral, grade 1
-Interstitial mineralization, multifocal, bilateral, grade 1
-Intratubular granular casts, unilateral, grade 1

UTERUS (INCLUDING CERVIX):
-Diestrus phase of the estrous cycle

VAGINA:
-Diestrus phase of the estrous cycle

PARATHYROID GLANDS:
Only one side on section

SPLEEN:
-Hemosiderin deposits, focal, within macrophages, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP	:	05, 1000 MG/KG/DAY	FEMALE
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* STATE AT NECROPSY: K0
 DAYS ON TEST : 28 * ANIMAL NO. : 49

* NECROPSY FINDINGS

CECUM:
 01: MUCOSA: DISCOLORATION, REDDISH.
 PANCREAS:
 01: DISCOLORATION, DARK RED.
 NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

CEREBRUM:
 -Neuronal fixation artefacts, grade 2
 CEREBELLUM:
 -Neuronal fixation artefacts, grade 1
 SCIATIC NERVE:
 -Infiltration mast cells, multifocal, bilateral, grade 1
 STOMACH:
 -Cytoplasmic inclusion, hyaline, grade 1
 -Granulocytic Infiltration, multifocal, grade 1
 -Mucosal gland dilation, multifocal, grade 1
 DUODENUM:
 -Autolysis, grade 1
 PEYER'S PATCHES, JEJUNUM:
 -Mineralization, focal, grade 1
 CECUM:
 Nothing abnormal discovered corresponding to necropsy observation no.01.
 -Autolysis, grade 3
 LIVER:
 -Lymphoid cell infiltration, multifocal, grade 1
 -Granuloma, single, grade 1
 -Bile duct hyperplasia, focal, grade 1
 -Vacuolation, diffuse, small vacuoles, grade 1

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TEST ARTICLE	:	AXN-DMS	PATHOL. NO.: 91003 WLA
TEST SYSTEM	:	RAT, 28-DAYS, ORAL (FEEDING)	DATE : 22-JUN-04
SPONSOR	:	DSM NUTRITIONAL PRODUCTS	PathData®System V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY FEMALE

CONT./FF. ANIMAL NO. : 49

PANCREAS:

Nothing abnormal discovered corresponding to necropsy observation no.01.

KIDNEYS:

- Tubular basophilia, focal, unilateral, grade 1
- Tubular simple dilation, multifocal, papilla, bilateral, grade 2
- Interstitial mineralization, multifocal, bilateral, grade 1
- Intratubular granular casts, bilateral, grade 1

UTERUS (INCLUDING CERVIX):

- Metestrus phase of the estrous cycle

VAGINA:

- Diestrus phase of the estrous cycle

ADRENAL CORTICES:

- Focal fatty change, solitary, bilateral, grade 1

SPLEEN:

- Hemosiderin deposits, multifocal, within macrophages, grade 1 and also focally next to insertion of ligament

MESENTERIC LYMPH NODE:

- Granulocytic Infiltration, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

* STATE AT NECROPSY: K0

DAYS ON TEST : 28

* ANIMAL NO. : 50

* NECROPSY FINDINGS

CECUM:

01: MUCOSA: DISCOLORATION, REDDISH.

NO OTHER NECROPSY OBSERVATIONS NOTED

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TEST ARTICLE : AXN-DMS		PATHOL. NO.: 91003 WLA		
TEST SYSTEM : RAT, 28-DAYS, ORAL (FEEDING)		DATE : 22-JUN-04		
SPONSOR : DSM NUTRITIONAL PRODUCTS		PathData®System V6.2a2		
TEXT OF GROSS AND MICROSCOPIC FINDINGS				
DOSE GROUP : 05, 1000 MG/KG/DAY				FEMALE

CONT./FF. ANIMAL NO. : 50

* MICROSCOPIC FINDINGS

CEREBRUM:
-Neuronal fixation artefacts, grade 3
CEREBELLUM:
-Neuronal fixation artefacts, grade 2
SCIATIC NERVE:
-Infiltration mast cells, multifocal, bilateral, grade 1
TRACHEA:
-Lymphoid cell infiltration, focal, grade 1
-Glandular ectasia, grade 2
STOMACH:
-Granulocytic Infiltration, multifocal, grade 1
-Mucosal gland dilation, multifocal, grade 2
DUODENUM:
-Autolysis, grade 1
JEJUNUM:
-Autolysis, grade 1
PEYER'S PATCHES, JEJUNUM:
-Mineralization, focal, grade 1
ILEUM:
-Autolysis, grade 2
CECUM:
Nothing abnormal discovered corresponding to necropsy observation no.01.
-Autolysis, grade 1
COLON:
-Autolysis, grade 3
LIVER:
-Lymphoid cell infiltration, multifocal, grade 1
-Granuloma, multiple, grade 1
-Vacuolation, diffuse, small vacuoles, grade 1
few scattered hepatocytes with one large size vacuole
KIDNEYS:
-Tubular simple dilation, multifocal, papilla, bilateral, grade 1
-Intratubular granular casts, unilateral, grade 1

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TEST ARTICLE	: AXN-DMS	PATHOL. NO.:	91003 WLA
TEST SYSTEM	: RAT, 28-DAYS, ORAL (FEEDING)	DATE	: 22-JUN-04
SPONSOR	: DSM NUTRITIONAL PRODUCTS	PathData®System	V6.2a2

TEXT OF GROSS AND MICROSCOPIC FINDINGS	
DOSE GROUP	: 05, 1000 MG/KG/DAY FEMALE

CONT./FF. ANIMAL NO. : 50

.....

UTERUS (INCLUDING CERVIX):
-Metestrus phase of the estrous cycle
VAGINA:
-Metestrus phase of the estrous cycle
SPLEEN:
-Hemosiderin deposits, multifocal, within macrophages, grade 1
-Congestion, diffuse, grade 1
THYMUS:
-Hemorrhage, multifocal, grade 1
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

RCC STUDY NUMBER 853022
AXN-DMS

REPORT

APPENDIX VIII:

CERTIFICATE OF ANALYSIS

DSM Nutritional Products

R&D Human Nutrition and Health, VFHA

P.O. Box 3255, Building 205/225, CH-4002 Basel, Switzerland
Telephone +41 (0)61 688 24 39, Telefax +41 (0)61 688 16 40
E-mail joseph.schierle@dsm.com
Internet www.dsmnutritionalproducts.com

DSM 

Certificate of Analysis

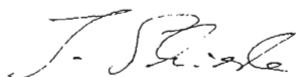
● Product name: **Carophyll Stay Pink 15% CWS**

Roche No.: RO4381139-000-001
Lot No.: B.2003.01.12/PC
Analysis No.: Lab_Order No. 008405_0001
Analytical method: HPLC, AMS_ZK
Quality system: ISO9001

Storage Conditions: Nominal 5°C in darkness (refrigerator) under argon or nitrogen

Retest date: December 09th, 2004

● Content: Astaxanthin dimethyl disuccinate: 163 g/kg
Astaxanthin equivalent: 118 g/kg



Dr. Joseph Schierle
January 22th, 2004

DSM Nutritional Products

R&D Human Nutrition and Health, VFHA

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E-mail joseph.schierle@dsm.com
Internet www.dsmnutritionalproducts.com

DSM 

Certificate of Analysis

● **Product Name:** **Placebo Carophyll Stay Pink 15% CWS**

Lot No.: B.2003.01.13/VN.002
Analysis No.: ANA_Order No. 001183_000001
Analytical Method: HPLC, AMS_ZK
Quality System: ISO9001

Storage Conditions: Nominal 5°C in darkness (refrigerator) under argon or nitrogen

Retest date: December 22th, 2004

Content: Astaxanthin dimethyl disuccinate: n.d.
Astaxanthin equivalent: n.d.

● (n.d. = not detected, detection limit = approx. 100 mg/kg)



Dr. Joseph Schierle
January 22th, 2004