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FINAL REPORT

28-Day Repeated Dose Dermal Toxicity Test

with

"Lehmannblausulfat"

in Guinea Pigs

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APPENDICES [Individual Values]

DECLARATION

We, the undersigned, hereby declare that the work performed under our supervision was conducted in accordance with the described procedures. It is assured that the reported results faithfully reproduce the raw data obtained during the experimental work. To the best of our knowledge, no circumstances have been left unreported which may have affected the quality or integrity of the data or which might have a potential bearing on the validity and reproducibility of this study.

The study director accepts overall responsibility for the technical conduct of the study as well as for the interpretation, analysis, documentation and reporting of the results.

Study Director:

Priv. Doz. Dr. med. vet. J. Lindena
Principal Scientist
Department of Toxicology II

Technical Supervision:

H. Böhm
Senior Technician

Histopathology:

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Board certified expert of pathology
Veterinary School, Hannover

Analytic:

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Head of Bioanalytics

6.2.1991
Date

GLP COMPLIANCE

To the best of my knowledge, this study was performed in accordance with the principles of Good Laboratory Practice for non-clinical laboratory studies as specified by national (BGBl. I, No. 13, § 19 a, March 22, 1990) and international (FDA Final Rule: U.S. Fed. Reg., Title 21, Part 58, September 4, 1987) legislation.

Study Director:

.....

Priv. Doz. Dr. med. vet. J. Lindena

5.3.91

.....

Date

QUALITY ASSURANCE STATEMENT

The testing facilities utilized in this study have been inspected regularly in accordance with the principles of Good Laboratory Practice for non-clinical laboratory studies as specified by national (BGB. I, No. 13, § 19 a, March 22, 1990) and international (FDA Final Rule: U.S. Fed. Reg., Title 21, Part 58, September 4, 1987) legislation.

This study was inspected/audited and the findings reported to management and to the study director on the dates shown below. Inspections were performed according to the standard operating procedures of the testing facility's quality assurance unit. The final report was audited in detail against the approved protocol and all pertinent raw data.

Inspections	Reports
Protocol:	
July 12, 1990	July 12, 1990
Study:	
August 28, 1990	September 4, 1990
Final Report / Raw Data Audit:	
February 11 - 13, 1991	February 14, 1991

i. A. [signature]
(p.p. Quality Assurance Unit)

6. 3. 91
Date

I. OBJECTIVE

It was the purpose of this study to provide information on possible hazards likely to arise from repeated exposures to the test article **"Lehmannblausulfat"** by the dermal route over 28 days in guinea pigs.

The study was carried out in accordance with the OECD guidelines for testing of chemicals, OECD 410, Repeated Dose Dermal Toxicity: 21/28-day Study, 12. May 1981.

The principles of Good Laboratory Practice Regulations (FDA Final Rule: U.S. Fed. Reg., Title 21, Part 58, September 4, 1987) were followed during the performance of the study. The IBR protocol, signed and dated on July 18 and 20, 1990 was valid.

II. SUMMARY

"Lehmannblausulfat" was applied dermally once daily on seven days a week for 28 days to guinea pigs at daily dose levels of 50 mg/kg, 150 mg/kg and 300 mg/kg. A control group received tap water only. Blood sampling for clinical chemical and hematological investigations was performed and skin irritation was assessed. Histopathological examination of skin, liver and kidney was performed.

Under the experimental conditions the following results were obtained:

No clinical signs of reaction to treatment were observed in any animal. No animal died during the entire observation period.

Comparable body weight development was observed for the animals between control and dose groups.

Daily observations on skin reaction were without any sign of erythema and edema.

Hematology parameters including prothrombin time did not display test article related alterations.

Clinical chemistry parameters were without changes which could be related to test article administration.

Organ weights did not reveal any intergroup differences.

No treatment related changes were observed for macroscopic necropsy observations and organ weight determinations.

The histopathological examination revealed, for target organs (heart, kidney, liver), no drug related changes. In the skin of some animals hyperplasia and hyperkeratoris was observed, which in all likelihood was not test article-related.

III. MATERIAL and METHOD

1. Animals

For this test SPF-Pirbright White Guinea Pigs of the substrain BOR: DHPW were used.

1.1 Specific Information

Supplied by:	Firma Winkelmann Gartenstraße 27 W-4799 Borchen
Number of animals:	20 males, 20 females
Weight range at study initiation:	males: 307 to 360 g females: 302 to 351 g
Date of receipt:	July 25, 1990
Acclimatization period:	7 days
Group allocation:	One untreated control group, three dose group.

1.2 Groups and Group Size

Group	Sex/Animal No.
I (Control)	m 101 - 105 f 151 - 155
II (low dose)	m 201 - 205 f 251 - 255
III (mid dose)	m 301 - 305 f 351 - 355
IV (high dose)	m 401 - 405 f 451 - 455

1.3 Animal Health

Animals used in this test were examined by a veterinarian when they arrived (entrance examination). Only animals in good health condition were used for the test. Before initiating the study a second veterinary examination was carried out to assure that all animals were still in the best condition for this investigation. Quarterly reports of the breeders veterinary examinations for specific pathogens and health condition are on record at IBR.

1.4 Randomization (Computer program)

All animals preliminarily received a serial number without distribution to groups. They were sorted according to weight (starting with the lightest animals), received a random number, were allocated to 4 blocks and sorted within the blocks according to rising numbers (starting with the lowest one). The classification into the test groups was done by attaching each first animal of a block to the control, the second one to group II etc. This procedure guaranteed a randomized distribution with regard to mean group body weights. This procedure was carried out for both sexes separately.

Randomization tables were established by use of a computes program according to:

Zufallszahlentabellen aus
"Grundriß der biologischen Statistik"
Erna Weber, 8th Edition, 1980, P. 686

1.5 **Animal Identification**

The animals are marked with a special pen. Additionally the cages are identified by individual animal identity cards with information about source, sex, arrival date, group/animal number and IBR project number.

1.6 **Justification for the Choice of the Species**

The guinea pig is, as a rodent, the standard experimental animal of choice. The large amount of available physiological data render it highly suitable for dermato-toxicologial investigations. The guinea pig is one of the recommended species according to the OECD guideline 410, "Repeated Dose Dermal Toxicity: 21/28-day Study".

2. **Husbandry**

The animals were housed singly in a battery of lattice plate boxes. The room temperature was adjusted to 19.5°C + 3.5°C and relative humidity was between 50 and 85 %. The recording was done by thermohygrometer. The animals' room was illuminated by artificial light for 12 hours daily from 7.00 to 19.00 p.m.. Air was changed 16 times per hour and was filtered adequately.

3. **Food and Feeding**

The animals received "Ssniff-G (Alleindiät für Meerschweinchen) produced by Ssniff-Spezial Diäten GmbH, 4770 Soest/Westf. Food consumption was allowed ad libitum.

3.1 Diet Quality Assurance

The diet was analysed periodically by order of the producer with respect to the content of chlorinated hydrocarbons, aflatoxins, heavy metals, arsenic and antibiotic activity. IBR verifies the results by analysing samples of delivered batches twice yearly. The analyses are carried out at the Agricultural Analysis and Research Institute, Kiel of the Ministry of Agriculture, Schleswig-Holstein. At IBR the reports are compared with the highest tolerated values (amended June 22nd, 1988) of the "Futtermittelverordnung (April 8th, 1981, BGBl. I, p. 352) and stored in the archive. (Diet composition and certifcates of analyses valid for the study period are presented in the appendix.)

4. Water Supply

The animals received aqua fontana ad libitum from automatic watering nipples.

4.1 Water Control

Samples of drinking water are collected twice yearly by an official laboratory. Chemical analysis, conducted by a governmental chemical institute (Untersuchungsamt) according to "Trinkwasserverordnung" from May 22nd, 1986 (BGBl. I, page 760) § 2, 1st section, enclosure 2, includes the content of chlorinated hydrocarbons, heavy metals and arsenic. Bacteriological tests are performed on the water supply to the housing area by a governmental institute for public health (Medizinaluntersuchungsamt). The certificates of all analyses are on record at IBR (copies of the certificates, valid for the test period, are presented in the appendix).

5. Treatment

Groups and Dosages

The following groups and dose levels (mg/kg) were used:

Group	Number of animals m	f	Daily total dose (mg/kg b.w.)	Application volume (ml/kg b.w.)	Test article concentration % (w/v)
I	5	5	0 (tap water)	1	0
II	5	5	50	1	5
III	5	5	150	1	15
IV	5	5	300	1	30

5.1 Test Article Preparation

The test article was prepared fresh daily immediately before application.

5.2 Administration of the Test Article

The test article was applied, in the appropriate dose, once daily (seven days per week) to a clipped area of skin on the animal's back (3 x 4 cm; about 10 percent of the total body surface) with a graduated pipette within 1 h post test article preparation. Doses were adapted weekly according to the weight development of the animals. Fur was clipped twice weekly. The test and control articles were applied in the early morning hours. Range finding studies have shown that it was not necessary to cover the test site to ensure that the animals cannot ingest the test substance.

5.3 Duration

Treatment was be continued for 28 days and, if all animals could not be necropsied on the same day, treatment was be continued up to the day preceding necropsy.

5.4 Justification for the Dosages Selected

Dose levels chosen for this study are based on the results of a range finding test. The intended human dose is a 3 % formulation of the test article. The 30 % (w/v) solution of "Lehmannblausulfat" and the application volume of 1 ml/kg represent technical limits with regard to solubility and application volume, respectively.

5.4 Justification for the Route of Administration

Adapted to human exposure.

6. Test Material

6.1 Details

Name:	**Lehmannblausulfat**
Supplied by:	
Chemical name:	1-Methoxy-2-amino-4-(2'-hydroxyethyl)-amino-sulfat
Physical state:	grey powder
Charge (Batch no.)	not communicated
Receipt on:	March 1, 1990
Identification:	Sticker with IBR project no., name of the compound, name of the sponsor, date of receipt, expiry date, hazards.
Storage:	room temperature, protected from light
Stability:	stable
Purity:	98 %
Solvent/vehicle used in this study:	**Lehmannblausulfat** was applied dermally as a 5 to 30 % solution in water.

6.2 Reanalyses

Sample of the used batch were analysed at the IBR's Bioanalytical Centre, Hannover with respect to identity, stability and homogenity prior to study initiation and at termination (see additional Certificate of Analysis, App. 6).

7. Observational Parameters

7.1 Clinical Observations

All animals were observed daily with regard to their sensory and motor behaviour, skin, body orifices, urine and fecal excretion, general health status and dose responses. The observations were recorded daily and dose responses were summarized in weekly reports. Viability or mortality checks were performed twice daily.

7.2 Body Weights

Body weights were recorded individually in weekly intervals.

7.3 Skin irritation

Skin irritation at the application site were assessed daily throughout the study according to the following scale (modified Draize scheme):

Erythema and Eschar Formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Maximum possible = 4	

Oedema Formation	
No oedema	0
Very slight oedema (barely perceptible)	1
Slight oedema (edges of area well defined by definite raising)	2
Moderate oedema (raised approximately 1 mm)	3
Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4
Maximum possible = 4	

Assessment of dermal irritation were performed and recorded in the early morning hours prior to each new administration.

8. Laboratory Examinations

a) Blood samples were collected from all animals for hematological (EDTA-blood) and clinical chemistry (heparin blood). Blood was taken from the retrobulbar venous plexus.

b) Dates of Blood Sampling

Blood samples for hematological and clinical chemical analyses were withdrawn on the day before initiating the study (0) and at termination of the study (28 days).

8.1 Investigational Parameters

8.1.1 Hematology

Erythrocytes (RBC)
Leukocytes (WBC)
Thrombocytes
Hemoglobin
Hematocrit
Reticulocytes
MCV, MCH and MCHC
Differential blood count
Prothrombin Time

8.1.2 Clinical Chemistry

a) Substrates
- Bilirubin (total)
- Creatinine
- Glucose
- Urea Nitrogen (BUN)
- Uric Acid

b) Lipids
- Triglyceride
- Cholesterol

c) Proteins
- Protein (total)
- Albumin
- Electrophoresis
  - Albumin
  - $alpha_1$ + $alpha_2$ -Globulin
  - beta - Globulin
  - gamma - Globulin

d) Elektrolytes
- Calcium
- Chloride
- Inorg. Phosphorus
- Iron
- Potassium
- Sodium
- Na/K ratio by statistical evaluation

e) Enyzmes
- Lactate Dehydrogenase (LDH) (EC 1.1.1.27)
- Alanine Aminotransferase (ALT) (EC 2.6.1.1)
- Aspartate Aminotransferase (AST) (EC 2.6.1.2)
- Alkaline Phosphatase (EC 3.1.3.1)
- Creatine Kinase (CK) (EC 2.7.3.2)
- Gamma-Glutamyl Transferase (EC 2.3.2.2)
- AST/ALT ratio by statistical evaluation

8.2 Performance of Laboratory Examinations

The investigations of hematology and clinical chemistry parameters were carried out at IBR-Laboratory.

8.3 METHODS used in HEMATOLOGY

Parameter	Method	Unit of Measurement
Erythrocytes	Contraves autolyzer 80	10^{12}/l
Hemoglobin	Contraves autolyzer 80	mmol/l
Hematocrit	Contraves autolyzer 80	1
MCV	By statistical evaluation	fl
MCH	"	fmol
MCHC	"	mmol/l
Reticulocytes	Sysmex R-1000	1
Thrombocytes	Contraves autolyzer 80	10^9/l
Leukocytes		
Total Count	Contraves autolyzer 80	10^9/l
Differential Count	Pappenheim stain	1
Prothrombin time (Quick)	Plasma-method in guinea pigs (Boehringer, Mannheim)	%

8.4 METHODS used in CLINICAL CHEMISTRY

[Currently available parameters determined on Hitachi 705 analyzer system and Beckmann Astra-AS4]

Parameter	Method	Unit of Measurement
Albumin	Bromocresol green complex B.T. Doumas et al., Clin. Chim.Acta 31 (1971) 87	g/l
Alanine Amino-transferase (ALT)	Opt. Standard Method DGKCH	U/l
Aspartate Amino-transferase AST)	UV-test Z.Klin. Chem. u. klin. Biochem. 8 (1970) 658; 9 (1971) 464; 10 (1972) 182	
Alkaline Phosphatase (AP)	Opt. Standard method DGKCH, colorimetric test Z. Klin.Chem. u. klin. Biochem. 8 (1970) 658; 9 (1971) 464; 10 (1972) 182	U/l
Bilirubin (total)	DPD-Method Wahlefeld, A.W., et al. Scand. J. Clin. Lab. Invest. Vol. 29, Suppl. 126 (1972) Abstract 11.12.	µmol/l
Calcium	o-Cresophthalein complexone without deproteinization Baginski, E. et al. Clin. Chim. Acta 46 (1973) 46	mmol/l
Chloride	Endpoint, titration, Ag^+ generator Beckman-Astra Kit	mmol/l
Cholesterol	CHOD-PAP enzymatic colorimetric test Siedel J., et al. J. Clin. Chem. Clin. Biochem. 19 (1981) 838	mmol/l
Creatinine	Jaffé, without deproteinization mod. Bartels, H. et al. Clin. Chim. Acta 37 (1972) 193	µmol/l

8.5 Methods used in Clinical Chemistry (cont'd)

Parameter	Method	Unit of Measurement
Creatine Kinase (CK)	Opt. Standard Method DGKCH NAC-activated with the addition of EDTA, UV-test J. Clin. Chem. Clin. Biochem. 15 (1977) 249 Z. Klin. Chem. u. Klin.Biochem. 9 (1971) 464 Dtsch. Med. Wochenschr. 104 (1979) 257	U/l
γ- Glutamyl Transferase	Substrate: L-γ-glutamyl-3-carboxy-4-nitroanilide Colorimetric Test Z. Klin. Chem. Klin.Biochem. 12 (1974) 228 J. Clin. Chem. Clin. Biochem. 14 (1976) 421	U/l
Glutamate Dehydrogenase (GLDH)	Opt. Standard Method DGKCH UV-method Z. Klin. Chem. u. Klin. Biochem. 8 (1970) 658; 9 (1971) 464; 10 (1972) 182; 12 (1974) 391	U/l
Glucose	Hexokinase/G6P-DH UV-test Schmidt, F.H. Klin. Wschr. 39 (1961) 1244	mmol/l
Inorg. Phosphorus	Enzymatic colorimetric test Sigiura, M. et al. Chem. Pharm. Bull. 29 (1981) 1451	mmol/l
Iron	Without deproteinization Siedel, J. et al. Clin. Chem. 30 (1984) 975	µmol/l
Amino Acid Acrylamidase (LAP)	Opt. Standard Method DGKCH Colorimetric test Z. Klin. Chem. Klin. Biochem. 8 (1970) 658; 9 (1971) 464; 10 (1972) 182	U/l
Lactate Dehydrogenase (LDH)	Opt. Standard Method DGKCH UV-test Z. Klin.Chem. u. Klin. Biochem. 8 (1970) 658; 9 (1971) 464; 10 (1972) 182	

8.5 Methods used in Clinical Chemistry (cont'd)

Parameter	Method	Unit of Measurement
Potassium	Endpoint, Ion-selective-electrode Valinomycin membrane Beckman-Astra Kit	mmol/l
Protein (total)	Biuret reaction, colorimetric test Weichselbaum, T.E., Am. J. Clin. Path. 16 (1946) 40 Beckman - Astra Kit	g/l
Sodium	Endpoint, Ion-selectiv-electrode Valinomycin membrane Beckman-Astra Kit	mmol/l
Triglyceride	GPO-PAP enzymatic colorimetric test mod. Wahlefeld, A.W. in H.U. Bergmeyer: Methoden der enzymatischen Analyse, 3. Aufl., Bd. II, Verlag Chemie Weinheim 1974, S. 1878	mmol/l
Uric Acid	PAP-method, enzymatic-colorimetric test, Town, M.-H., et al. J. Clin. Chem. Clin. Biochem. 23 (1985) 591	µmol/l
Urea Nitrogen (BUN)	Timed rate, conductivity urease (liquid) Beckman - Astra Kit	mmol/l
Electrophoresis	Beckman Microzone(R) Cellulose Acetate Membrane (Mod. CD 1-100) Microzone-electrophoresis system Beckman-Bulletin M-308, May 1971	ratio 1

9. Necropsy

The animals were sacrificed at the end of the experiment by an intravenous injection of 0.5 ml/kg T 61 (Hoechst). The blood was removed by cutting the A. carotis. A complete autopsy was performed in all animals in random order. The macropathological examination which includes an inspection of the cranial, thoracic, abdominal and pelvic cavities was conducted under direct veterinary supervision. At autopsy terminal body weights were be measured in order to calculate relative organ weights.

9.1 Determination of Organ Weights

From all animals the following organ weights were determined and recorded:

Liver
Kidneys (l. + r.)
Heart
Spleen
Testes with Epididymides
Ovary (l. + r.)
Uterus
Adrenals

10. Histopathology

Samples from tissues listed below were removed from all males or females. Blocks and slides were prepared from all males and all females of groups I and IV (control and high dose group) at termination and slides were evaluated by qualified and board certified veterinary pathologists (additional expert report).

These examinations may be extended to animals of other dosage groups, if considered necessary.

The skin (treated and untreated areas) was examined from all animals of all groups.

The following organs and tissues were examined:
Skin (treated and untreated)
Liver
Kidney
Target organs, i.e., those organs showing gross lesions or changes in size (additional costs)

10.1 Organ Fixation and Tissue Preperation

All dissected organs were preserved in 8 % buffered formalin. Samples of all tissues destined for histopathological investigation were trimmed, embedded in tissue wax and stained with hematoxylin and eosin. In addition frozen sections were prepared from liver and kidney and stained with Sudan Red for assessment of fat content.

11. Statistics

Statistical analyses of data were performed seperately for male and female animals. For the evaluation of weight changes a one- rep. two-factorical analysis of variance was performed. To compare the group mean values the method of "Scheffé" was employed.

The organ weights were evaluated by analysis of co-variance. Hereby the animal weight is the independent variable, the organ weight the dependent one. The comparison of the mean values was performed by the method of "Scheffé" for the analysis of co-variance.

Values of clinical chemistry and hematology were analysed as follows:

a) Analysis of variance for dose-effect curves with the factors group and time and the interaction group/time. The degrees of freedom for the factor time and the interaction group/time were corrected according to Greenhouse and Geisser (Epsilon-correction).

b) Mean values were compared according to the method of Scheffé after a preceding analysis of co-variance. The comparison (of the mean values) was carried out by correction with analysis of co-variance in such a manner as if the curves originated from the same starting-point.

c) If there were available one point time values only, an analysis of variance with subsequent Scheffé test for analysis of variance was performed. Significance levels in the tables were marked by asterix.

*	$p < 0.05$
**	$p < 0.01$
***	$p < 0.001$

References:

1. Winer, B.J. (1971)
   Statistical Principles in Experimental Design
   McGraw Hill, Kogakusha Ltd.

2. Snedecor, G.W. and Cochran, W.G.
   Statistical Methods
   Sixth Edition, 1967
   IOWA State University Press

11.1 Tabulation of Statistical Data

Mean values per group (XM) and the corresponding standard deviation (± SD) are tabulated. In the case of body weights, food consumption and organ weights percentages are also compiled, whereby the control mean values are taken as 100 %. In the Scheffé test group means are compared as indicated. Asterisks represent the level of significance (see above), reduced or increased values being designated by sign in parentheses = (-) or (+). In the organ weight histograms the bars represent standard deviation and the columns picture uncorrected and corrected organ weights.

12. General Information

Experimental period:	July 30, 1990 to August 29, 1990
First and last day of dosing:	August 1, 1990; August 28, 1990
Testing facility:	**I B R** Forschungs GmbH Südkampen Nr. 31 W-3030 Walsrode
Study director:	Priv. Doz. Dr. med. vet. J. Lindena
Pathologist:	Prof. Dr. med. vet. K. Messow Department of Pathology Veterinary School, Hannover
Responsible technicians:	H. Böhm, biology technician, C. Kautz, medical laboratory technician P. Koch, biology technician, Histology
Statistics:	Dr. rer. hum. biol. J. Gebert Dipl. Ing. I. Giebel H. Utke D. Kownatzki
Quality Assurance Unit:	M. Schaardt Dr. med. vet. A. Stöcker Dr. A. Burt
Archives and documents:	All raw data, documentation and specimens, the protocol and a copy of the final report will be stored in the IBR archives for the minimum period of time specified by current national and international legislation on GLP. Biological specimens will be retained only as long as they afford a meaningful re-evaluation. At the end of the study, any remaining test article will be returned to the sponsor. IBR reserves the right to retain a sample of the test article.

VI. RESULTS

1. Histopathological Findings (see Table 1, page 26 - 37)

In the skin of some animals hyperplasia and hyperkeratosis were observed which predominantly were the result of mechanical irritations brought about by the clipping machine rather than by test article-related reactions.

For other target organs (heart, kidney, liver) no test article related changes were observed.

2. Clinical Signs (see Table 2, page 38 - 39)

All animals of the control and dose groups displayed a normal habit and behaviour during the entire study. No signs attributable to treatment were noticed in animals treated with "**Lehmannblausulfat**".

3. Death

No animals died or had to be sacrificed in extremis during the whole study period.

4. Body Weight Development (see Table 3, page 40 - 44)

Similar weight changes were observed in all animals.

5. Skin Reaction (see Table 4, page 45 - 100)

Daily observations on skin reactins were without any sign of erythema and edema.

6. **Hematology** (see Table 5, page 101 - 125)

Hematology parameters generally were within normal range during the entire study period or did not essentially differ from controls. The increased value for prothrombin time (%) in high dose males was considered as a coincidental finding.

7. **Clinical Chemistry** (see Table 6, page 126 - 180)

Clinical chemical values generally were within normal ranges or did not essentially differ from controls. The decreased globulin G fraction in mid dose females was considered as a coincidental finding.

8. **Macroscopic Findings** (see Table 7, page 181 - 184)

There were no gross findings which were considered to be test article related. The described findings on lung, liver intestine and salivary gland are common for the control and all test groups.

9. **Organ Weights** (see Table 8, page 185 - 205)

Among organ weights no abnormal change was noticed.

HISTOPATHOLOGY REPORT

28-Day Repeated Dose Dermal Toxicity Test

with

"Lehmannblausulfat"

in Guinea Pigs

Author:

Prof. Dr. C. Messow

1. SUMMARY

A total of 40 guinea pigs, i.e. 5 male and 5 female animals of the control group and 5 male and 5 female animals of each experimental group (II to IV), were examined histopathologically. The animals were sacrificed at termination of the study after 28 days.

Liver and skin (untreated and treated site) were examined in the control- and all three dose groups. The kidney (2x) was examined from control and high-dose group animals.

Heart, kidney and liver from control and high-dose group animals were subjected to fat stain for histopathological assessment.

The test article "**Lehmannblausulfat**" was applied, in the appropriate dose, once daily (seven days per week) to a clipped area of skin on the animals back (3 x 4 cm; about 10 percent of the total body surface) with a graduated pipette. Doses were adapted weekly according to the weight development of the animals.

The histopathological examination of organs from guinea pigs in a 28-day dermal toxicity study with "**Lehmannblausulfat**" revealed hyperplasia and hyperkeratosis in the skin of some animals, which in all likelihood were not test compound-related.

The other findings in this study are incidental findings and commonly encountered in guinea pigs of this strain and age. Type, incidence and severity of the lesions recorded were not increased in treated animals as compared to the concurrent control animals.

2. MATERIALS and METHODS

2.1 Experimental Design

Group	Number of animals m	f	Daily total dose (mg/kg)	Application volume (ml/kg)	Test article concentration % (w/v)
I	5	5	0 (tap water)	1	0
II	5	5	50	1	5
III	5	5	150	1	15
IV	5	5	300	1	30

2.2 Evaluation of organs tissues

The following H.-E. stained paraffin sections were submitted to histopathological evaluation (in alphabetical order):

<u>All groups (I to IV) [5 male / 5 female animals/group]</u>

Liver, skin (treated and untreated)

<u>Group I and IV [5 male / 5 female animals/group]</u>

Kidney (2x)

<u>Sudan red-stained frozen sections were examined of groups I and IV [5 male / 5 female animals/group] from</u>

Heart, kidney, liver.

2.3 Data compilation

The animal data and macroscopic findings were taken from the post-mortem records, translated into English and entered into the "*LABCAT Histopathology*" computer system.

The histological and macroscopic findings are given for each animal in test form under "*Individual Animal Data*". The incidence of microscopic findings is also presented in tabular form.

Incidence tables were generated by computer unless otherwise specified.

Histological changes were described according to their distribution, severity and morphological character.

3. RESULTS and DISCUSSION

3.1 Findings possibly related to treatment and/or clipping

In the skin an increased incidence of hyperplasia and hyperkeratosis in the epidermis of treated animals was observed; especially in the male high-dose group.

Characteristic for hyperplasia is an increase of epidermal cell layers, i.e. in opposite to controls showing 2-3 layers with nuclei, 3-5 cell layers were present in dose group animals. These layers extend evenly within the section and do not show focal tendencies towards proliferation or nuclear anomalies.

The hyperkeratosis is unevenly distributed over the section. Hence not all areas showed evidence of this finding.

The incidence of findings as described above is presented in table 1.

Under the experimental conditions of this study, where the application area has been clipped, the control groups are virtually the groups I (male/female) treated with tap water, rather than the mechanically not disturbed untreated skin.

Clipping of skin occured every 3 days during the test and macro- and microlesions were set by the clipping machine and the vivid reactions of the animals.

Taking this into account it can be said that the observed skin alterations in the treated groups were predominantly the results of mechanical irritations brought about by the clipping machine.

Application of a test article to irritated skin will in all likelihood produce more severe alterations than to normal skin.

In summary, there seemed to be no direct dermatotoxic effect of the test substance. The observed incidences of lesions and distribution within the test groups more likely represent incidental findings under this special test regimen.

Table 1: Findings of the skin

MALE								**FEMALE**							
untreated				treated				untreated				treated			
I (5)	II (5)	III (5)	IV (5)	I (5)	II (5)	III (5)	IV (5)	I (5)	II (5)	III (5)	IV (4)	I (5)	II (5)	III (5)	IV (5)
Hyperplasia				1	2		5	1					2	1	2
Hyperkeratosis						1	3					0	2	2	1
Epidermis incomplete					1							2			
Not present											1				

3.2 **Findings unrelated to treatment**

3.2.1 Reactive inflammatory processes, independent of treatment

Heart:	lympho-histiocytic infiltrations	1 x IV
Kidney:	lympho-histiocytic infiltrations	2 x I; 2 x IV
	lympho-histiocyitc infiltrations in pelvis	2 x IV
	cortical fibrosis	5 x I; 6 x IV
Liver:	pericholangitis	8 x I; 10 x II; 10 x III; 8 x IV
	MPS-cell-proliferation:	8 x I; 9 x II; 10 x III; 9 x IV
	Sinusoidal leukocytosis:	1 x II; 4 x III, 8 x IV

3.2.2 Individual Findings

Kidney:	hyaline tubular casts	2 x I; 2 x IV
	calcified tubular casts	2 x I; 3 x IV
	regeneration of tubules	7 x I, 3 x IV
Liver:	plant cell structure	1 x IV
	focal necrosis	2 x I; 2 x III, 2 x IV

3.2.3 Fat Stains

There were no differences with regard to fat-stains in heart and kidney between control and high-dose group animals.

In the liver there is a slight increase of diffuse fatty infiltration:

Fatty infiltration of single cells	9 x I; 6 x IV
Diffuse fatty infiltration	1 x I; 3 x IV

The difference, however, between control and high-dose group is so small that it might be still coincidental.

Prof. Dr. C. Messow

22.1.1991
Date

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

Project Summary Table
SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 0387-90 FATES: ALLWEEKS: ALL SEX: MALE

GROUP:		Control	50mg/kg	150mg/kg	300mg/kg
NUMBER OF ANIMALS:		5	5	5	5
		#	#	#	#
Heart (Sudan red)	# Ex	5	0	0	5
Lympho-histioc.infiltration		0	0	0	1
Kidney I (H.E.)	# Ex	5	0	0	5
Hyaline tubular casts		0	0	0	1
Lympho-histiocytic infiltr.		1	0	0	0
Cortical fibrosis		2	0	0	3
Regeneration of tubules		3	0	0	0
Calcified tubular casts		0	0	0	1
Lymph.-hist. infiltr.in pelvis		0	0	0	2
Kidney I (Sudan red)	# Ex	5	0	0	5
Cortical fibrosis		2	0	0	3
Calcified tubular casts		0	0	0	1
Kidney II (H.E.)	# Ex	5	0	0	5
Hyaline tubular casts		0	0	0	2
Lympho-histiocytic infiltr.		1	0	0	0
Cortical fibrosis		0	0	0	1
Regeneration of tubules		1	0	0	0
Lymph.-hist. infiltr.in pelvis		0	0	0	1
Liver (H.E.)	# Ex	5	5	5	5
Pericholangitis		3	5	5	3
Focal necrosis of hepatoc.		2	0	1	0
MPS-cell proliferation		5	4	5	4
Sinusoidal leukocytosis		0	1	1	4
Plant cell structure		0	0	0	1
Liver (Sudan red)	# Ex	5	0	0	5
Fatty infiltr.single hepatoc.		5	0	0	3
Diffuse fatty infiltration		0	0	0	3
Skin (treated)	# Ex	5	5	5	5
Hyperkeratosis		0	0	1	3

Project Summary Table
SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 0387-90 FATES: ALLWEEKS: ALL SEX: MALE

GROUP:		Control	50mg/kg	150mg/kg	300mg/kg
NUMBER OF ANIMALS:		5	5	5	5
		#	#	#	#
Skin (treated)	# Ex	5	5	5	5
Epidermal hyperplasia		1	2	0	5
Epidermis, incomplete		0	1	0	0
Skin (untreated)	# Ex	5	5	5	5

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

Project Summary Table
SUMMARY: Incidence of NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: 0387-90 FATES: ALLWEEKS: ALL SEX: FEMALE

GROUP:		Control	50mg/kg	150mg/kg	300mg/kg
NUMBER OF ANIMALS:		5	5	5	5
		#	#	#	#
Heart (Sudan red)	# Ex	5	0	0	5
Kidney I (H.E.)	# Ex	5	0	0	5
Hyaline tubular casts		1	0	0	0
Lympho-histiocytic infiltr.		1	0	0	2
Cortical fibrosis		2	0	0	2
Fibrosis		2	0	0	0
Regeneration of tubules		4	0	0	3
Calcified tubular casts		2	0	0	2
Kidney I (Sudan red)	# Ex	5	0	0	5
Cortical fibrosis		2	0	0	2
Kidney II (H.E.)	# Ex	5	0	0	5
Hyaline tubular casts		2	0	0	0
Lympho-histiocytic infiltr.		1	0	0	1
Regeneration of tubules		2	0	0	1
Calcified tubular casts		0	0	0	2
Liver (H.E.)	# Ex	5	5	5	5
Pericholangitis		5	5	5	5
Focal necrosis of hepatoc.		0	0	1	2
MPS-cell proliferation		3	5	5	5
Sinusoidal leukocytosis		0	0	3	4
Liver (Sudan red)	# Ex	5	0	0	5
Fatty infiltr.single hepatoc.		4	0	0	3
Diffuse fatty infiltration		1	0	0	0
Skin (treated)	# Ex	5	5	5	5
Hyperkeratosis		0	2	1	1
Epidermal hyperplasia		0	2	1	2
Epidermis, incomplete		2	0	0	0

24-Jan-1991

Project Summary Table
SUMMARY: Incidence of NON-NEOPLASTIC Microscopic findings

PROJECT ID. NO: 0387-90 FATES: ALLWEEKS: ALL SEX: FEMALE

GROUP:		Control	50mg/kg	150mg/kg	300mg/kg
NUMBER OF ANIMALS:		5	5	5	5
		#	#	#	#
Skin (untreated)	# Ex	5	5	5	4
Epidermal hyperplasia		1	0	0	0

24-Jan-1991

Table 2

SPEZIELLE KLINISCH-TOXIKOLOGISCHE BEOBACHTUNGEN (Guinea Pig)
SPECIAL PHARMACO-TOXICOLOGICAL OBSERVATIONS (Guinea Pig)

(modifiziert nach Irwin / modified Irwin Screen)

Projekt/project: 30-05-0387-90
Spezies/spezies: Guinea Pig
Substanz/compound: Lehmannblausulfat

Week of observation: 0, 28 days
Time of observation p.a. continuous

Bewertung/score:

-3 -2 -1 0 +1 +2 +3

vermindert/ decreased — normal — verstärkt/ increased

0 = normal
-1/+1 = geringgradig/slightly
-2/+2 = mittelgradig/moderate
-3/+3 = hochgradig/severe

		Dose: 0 Group I (Water)		Dose: 50 mg/kg Group II	
		male	female	male	female
Beobachtungen/Observations	rounded	XM	XM	XM	XM
1. Aktivität;allgem.Reak./activity;gen.reaction		0	0	0	0
Schmerzreaktion/pain reaction		0	0	0	0
Lautäußerung/vocalisation		0	0	0	0
Unruhe/restlessness		0	0	0	0
Reizbark.;Aggressivität/irritability		0	0	0	0
Stereotypie/stereotypy		0	0	0	0
Tremor/tremor		0	0	0	0
Zuckungen/twitches		0	0	0	0
Tonisches Krämpfe/tonic convulsions		0	0	0	0
Klonische Krämpfe/clonic convulsions		0	0	0	0
2. Ataxien;Taumeln/abnormal gait		0	0	0	0
Bauchlage/ventral position		0	0	0	0
Seitenlage/limb position		0	0	0	0
Hockstellung/squatting position		0	0	0	0
Haltungs-Stellungsanomalien/abnormal body posture		0	0	0	0
Greif- u. Gliedmaßentonus/grip- and limb tone		0	0	0	0
Körpertonus/body tone		0	0	0	0
Bauchdeckenspannung/abdominal tone		0	0	0	0
Hautturgor/skin turgor		0	0	0	0
Ohr-Reflex/ear-reflex		0	0	0	0
Corneal-Reflex/corneal-reflex		0	0	0	0
4. Pupillengröße/pupil size		0	0	0	0
Exophthalmus/exophthalmus		0	0	0	0
Haut- u. Schleimhautfarbe/ skin- a. membr.color:		0	0	0	0
Cyanose/cyanosis		0	0	0	0
Blässe/paleness		0	0	0	0
Rötung/redness		0	0	0	0
Diarrhoe/diarrhea		0	0	0	0
Diurese/diuresis		0	0	0	0
Salivation/salivation		0	0	0	0
Atemfrequenz/respiration rate		0	0	0	0
Gehör/Geräuschprüfung/auditory examination		0	0	0	0
Körpertemperatur/body temperature		0	0	0	0

1. Zentrale Symptome, Bewußtseins, Emotion/CNS-syptoms, awareness, emotion
2. Koordination/coordination
3. Reflexe/reflex, Tonus/tone
4. Autonome Funktionen/autonomic functions

Table 2

SPEZIELLE KLINISCH-TOXIKOLOGISCHE BEOBACHTUNGEN (Guinea Pig)
SPECIAL PHARMACO-TOXICOLOGICAL OBSERVATIONS (Guinea Pig)

(modifiziert nach Irwin / modified Irwin Screen)

Projekt/project: 30-05-0387-90
Spezies/spezies: Guinea Pig
Substanz/compound: Lehmannblausulfat

Week of observation: 0, 28 days
Time of observation p.a. continuous

Bewertung/score:

-3 -2 -1 0 +1 +2 +3

vermindert/ decreased — normal — verstärkt/ increased

0 = normal
-1/+1 = geringgradig/slightly
-2/+2 = mittelgradig/moderate
-3/+3 = hochgradig/severe

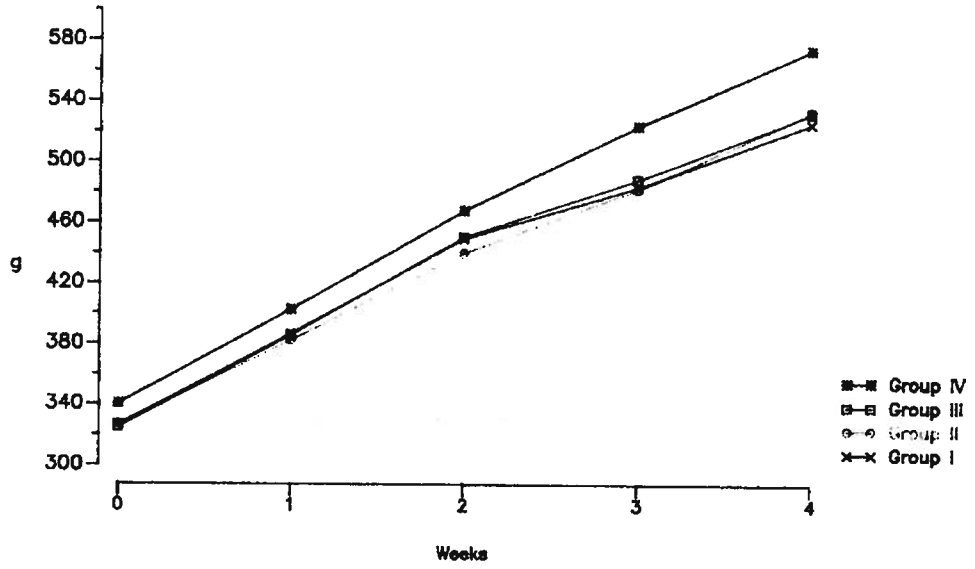
		Dose: 150 mg/kg Group III		Dose: 300 mg/kg Group IV	
		male	female	male	female
Beobachtungen/Observations	rounded	XM	XM	XM	XM
1. Aktivität;allgem.Reak./activity;gen.reaction		0	0	0	0
Schmerzreaktion/pain reaction		0	0	0	0
Lautäußerung/vocalisation		0	0	0	0
Unruhe/restlessness		0	0	0	0
Reizbark.;Aggressivität/irritability		0	0	0	0
Stereotypie/stereotypy		0	0	0	0
Tremor/tremor		0	0	0	0
Zuckungen/twitches		0	0	0	0
Tonisches Krämpfe/tonic convulsions		0	0	0	0
Klonische Krämpfe/clonic convulsions		0	0	0	0
2. Ataxien;Taumeln/abnormal gait		0	0	0	0
Bauchlage/ventral position		0	0	0	0
Seitenlage/limb position		0	0	0	0
Hockstellung/squatting position		0	0	0	0
Haltungs-Stellungsanomalien/abnormal body posture		0	0	0	0
Greif- u. Gliedmaßentonus/grip- and limb tone		0	0	0	0
Körpertonus/body tone		0	0	0	0
Bauchdeckenspannung/abdominal tone		0	0	0	0
Hautturgor/skin turgor		0	0	0	0
Ohr-Reflex/ear-reflex		0	0	0	0
Corneal-Reflex/corneal-reflex		0	0	0	0
4. Pupillengröße/pupil size		0	0	0	0
Exophthalmus/exophthalmus		0	0	0	0
Haut- u. Schleimhautfarbe/ skin- a. membr.color:		0	0	0	0
Cyanose/cyanosis		0	0	0	0
Blässe/paleness		0	0	0	0
Rötung/redness		0	0	0	0
Diarrhoe/diarrhea		0	0	0	0
Diurese/diuresis		0	0	0	0
Salivation/salivation		0	0	0	0
Atemfrequenz/respiration rate		0	0	0	0
Gehör/Geräuschprüfung/auditory examination		0	0	0	0
Körpertemperatur/body temperature		0	0	0	0

1. Zentrale Symptome, Bewußtseins, Emotion/CNS-syptoms, awareness, emotion
2. Koordination/coordination
3. Reflexe/reflex, Tonus/tone
4. Autonome Funktionen/autonomic functions

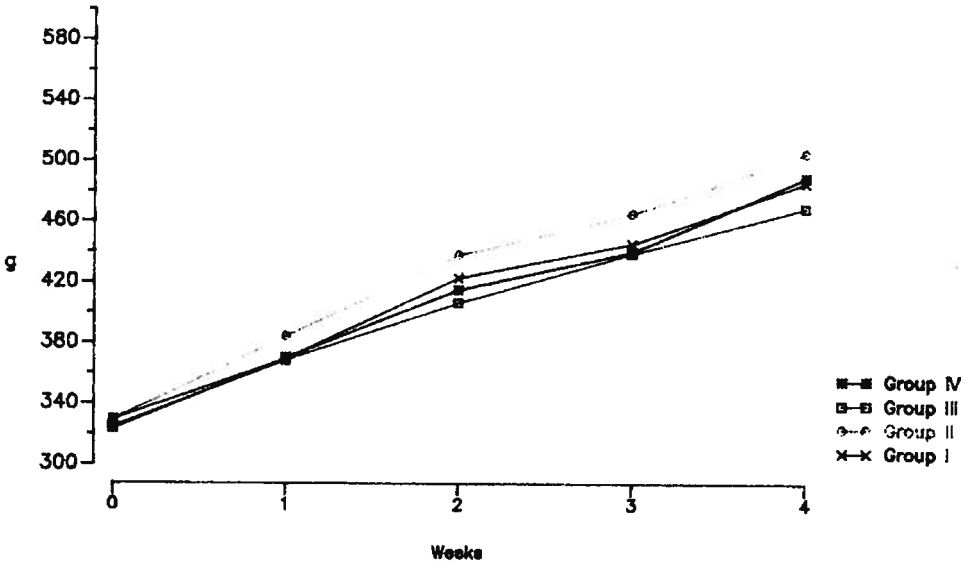
Body weights

30-05-0387-90

Males



Females



Weight changes (g) 30-05-0387-90

Analysis of variance - Startweight to Week 4

Source of variation	MS	DF	F
Groups (treatment)	1286.5	3	1.5
Sex	26163.1	1	29.8 ***
Interaction group/sex	780.3	3	.9
Error	877.3	32	
Summary		39	

Group		Males	Percent	Females	Percent
I	XM	199.8	100.0	157.0	100.0
	SD	16.3		31.1	
II	XM	207.0	103.6	176.6	112.5
	SD	31.3		21.9	
III	XM	208.0	104.1	144.8	92.2
	SD	42.4		17.3	
IV	XM	234.4	117.3	166.2	105.9
	SD	36.3		30.1	

Weight changes (g) 30-05-0387-90

Analysis of variance - Startweight to Week 2

Source of variation	MS	DF	F
Groups (treatment)	95.7	3	.3
Sex	8122.6	1	25.9 ***
Interaction group/sex	734.8	3	2.3
Error	314.0	32	
Summary		39	

Group		Males	Percent	Females	Percent
I	XM	123.4	100.0	93.8	100.0
	SD	6.9		23.5	
II	XM	113.2	91.7	108.8	116.0
	SD	26.1		8.0	
III	XM	126.0	102.1	81.8	87.2
	SD	24.6		12.0	
IV	XM	127.6	103.4	91.8	97.9
	SD	10.3		17.6	

Weight changes (g) 30-05-0387-90

Analysis of variance - Week 2 to 4

Source of variation	MS	DF	F
Groups (treatment)	877.9	3	1.8
Sex	5130.2	1	10.4 **
Interaction group/sex	174.1	3	.4
Error	495.0	32	
Summary		39	

Group		Males	Percent	Females	Percent
I	XM	76.4	100.0	63.2	100.0
	SD	13.5		10.6	
II	XM	93.8	122.8	67.8	107.3
	SD	21.5		19.5	
III	XM	82.0	107.3	63.0	99.7
	SD	40.1		14.7	
IV	XM	106.8	139.8	74.4	117.7
	SD	28.5		14.0	

Body weights (g)

30-05-0387-90

Group		Start-weight	Weeks 1	2	3	4
males						
I	XM	326.0	386.2	449.4	483.6	525.8
	SD	14.8	10.2	12.2	14.4	22.5
II	XM	327.0	382.4	440.2	482.4	534.0
	SD	8.3	23.4	31.1	29.6	38.3
III	XM	325.0	386.0	451.0	489.0	533.0
	SD	11.9	24.3	29.5	33.3	38.1
IV	XM	340.4	402.8	468.0	524.0	574.8
	SD	13.4	20.5	22.9	34.1	46.1
females						
I	XM	329.0	369.0	422.8	445.6	486.0
	SD	18.2	34.9	40.0	30.2	47.7
II	XM	329.4	384.4	438.2	465.6	506.0
	SD	10.9	9.3	14.4	26.3	32.1
III	XM	325.0	369.0	406.8	439.6	469.8
	SD	7.1	13.9	15.1	24.7	21.9
IV	XM	323.4	370.2	415.2	440.4	489.6
	SD	16.2	25.5	30.0	31.2	41.1

SKIN REACTION (IRRITATION) DAY- 1 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 1 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 2 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 2 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 3 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 3 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 4 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 4 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 5 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 5 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 6 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 6 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 7 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 7 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 8 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 8 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 9 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 9 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 10 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
		XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 10 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 11 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 11 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 12 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 12 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 13 30-05-0387-90

Group	Anim.-No.		E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 13 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 14 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 14 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 15 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 15 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 16 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 16 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 17 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 17 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 18 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 18 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 19 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 19 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 20 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 20 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 21 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 21 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 22 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 22 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 23 30-05-0387-90

Group	Anim.-No.		E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 23 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 24 30-05-0387-90

Group	Anim.-No.		E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 24 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 25 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 25 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 26 30-05-0387-90

Group Anim.-No.			E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 26 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 27 30-05-0387-90

Group	Anim.-No.		E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 27 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 28 30-05-0387-90

Group	Anim.-No.		E	O
Male	I	101	0	0
	I	102	0	0
	I	103	0	0
	I	104	0	0
	I	105	0	0
Female	I	151	0	0
	I	152	0	0
	I	153	0	0
	I	154	0	0
	I	155	0	0
	I	XM	.0	.0
Male	II	201	0	0
	II	202	0	0
	II	203	0	0
	II	204	0	0
	II	205	0	0
Female	II	251	0	0
	II	252	0	0
	II	253	0	0
	II	254	0	0
	II	255	0	0
	II	XM	.0	.0

E= Erythema O= Edema

SKIN REACTION (IRRITATION) DAY- 28 30-05-0387-90

Group Anim.-No.		E	O
Male	III 301	0	0
	III 302	0	0
	III 303	0	0
	III 304	0	0
	III 305	0	0
Female	III 351	0	0
	III 352	0	0
	III 353	0	0
	III 354	0	0
	III 355	0	0
	III XM	.0	.0
Male	IV 401	0	0
	IV 402	0	0
	IV 403	0	0
	IV 404	0	0
	IV 405	0	0
Female	IV 451	0	0
	IV 452	0	0
	IV 453	0	0
	IV 454	0	0
	IV 455	0	0
	IV XM	.0	.0

E= Erythema O= Edema

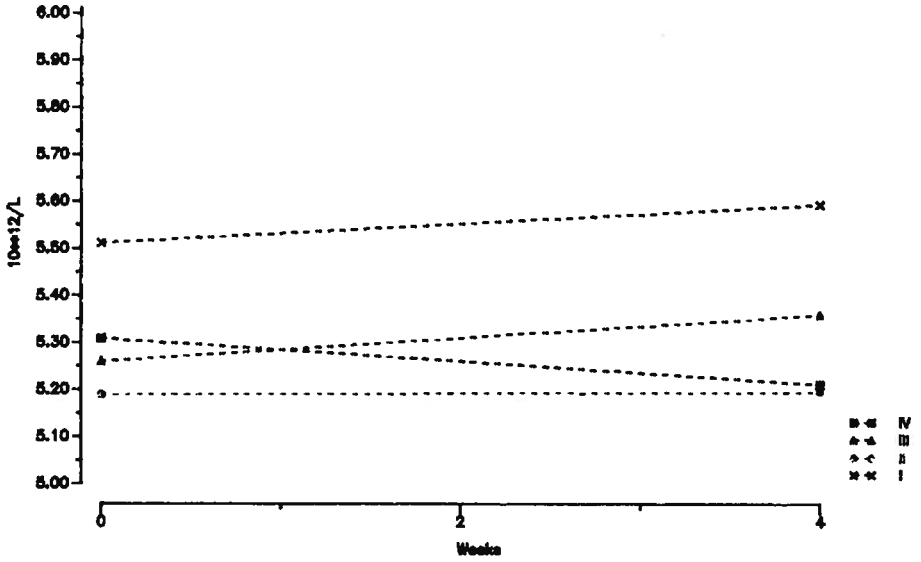
Hematology

Reference values - Guinea Pig (mean values with ranges ± 2 SD)

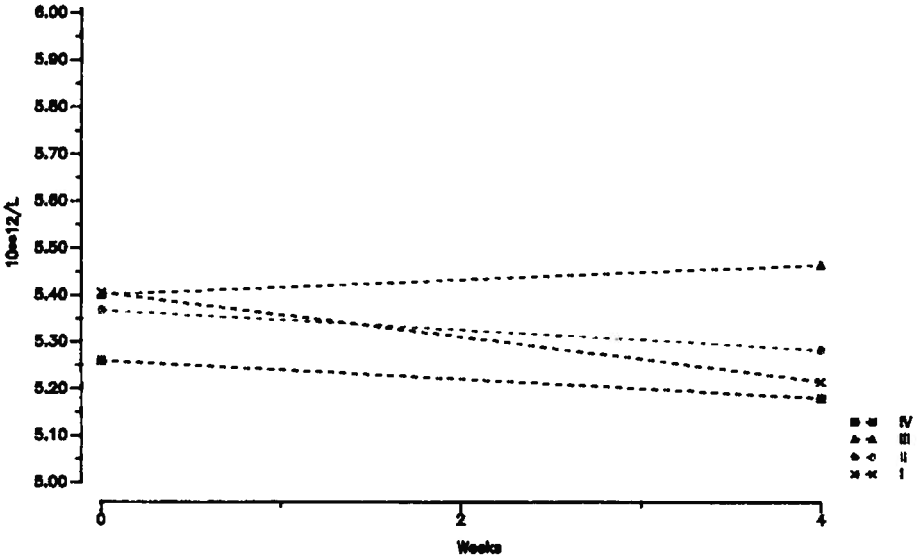
	Sex	x	- SD	+ SD	
Erythrocytes	m	5.0	4.3	5.8	x 10^{12}/l
	f	4.9	4.4	5.4	
Thrombocytes	m	426	301	552	x 10^{9}/l
	f	423	300	546	
Reticulocytes	m	0.023	0.010	0.035	1
	f	0.018	0.006	0.031	
Hemoglobin	m	8.3	7.5	9.1	mmol/l
	f	8.0	7.2	8.8	
Hematocrit	m	0.41	0.35	0.47	1
	f	0.40	0.37	0.44	
MCV	m	81.6	77.4	85.8	fl
	f	81.7	76.9	86.5	
MCH	m	1.7	1.4	1.9	fmol
	f	1.6	1.5	1.8	
MCHC	m	20.2	17.1	23.4	mmol/l
	f	19.9	18.9	21.1	
Total leukocytes	m	6.0	3.5	8.6	x 10^{9}/l
	f	5.8	3.2	8.4	
Differential count:					
Eosinophil - granulocytes	m	0.01	0.004	0.016	1
	f	0.01	0.004	0.016	
Basophil - granulocytes	m	0.01	0.003	0.017	1
	f	0.01	0.003	0.017	
Neutrophil - granulocytes					
- juvenile	m	0.0			1
	f	0.0			
- stab	m	0.0			1
	f	0.0			
- polymorphonuclear	m	0.450	0.300	0.600	1
	f	0.400	0.250	0.550	
Lymphocytes	m	0.550	0.700	0.400	1
	f	0.500	0.650	0.350	
Monocytes	m	0.025	0.000	0.050	1
	f	0.025	0.000	0.050	
Normoblasts	m	0.0			1
	f	0.0			
Prothrombin time	m	93.7	81.3	106	%
	f	99.1	83.5	115	

ERYTHROCYTES

30-05-0387-90 Males



Females



ERYTHROCYTES (10**12/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	5.510	5.592
	SD	.367	.383
II	XM	5.190	5.196
	SD	.197	.628
III	XM	5.260	5.360
	SD	.336	.639
IV	XM	5.310	5.212
	SD	.172	.280

Group	F(3, 16) =	1.0
Time	F(1, 16) =	.1
Group X Time	F(3, 16) =	.2

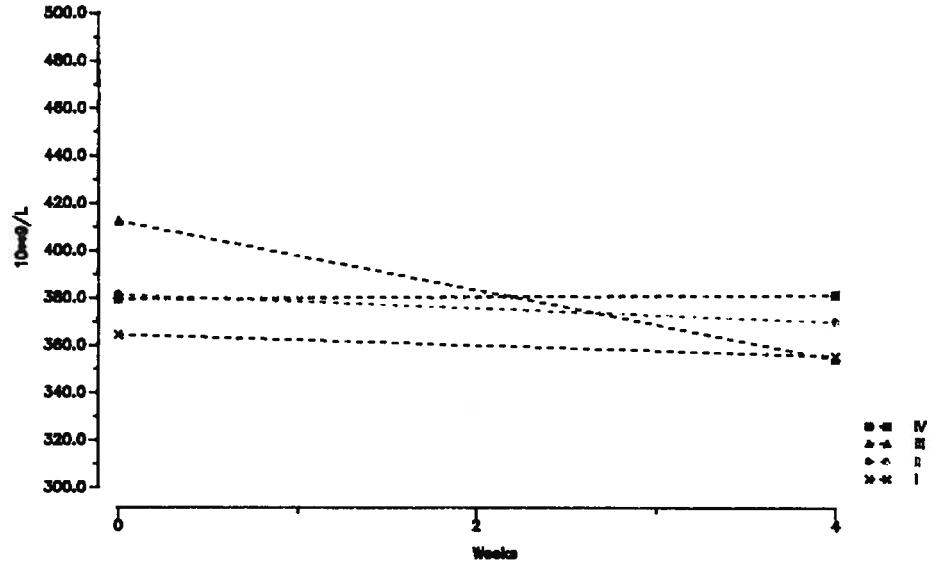
Females

Group		Week 0	Week 4
I	XM	5.404	5.214
	SD	.512	.139
II	XM	5.370	5.284
	SD	.313	.151
III	XM	5.402	5.466
	SD	.328	.319
IV	XM	5.262	5.182
	SD	.255	.312

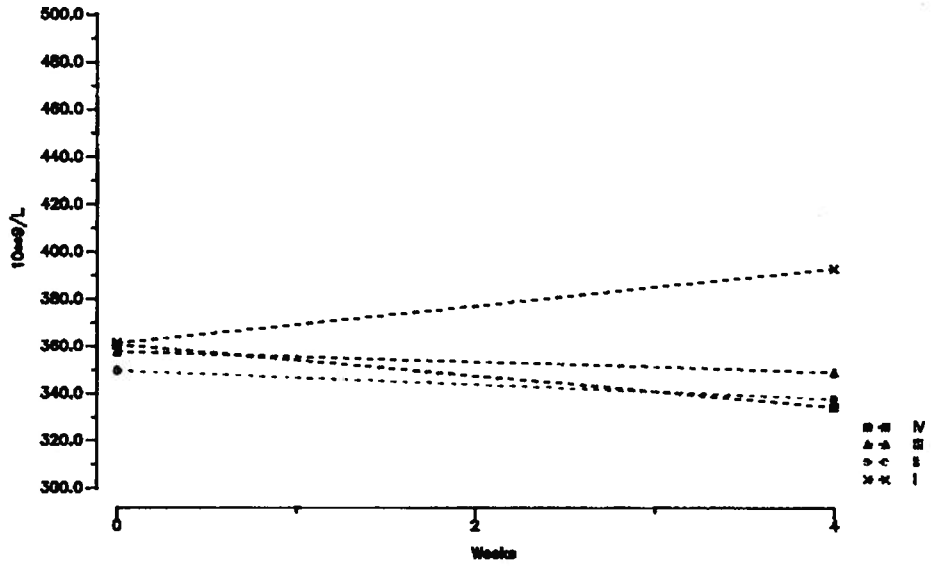
Group	F(3, 16) =	.9
Time	F(1, 16) =	.5
Group X Time	F(3, 16) =	.3

THROMBOCYTES

30–05–0387–90 Males



Females



THROMBOCYTES (10**9/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	364.2	355.2
	SD	71.5	53.6
II	XM	381.2	369.8
	SD	39.4	64.3
III	XM	412.4	354.0
	SD	54.3	60.0
IV	XM	379.6	381.4
	SD	44.6	43.0

Group	F(3, 16) =	.3
Time	F(1, 16) =	1.5
Group X Time	F(3, 16) =	.7

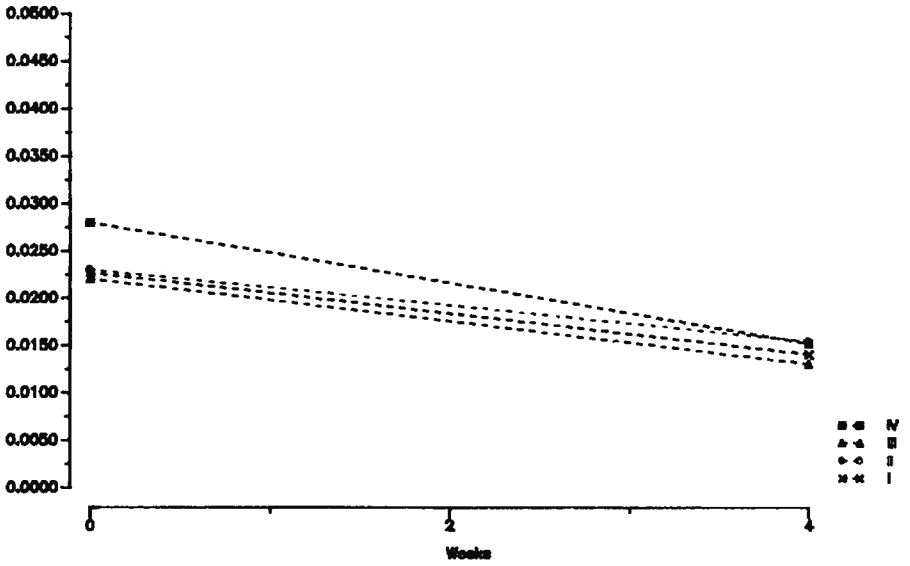
Females

Group		Week 0	Week 4
I	XM	361.2	392.8
	SD	34.5	31.9
II	XM	349.8	337.8
	SD	74.5	40.9
III	XM	357.8	349.0
	SD	64.0	76.9
IV	XM	360.8	334.4
	SD	24.8	28.8

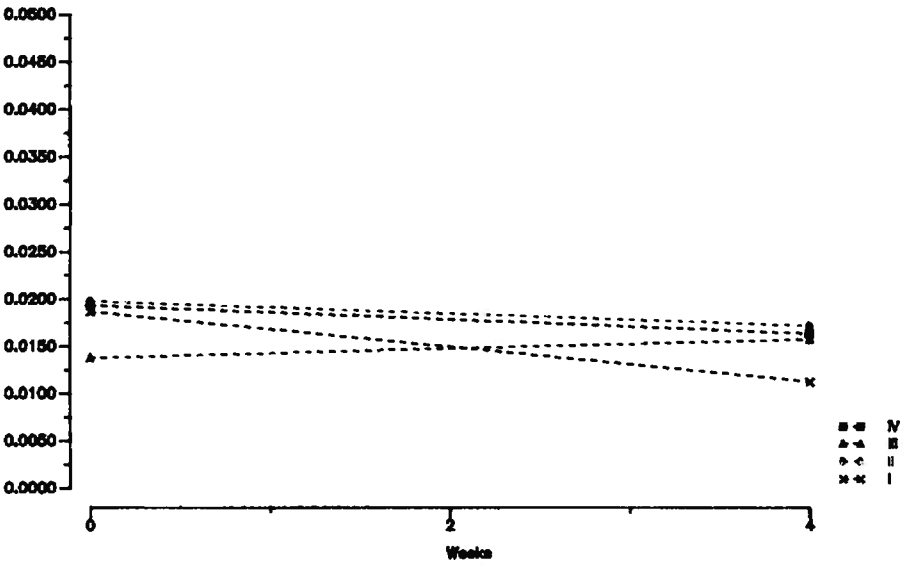
Group	F(3, 16) =	.6
Time	F(1, 16) =	.1
Group X Time	F(3, 16) =	1.2

RETICULOCYTES

30–05–0387–90 Males



Females



Males

Group		Week 0	Week 4
I	XM	.0226	.0140
	SD	.0032	.0045
II	XM	.0230	.0154
	SD	.0030	.0045
III	XM	.0220	.0130
	SD	.0037	.0039
IV	XM	.0280	.0152
	SD	.0043	.0043

Group	F(3, 16) =	1.8
Time	F(1, 16) =	66.7 ***
Group X Time	F(3, 16) =	1.0

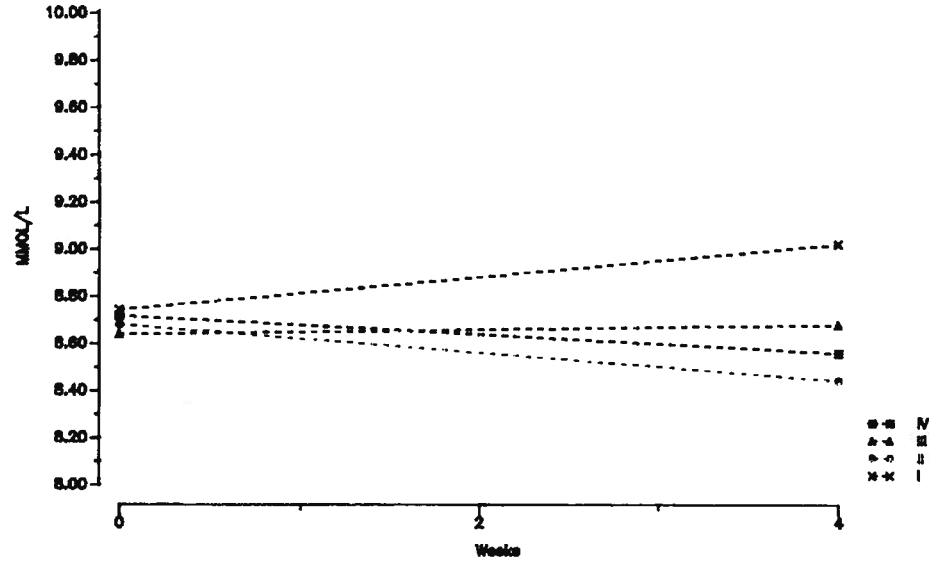
Females

Group		Week 0	Week 4
I	XM	.0186	.0112
	SD	.0073	.0067
II	XM	.0198	.0172
	SD	.0090	.0111
III	XM	.0138	.0158
	SD	.0027	.0051
IV	XM	.0194	.0164
	SD	.0105	.0057

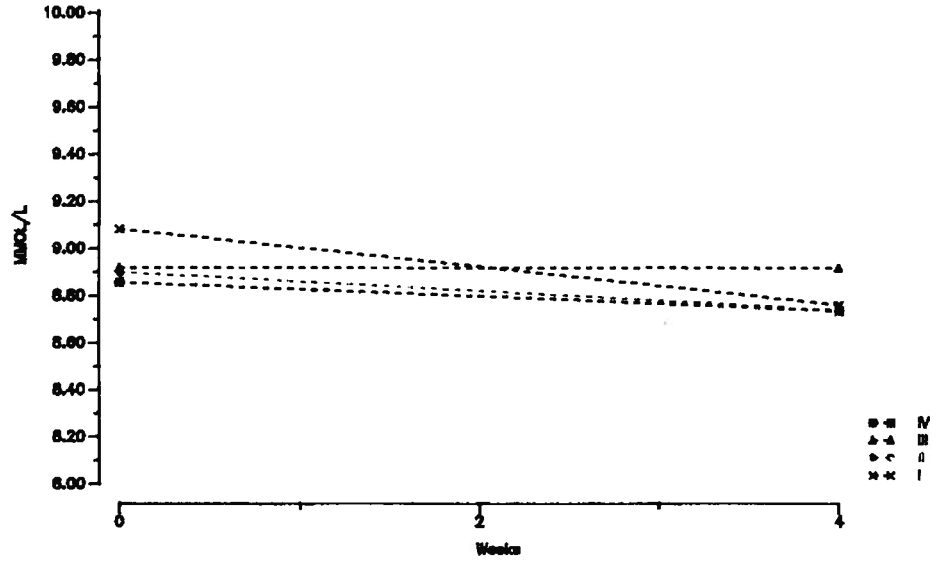
Group	F(3, 16) =	.8
Time	F(1, 16) =	1.1
Group X Time	F(3, 16) =	.5

HEMOGLOBIN

30–05–0387–90 Males



Females



HEMOGLOBIN (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	8.74	9.02
	SD	.61	.64
II	XM	8.68	8.44
	SD	.16	.94
III	XM	8.64	8.68
	SD	.32	1.00
IV	XM	8.72	8.56
	SD	.36	.23

Group	F(3, 16) =	.4
Time	F(1, 16) =	.0
Group X Time	F(3, 16) =	.6

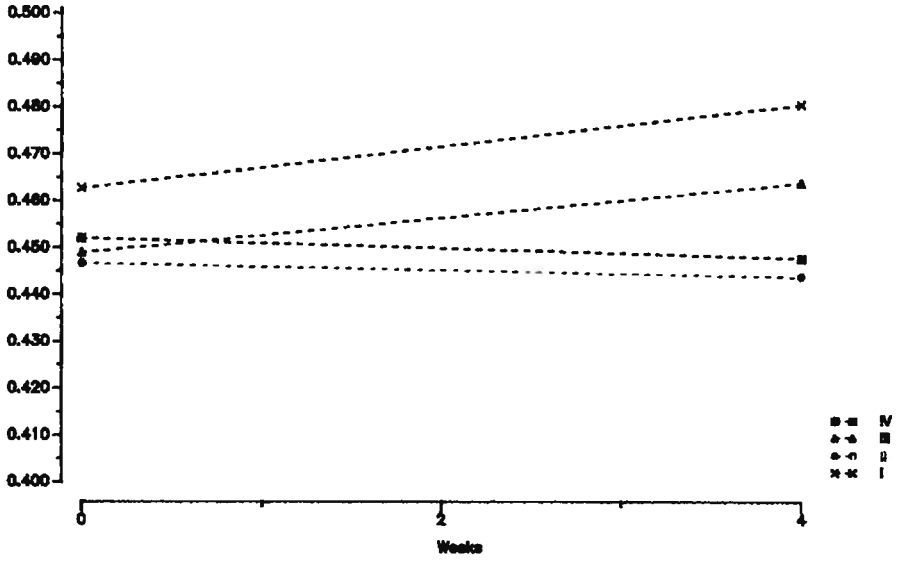
Females

Group		Week 0	Week 4
I	XM	9.08	8.76
	SD	.72	.36
II	XM	8.90	8.74
	SD	.46	.24
III	XM	8.92	8.92
	SD	.54	.58
IV	XM	8.86	8.74
	SD	.36	.46

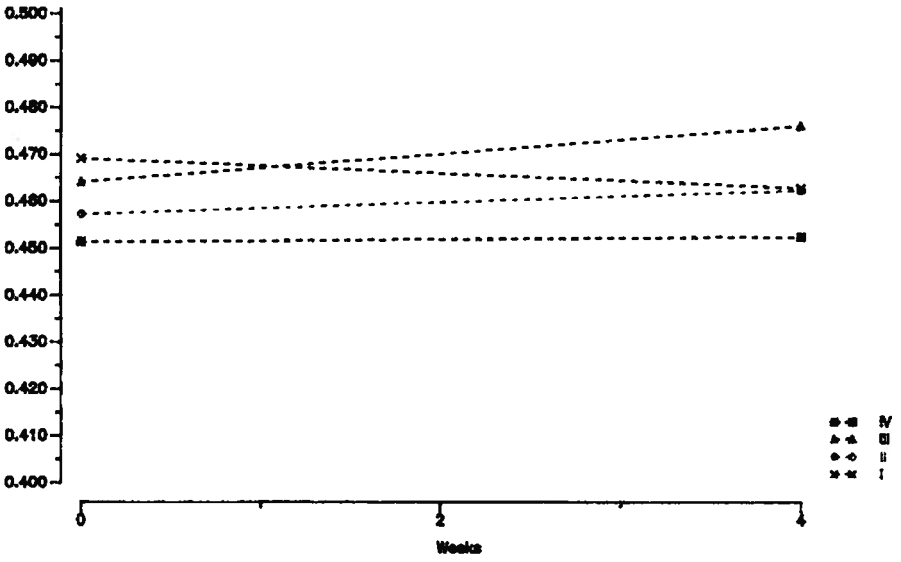
Group	F(3, 16) =	.1
Time	F(1, 16) =	1.2
Group X Time	F(3, 16) =	.2

HEMATOCRIT

30–05–0387–90 Males



Females



HEMATOCRIT

30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	.4626	.4804
	SD	.0267	.0344
II	XM	.4468	.4438
	SD	.0096	.0493
III	XM	.4490	.4638
	SD	.0194	.0537
IV	XM	.4522	.4478
	SD	.0157	.0156

Group	F(3, 16) =	.9
Time	F(1, 16) =	.6
Group X Time	F(3, 16) =	.5

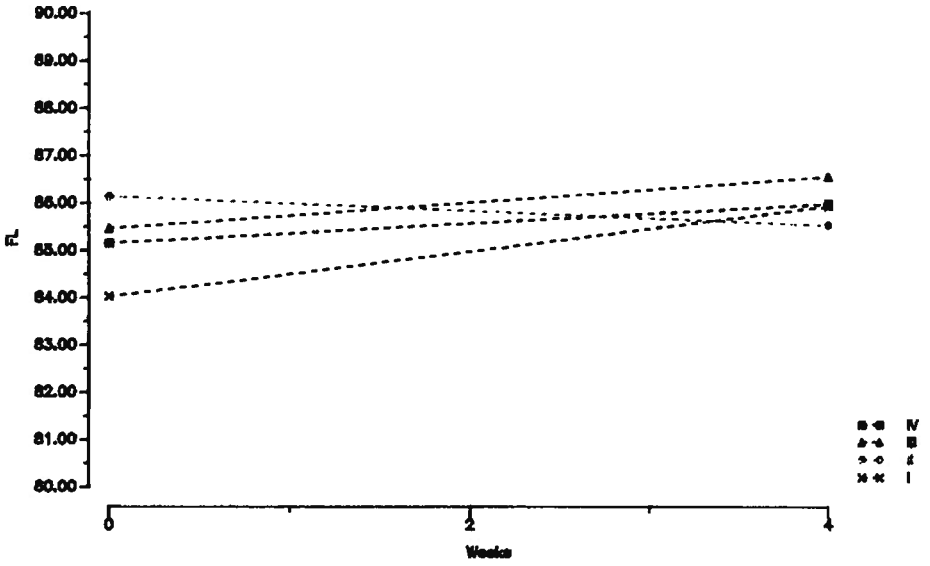
Females

Group		Week 0	Week 4
I	XM	.4690	.4628
	SD	.0384	.0181
II	XM	.4574	.4626
	SD	.0254	.0090
III	XM	.4642	.4764
	SD	.0282	.0293
IV	XM	.4516	.4528
	SD	.0202	.0273

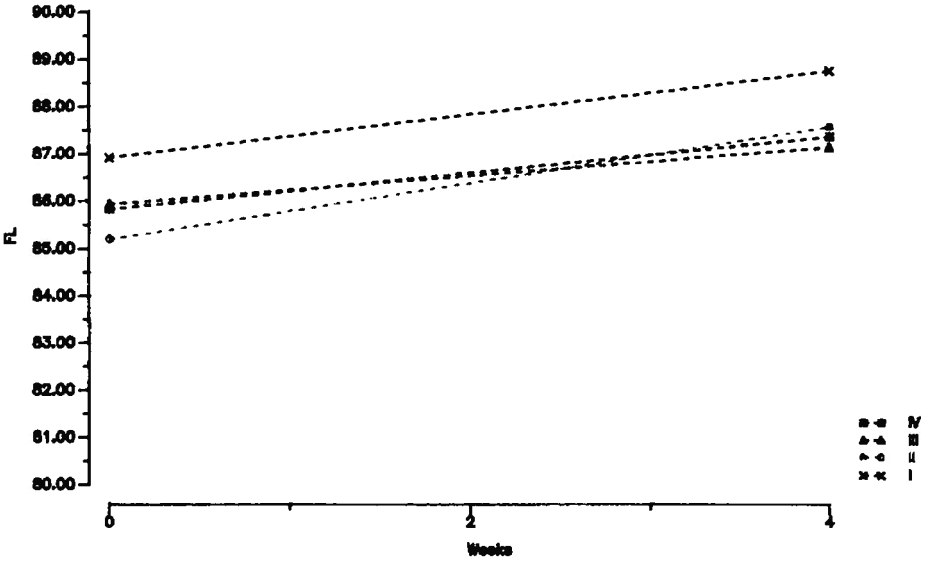
Group	F(3, 16) =	.8
Time	F(1, 16) =	.2
Group X Time	F(3, 16) =	.2

MCV

30–05–0387–90 Males



Females



Males

Group		Week 0	Week 4
I	XM	84.014	85.920
	SD	2.374	2.688
II	XM	86.132	85.510
	SD	1.861	1.741
III	XM	85.462	86.552
	SD	2.526	1.652
IV	XM	85.164	85.992
	SD	1.621	2.043

Group	F(3, 16) =	.3
Time	F(1, 16) =	8.8 **
Group X Time	F(3, 16) =	3.7 *

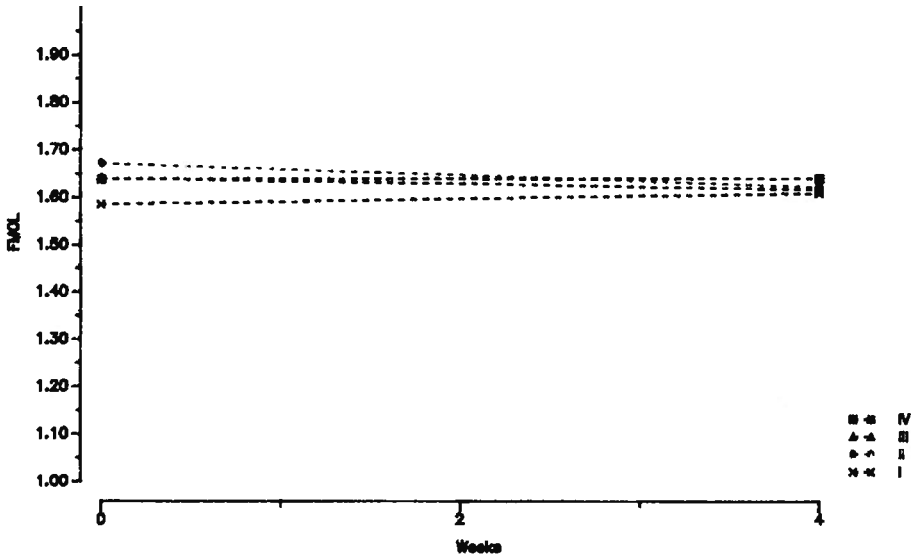
Females

Group		Week 0	Week 4
I	XM	86.908	88.760
	SD	3.151	2.797
II	XM	85.192	87.570
	SD	1.382	1.797
III	XM	85.938	87.150
	SD	1.407	1.529
IV	XM	85.842	87.380
	SD	1.653	1.201

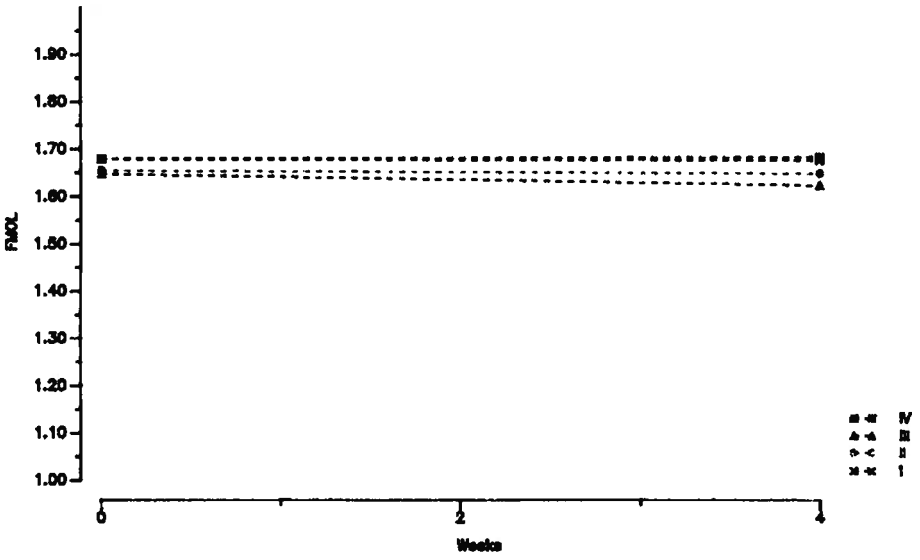
Group	F(3, 16) =	.9
Time	F(1, 16) =	11.6 **
Group X Time	F(3, 16) =	.2

MCH

30–05–0387–90 Males



Females



MCH (FMOL) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	1.584	1.608
	SD	.057	.041
II	XM	1.670	1.620
	SD	.046	.058
III	XM	1.640	1.616
	SD	.074	.033
IV	XM	1.638	1.640
	SD	.042	.056

Group	F(3, 16) =	1.1
Time	F(1, 16) =	1.4
Group X Time	F(3, 16) =	2.5

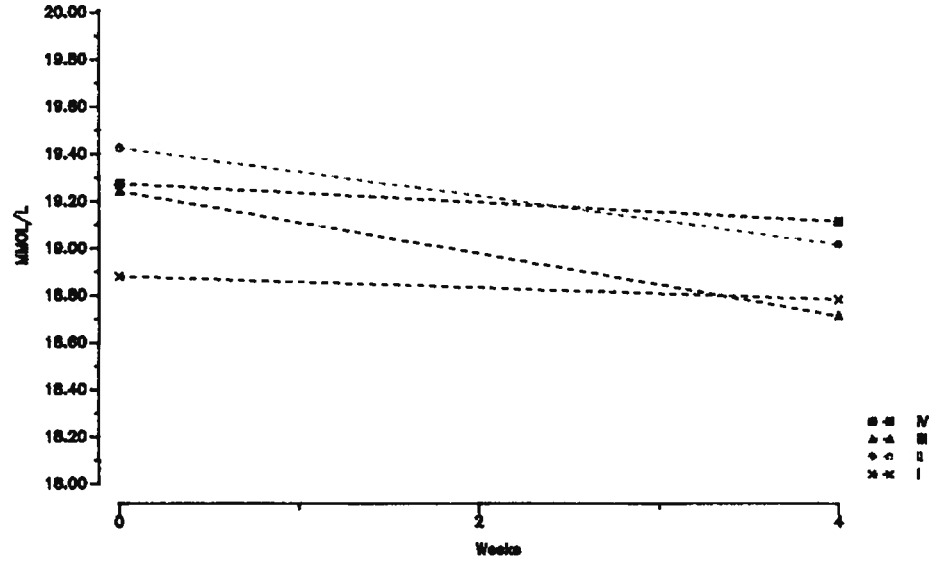
Females

Group		Week 0	Week 4
I	XM	1.678	1.676
	SD	.065	.048
II	XM	1.654	1.648
	SD	.032	.024
III	XM	1.648	1.624
	SD	.040	.039
IV	XM	1.680	1.684
	SD	.053	.034

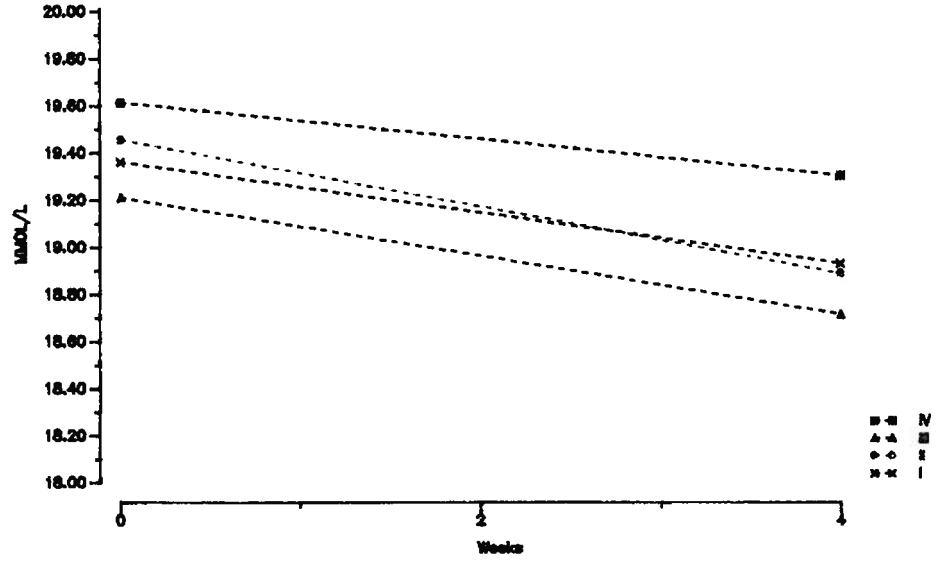
Group	F(3, 16) =	1.8
Time	F(1, 16) =	.5
Group X Time	F(3, 16) =	.3

MCHC

30–05–0387–90 Males



Females



MCHC (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	18.878	18.780
	SD	.279	.366
II	XM	19.424	19.014
	SD	.197	.344
III	XM	19.242	18.712
	SD	.342	.242
IV	XM	19.276	19.114
	SD	.231	.209

Group	F(3, 16) =	3.8 *
Time	F(1, 16) =	12.9 **
Group X Time	F(3, 16) =	1.5

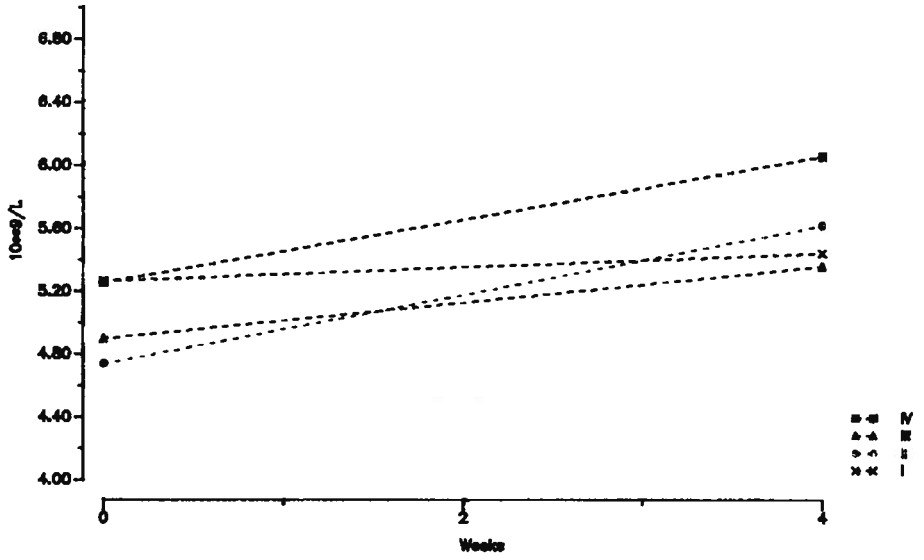
Females

Group		Week 0	Week 4
I	XM	19.360	18.930
	SD	.108	.619
II	XM	19.456	18.888
	SD	.189	.261
III	XM	19.212	18.716
	SD	.339	.199
IV	XM	19.616	19.306
	SD	.352	.449

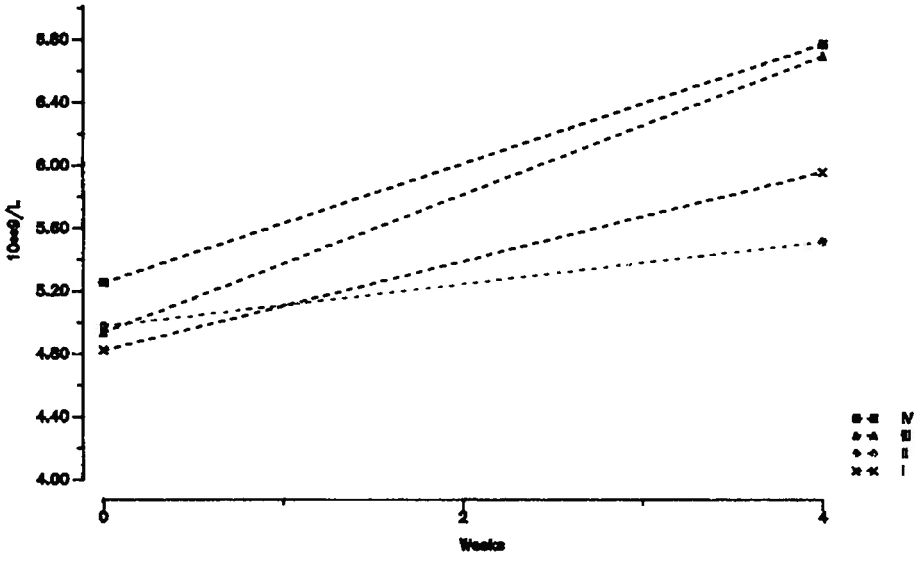
Group	F(3, 16) =	3.2
Time	F(1, 16) =	18.0 ***
Group X Time	F(3, 16) =	.3

LEUKOCYTES

30–05–0387–90 Males



Females



LEUKOCYTES (10**9/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	5.26	5.44
	SD	.91	.59
II	XM	4.74	5.62
	SD	.68	.68
III	XM	4.90	5.36
	SD	1.49	.34
IV	XM	5.26	6.06
	SD	.65	1.51

Group	F(3, 16) =	.7
Time	F(1, 16) =	3.7
Group X Time	F(3, 16) =	.3

Females

Group		Week 0	Week 4
I	XM	4.82	5.96
	SD	.70	1.59
II	XM	4.98	5.52
	SD	.55	.93
III	XM	4.94	6.70
	SD	1.31	1.94
IV	XM	5.26	6.78
	SD	1.00	1.53

Group	F(3, 16) =	.5
Time	F(1, 16) =	20.0 ***
Group X Time	F(3, 16) =	.9

DIFFERENTIAL COUNT

0. DAY

Males

GR./ANIM.	EO.	BASO.	JUV.	STAB.	SEG.	LYMPH	MONO.	NORM.
I 101	.02	.00	.00	.00	.40	.57	.01	.00
I 102	.05	.01	.00	.00	.38	.52	.04	.00
I 103	.00	.00	.00	.00	.42	.54	.04	.00
I 104	.02	.00	.00	.00	.32	.62	.04	.00
I 105	.01	.00	.00	.00	.28	.69	.02	.00
I XM	.020	.002	.000	.000	.360	.588	.030	.000
II 201	.00	.00	.00	.00	.31	.59	.10	.00
II 202	.02	.00	.00	.00	.43	.55	.00	.00
II 203	.00	.00	.00	.00	.41	.56	.03	.00
II 204	.01	.00	.00	.00	.42	.57	.00	.00
II 205	.01	.00	.00	.00	.35	.62	.02	.00
II XM	.008	.000	.000	.000	.384	.578	.030	.000
III 301	.03	.01	.00	.00	.33	.62	.01	.00
III 302	.01	.00	.00	.00	.48	.50	.01	.00
III 303	.01	.01	.00	.00	.25	.69	.04	.00
III 304	.05	.00	.00	.00	.32	.61	.02	.00
III 305	.00	.00	.00	.00	.24	.73	.03	.00
III XM	.020	.004	.000	.000	.324	.630	.022	.000
IV 401	.00	.00	.00	.00	.55	.40	.05	.00
IV 402	.02	.00	.00	.00	.34	.60	.04	.00
IV 403	.01	.00	.00	.00	.27	.72	.00	.00
IV 404	.01	.01	.00	.00	.29	.62	.07	.00
IV 405	.00	.00	.00	.00	.30	.63	.07	.00
IV XM	.008	.002	.000	.000	.350	.594	.046	.000

DIFFERENTIAL COUNT 30-05-0387-90

28. DAY

Males

GR./ANIM.	EO.	BASO.	JUV.	STAB.	SEG.	LYMPH	MONO.	NORM.
I 101	.03	.00	.00	.00	.24	.71	.02	.00
I 102	.03	.00	.00	.00	.33	.58	.06	.00
I 103	.02	.00	.00	.00	.33	.60	.05	.00
I 104	.01	.01	.00	.00	.32	.66	.00	.00
I 105	.04	.02	.00	.00	.32	.61	.01	.00
I XM	.026	.006	.000	.000	.308	.632	.028	.000
II 201	.03	.00	.00	.00	.53	.42	.02	.00
II 202	.00	.00	.00	.00	.44	.56	.00	.00
II 203	.01	.00	.00	.00	.36	.61	.02	.00
II 204	.01	.00	.00	.00	.28	.67	.04	.00
II 205	.03	.00	.00	.00	.14	.75	.08	.00
II XM	.016	.000	.000	.000	.350	.602	.032	.000
III 301	.02	.00	.00	.00	.32	.66	.00	.00
III 302	.04	.00	.00	.00	.25	.66	.05	.00
III 303	.00	.00	.00	.00	.16	.82	.02	.00
III 304	.03	.01	.00	.00	.15	.74	.07	.00
III 305	.01	.01	.00	.00	.36	.59	.03	.00
III XM	.020	.004	.000	.000	.248	.694	.034	.000
IV 401	.02	.00	.00	.00	.41	.54	.03	.00
IV 402	.01	.00	.00	.00	.33	.65	.01	.00
IV 403	.02	.00	.00	.00	.38	.60	.00	.00
IV 404	.01	.00	.00	.00	.20	.75	.04	.00
IV 405	.01	.01	.00	.00	.14	.83	.01	.00
IV XM	.014	.002	.000	.000	.292	.674	.018	.000

DIFFERENTIAL COUNT

0. DAY

Females

GR./ANIM.	EO.	BASO.	JUV.	STAB.	SEG.	LYMPH	MONO.	NORM.
I 151	.00	.00	.00	.00	.12	.80	.08	.00
I 152	.01	.00	.00	.00	.29	.67	.03	.00
I 153	.02	.01	.00	.00	.20	.75	.02	.00
I 154	.03	.00	.00	.00	.24	.72	.01	.00
I 155	.04	.00	.00	.00	.09	.84	.03	.00
I XM	.020	.002	.000	.000	.188	.756	.034	.000
II 251	.01	.00	.00	.00	.16	.79	.04	.00
II 252	.02	.00	.00	.00	.16	.74	.08	.00
II 253	.00	.01	.00	.00	.32	.66	.01	.00
II 254	.01	.01	.00	.00	.32	.63	.03	.00
II 255	.01	.01	.00	.00	.15	.80	.03	.00
II XM	.010	.006	.000	.000	.222	.724	.038	.000
III 351	.02	.00	.00	.00	.26	.69	.03	.00
III 352	.03	.00	.00	.00	.17	.73	.07	.00
III 353	.01	.00	.00	.00	.19	.77	.03	.00
III 354	.02	.00	.00	.00	.18	.68	.12	.00
III 355	.02	.00	.00	.00	.30	.65	.03	.00
III XM	.020	.000	.000	.000	.220	.704	.056	.000
IV 451	.01	.02	.00	.00	.15	.80	.02	.00
IV 452	.04	.02	.00	.00	.20	.69	.05	.00
IV 453	.02	.02	.00	.00	.15	.76	.05	.00
IV 454	.00	.01	.00	.00	.24	.64	.11	.00
IV 455	.02	.02	.00	.00	.13	.68	.15	.00
IV XM	.018	.018	.000	.000	.174	.714	.076	.000

DIFFERENTIAL COUNT 30-05-0387-90

28. DAY

Females

GR./ANIM.	EO.	BASO.	JUV.	STAB.	SEG.	LYMPH	MONO.	NORM.
I 151	.01	.00	.00	.00	.23	.70	.06	.00
I 152	.02	.00	.00	.00	.35	.55	.08	.00
I 153	.06	.00	.00	.00	.29	.60	.05	.00
I 154	.02	.00	.00	.00	.34	.57	.07	.00
I 155	.04	.00	.00	.00	.31	.60	.05	.00
I XM	.030	.000	.000	.000	.304	.604	.062	.000
II 251	.02	.01	.00	.00	.24	.63	.10	.00
II 252	.04	.00	.00	.00	.18	.68	.10	.00
II 253	.04	.01	.00	.00	.23	.66	.06	.00
II 254	.03	.00	.00	.00	.09	.76	.12	.00
II 255	.03	.00	.00	.00	.26	.60	.11	.00
II XM	.032	.004	.000	.000	.200	.666	.098	.000
III 351	.02	.01	.00	.00	.35	.52	.10	.00
III 352	.02	.00	.00	.00	.32	.61	.05	.00
III 353	.06	.02	.00	.00	.25	.53	.14	.00
III 354	.00	.00	.00	.00	.41	.55	.04	.00
III 355	.01	.00	.00	.00	.31	.63	.05	.00
III XM	.022	.006	.000	.000	.328	.568	.076	.000
IV 451	.02	.01	.00	.00	.36	.52	.09	.00
IV 452	.01	.00	.00	.00	.33	.47	.19	.00
IV 453	.01	.00	.00	.00	.44	.46	.09	.00
IV 454	.07	.01	.00	.00	.19	.65	.08	.00
IV 455	.01	.02	.00	.00	.33	.52	.12	.00
IV XM	.024	.008	.000	.000	.330	.524	.114	.000

ANALYSIS OF VARIANCE: SEGMENTED NEUTROPHIL GRANULOCYTES

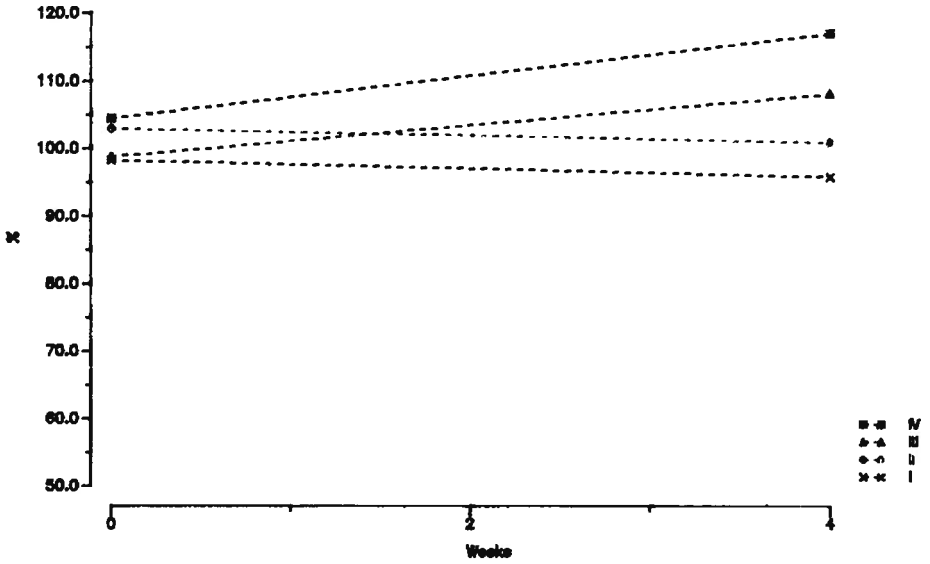
F - VALUE: (3/ 16) = 4.09 * p = .0247

TUKEY- TEST:

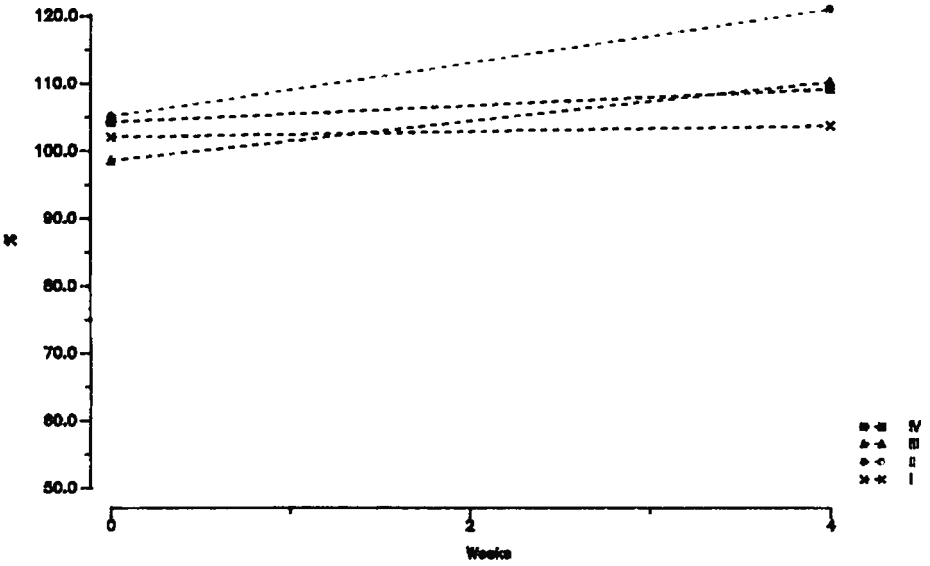
II - III = *
II - IV = *

PROTHROMBIN TIME

30-05-0387-90 Males



Females



PROTHROMBIN TIME (%)

30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	98.2	95.8
	SD	10.4	2.9
II	XM	103.0	101.0
	SD	4.9	12.0
III	XM	98.8	108.2
	SD	5.0	9.9
			*
IV	XM	104.6	117.2
	SD	17.6	11.7

Group	F(3, 16) =	2.8
Time	F(1, 16) =	2.0
Group X Time	F(3, 16) =	1.6

Females

Group		Week 0	Week 4
I	XM	102.0	103.8
	SD	5.5	9.2
II	XM	105.2	121.2
	SD	13.6	10.8
III	XM	98.6	110.4
	SD	4.9	13.7
IV	XM	104.4	109.4
	SD	3.9	7.9

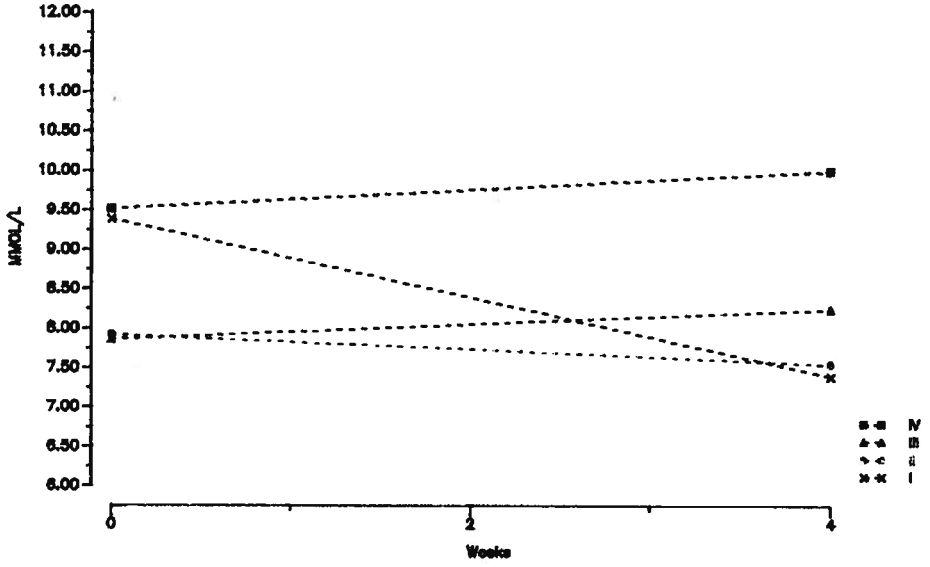
Group	F(3, 16) =	2.0
Time	F(1, 16) =	10.1 **
Group X Time	F(3, 16) =	1.4

Clinical Chemistry
Reference values - Guinea Pig (mean value with ranges ± 2 SD)

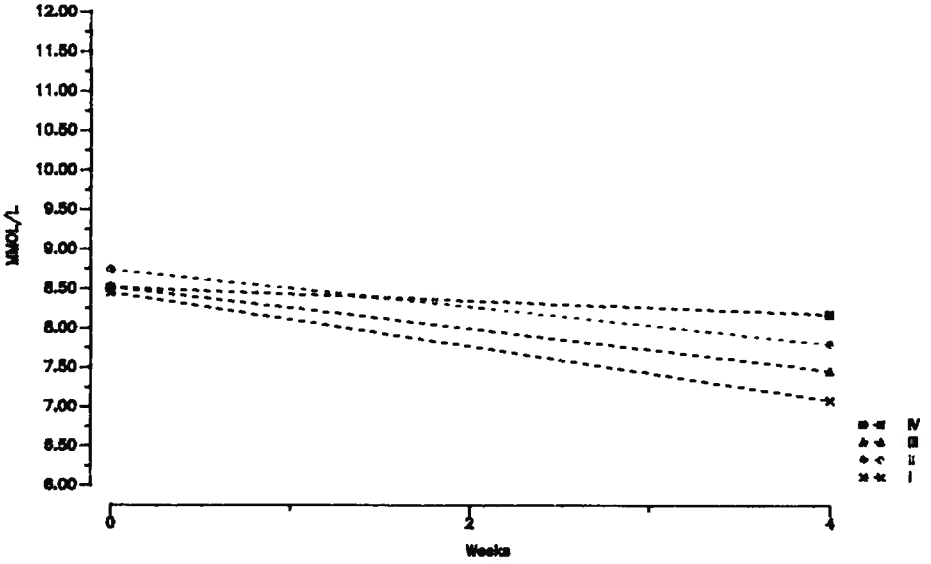
	Sex	x	- 2 SD	+ 2 SD	
Glucose	m	7.7	6.5	8.8	mmol/l
	f	7.5	6.3	8.8	
Cholesterol	m	0.77	0.43	1.1	mmol/l
	f	0.89	0.43	1.3	
Triglyceride	m	0.40	0.20	0.60	mmol/l
	f	0.39	0.23	0.55	
Total Protein	m	41.7	36.7	46.7	g/l
	f	41.4	37.6	45.2	
Albumin	m	28.2	25.9	30.5	g/l
	f	28.1	25.9	30.8	
Electrophoresis:					
- Albumin	not yet available				1
- Globulin $A_1 + A_2$	not yet available				1
- Globulin B	not yet available				1
- Globulin G	not yet available				1
ALT (SGPT)	m	20.7	13.5	27.9	U/l
	f	18.4	8.2	28.6	
AST (SGOT)	m	20.3	8.3	32.3	U/l
	f	19.8	7.0	32.6	
AST/ALT	m	0.98	0.58	1.4	U/l
	f	1.10	0.52	1.7	
Alk. Phosphatase	m	443	191	695	U/l
	f	362	253	472	
LDH	m	58.3	33.1	83.5	U/l
	f	58.3	19.1	97.5	
Gamma-GT	m	3.8	2.6	5.0	U/l
	f	3.7	2.3	5.1	
CK	m	103	59.0	146	U/l
	f	100	38.2	162	
Total Bilirubin	m	0.71	0.53	0.89	µmol/l
	f	0.76	0.58	0.94	
Uric Acid	m	19.1	7.5	30.7	µmol/l
	f	17.8	8.8	26.8	
BUN	m	8.7	6.5	11.0	mmol/l
	f	8.6	7.0	10.2	
Creatinine	m	32.2	25.4	39.0	µmol/l
	f	31.9	25.3	38.5	
Sodium	m	142	134	150	mmol/l
	f	142	135	149	
Potassium	m	6.2	4.8	7.6	mmol/l
	f	6.4	4.9	7.9	
Na/K-Ratio	m	23.3	17.8	28.7	
	f	22.4	17.1	27.7	
Calcium	m	2.8	2.6	3.0	mmol/l
	f	2.8	2.6	3.0	
Iron	m	43.0	25.9	60.2	µmol/l
	f	42.6	26.9	58.3	
Chloride	m	104	98.1	110	mmol/l
	f	103	98.8	108	
Inorg. Phosphorus	m	1.7	1.3	2.1	mmol/l
	f	1.7	1.4	1.9	

GLUCOSE

30–05–0387–90 Males



Females



GLUCOSE (MMOL/L)

30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	9.38	7.38
	SD	2.53	.47
II	XM	7.92	7.54
	SD	.71	.83
III	XM	7.86	8.24
	SD	.47	1.36
IV	XM	9.52	10.00
	SD	1.00	2.20

Group	F(3, 16) =	4.0 *
Time	F(1, 16) =	.8
Group X Time	F(3, 16) =	1.7

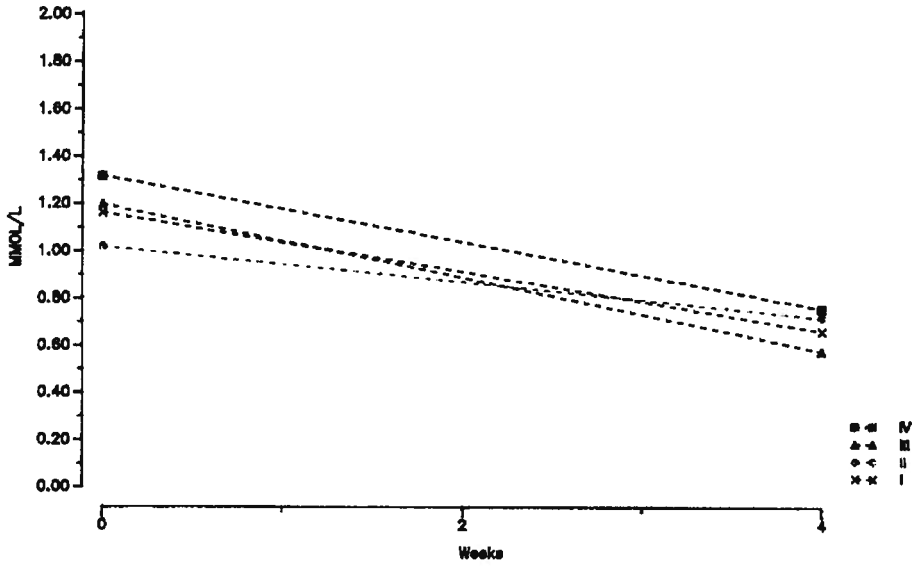
Females

Group		Week 0	Week 4
I	XM	8.44	7.08
	SD	.32	.65
II	XM	8.74	7.80
	SD	.94	.61
III	XM	8.52	7.46
	SD	.70	.43
IV	XM	8.52	8.18
	SD	.16	.65

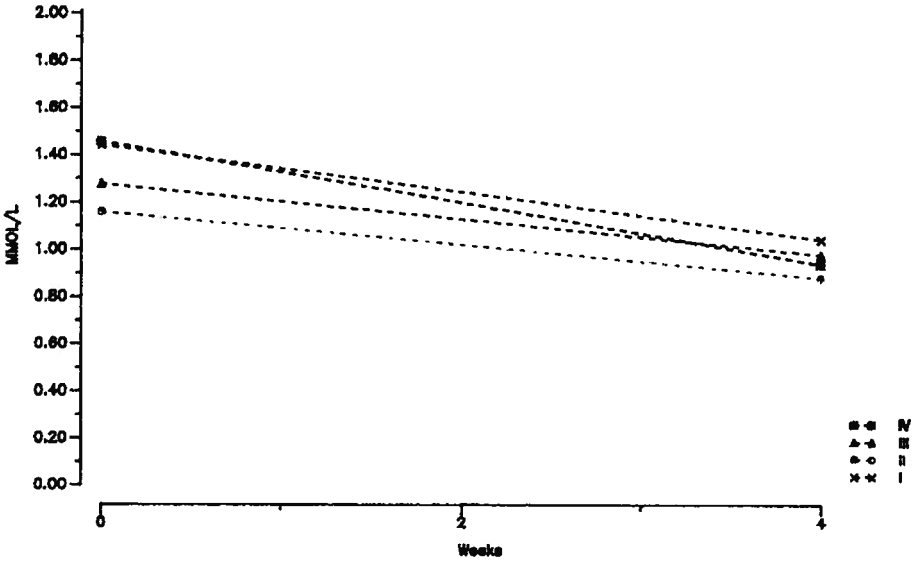
Group	F(3, 16) =	1.4
Time	F(1, 16) =	42.7 ***
Group X Time	F(3, 16) =	2.3

CHOLESTEROL

30-05-0387-90 Males



Females



CHOLESTEROL (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	1.16	.66
	SD	.26	.09
II	XM	1.02	.72
	SD	.28	.18
III	XM	1.20	.58
	SD	.16	.22
IV	XM	1.32	.76
	SD	.24	.11

Group	F(3, 16) =	1.8
Time	F(1, 16) =	50.3 ***
Group X Time	F(3, 16) =	1.0

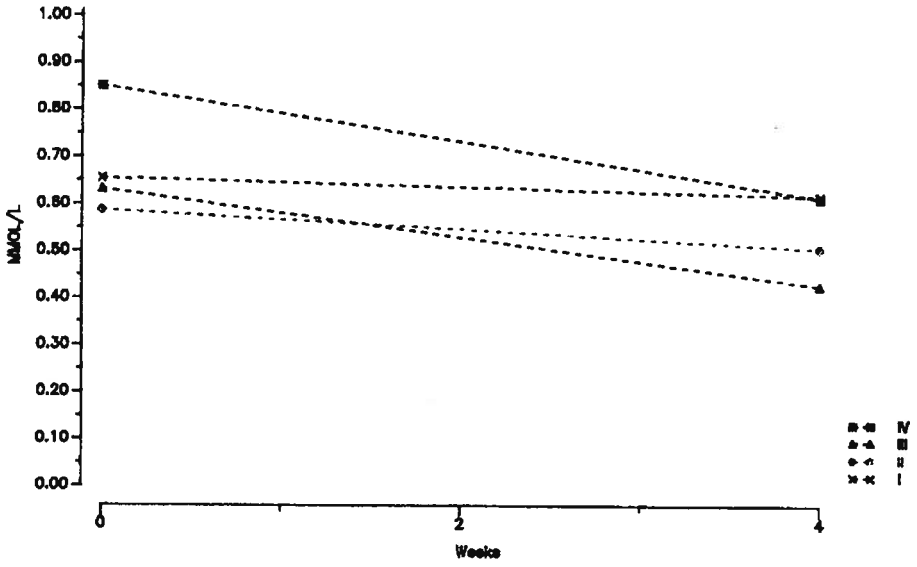
Females

Group		Week 0	Week 4
I	XM	1.44	1.04
	SD	.27	.11
II	XM	1.16	.88
	SD	.13	.23
III	XM	1.28	.98
	SD	.33	.23
IV	XM	1.46	.94
	SD	.17	.21

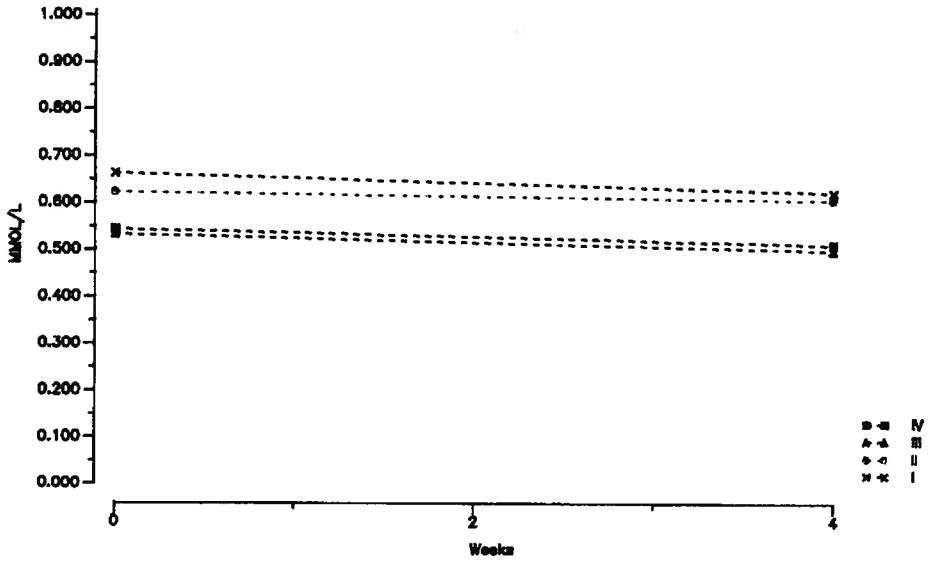
Group	F(3, 16) =	1.9
Time	F(1, 16) =	28.9 ***
Group X Time	F(3, 16) =	.6

TRIGLYCERIDE

30–05–0387–90 Males



Females



TRIGLYCERIDE (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	.654	.616
	SD	.241	.156
II	XM	.588	.506
	SD	.122	.231
III	XM	.632	.426
	SD	.235	.135
IV	XM	.852	.614
	SD	.134	.154

Group	F(3, 16) =	2.0
Time	F(1, 16) =	8.5 *
Group X Time	F(3, 16) =	1.0

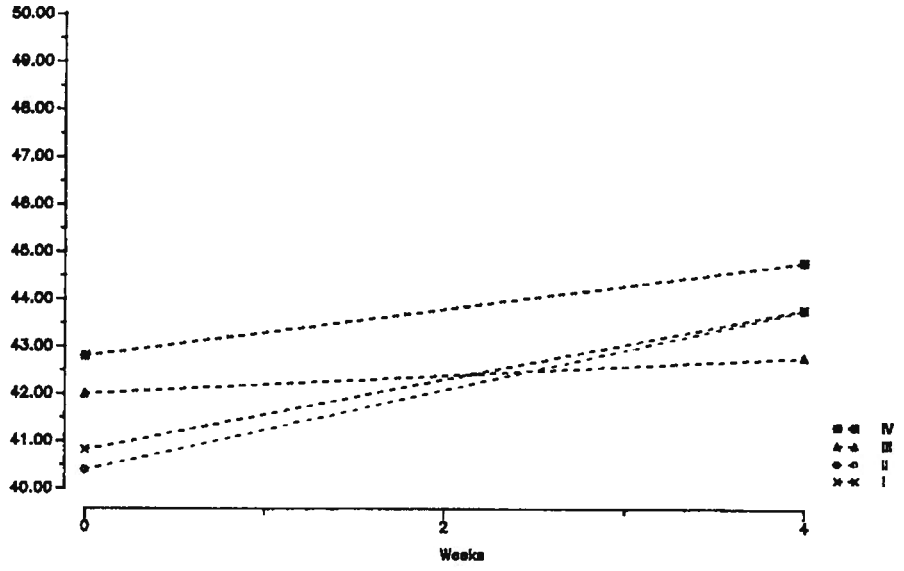
Females

Group		Week 0	Week 4
I	XM	.662	.622
	SD	.138	.214
II	XM	.624	.608
	SD	.112	.294
III	XM	.534	.500
	SD	.182	.122
IV	XM	.546	.514
	SD	.123	.113

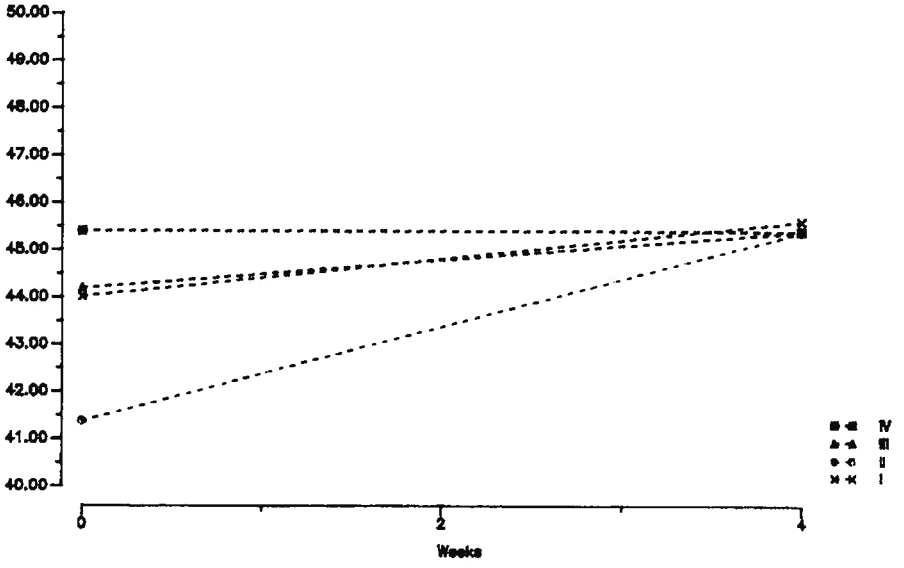
Group	F(3, 16) =	1.5
Time	F(1, 16) =	.3
Group X Time	F(3, 16) =	.0

TOTAL PROTEIN (G/L)

30-05-0387-90 Males



Females



TOTAL PROTEIN (G/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	40.8	43.8
	SD	3.3	2.3
II	XM	40.4	43.8
	SD	3.8	3.3
III	XM	42.0	42.8
	SD	2.0	3.8
IV	XM	42.8	44.8
	SD	2.2	2.3

Group	F(3, 16) =	.5
Time	F(1, 16) =	9.2 **
Group X Time	F(3, 16) =	.6

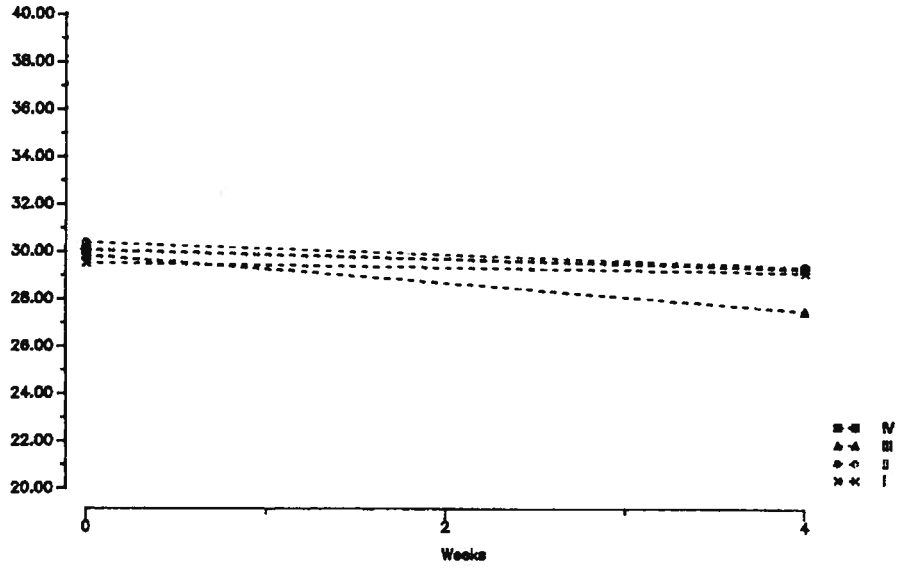
Females

Group		Week 0	Week 4
I	XM	44.0	45.6
	SD	3.6	4.2
II	XM	41.4	45.4
	SD	3.3	2.5
III	XM	44.2	45.4
	SD	4.3	2.9
IV	XM	45.4	45.4
	SD	3.4	2.7

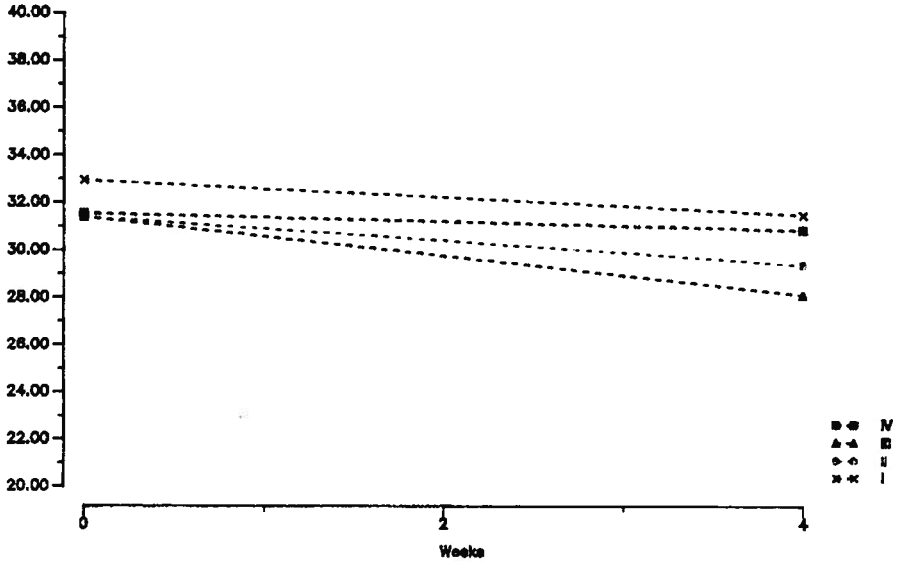
Group	F(3, 16) =	.4
Time	F(1, 16) =	4.0
Group X Time	F(3, 16) =	1.0

ALBUMIN (G/L)

30-05-0387-90 Males



Females



ALBUMIN (G/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	29.50	29.10
	SD	2.07	1.12
II	XM	30.40	29.38
	SD	3.25	1.31
III	XM	29.86	27.50
	SD	1.49	2.07
IV	XM	30.06	29.28
	SD	.92	1.04

Group	F(3, 16) =	.7
Time	F(1, 16) =	5.1 *
Group X Time	F(3, 16) =	.7

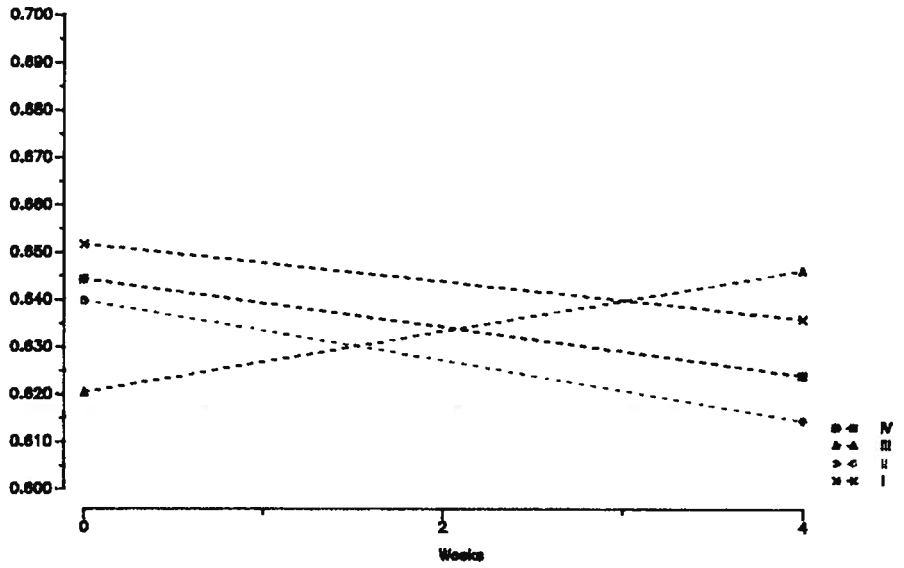
Females

Group		Week 0	Week 4
I	XM	32.92	31.46
	SD	3.59	1.54
II	XM	31.42	29.40
	SD	1.19	2.49
III	XM	31.40	28.12
	SD	2.76	1.15
IV	XM	31.54	30.84
	SD	1.34	1.14

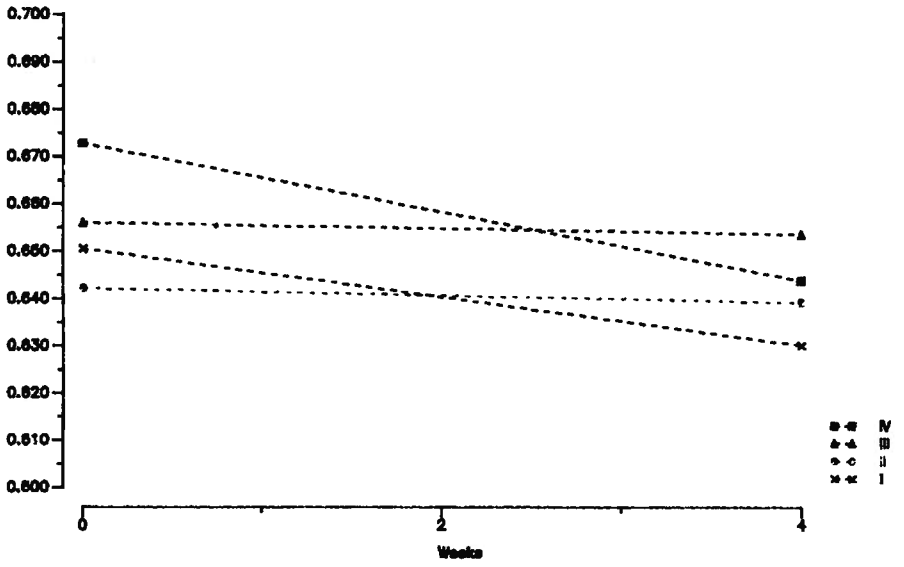
Group	F(3, 16) =	2.1
Time	F(1, 16) =	9.7 **
Group X Time	F(3, 16) =	.8

ELECTROPHORESIS: ALBUMIN

30–05–0387–90 Males



Females



Males

Group		Week 0	Week 4
I	XM	.6516	.6358
	SD	.0148	.0209
II	XM	.6398	.6144
	SD	.0054	.0298
III	XM	.6204	.6462
	SD	.0361	.0254
IV	XM	.6444	.6240
	SD	.0187	.0312

Group	F(3, 16) =	.7
Time	F(1, 16) =	1.6
Group X Time	F(3, 16) =	2.7

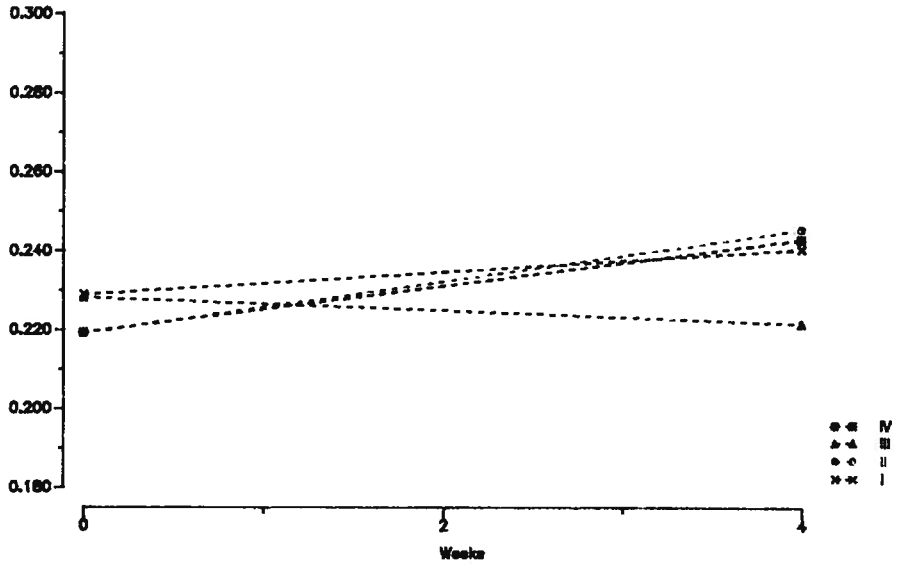
Females

Group		Week 0	Week 4
I	XM	.6504	.6300
	SD	.0201	.0233
II	XM	.6422	.6392
	SD	.0118	.0197
III	XM	.6560	.6536
	SD	.0256	.0188
IV	XM	.6728	.6438
	SD	.0217	.0300

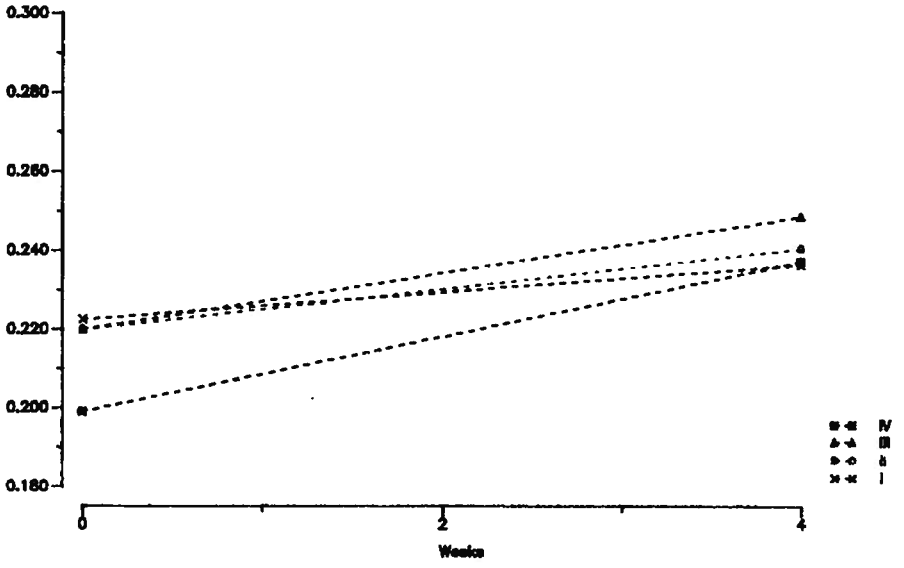
Group	F(3, 16) =	1.4
Time	F(1, 16) =	5.6 *
Group X Time	F(3, 16) =	1.3

ELECTROPHORESIS: GLOBULIN A1 + A2

30-05-0387-90 Males



Females



Males

Group		Week 0	Week 4
I	XM	.2288	.2404
	SD	.0101	.0084
II	XM	.2192	.2454
	SD	.0069	.0129
III	XM	.2282	.2214
	SD	.0150	.0159
IV	XM	.2194	.2430
	SD	.0078	.0090

Group	F(3, 16) =	1.3
Time	F(1, 16) =	16.4 ***
Group X Time	F(3, 16) =	5.0 *

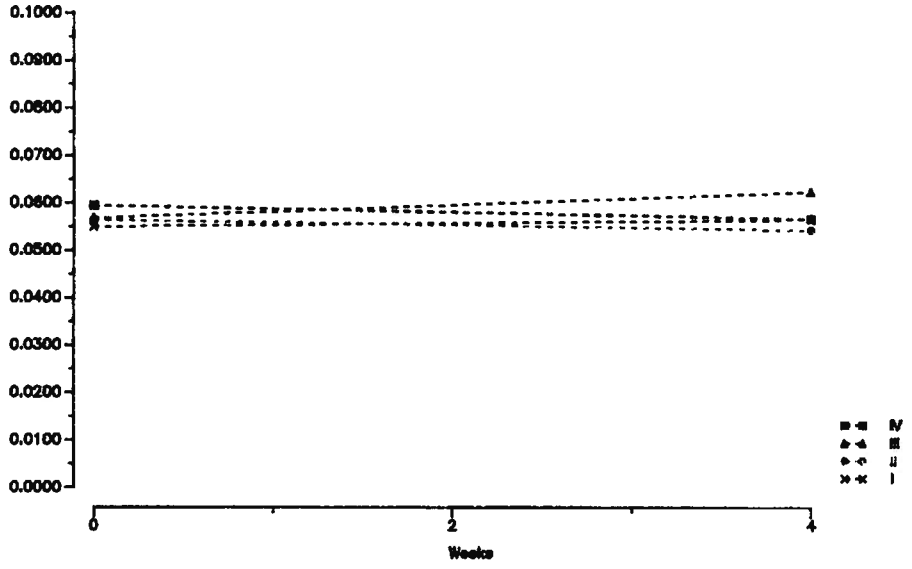
Females

Group		Week 0	Week 4
I	XM	.2224	.2364
	SD	.0151	.0191
II	XM	.2200	.2406
	SD	.0041	.0126
III	XM	.2200	.2486
	SD	.0084	.0173
IV	XM	.1992	.2374
	SD	.0210	.0134

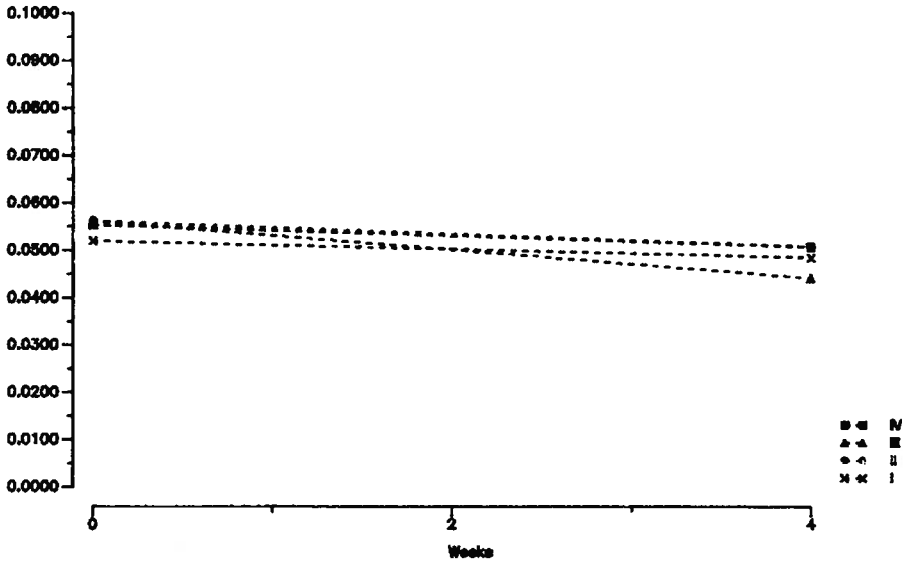
Group	F(3, 16) =	2.3
Time	F(1, 16) =	27.5 ***
Group X Time	F(3, 16) =	1.2

ELECTROPHORESIS: GLOBULIN B

30-05-0387-90 Males



Females



ELECTROPHORESIS: GLOBULIN β 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	.0548	.0564
	SD	.0112	.0049
II	XM	.0564	.0542
	SD	.0070	.0073
III	XM	.0568	.0624
	SD	.0075	.0052
IV	XM	.0594	.0566
	SD	.0071	.0078

Group	F(3, 16) =	.6
Time	F(1, 16) =	.1
Group X Time	F(3, 16) =	.9

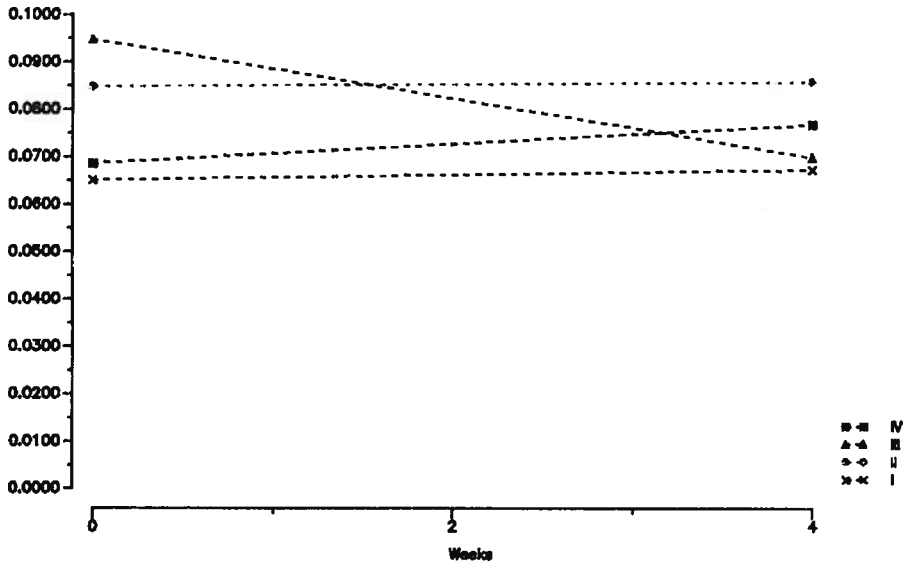
Females

Group		Week 0	Week 4
I	XM	.0518	.0484
	SD	.0043	.0057
II	XM	.0562	.0508
	SD	.0108	.0045
III	XM	.0562	.0442
	SD	.0092	.0076
IV	XM	.0554	.0508
	SD	.0086	.0094

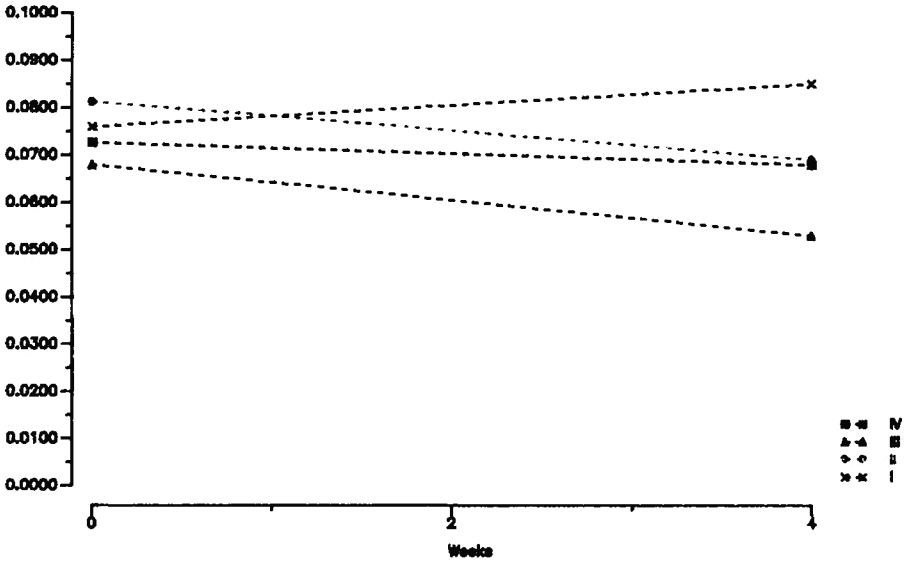
Group	F(3, 16) =	.4
Time	F(1, 16) =	9.9 **
Group X Time	F(3, 16) =	.9

ELECTROPHORESIS: GLOBULIN G

30-05-0387-90 Males



Females



ELECTROPHORESIS: GLOBULIN G

30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	.0650	.0672
	SD	.0082	.0196
II	XM	.0848	.0858
	SD	.0033	.0330
III	XM	.0948	.0698
	SD	.0173	.0199
IV	XM	.0686	.0768
	SD	.0137	.0200

Group	F(3, 16) =	2.3
Time	F(1, 16) =	.3
Group X Time	F(3, 16) =	1.5

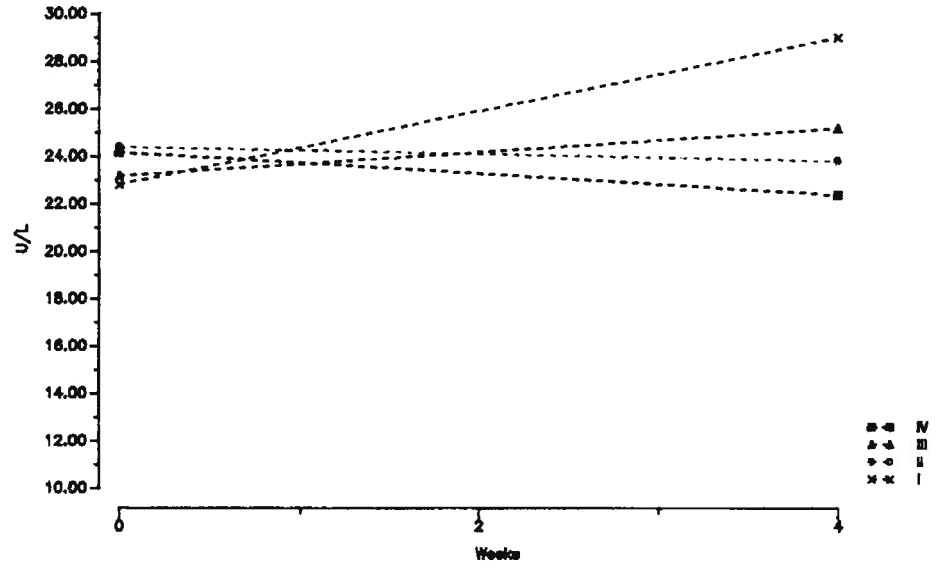
Females

Group		Week 0	Week 4
I	XM	.0758	.0852
	SD	.0175	.0220
II	XM	.0812	.0690
	SD	.0143	.0130
			*
III	XM	.0680	.0530
	SD	.0119	.0203
IV	XM	.0726	.0680
	SD	.0056	.0108

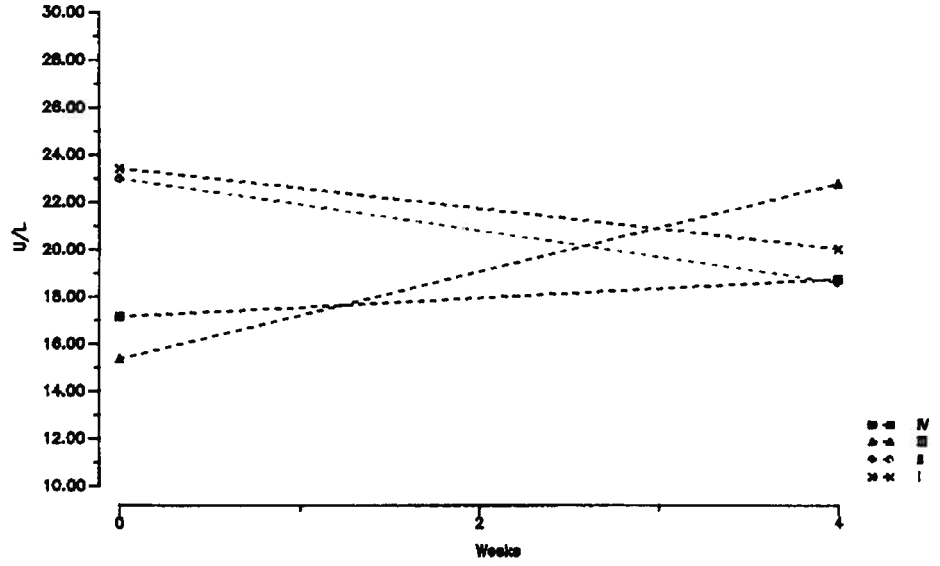
Group	F(3, 16) =	1.8
Time	F(1, 16) =	4.8 *
Group X Time	F(3, 16) =	4.6 *

ALT

30-05-0387-90 Males



Females



ALT (U/L)

Males

Group		Week 0	Week 4
I	XM	22.8	29.0
	SD	8.9	13.2
II	XM	24.4	23.8
	SD	5.6	3.6
III	XM	23.2	25.2
	SD	10.6	8.8
IV	XM	24.2	22.4
	SD	12.5	3.6

Group	F(3, 16) =	.1
Time	F(1, 16) =	.3
Group X Time	F(3, 16) =	.4

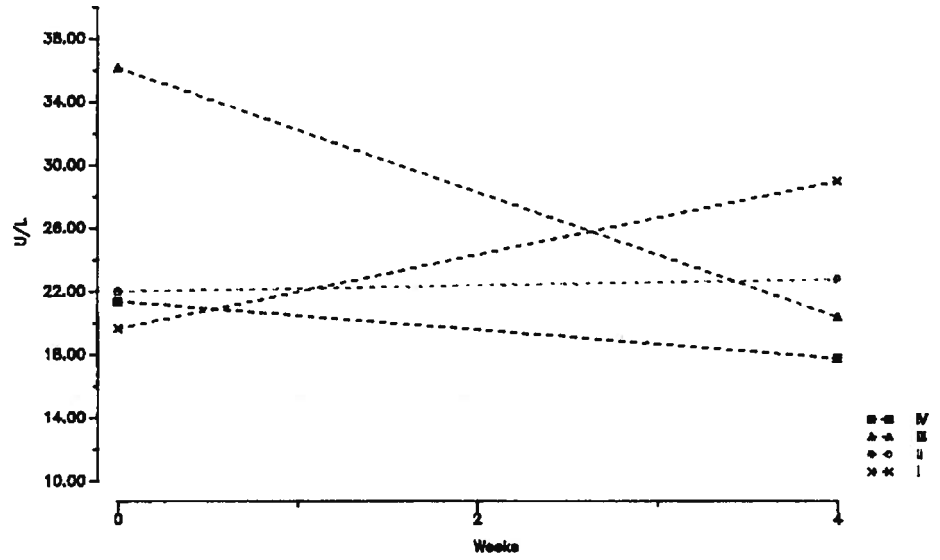
Females

Group		Week 0	Week 4
I	XM	23.4	20.0
	SD	6.3	4.1
II	XM	23.0	18.6
	SD	11.7	3.7
III	XM	15.4	22.8
	SD	6.4	10.4
IV	XM	17.2	18.8
	SD	2.9	3.0

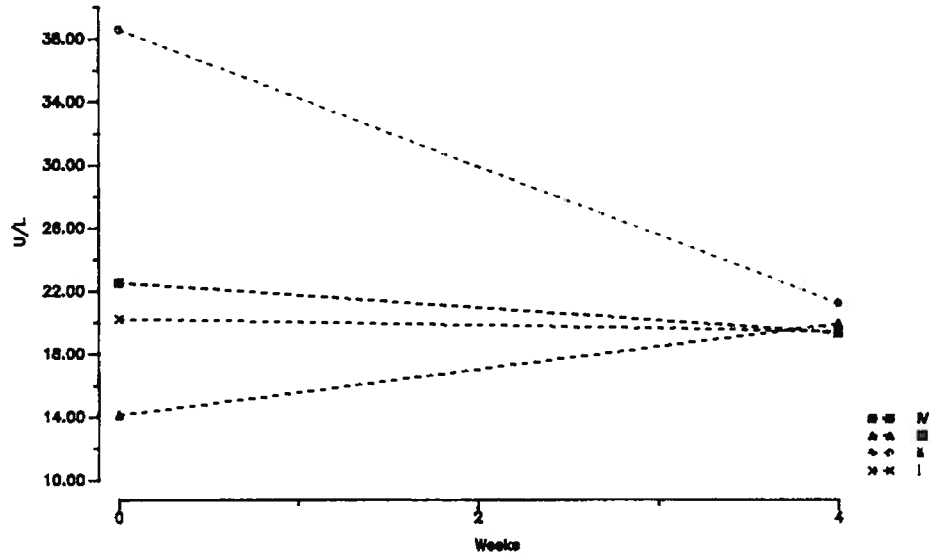
Group	F(3, 16) =	.5
Time	F(1, 16) =	.0
Group X Time	F(3, 16) =	2.0

AST

30–05–0387–90 Males



Females



AST (U/L)

30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	19.6	29.0
	SD	5.2	19.3
II	XM	22.0	22.8
	SD	10.2	6.0
III	XM	36.2	20.4
	SD	42.4	3.3
IV	XM	21.4	17.8
	SD	8.1	4.2

Group	F(3, 16) =	.5
Time	F(1, 16) =	.2
Group X Time	F(3, 16) =	.9

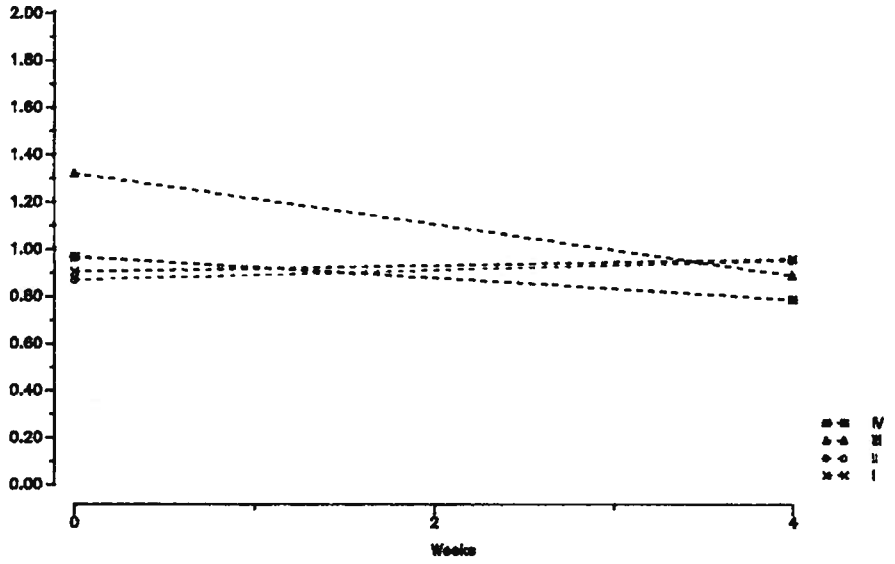
Females

Group		Week 0	Week 4
I	XM	20.2	19.4
	SD	7.6	3.3
II	XM	38.6	21.2
	SD	49.0	5.2
III	XM	14.2	20.0
	SD	5.8	9.2
IV	XM	22.6	19.4
	SD	9.5	4.7

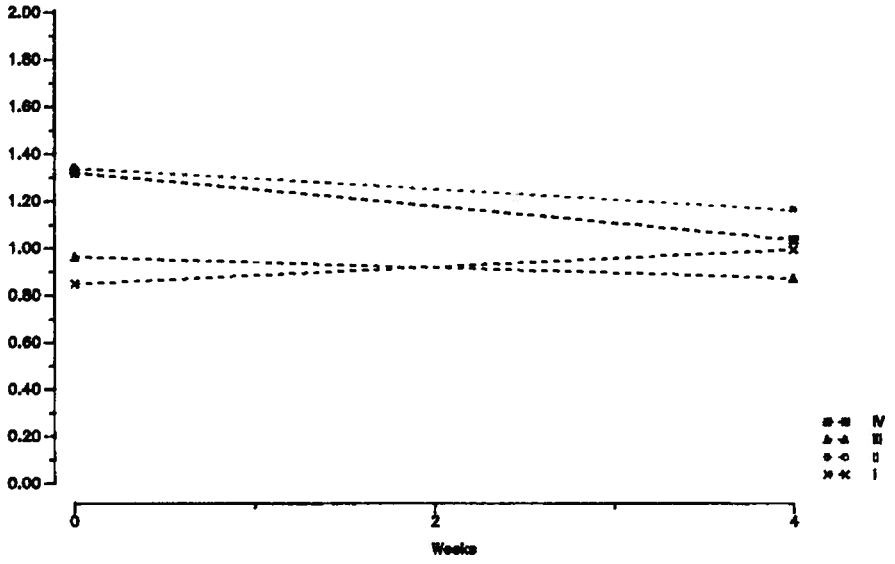
Group	F(3, 16) =	.9
Time	F(1, 16) =	.4
Group X Time	F(3, 16) =	.7

AST/ALT

30-05-0387-90 Males



Females



Males

Group		Week 0	Week 4
I	XM	.902	.958
	SD	.242	.335
II	XM	.872	.956
	SD	.250	.218
III	XM	1.322	.888
	SD	.854	.351
IV	XM	.970	.788
	SD	.249	.106

Group	F(3, 16) =	.6
Time	F(1, 16) =	1.0
Group X Time	F(3, 16) =	1.1

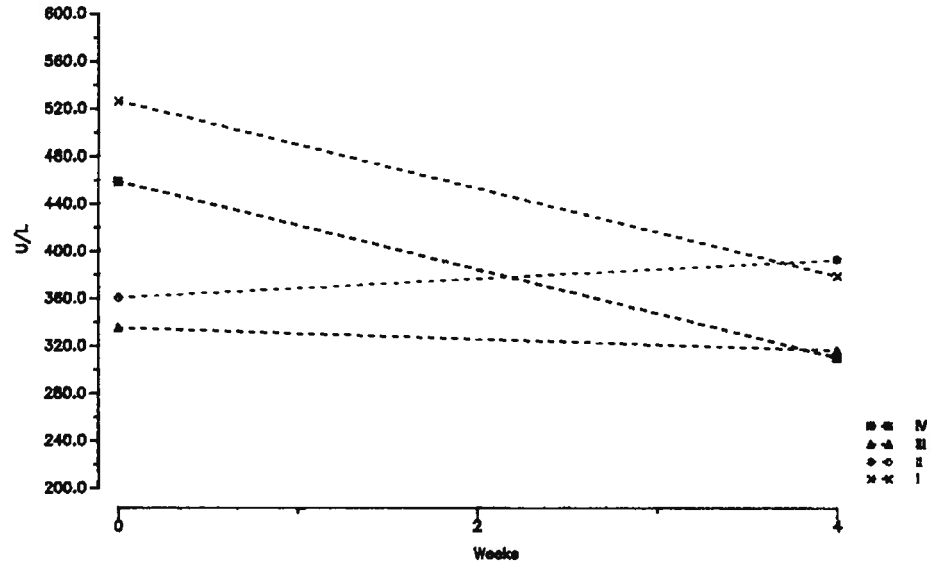
Females

Group		Week 0	Week 4
I	XM	.846	.994
	SD	.119	.256
II	XM	1.342	1.164
	SD	.922	.341
III	XM	.964	.874
	SD	.280	.094
IV	XM	1.322	1.038
	SD	.589	.259

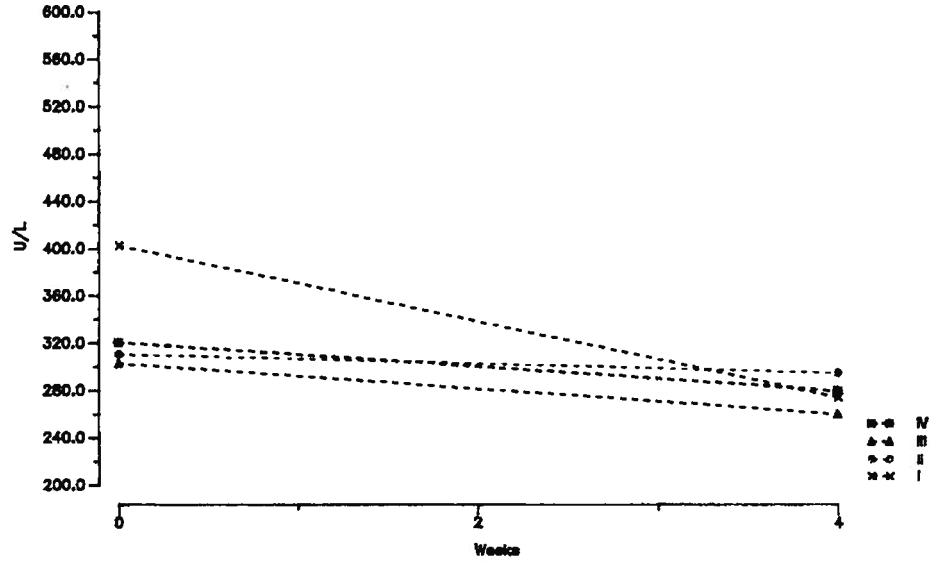
Group	F(3, 16) =	1.6
Time	F(1, 16) =	.5
Group X Time	F(3, 16) =	.4

ALK. PHOSPHATASE

30-05-0387-90 Males



Females



ALK. PHOSPHATASE (U/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	526.2	378.6
	SD	134.9	86.7
II	XM	361.4	393.6
	SD	58.2	80.0
III	XM	335.6	316.4
	SD	54.4	75.0
IV	XM	459.0	310.0
	SD	86.0	42.9

Group	F(3, 16) =	2.9
Time	F(1, 16) =	12.2 **
Group X Time	F(3, 16) =	5.1 *

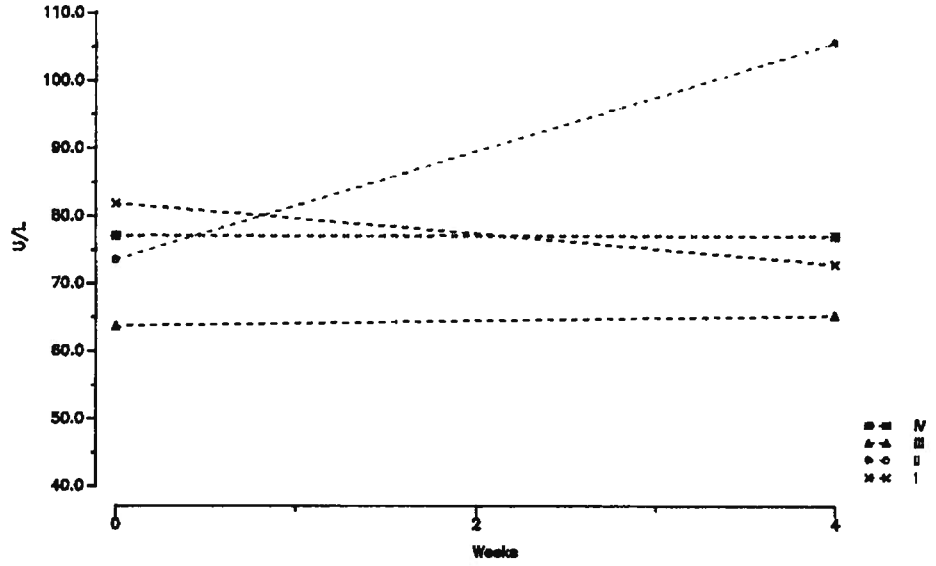
Females

Group		Week 0	Week 4
I	XM	402.0	274.0
	SD	126.6	59.7
II	XM	311.6	295.6
	SD	46.4	37.8
III	XM	303.6	260.6
	SD	25.0	18.7
IV	XM	321.0	280.2
	SD	43.2	59.4

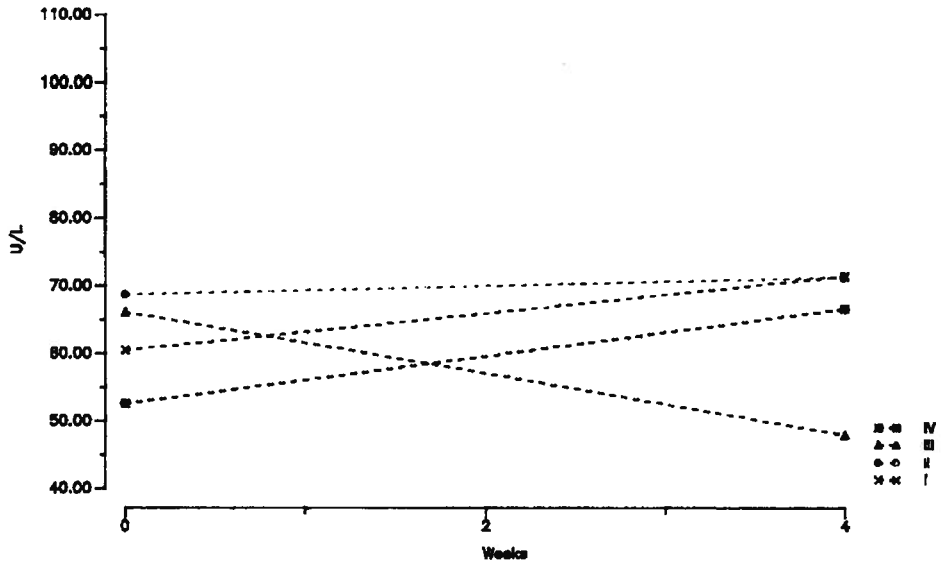
Group	F(3, 16) =	1.2
Time	F(1, 16) =	10.7 **
Group X Time	F(3, 16) =	2.0

LDH

30-05-0387-90 Males



Females



LDH (U/L)

30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	81.8	72.8
	SD	17.6	7.9
II	XM	73.6	105.6
	SD	25.2	38.0
III	XM	63.8	65.4
	SD	38.7	21.6
IV	XM	77.2	77.2
	SD	13.2	13.7

Group	F(3, 16) =	1.3
Time	F(1, 16) =	1.0
Group X Time	F(3, 16) =	2.2

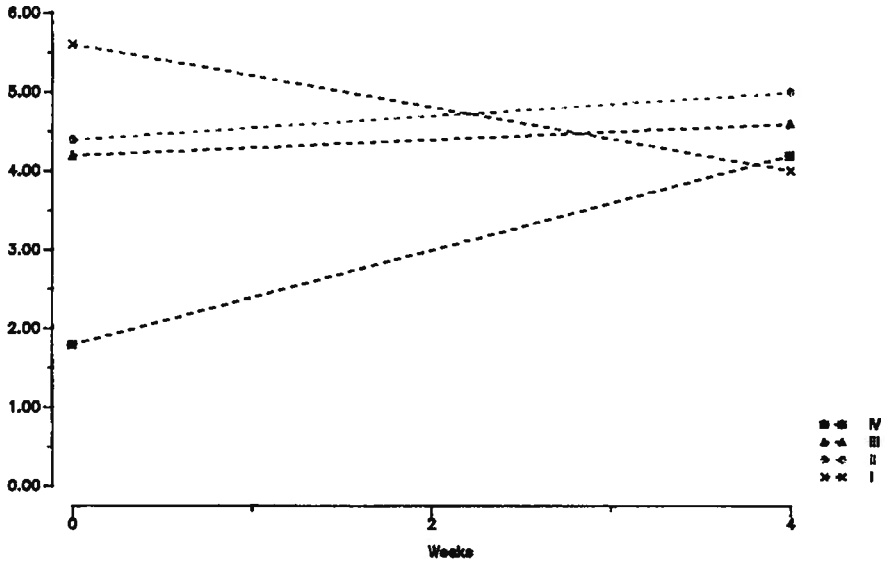
Females

Group		Week 0	Week 4
I	XM	60.4	71.4
	SD	16.9	17.5
II	XM	68.8	71.4
	SD	12.5	32.3
III	XM	66.2	48.0
	SD	28.1	12.0
IV	XM	52.8	66.8
	SD	22.3	20.1

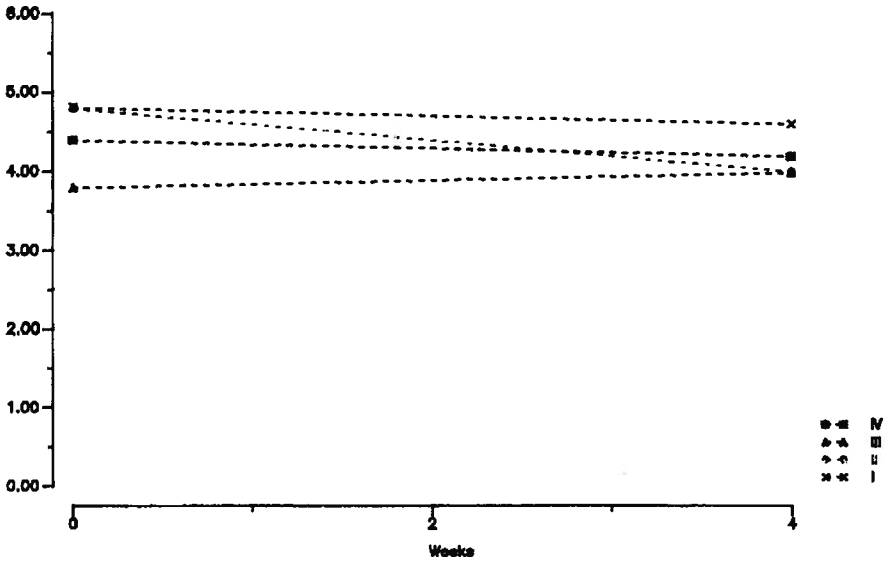
Group	F(3, 16) =	.9
Time	F(1, 16) =	.1
Group X Time	F(3, 16) =	1.0

GAMMA GT (U/L)

30-05-0387-90 Males



Females



GAMMA- GT /U/L)

30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	5.6	4.0
	SD	3.6	.7
II	XM	4.4	5.0
	SD	1.1	1.0
III	XM	4.2	4.6
	SD	2.8	.5
IV	XM	1.8	4.2
	SD	1.3	.4

Group	F(3, 16) =	2.2
Time	F(1, 16) =	.6
Group X Time	F(3, 16) =	2.0

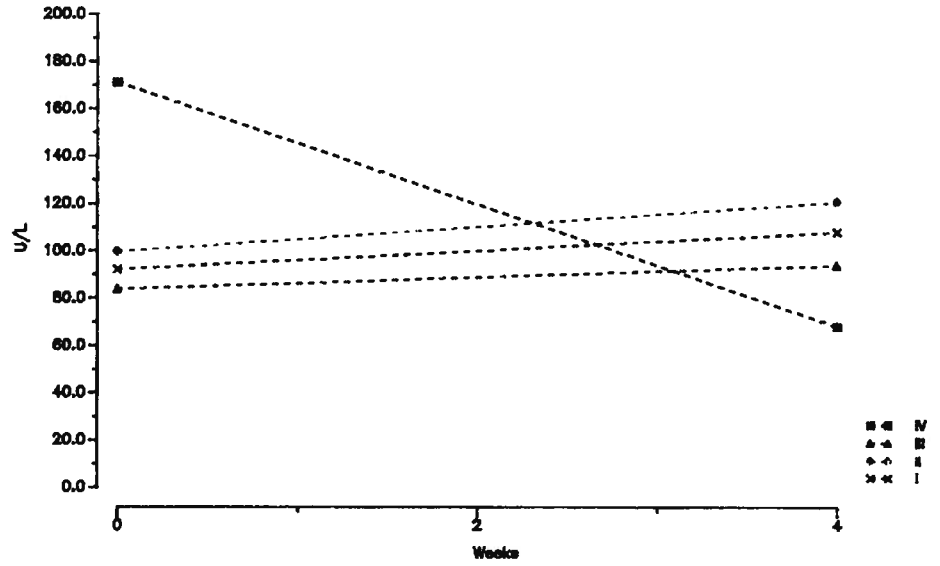
Females

Group		Week 0	Week 4
I	XM	4.8	4.6
	SD	2.8	.5
II	XM	4.8	4.0
	SD	3.3	1.2
III	XM	3.8	4.0
	SD	.8	.0
IV	XM	4.4	4.2
	SD	2.6	.4

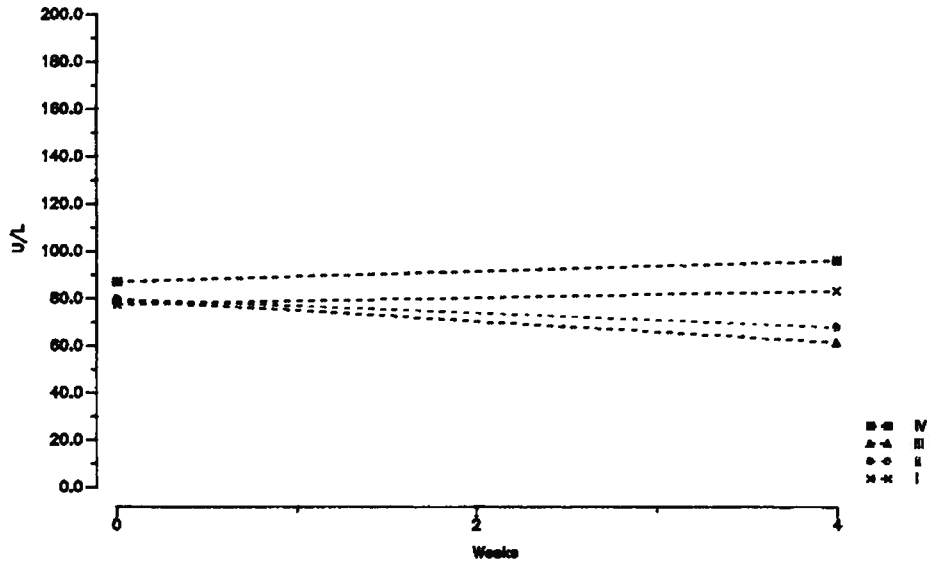
Group	F(3, 16) =	.3
Time	F(1, 16) =	.2
Group X Time	F(3, 16) =	.1

CK

30–05–0387–90 Males



Females



CK (U/L)

30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	91.8	107.8
	SD	32.9	38.8
II	XM	99.8	120.8
	SD	62.0	61.2
III	XM	83.8	94.0
	SD	17.4	37.0
IV	XM	171.0	67.8
	SD	42.8	15.2

Group	F(3, 16) =	1.5
Time	F(1, 16) =	.8
Group X Time	F(3, 16) =	3.8 *

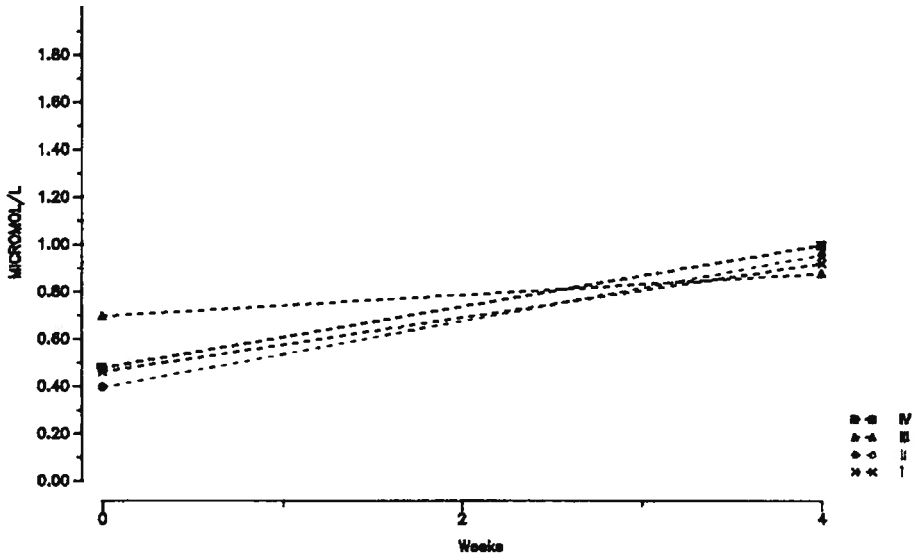
Females

Group		Week 0	Week 4
I	XM	77.2	83.2
	SD	24.0	23.3
II	XM	80.0	68.2
	SD	42.9	25.6
III	XM	79.4	61.6
	SD	19.7	12.7
IV	XM	87.2	96.4
	SD	63.2	48.4

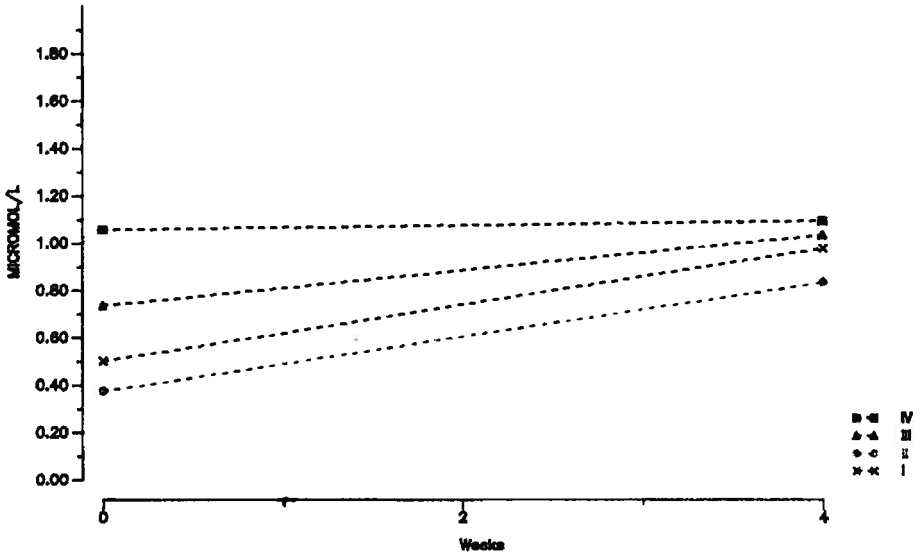
Group	F(3, 16) =	.9
Time	F(1, 16) =	.1
Group X Time	F(3, 16) =	.3

TOTAL BILIRUBIN

30–05–0387–90 Males



Females



TOTAL BILIRUBIN (MICROMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	.46	.92
	SD	.31	.19
II	XM	.40	.96
	SD	.07	.19
III	XM	.70	.88
	SD	.25	.18
IV	XM	.48	1.00
	SD	.11	.19

Group	F(3, 16) =	.6
Time	F(1, 16) =	49.3 ***
Group X Time	F(3, 16) =	2.0

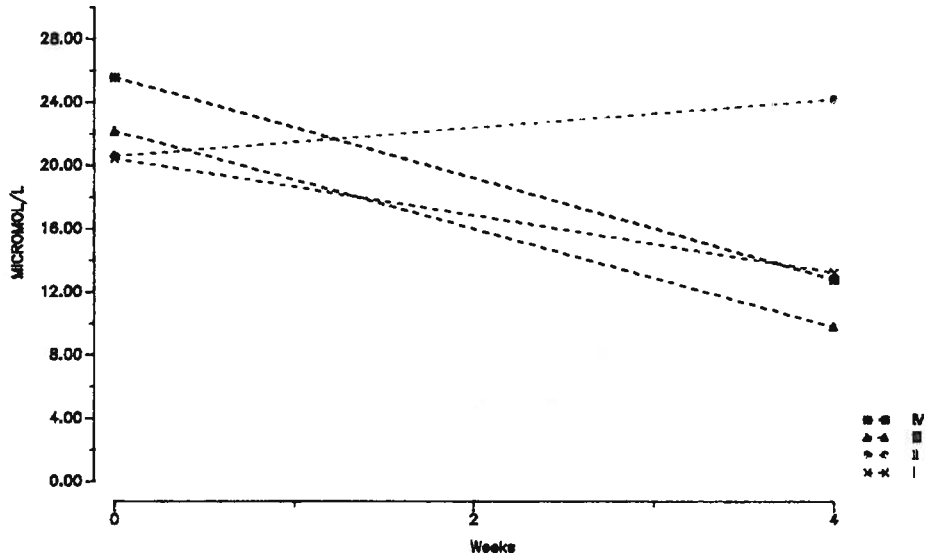
Females

Group		Week 0	Week 4
I	XM	.50	.98
	SD	.22	.08
II	XM	.38	.84
	SD	.11	.11
III	XM	.74	1.04
	SD	.42	.23
IV	XM	1.06	1.10
	SD	.87	.07

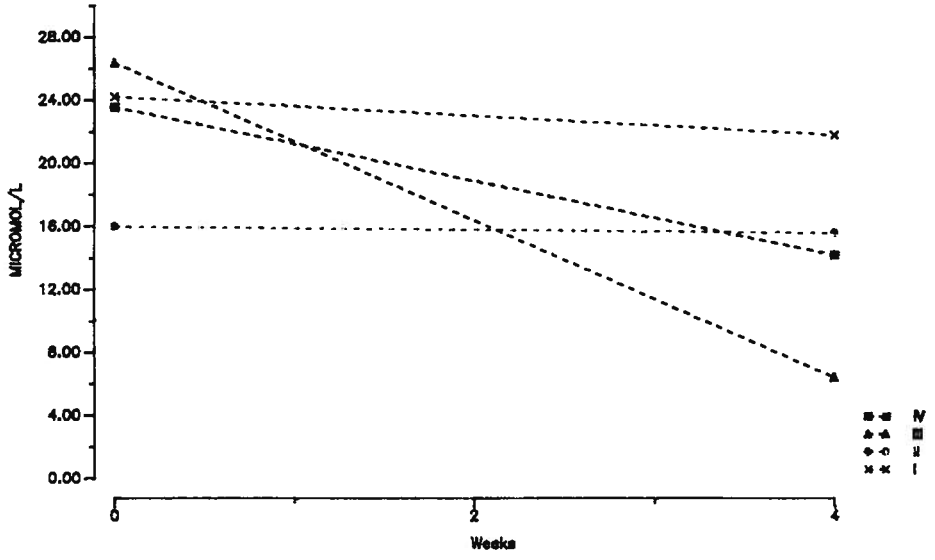
Group	F(3, 16) =	3.5 *
Time	F(1, 16) =	6.7 *
Group X Time	F(3, 16) =	.7

URIC ACID

30-05-0387-90 Males



Females



URIC ACID (MICROMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	20.4	13.2
	SD	10.7	3.9
II	XM	20.6	24.2
	SD	6.3	19.1
III	XM	22.2	9.8
	SD	10.9	7.8
IV	XM	25.6	12.8
	SD	6.2	6.3

Group	F(3, 16) =	.8
Time	F(1, 16) =	5.2 *
Group X Time	F(3, 16) =	1.5

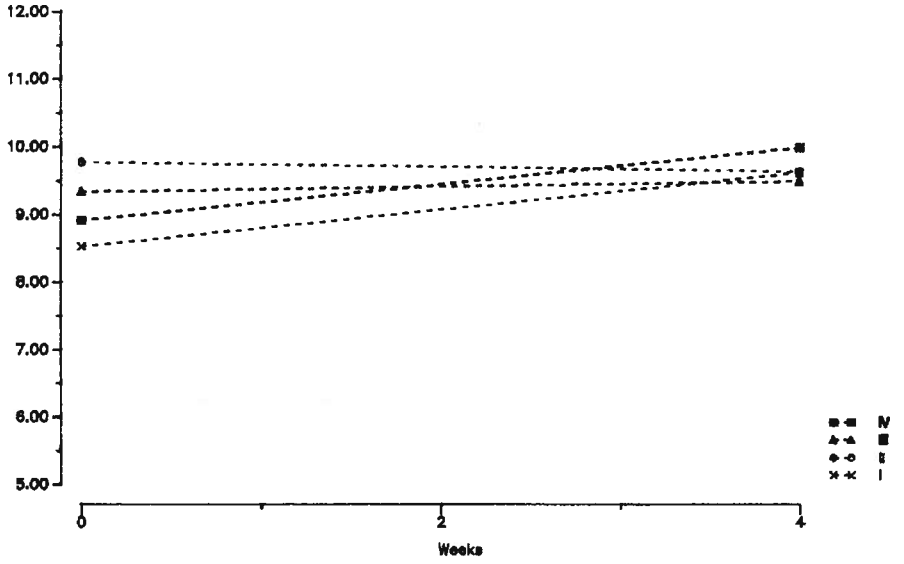
Females

Group		Week 0	Week 4
I	XM	24.2	21.8
	SD	7.5	11.6
II	XM	16.0	15.6
	SD	7.0	16.0
III	XM	26.4	6.4
	SD	14.1	4.0
IV	XM	23.6	14.2
	SD	7.6	4.8

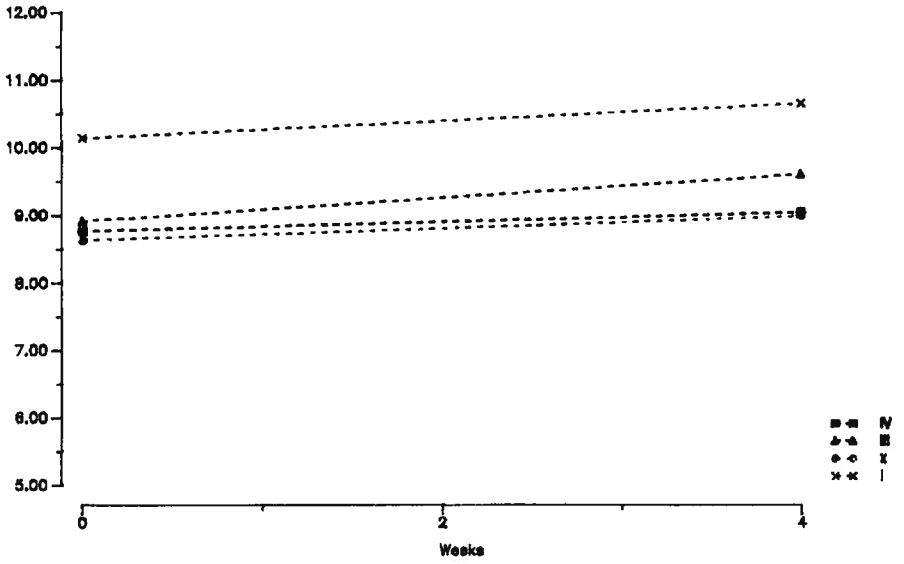
Group	F(3, 16) =	.8
Time	F(1, 16) =	10.8 **
Group X Time	F(3, 16) =	3.3 *

BUN (MMOL/L)

30-05-0387-90 Males



Females



Males

Group		Week 0	Week 4
I	XM	8.52	9.62
	SD	.88	.91
II	XM	9.78	9.64
	SD	.91	.85
III	XM	9.34	9.50
	SD	1.22	1.14
IV	XM	8.92	10.00
	SD	.83	1.20

Group	F(3, 16) =	.5
Time	F(1, 16) =	5.9 *
Group X Time	F(3, 16) =	2.0

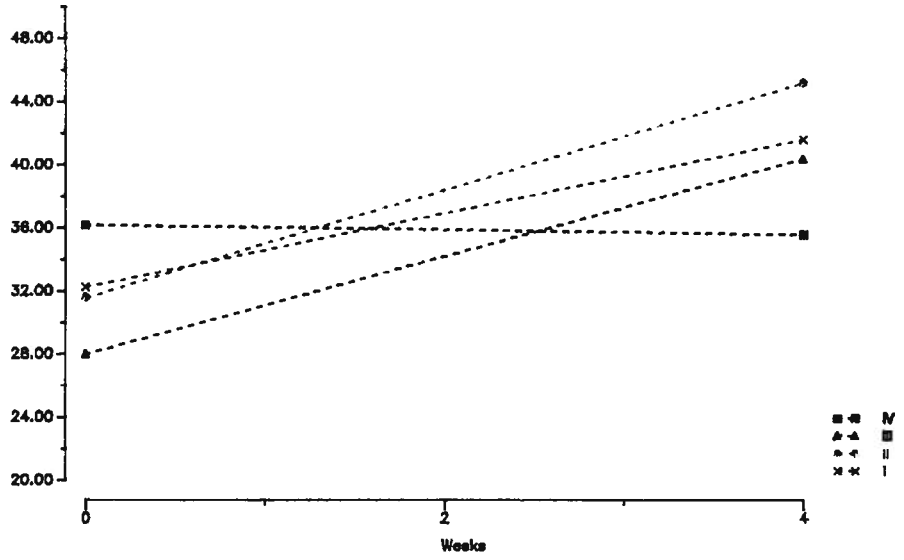
Females

Group		Week 0	Week 4
I	XM	10.14	10.66
	SD	1.40	.78
II	XM	8.64	9.00
	SD	.47	1.16
III	XM	8.92	9.62
	SD	.93	.90
IV	XM	8.78	9.06
	SD	.52	1.33

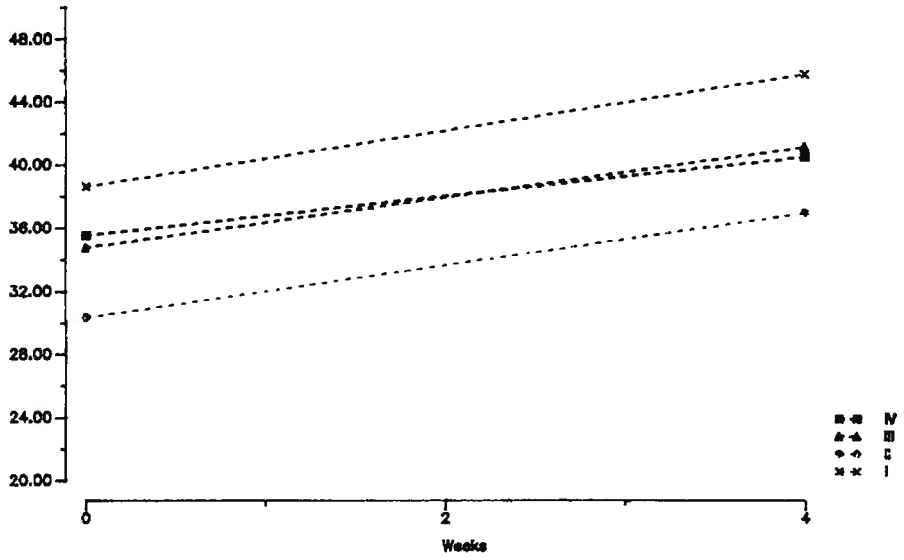
Group	F(3, 16) =	5.4 **
Time	F(1, 16) =	2.2
Group X Time	F(3, 16) =	.1

CREATININE (MICROMOL/L)

30–05–0387–90 Males



Females



CREATININE (MICROMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	32.2	41.6
	SD	7.6	4.9
II	XM	31.6	45.2
	SD	3.5	5.2
III	XM	28.0	40.4
	SD	13.9	4.9
IV	XM	36.2	35.6
	SD	3.0	5.9

Group	F(3, 16) =	.6
Time	F(1, 16) =	17.6 ***
Group X Time	F(3, 16) =	2.4

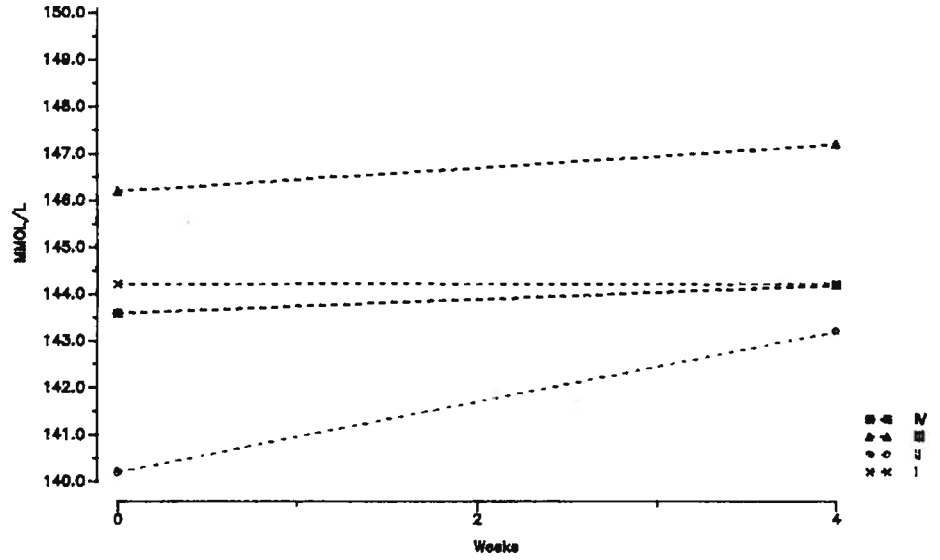
Females

Group		Week 0	Week 4
I	XM	38.6	45.8
	SD	4.5	5.4
II	XM	30.4	37.0
	SD	5.0	8.6
III	XM	34.8	41.2
	SD	6.8	4.1
IV	XM	35.6	40.6
	SD	4.0	7.1

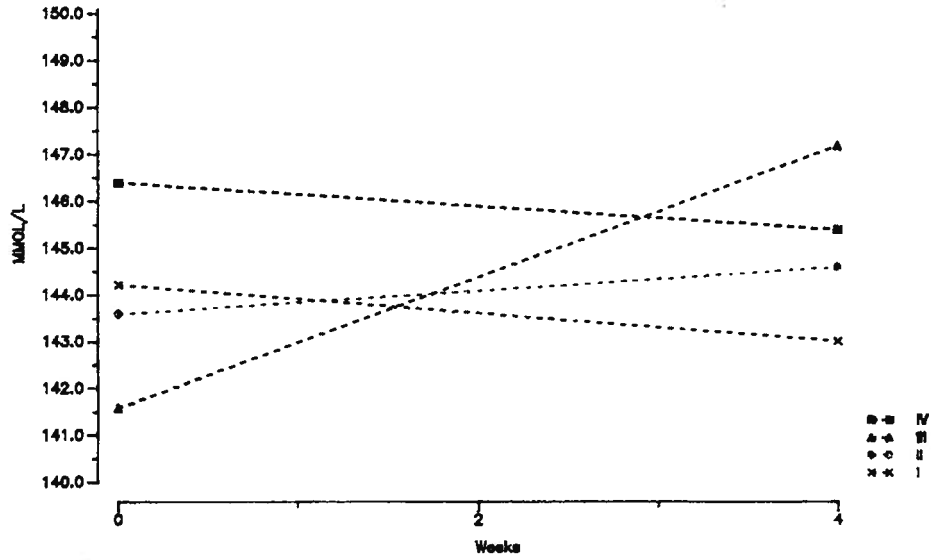
Group	F(3, 16) =	3.3 *
Time	F(1, 16) =	11.9 **
Group X Time	F(3, 16) =	.1

SODIUM

30-05-0387-90 Males



Females



SODIUM (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	144.2	144.2
	SD	4.4	4.2
II	XM	140.2	143.2
	SD	8.6	4.2
III	XM	146.2	147.2
	SD	.4	5.4
IV	XM	143.6	144.2
	SD	3.0	2.2

Group	F(3, 16) =	1.7
Time	F(1, 16) =	.7
Group X Time	F(3, 16) =	.2

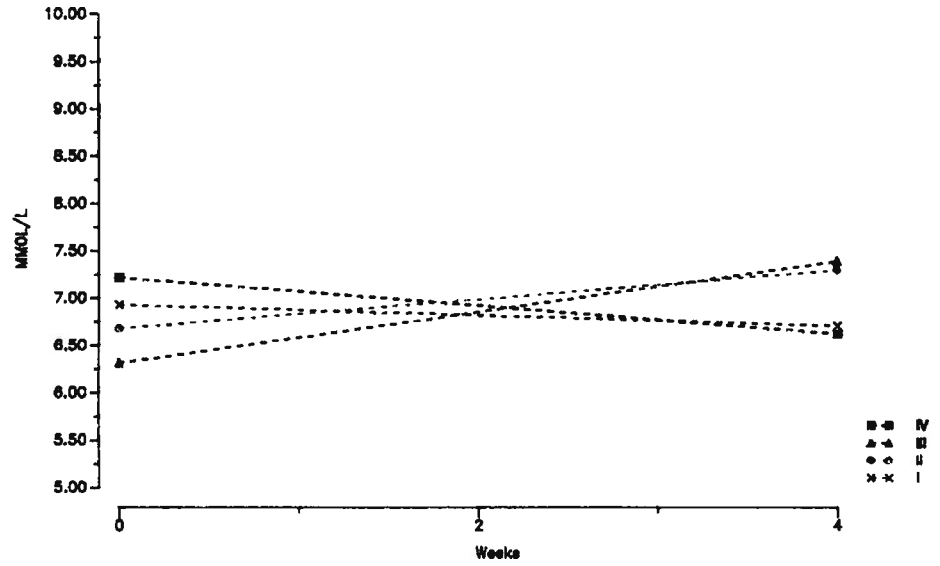
Females

Group		Week 0	Week 4
I	XM	144.2	143.0
	SD	3.8	1.2
II	XM	143.6	144.6
	SD	3.1	1.8
III	XM	141.6	147.2
	SD	4.7	2.4
IV	XM	146.4	145.4
	SD	2.6	3.0

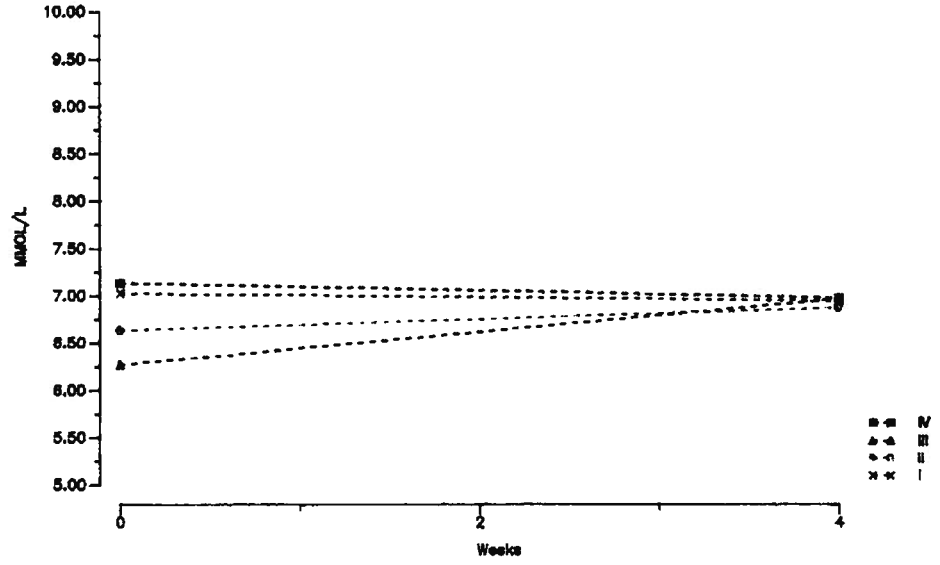
Group	F(3, 16) =	1.0
Time	F(1, 16) =	1.5
Group X Time	F(3, 16) =	3.1

POTASSIUM

30–05–0387–90 Males



Females



POTASSIUM (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	6.92	6.70
	SD	.72	.97
II	XM	6.68	7.30
	SD	1.11	1.28
III	XM	6.32	7.40
	SD	.47	.42
IV	XM	7.22	6.62
	SD	.81	.58

Group	F(3, 16) =	.1
Time	F(1, 16) =	2.0
Group X Time	F(3, 16) =	6.0 **

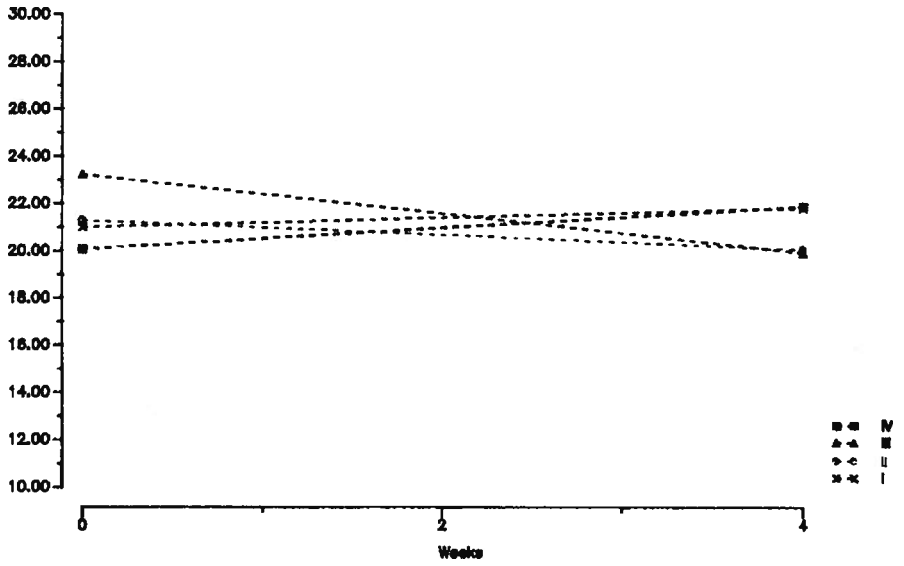
Females

Group		Week 0	Week 4
I	XM	7.02	6.94
	SD	1.03	.66
II	XM	6.64	6.88
	SD	.70	.41
III	XM	6.28	6.98
	SD	.88	.52
IV	XM	7.14	6.98
	SD	1.06	.46

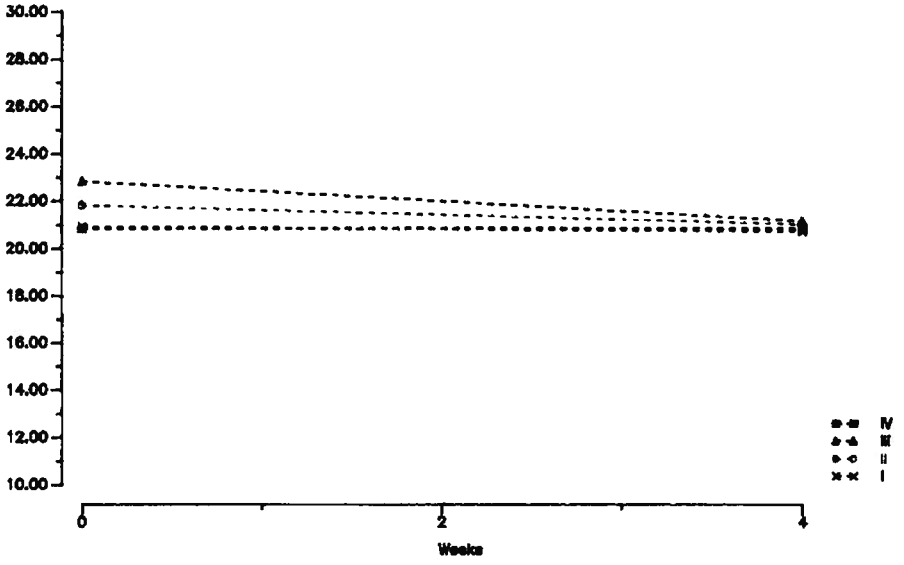
Group	F(3, 16) =	.5
Time	F(1, 16) =	.7
Group X Time	F(3, 16) =	.9

SODIUM/POTASSIUM

30-05-0387-90 Males



Females



Males

Group		Week 0	Week 4
I	XM	20.974	21.804
	SD	1.811	2.558
II	XM	21.312	20.070
	SD	2.739	3.279
III	XM	23.232	19.914
	SD	1.778	.810
IV	XM	20.104	21.906
	SD	2.487	1.804

Group	F(3, 16) =	.2
Time	F(1, 16) =	1.0
Group X Time	F(3, 16) =	5.9 **

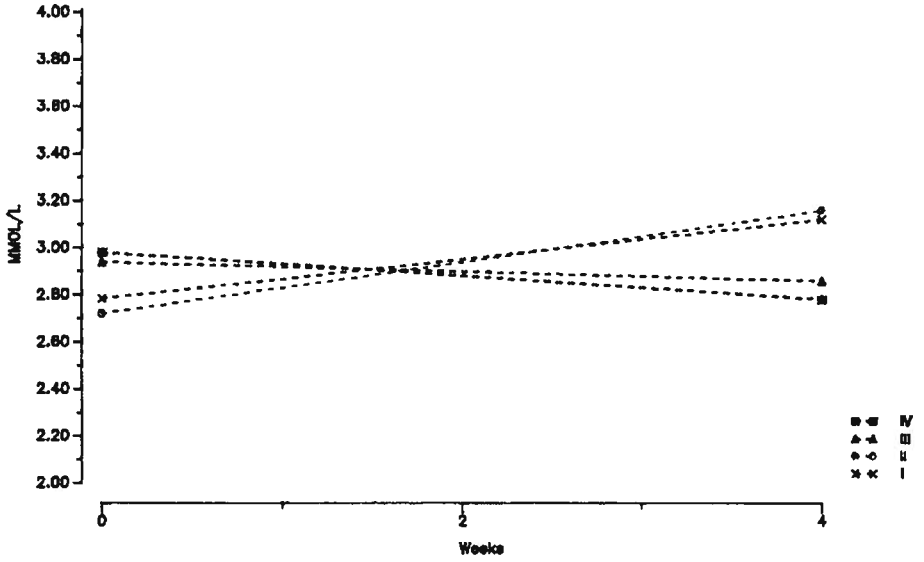
Females

Group		Week 0	Week 4
I	XM	20.884	20.738
	SD	3.029	1.796
II	XM	21.848	21.064
	SD	2.674	1.077
III	XM	22.846	21.180
	SD	2.814	1.615
IV	XM	20.878	20.898
	SD	3.212	1.451

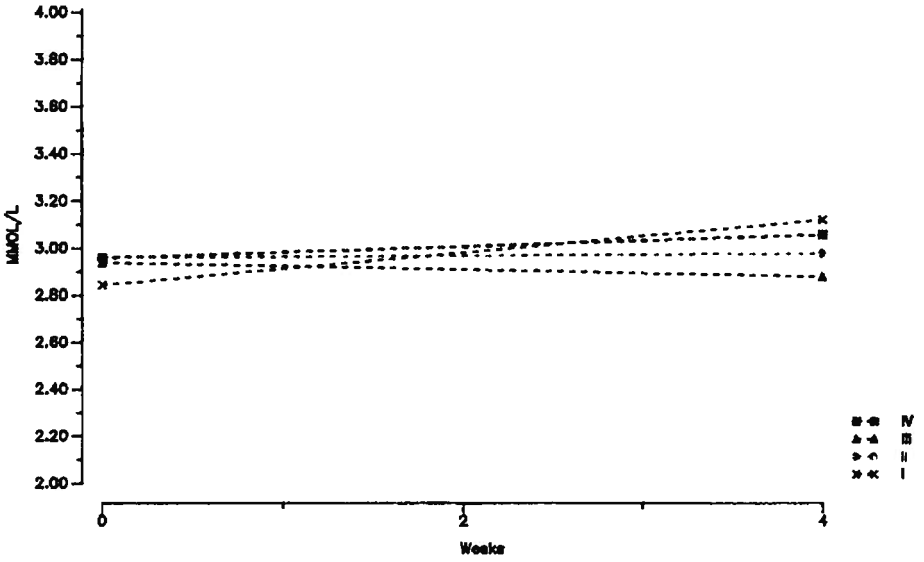
Group	F(3, 16) =	.5
Time	F(1, 16) =	1.0
Group X Time	F(3, 16) =	.4

CALCIUM

30–05–0387–90 Males



Females



CALCIUM (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	2.78	3.12
	SD	.28	.08
II	XM	2.72	3.16
	SD	.13	.24
III	XM	2.94	2.86
	SD	.15	.15
IV	XM	2.98	2.78
	SD	.22	.45

Group	F(3, 16) =	.2
Time	F(1, 16) =	3.4
Group X Time	F(3, 16) =	5.3 **

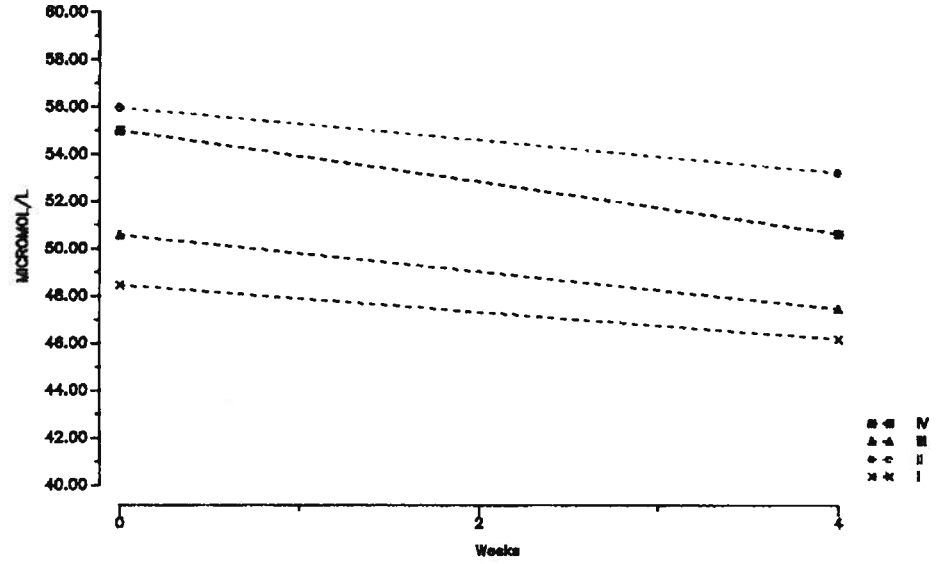
Females

Group		Week 0	Week 4
I	XM	2.84	3.12
	SD	.15	.24
II	XM	2.96	2.98
	SD	.13	.29
III	XM	2.94	2.88
	SD	.19	.20
IV	XM	2.96	3.06
	SD	.21	.17

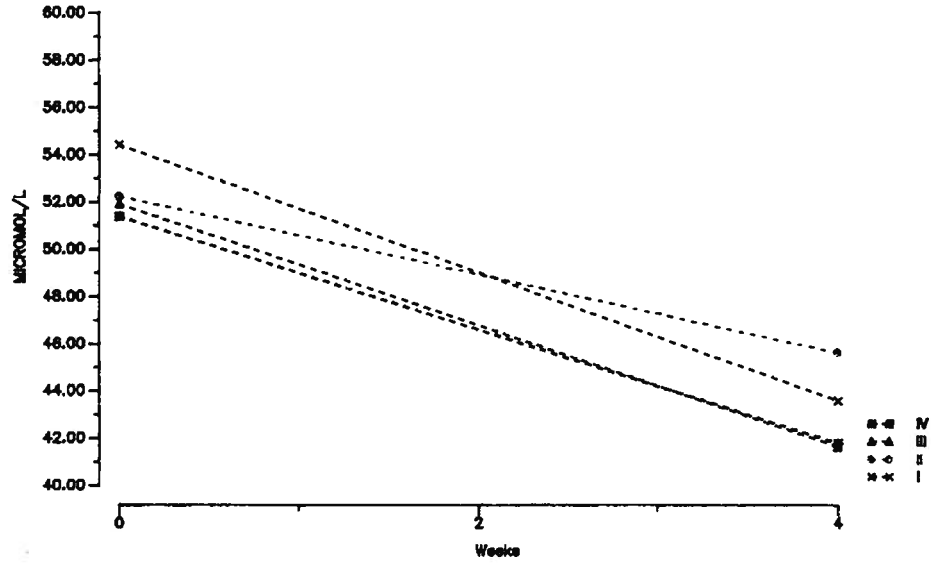
Group	F(3, 16) =	.4
Time	F(1, 16) =	1.7
Group X Time	F(3, 16) =	1.3

IRON

30–05–0387–90 Males



Females



IRON (MICROMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	48.42	46.16
	SD	5.34	3.33
II	XM	55.98	53.22
	SD	7.67	8.18
III	XM	50.58	47.46
	SD	6.36	5.68
IV	XM	55.00	50.62
	SD	6.95	7.08

Group	F(3, 16) =	1.8
Time	F(1, 16) =	4.8 *
Group X Time	F(3, 16) =	.1

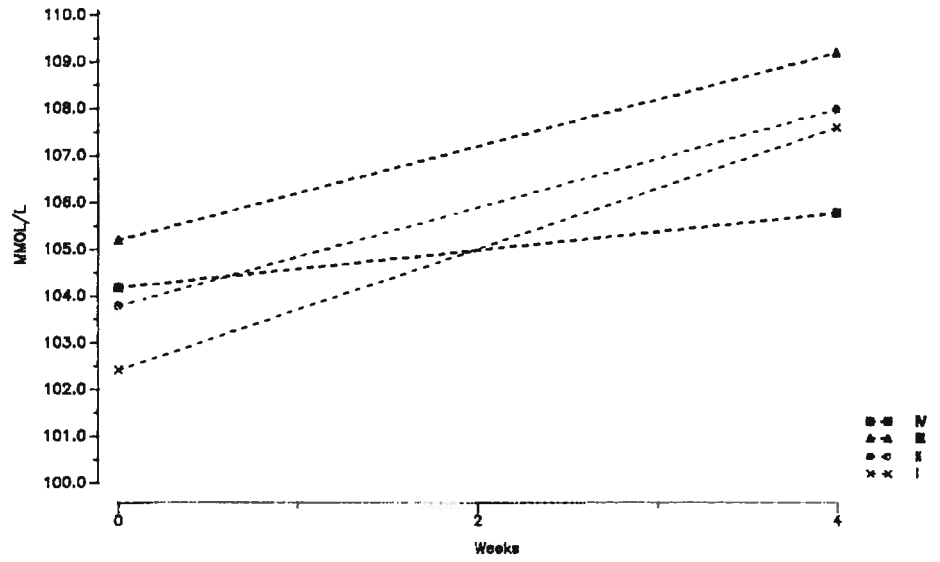
Females

Group		Week 0	Week 4
I	XM	54.40	43.56
	SD	7.78	8.47
II	XM	52.26	45.64
	SD	2.72	9.68
III	XM	51.92	41.64
	SD	6.49	9.71
IV	XM	51.38	41.78
	SD	9.73	4.93

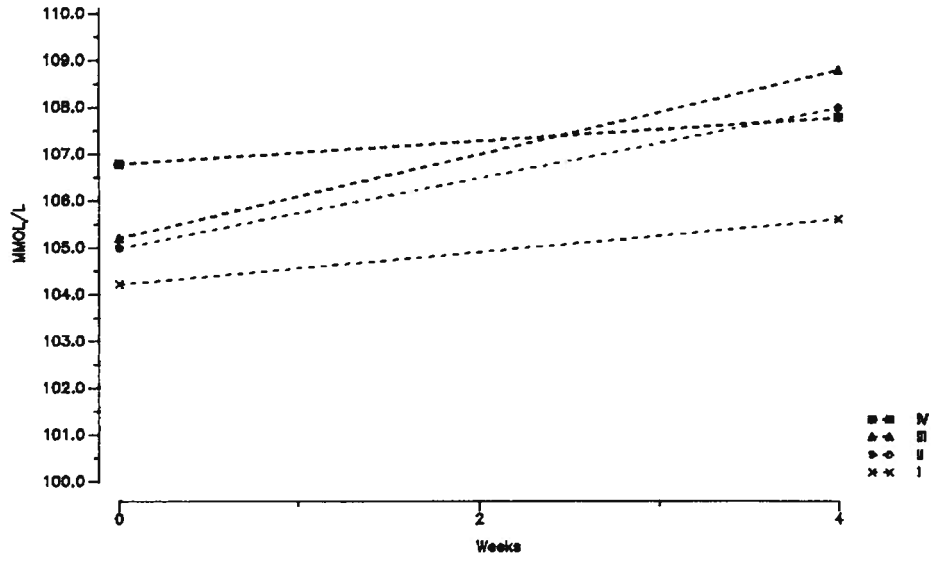
Group	F(3, 16) =	.2
Time	F(1, 16) =	24.2 ***
Group X Time	F(3, 16) =	.2

CHLORIDE

30–05–0387–90 Males



Females



CHLORIDE (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	102.4	107.6
	SD	2.1	1.8
II	XM	103.8	108.0
	SD	2.8	2.5
III	XM	105.2	109.2
	SD	1.3	2.9
IV	XM	104.2	105.8
	SD	2.4	3.3

Group	F(3, 16) =	1.6
Time	F(1, 16) =	27.3 ***
Group X Time	F(3, 16) =	1.1

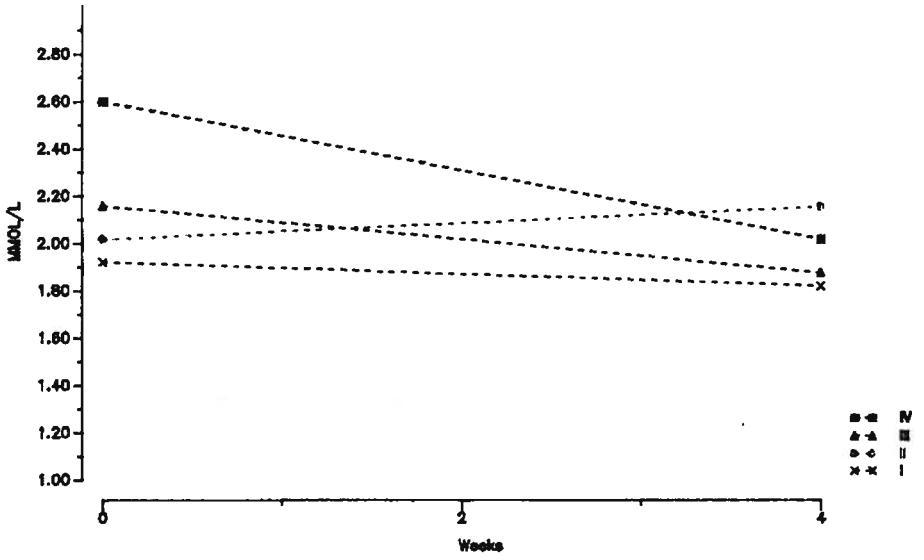
Females

Group		Week 0	Week 4
I	XM	104.2	105.6
	SD	2.4	2.7
II	XM	105.0	108.0
	SD	2.9	1.6
III	XM	105.2	108.8
	SD	4.1	1.3
IV	XM	106.8	107.8
	SD	2.7	2.2

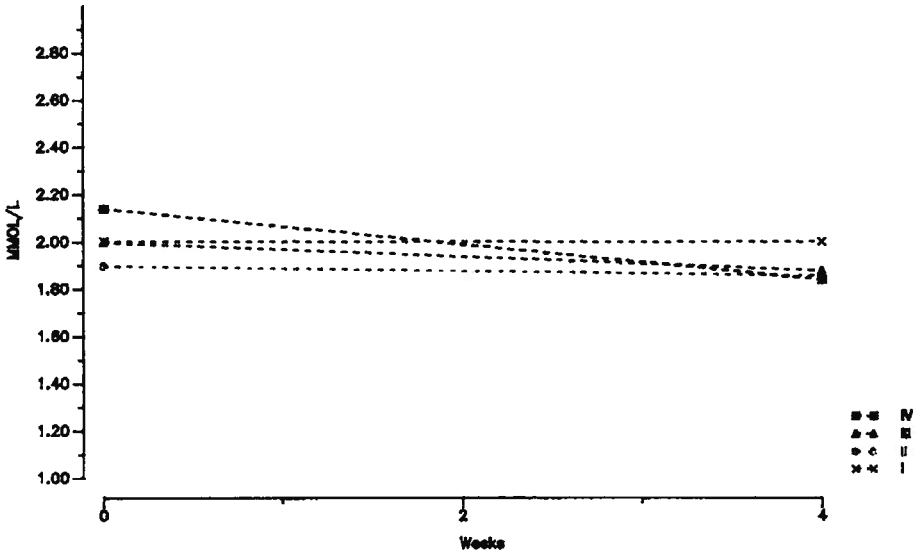
Group	F(3, 16) =	1.2
Time	F(1, 16) =	12.4 **
Group X Time	F(3, 16) =	1.0

INORG.PHOSPHORUS

30–05–0387–90 Males



Females



INORG.PHOSPHORUS (MMOL/L) 30-05-0387-90

Males

Group		Week 0	Week 4
I	XM	1.92	1.82
	SD	.22	.15
II	XM	2.02	2.16
	SD	.26	.23
III	XM	2.16	1.88
	SD	.17	.13
IV	XM	2.60	2.02
	SD	.36	.25

Group	F(3, 16) =	4.1 *
Time	F(1, 16) =	17.1 ***
Group X Time	F(3, 16) =	9.4 ***

Females

Group		Week 0	Week 4
I	XM	2.00	2.00
	SD	.23	.16
II	XM	1.90	1.86
	SD	.12	.24
III	XM	2.00	1.88
	SD	.24	.16
IV	XM	2.14	1.84
	SD	.17	.24

Group	F(3, 16) =	.6
Time	F(1, 16) =	4.3
Group X Time	F(3, 16) =	1.4

Table 7

Macroscopic organ findings

Group	Animal-No. Sex	Organ	Finding
I	101 m	Liver	irregular light areas
		Large intestine	irregular white spots (2-3 mm diam.)
I	102 m		no specific finding
I	103 m	Lung	flecked, dark red
		Large intestine	irregular white spots (2-3 mm diam.)
I	104 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
I	105 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
I	151 f	Lung	flecked, dark red
		Large intestine	irregular white spots (2-3 mm diam.)
I	152 f	Liver	irregular grey-white areas (3-4 diam.)
I	153 f	Lung	flecked, dark red
		Large intestine	irregular white spots (2-3 mm diam.)
I	154 f	Liver	irregular grey-white areas (3-4 diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
I	155 f	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
		Salivary gland	hemorrhagic infiltrated

Table 7 (cont'd)

Group	Animal-No. Sex	Organ	Finding
II	201 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
II	202 m	Liver	irregular grey-white areas (3-4 mm diam.)
II	203 m		no specific finding
II	204 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
II	205 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
		Salivary gland	hemorrhagic infiltrated
II	251 f	Liver	irregular grey-white areas (3-4 mm diam.)
II	252 f	Liver	irregular grey-white areas (3-4 mm diam.)
II	253 f	Liver	irregular grey-white areas (3-4 mm diam.)
II	254 f	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
		Salivary gland	hemorrhagic infiltrated
II	255 f	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
		Salivary gland	hemorrhagic infiltrated

Table 7 (cont'd)

Group	Animal-No. Sex	Organ	Finding
III	301 m	Liver	irregular grey-white areas (3-4 mm diam.)
III	302 m	Liver	irregular grey-white areas (3-4 mm diam.)
III	303 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
		Ovary, left	missing
III	304 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
		Salivary gland	hemorrhagic infiltrated
III	305 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
III	351 f		no specific findings
III	352 f	Liver	irregular grey-white areas (3-4 mm diam.)
III	353 f	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
III	354 f	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (3- 4 mm diam.)
III	355 f	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (3- 4 mm diam.)

Table 7 (cont'd)

Group	Animal-No. Sex	Organ	Finding
IV	401 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
IV	402 m	Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
IV	403 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
		Salivary gland	hemorrhagic infiltrated
IV	404 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
IV	405 m	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.) single yellow discoloration (6mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
IV	451 f	Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
IV	452 f	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
IV	453 f	Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)
IV	454 f	Liver	irregular grey-white areas (3-4 mm diam.)
IV	455 f	Lung	flecked, dark red
		Liver	irregular grey-white areas (3-4 mm diam.)
		Large intestine	irregular white spots (2-3 mm diam.)

HEART (G) 30-05-0387-90

Terminal sacrifice, day 28

Analysis of covariance

males

Source of variation	DF	F
Groups (not corrected)	3/ 16	.4
Regression	1/ 15	9.8 **
Groups (corrected)	3/ 15	1.1

Group		not corrected	Percent	corrected	Percent
I	XM	2.178	100.0	2.256	100.0
	SD	.234		.191	
II	XM	2.190	100.6	2.228	98.8
	SD	.304		.204	
III	XM	2.346	107.8	2.390	105.9
	SD	.266		.147	
IV	XM	2.259	103.7	2.099	93.0
	SD	.338		.319	

HEART (G) 30-05-0387-90

Terminal sacrifice, day 28

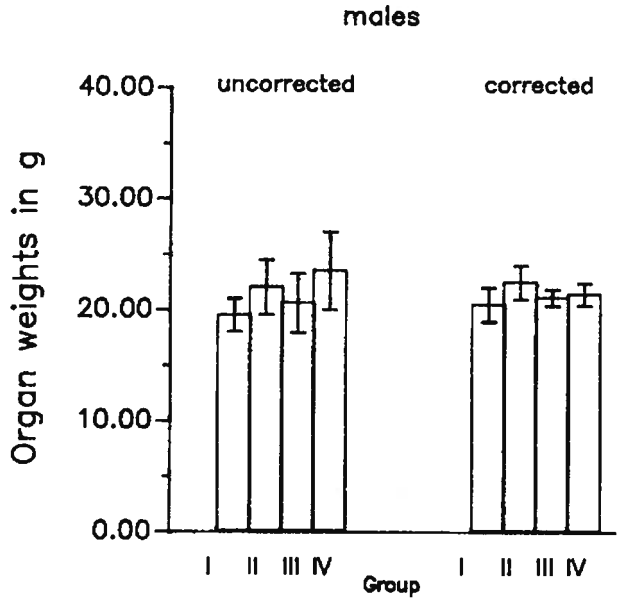
Analysis of covariance

females

Source of variation	DF	F
Groups (not corrected)	3/ 16	.3
Regression	1/ 15	11.5 **
Groups (corrected)	3/ 15	.1

Group		not corrected	Percent	corrected	Percent
I	XM	1.837	100.0	1.845	100.0
	SD	.285		.194	
II	XM	1.935	105.3	1.852	100.4
	SD	.239		.230	
III	XM	1.792	97.5	1.873	101.5
	SD	.236		.163	
IV	XM	1.901	103.5	1.893	102.6
	SD	.253		.170	

LIVER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uncorrected
corrected
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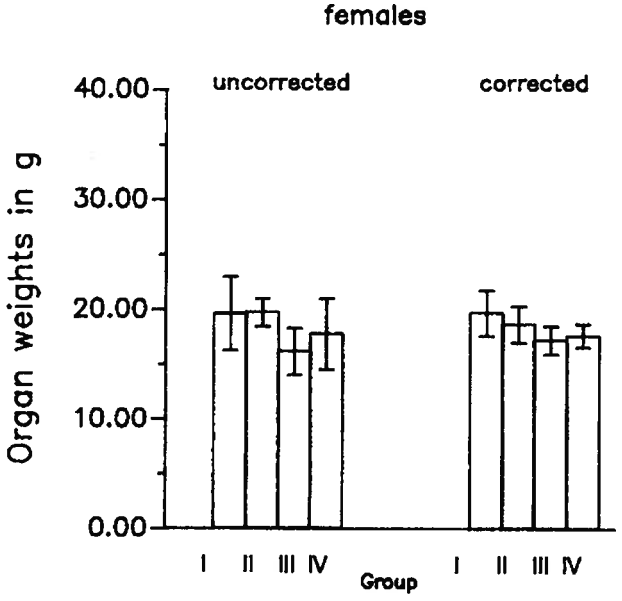
30.00
20.00
10.00
0.00
Organ weights in g
I II III IV
Group
I II III IV

I = SD


females
uncorrected
corrected
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30.00
20.00
10.00
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Organ weights in g
I II III IV
Group
I II III IV

LIVER (G) 30-05-0387-90

Terminal sacrifice, day 28

Analysis of covariance

males

Source of variation	DF	F
Groups (not corrected)	3/ 16	2.2
Regression	1/ 15	50.6 ***
Groups (corrected)	3/ 15	2.1

Group		not corrected	Percent	corrected	Percent
I	XM	19.483	100.0	20.489	100.0
	SD	1.519		1.562	
II	XM	22.020	113.0	22.513	109.9
	SD	2.487		1.537	
III	XM	20.587	105.7	21.143	103.2
	SD	2.689		.757	
IV	XM	23.524	120.7	21.469	104.8
	SD	3.512		1.017	

LIVER (G) 30-05-0387-90

Terminal sacrifice, day 28

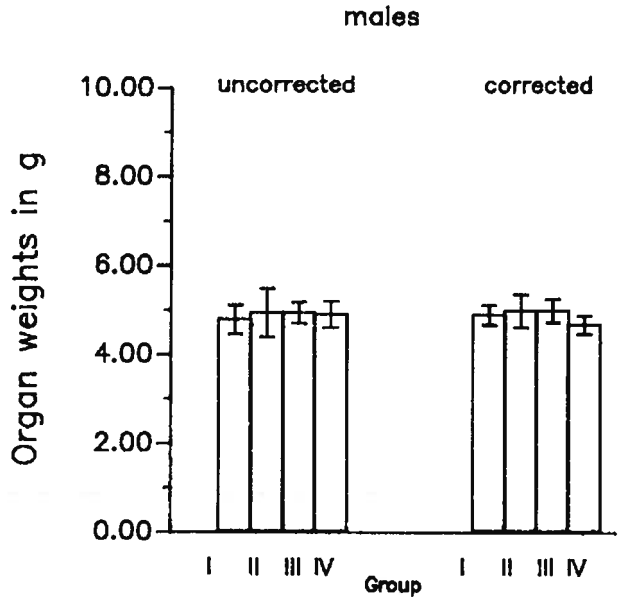
Analysis of covariance

females

Source of variation	DF	F
Groups (not corrected)	3/ 16	2.0
Regression	1/ 15	27.4 ***
Groups (corrected)	3/ 15	2.2

Group		not corrected	Percent	corrected	Percent
I	XM	19.617	100.0	19.723	100.0
	SD	3.370		2.067	
II	XM	19.736	100.6	18.690	94.8
	SD	1.287		1.666	
III	XM	16.206	82.6	17.246	87.4
	SD	2.141		1.308	
IV	XM	17.781	90.6	17.680	89.6
	SD	3.241		1.088	

KIDNEYS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uncorrected
corrected
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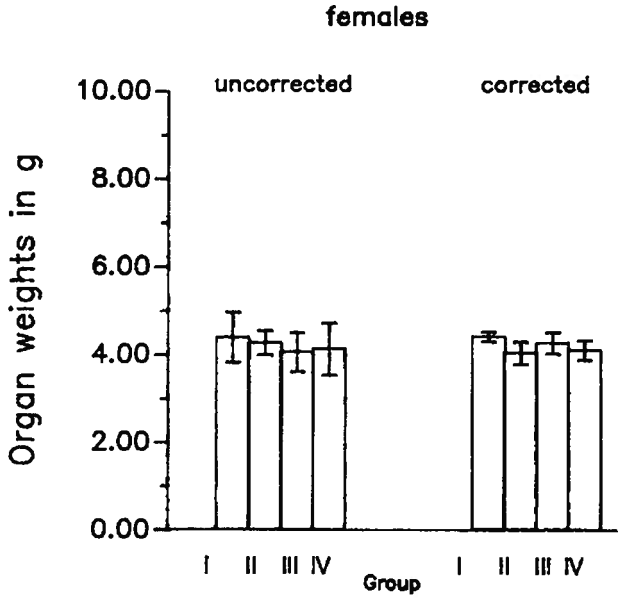
6.00
4.00
2.00
0.00
Organ weights in g
I II III IV
Group
I II III IV

I = SD


females
uncorrected
corrected
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6.00
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2.00
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Organ weights in g
I II III IV
Group
I II III IV

KIDNEYS (G) 30-05-0387-90

Terminal sacrifice, day 28

Analysis of covariance

males

Source of variation	DF	F
Groups (not corrected)	3/ 16	.2
Regression	1/ 15	12.1 **
Groups (corrected)	3/ 15	1.0

Group		not corrected	Percent	corrected	Percent
I	XM	4.781	100.0	4.889	100.0
	SD	.328		.225	
II	XM	4.938	103.3	4.992	102.1
	SD	.553		.379	
III	XM	4.934	103.2	4.994	102.1
	SD	.242		.271	
IV	XM	4.904	102.6	4.683	95.8
	SD	.301		.209	

KIDNEYS (G) 30-05-0387-90

Terminal sacrifice, day 28

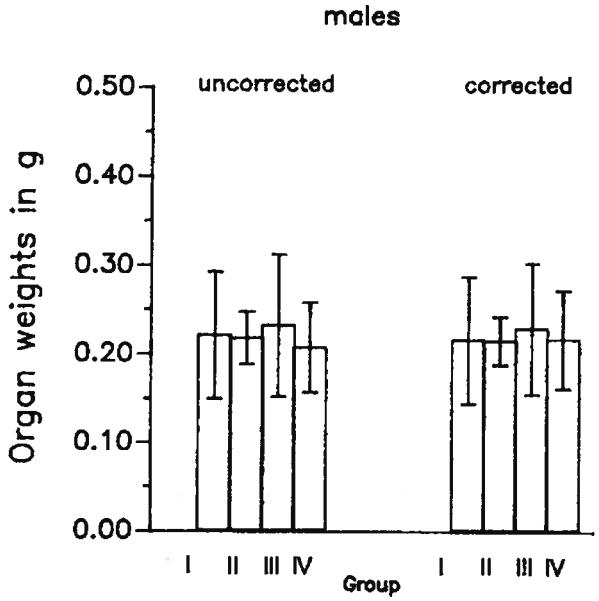
Analysis of covariance

females

Source of variation	DF	F
Groups (not corrected)	3/ 16	.5
Regression	1/ 15	60.0 ***
Groups (corrected)	3/ 15	2.5

Group		not corrected	Percent	corrected	Percent
I	XM	4.395	100.0	4.417	100.0
	SD	.576		.113	
II	XM	4.265	97.1	4.049	91.7
	SD	.283		.258	
III	XM	4.059	92.4	4.274	96.8
	SD	.449		.250	
IV	XM	4.134	94.1	4.113	93.1
	SD	.600		.229	

ADRENALS



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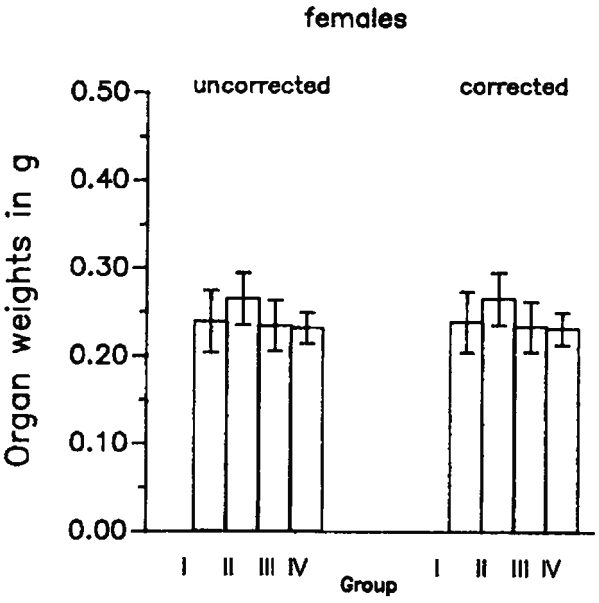


ADRENALS (G) 30-05-0387-90

Terminal sacrifice, day 28

Analysis of covariance

males

Source of variation	DF	F
Groups (not corrected)	3/ 16	.1
Regression	1/ 15	.5
Groups (corrected)	3/ 15	.1

Group		not corrected	Percent	corrected	Percent
I	XM	.221	100.0	.216	100.0
	SD	.072		.072	
II	XM	.218	98.6	.215	99.7
	SD	.030		.027	
III	XM	.232	105.0	.229	106.1
	SD	.080		.074	
IV	XM	.207	93.7	.217	100.5
	SD	.051		.056	

ADRENALS (G) 30-05-0387-90

Terminal sacrifice, day 28

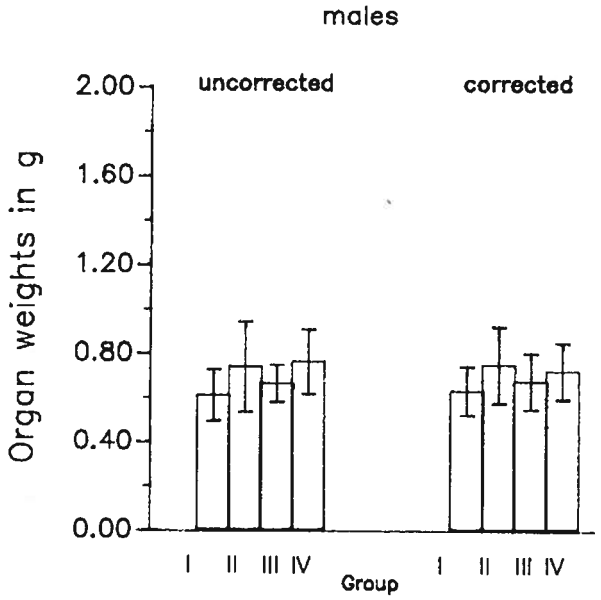
Analysis of covariance

females

Source of variation	DF	F
Groups (not corrected)	3/ 16	1.4
Regression	1/ 15	.0
Groups (corrected)	3/ 15	1.3

Group		not corrected	Percent	corrected	Percent
I	XM	.239	100.0	.239	100.0
	SD	.035		.035	
II	XM	.265	110.9	.266	111.1
	SD	.030		.030	
III	XM	.235	98.1	.234	97.9
	SD	.029		.029	
IV	XM	.232	96.9	.232	97.0
	SD	.018		.019	

SPLEEN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uncorrected
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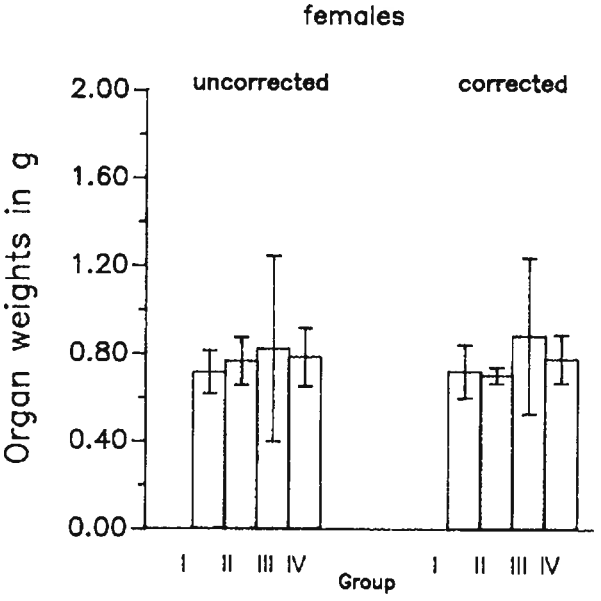
0.80
0.40
0.00
Organ weights in g
I II III IV
Group
I II III IV

I = SD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uncorrected
corrected
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1.20
0.80
0.40
0.00
Organ weights in g
I II III IV
Group
I II III IV

SPLEEN (G) 30-05-0387-90

Terminal sacrifice, day 28

Analysis of covariance

males

Source of variation	DF	F
Groups (not corrected)	3/ 16	1.2
Regression	1/ 15	1.8
Groups (corrected)	3/ 15	.6

Group		not corrected	Percent	corrected	Percent
I	XM	.609	100.0	.630	100.0
	SD	.116		.110	
II	XM	.739	121.2	.749	118.9
	SD	.205		.174	
III	XM	.663	108.8	.674	107.1
	SD	.085		.128	
IV	XM	.762	125.1	.721	114.5
	SD	.146		.128	

SPLEEN (G) 30-05-0387-90

Terminal sacrifice, day 28

Analysis of covariance

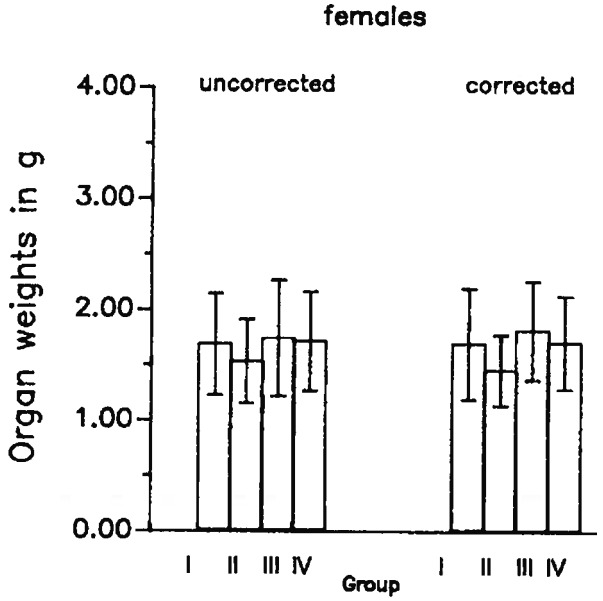
females

Source of variation	DF	F
Groups (not corrected)	3/ 16	.2
Regression	1/ 15	6.2 *
Groups (corrected)	3/ 15	.7

Group		not corrected	Percent	corrected	Percent
I	XM	.715	100.0	.721	100.0
	SD	.099		.121	
II	XM	.766	107.2	.704	97.6
	SD	.109		.037	
III	XM	.822	115.0	.884	122.6
	SD	.424		.356	
IV	XM	.784	109.7	.778	107.9
	SD	.133		.111	

Proj. 30-05-0387-90

UTERUS



UTERUS (G) 30-05-0387-90

Terminal sacrifice, day 28

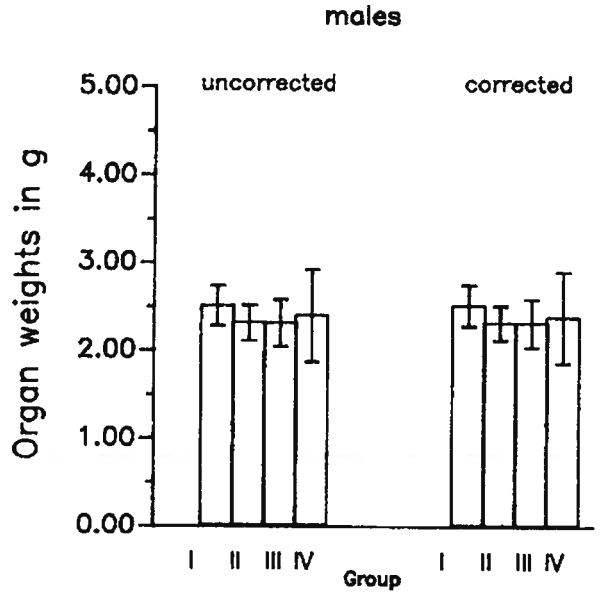
Analysis of covariance

females

Source of variation	DF	F
Groups (not corrected)	3/ 16	.2
Regression	1/ 15	1.9
Groups (corrected)	3/ 15	.5

Group		not corrected	Percent	corrected	Percent
I	XM	1.685	100.0	1.692	100.0
	SD	.460		.506	
II	XM	1.529	90.8	1.453	85.9
	SD	.380		.321	
III	XM	1.739	103.2	1.815	107.2
	SD	.526		.448	
IV	XM	1.713	101.7	1.705	100.8
	SD	.451		.423	

TESTES/OVARIES



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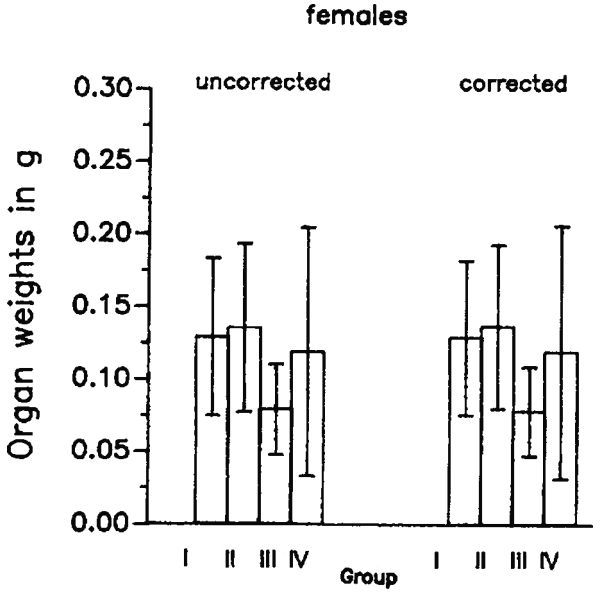

TESTES (G) 30-05-0387-90

Terminal sacrifice, day 28

Analysis of covariance

males

Source of variation	DF	F
Groups (not corrected)	3/ 16	.4
Regression	1/ 15	.0
Groups (corrected)	3/ 15	.4

Group		not corrected	Percent	corrected	Percent
I	XM	2.507	100.0	2.513	100.0
	SD	.230		.237	
II	XM	2.311	92.2	2.314	92.1
	SD	.206		.199	
III	XM	2.310	92.2	2.314	92.1
	SD	.270		.276	
IV	XM	2.394	95.5	2.382	94.8
	SD	.528		.524	

OVARIES (G) 30-05-0387-90

Terminal sacrifice, day 28

Analysis of covariance

females

Source of variation	DF	F
Groups (not corrected)	3/ 16	.9
Regression	1/ 15	.0
Groups (corrected)	3/ 15	.8

Group		not corrected	Percent	corrected	Percent
I	XM	.129	100.0	.129	100.0
	SD	.054		.053	
II	XM	.135	105.0	.136	105.9
	SD	.058		.057	
III	XM	.079	61.4	.078	60.6
	SD	.031		.031	
IV	XM	.119	92.2	.119	92.4
	SD	.086		.087	

Body weights (g) 30-05-0387-90

Anim.-No.	Start	Weeks 1	2	3	4
IV males					
401	344	413	476	523	558
402	337	390	458	503	554
403	338	404	472	539	615
404	323	377	436	483	518
405	360	430	498	572	629
IV females					
451	347	402	451	464	524
452	319	355	387	411	452
453	322	371	413	445	489
454	327	386	440	476	537
455	302	337	385	406	446

Body weights (g) 30-05-0387-90

Anim.-No.	Start	Weeks 1	2	3	4
I males					
101	307	376	438	464	504
102	319	382	449	492	537
103	324	379	439	474	499
104	346	395	468	500	545
105	334	399	453	488	544
I females					
151	324	342	397	435	449
152	345	418	445	472	520
153	310	347	392	422	444
154	315	344	397	416	465
155	351	394	483	483	552
II males					
201	315	382	424	454	482
202	323	342	393	447	506
203	330	397	466	507	573
204	330	395	458	508	556
205	337	396	460	496	553
II females					
251	315	368	413	423	455
252	343	388	447	487	542
253	330	388	441	485	514
254	336	391	448	474	518
255	323	387	442	459	501
III males					
301	326	392	468	506	582
302	312	391	449	495	564
303	315	344	402	434	499
304	331	407	478	522	499
305	341	396	458	488	521
III females					
351	323	355	393	424	449
352	333	388	431	482	502
353	328	360	411	432	461
354	327	379	397	439	482
355	314	363	402	421	455

ERYTHROCYTES (10**12/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	5.40	5.23	102	5.14	5.22
103	5.68	5.87	104	6.06	6.08
105	5.27	5.56			
Females					
151	5.41	5.18	152	5.32	5.15
153	6.03	5.23	154	5.63	5.07
155	4.63	5.44			
II					
Males					
201	5.27	5.73	202	5.49	5.71
203	4.99	5.35	204	5.06	4.22
205	5.14	4.97			
Females					
251	4.90	5.27	252	5.78	5.13
253	5.38	5.48	254	5.37	5.15
255	5.42	5.39			
III					
Males					
301	4.92	5.53	302	5.50	5.36
303	5.17	4.61	304	5.71	6.31
305	5.00	4.99			
Females					
351	4.95	5.35	352	5.40	4.97
353	5.82	5.63	354	5.58	5.59
355	5.26	5.79			
IV					
Males					
401	5.08	5.52	402	5.43	5.35
403	5.43	4.89	404	5.44	5.36
405	5.17	4.94			
Females					
451	4.93	5.08	452	5.29	5.44
453	5.64	4.93	454	5.19	4.88
455	5.26	5.58			

THROMBOCYTES (10**9/L) 30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	396	261	102	435	395
103	408	377	104	261	368
105	321	375			
Females					
151	364	403	152	346	435
153	314	354	154	407	403
155	375	369			
II					
Males					
201	377	459	202	372	312
203	441	414	204	331	317
205	385	347			
Females					
251	360	285	252	250	338
253	340	397	254	459	348
255	340	321			
III					
Males					
301	351	316	302	462	325
303	476	408	304	396	428
305	377	293			
Females					
351	313	251	352	275	298
353	407	396	354	429	445
355	365	355			
IV					
Males					
401	425	337	402	326	340
403	359	438	404	427	390
405	361	402			
Females					
451	381	304	452	345	327
453	368	346	454	384	378
455	326	317			

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	.025	.015	102	.023	.013
103	.024	.009	104	.024	.021
105	.017	.012			
Females					
151	.014	.009	152	.025	.023
153	.012	.010	154	.014	.007
155	.028	.007			
II					
Males					
201	.023	.009	202	.022	.020
203	.022	.016	204	.020	.019
205	.028	.013			
Females					
251	.035	.010	252	.013	.014
253	.021	.025	254	.016	.032
255	.014	.005			
III					
Males					
301	.021	.017	302	.022	.011
303	.028	.017	304	.018	.008
305	.021	.012			
Females					
351	.015	.012	352	.017	.021
353	.011	.015	354	.015	.010
355	.011	.021			
IV					
Males					
401	.028	.009	402	.026	.013
403	.031	.020	404	.022	.018
405	.033	.016			
Females					
451	.038	.008	452	.017	.024
453	.013	.016	454	.015	.016
455	.014	.018			

HEMOGLOBIN (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	8.1	8.4	102	8.5	8.7
103	8.9	9.3	104	9.7	10.0
105	8.5	8.7			
Females					
151	9.6	9.1	152	8.8	8.4
153	9.8	8.6	154	9.2	8.5
155	8.0	9.2			
II					
Males					
201	8.6	9.2	202	8.9	9.3
203	8.5	8.8	204	8.8	7.2
205	8.6	7.7			
Females					
251	8.2	8.5	252	9.4	8.6
253	9.1	9.0	254	8.7	8.6
255	9.1	9.0			
III					
Males					
301	8.5	9.1	302	8.9	8.5
303	8.2	7.4	304	9.0	10.1
305	8.6	8.3			
Females					
351	8.2	8.6	352	8.6	8.1
353	9.5	9.0	354	9.4	9.5
355	8.9	9.4			
IV					
Males					
401	8.2	8.8	402	8.6	8.5
403	9.1	8.4	404	9.0	8.8
405	8.7	8.3			
Females					
451	8.4	8.7	452	9.3	9.2
453	9.1	8.2	454	8.6	8.4
455	8.9	9.2			

HEMATOCRIT

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	.438	.435	102	.450	.471
103	.474	.500	104	.504	.526
105	.447	.470			
Females					
151	.495	.475	152	.456	.471
153	.510	.446	154	.473	.441
155	.411	.481			
II					
Males					
201	.447	.485	202	.460	.483
203	.433	.464	204	.448	.371
205	.446	.416			
Females					
251	.419	.453	252	.486	.464
253	.461	.474	254	.449	.454
255	.472	.468			
III					
Males					
301	.430	.482	302	.468	.464
303	.433	.391	304	.471	.538
305	.443	.444			
Females					
351	.429	.463	352	.456	.434
353	.495	.479	354	.491	.499
355	.450	.507			
IV					
Males					
401	.428	.466	402	.453	.447
403	.471	.432	404	.459	.461
405	.450	.433			
Females					
451	.423	.443	452	.463	.483
453	.473	.436	454	.439	.422
455	.460	.480			

LEUKOCYTES (10**9/L) 30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	4.8	5.3	102	5.7	5.4
103	6.4	5.7	104	4.0	4.6
105	5.4	6.2			
Females					
151	5.3	5.4	152	4.7	8.6
153	3.7	4.9	154	4.9	4.7
155	5.5	6.2			
II					
Males					
201	4.0	4.9	202	5.3	4.9
203	5.3	6.0	204	4.0	5.9
205	5.1	6.4			
Females					
251	4.9	6.1	252	5.8	6.6
253	4.4	5.1	254	5.2	4.2
255	4.6	5.6			
III					
Males					
301	3.4	5.4	302	3.2	5.9
303	6.4	5.3	304	5.9	5.2
305	5.6	5.0			
Females					
351	3.2	5.4	352	4.2	4.8
353	6.6	9.3	354	5.0	8.2
355	5.7	5.8			
IV					
Males					
401	6.1	4.6	402	5.0	8.0
403	4.6	6.3	404	5.8	6.9
405	4.8	4.5			
Females					
451	6.8	8.3	452	5.2	7.9
453	5.3	7.4	454	4.0	5.0
455	5.0	5.3			

PROTHROMBIN TIME (%)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	92	95	102	96	100
103	97	95	104	116	92
105	90	97			
Females					
151	95	105	152	109	112
153	104	113	154	104	92
155	98	97			
II					
Males					
201	103	88	202	107	117
203	103	95	204	107	95
205	95	110			
Females					
251	102	109	252	99	119
253	95	126	254	129	137
255	101	115			
III					
Males					
301	97	103	302	105	109
303	103	125	304	96	100
305	93	104			
Females					
351	102	94	352	98	116
353	105	110	354	93	130
355	95	102			
IV					
Males					
401	105	130	402	75	112
403	113	100	404	109	119
405	121	125			
Females					
451	99	120	452	108	101
453	108	107	454	102	115
455	105	104			

GLUCOSE (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	10.5	7.3	102	13.3	7.0
103	7.3	6.9	104	7.6	8.0
105	8.2	7.7			
Females					
151	8.5	6.5	152	8.4	6.9
153	8.0	6.9	154	8.4	6.9
155	8.9	8.2			
II					
Males					
201	7.9	6.1	202	7.8	7.9
203	9.1	8.2	204	7.6	7.7
205	7.2	7.8			
Females					
251	8.7	7.5	252	7.8	7.7
253	8.3	8.3	254	8.6	7.0
255	10.3	8.5			
III					
Males					
301	7.7	8.9	302	7.2	10.2
303	8.4	7.8	304	8.2	6.6
305	7.8	7.7			
Females					
351	8.2	7.2	352	8.7	7.5
353	7.6	6.9	354	9.5	8.0
355	8.6	7.7			
IV					
Males					
401	10.7	13.6	402	9.2	9.4
403	8.0	9.5	404	9.8	7.6
405	9.9	9.9			
Females					
451	8.6	8.9	452	8.3	8.5
453	8.7	7.4	454	8.6	7.6
455	8.4	8.5			

CHOLESTEROL (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	1.6	.6	102	1.2	.6
103	1.0	.8	104	1.0	.7
105	1.0	.6			
Females					
151	1.3	1.2	152	1.4	1.0
153	1.6	.9	154	1.8	1.1
155	1.1	1.0			
II					
Males					
201	.7	1.0	202	1.3	.7
203	1.3	.7	204	1.0	.7
205	.8	.5			
Females					
251	1.3	1.2	252	1.1	.8
253	1.0	.8	254	1.3	1.0
255	1.1	.6			
III					
Males					
301	1.0	.8	302	1.3	.7
303	1.1	.4	304	1.2	.7
305	1.4	.3			
Females					
351	1.0	.9	352	1.3	.7
353	1.3	1.3	354	1.8	.9
355	1.0	1.1			
IV					
Males					
401	1.4	.8	402	1.2	.7
403	1.7	.8	404	1.2	.9
405	1.1	.6			
Females					
451	1.4	1.3	452	1.5	.8
453	1.6	.8	454	1.6	.9
455	1.2	.9			

TRIGLYCERIDE (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	1.00	.73	102	.76	.58
103	.38	.82	104	.64	.50
105	.49	.45			
Females					
151	.59	.74	152	.76	.51
153	.70	.94	154	.80	.50
155	.46	.42			
II					
Males					
201	.39	.51	202	.66	.44
203	.66	.23	204	.68	.87
205	.55	.48			
Females					
251	.61	1.05	252	.47	.46
253	.78	.55	254	.60	.71
255	.66	.27			
III					
Males					
301	.36	.47	302	.80	.57
303	.57	.31	304	.49	.26
305	.94	.52			
Females					
351	.32	.68	352	.67	.36
353	.44	.43	354	.77	.55
355	.47	.48			
IV					
Males					
401	.96	.71	402	.88	.56
403	.84	.52	404	.95	.83
405	.63	.45			
Females					
451	.44	.51	452	.49	.59
453	.57	.39	454	.75	.42
455	.48	.66			

TOTAL PROTEIN (G/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	40	41	102	37	42
103	41	46	104	46	46
105	40	44			
Females					
151	49	50	152	43	50
153	45	41	154	44	43
155	39	44			
II					
Males					
201	38	49	202	45	44
203	37	41	204	44	44
205	38	41			
Females					
251	39	46	252	39	43
253	41	46	254	47	49
255	41	43			
III					
Males					
301	40	39	302	45	42
303	41	41	304	43	49
305	41	43			
Females					
351	41	41	352	41	45
353	46	46	354	51	46
355	42	49			
IV					
Males					
401	40	45	402	41	43
403	44	47	404	45	47
405	44	42			
Females					
451	42	42	452	43	44
453	50	45	454	48	47
455	44	49			

ALBUMIN (G/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	28.4	28.9	102	27.6	28.6
103	30.8	30.4	104	32.5	27.6
105	28.2	30.0			
Females					
151	35.8	33.0	152	31.1	33.1
153	35.8	31.0	154	34.4	29.6
155	27.5	30.6			
II					
Males					
201	28.4	30.3	202	32.4	30.7
203	29.2	27.5	204	35.0	29.8
205	27.0	28.6			
Females					
251	30.0	31.6	252	30.8	29.3
253	32.8	26.8	254	32.5	32.2
255	31.0	27.1			
III					
Males					
301	28.3	24.9	302	30.9	25.9
303	29.2	28.1	304	31.9	30.0
305	29.0	28.6			
Females					
351	29.2	27.2	352	29.5	27.6
353	34.8	30.0	354	34.0	27.4
355	29.5	28.4			
IV					
Males					
401	28.7	29.8	402	29.8	27.5
403	30.8	29.5	404	31.0	30.2
405	30.0	29.4			
Females					
451	30.4	29.9	452	31.6	30.9
453	33.5	32.1	454	32.0	31.8
455	30.2	29.5			

ELECTROPHORESIS: ALBUMIN

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	.645	.614	102	.676	.636
103	.653	.618	104	.647	.665
105	.637	.646			
Females					
151	.646	.608	152	.648	.659
153	.635	.650	154	.685	.623
155	.638	.610			
II					
Males					
201	.635	.578	202	.638	.651
203	.638	.625	204	.649	.628
205	.639	.590			
Females					
251	.660	.637	252	.644	.673
253	.643	.632	254	.636	.622
255	.628	.632			
III					
Males					
301	.636	.637	302	.558	.648
303	.629	.661	304	.651	.676
305	.628	.609			
Females					
351	.627	.660	352	.659	.657
353	.634	.637	354	.688	.634
355	.672	.680			
IV					
Males					
401	.652	.661	402	.619	.622
403	.664	.649	404	.656	.601
405	.631	.587			
Females					
451	.650	.603	452	.662	.652
453	.660	.623	454	.696	.668
455	.696	.673			

ELECTROPHORESIS: GLOBULIN α1 + α2 30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	.245	.240	102	.221	.251
103	.227	.239	104	.231	.244
105	.220	.228			
Females					
151	.216	.238	152	.234	.204
153	.242	.245	154	.205	.254
155	.215	.241			
II					
Males					
201	.218	.230	202	.222	.243
203	.222	.263	204	.208	.253
205	.226	.238			
Females					
251	.216	.253	252	.220	.226
253	.216	.253	254	.223	.241
255	.225	.230			
III					
Males					
301	.220	.238	302	.254	.228
303	.224	.213	304	.216	.198
305	.227	.230			
Females					
351	.233	.234	352	.219	.256
353	.221	.234	354	.210	.275
355	.217	.244			
IV					
Males					
401	.227	.238	402	.223	.250
403	.210	.238	404	.225	.234
405	.212	.255			
Females					
451	.228	.261	452	.204	.233
453	.206	.234	454	.174	.230
455	.184	.229			

ELECTROPHORESIS: GLOBULIN β

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	.047	.059	102	.046	.049
103	.062	.062	104	.048	.055
105	.071	.057			
Females					
151	.048	.053	152	.051	.045
153	.059	.048	154	.052	.055
155	.049	.041			
II					
Males					
201	.067	.064	202	.052	.044
203	.053	.052	204	.060	.054
205	.050	.057			
Females					
251	.053	.049	252	.068	.044
253	.066	.052	254	.042	.053
255	.052	.056			
III					
Males					
301	.049	.069	302	.065	.060
303	.064	.064	304	.056	.064
305	.050	.055			
Females					
351	.060	.051	352	.064	.053
353	.064	.043	354	.044	.037
355	.049	.037			
IV					
Males					
401	.056	.050	402	.066	.053
403	.058	.050	404	.050	.064
405	.067	.066			
Females					
451	.058	.060	452	.063	.049
453	.060	.061	454	.055	.044
455	.041	.040			

ELECTROPHORESIS: GLOBULIN G

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	.063	.087	102	.057	.064
103	.058	.080	104	.075	.036
105	.072	.069			
Females					
151	.091	.101	152	.067	.091
153	.064	.057	154	.059	.068
155	.098	.109			
II					
Males					
201	.080	.128	202	.088	.062
203	.087	.059	204	.083	.065
205	.086	.115			
Females					
251	.071	.060	252	.067	.056
253	.075	.063	254	.098	.084
255	.095	.082			
III					
Males					
301	.095	.056	302	.123	.063
303	.084	.062	304	.078	.063
305	.094	.105			
Females					
351	.081	.055	352	.058	.033
353	.081	.085	354	.059	.054
355	.061	.038			
IV					
Males					
401	.064	.052	402	.052	.075
403	.068	.064	404	.069	.101
405	.090	.092			
Females					
451	.064	.076	452	.071	.066
453	.074	.082	454	.075	.058
455	.079	.058			

ALT (U/L)

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	37	28	102	13	22
103	24	20	104	21	52
105	19	23			
Females					
151	22	14	152	18	25
153	33	20	154	26	22
155	18	19			
II					
Males					
201	29	20	202	26	29
203	18	25	204	30	24
205	19	21			
Females					
251	19	14	252	43	20
253	23	17	254	14	18
255	16	24			
III					
Males					
301	40	20	302	14	24
303	18	35	304	17	14
305	27	33			
Females					
351	6	19	352	17	18
353	12	15	354	21	21
355	21	41			
IV					
Males					
401	22	28	402	30	24
403	23	20	404	40	19
405	6	21			
Females					
451	14	15	452	16	19
453	17	23	454	17	20
455	22	17			

AST (U/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	23	20	102	11	14
103	19	17	104	21	61
105	24	33			
Females					
151	18	20	152	17	24
153	33	20	154	20	18
155	13	15			
II					
Males					
201	37	18	202	17	21
203	15	31	204	28	27
205	13	17			
Females					
251	14	15	252	126	19
253	22	29	254	19	23
255	12	20			
III					
Males					
301	112	16	302	18	19
303	15	21	304	17	21
305	19	25			
Females					
351	8	19	352	20	14
353	8	14	354	19	17
355	16	36			
IV					
Males					
401	26	25	402	25	17
403	25	16	404	24	17
405	7	14			
Females					
451	14	12	452	38	21
453	19	18	454	17	22
455	25	24			

ALK. PHOSPHATASE (U/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	538	319	102	718	380
103	374	373	104	425	300
105	576	521			
Females					
151	356	212	152	400	238
153	620	288	154	322	368
155	312	264			
II					
Males					
201	334	337	202	348	492
203	450	418	204	380	431
205	295	290			
Females					
251	355	328	252	284	329
253	332	248	254	343	310
255	244	263			
III					
Males					
301	288	278	302	389	367
303	372	358	304	267	202
305	362	377			
Females					
351	300	267	352	343	288
353	288	239	354	309	260
355	278	249			
IV					
Males					
401	585	293	402	364	288
403	409	363	404	437	260
405	500	346			
Females					
451	295	190	452	386	332
453	325	319	454	328	310
455	271	250			

LDH (U/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	97	68	102	58	69
103	94	86	104	92	74
105	68	67			
Females					
151	49	90	152	57	62
153	67	87	154	86	70
155	43	48			
II					
Males					
201	59	100	202	69	83
203	63	73	204	118	170
205	59	102			
Females					
251	53	79	252	81	85
253	59	46	254	80	114
255	71	33			
III					
Males					
301	84	53	302	35	54
303	16	91	304	71	43
305	113	86			
Females					
351	41	49	352	100	43
353	57	68	354	92	37
355	41	43			
IV					
Males					
401	92	77	402	76	64
403	82	98	404	80	81
405	56	66			
Females					
451	71	69	452	24	95
453	42	61	454	48	70
455	79	39			

GAMMA- GT (U/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	12	4	102	4	5
103	5	4	104	4	3
105	3	4			
Females					
151	9	5	152	3	4
153	4	5	154	6	5
155	2	4			
II					
Males					
201	3	6	202	5	5
203	4	4	204	6	4
205	4	6			
Females					
251	1	3	252	5	4
253	3	4	254	5	6
255	10	3			
III					
Males					
301	3	4	302	3	4
303	9	5	304	4	5
305	2	5			
Females					
351	4	4	352	3	4
353	3	4	354	5	4
355	4	4			
IV					
Males					
401	3	4	402	2	4
403	0	4	404	1	5
405	3	4			
Females					
451	9	4	452	4	4
453	3	4	454	3	5
455	3	4			

CK (U/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	69	92	102	146	99
103	74	60	104	70	124
105	100	164			
Females					
151	67	52	152	93	92
153	53	110	154	111	67
155	62	95			
II					
Males					
201	98	85	202	66	137
203	205	66	204	46	220
205	84	96			
Females					
251	57	67	252	63	61
253	82	40	254	153	110
255	45	63			
III					
Males					
301	78	72	302	94	89
303	109	150	304	68	53
305	70	106			
Females					
351	114	70	352	77	45
353	69	69	354	68	51
355	69	73			
IV					
Males					
401	160	67	402	127	66
403	207	82	404	137	80
405	224	44			
Females					
451	187	52	452	111	60
453	46	155	454	59	142
455	33	73			

TOTAL BILIRUBIN (MICROMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	.2	1.0	102	.8	.9
103	.2	1.0	104	.8	1.1
105	.3	.6			
Females					
151	.4	.9	152	.8	1.1
153	.6	1.0	154	.2	1.0
155	.5	.9			
II					
Males					
201	.4	1.1	202	.4	1.2
203	.4	.7	204	.3	.9
205	.5	.9			
Females					
251	.4	.9	252	.5	.8
253	.4	.7	254	.2	1.0
255	.4	.8			
III					
Males					
301	.9	.7	302	.3	.7
303	.9	1.0	304	.6	1.1
305	.8	.9			
Females					
351	.9	.9	352	.6	.8
353	1.4	1.0	354	.4	1.1
355	.4	1.4			
IV					
Males					
401	.6	.8	402	.6	.9
403	.4	1.3	404	.4	1.0
405	.4	1.0			
Females					
451	2.5	1.0	452	.8	1.1
453	1.1	1.2	454	.7	1.1
455	.2	1.1			

URIC ACID (MICROMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	12	12	102	7	12
103	30	16	104	31	8
105	22	18			
Females					
151	31	40	152	23	16
153	32	24	154	21	20
155	14	9			
II					
Males					
201	11	27	202	22	21
203	23	5	204	28	55
205	19	13			
Females					
251	11	12	252	17	24
253	7	2	254	21	39
255	24	1			
III					
Males					
301	18	2	302	28	5
303	22	16	304	36	6
305	7	20			
Females					
351	24	2	352	24	4
353	22	12	354	50	9
355	12	5			
IV					
Males					
401	27	11	402	22	7
403	29	23	404	17	14
405	33	9			
Females					
451	17	7	452	33	20
453	16	13	454	22	15
455	30	16			

BUN (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	7.9	8.2	102	7.9	9.6
103	8.6	9.6	104	10.0	10.7
105	8.2	10.0			
Females					
151	9.3	11.8	152	10.7	10.0
153	11.8	10.0	154	10.7	10.4
155	8.2	11.1			
II					
Males					
201	10.7	11.1	202	9.3	9.6
203	8.6	8.9	204	10.7	9.3
205	9.6	9.3			
Females					
251	9.3	10.7	252	8.9	7.5
253	8.6	9.3	254	8.2	8.9
255	8.2	8.6			
III					
Males					
301	9.6	9.3	302	10.0	9.6
303	10.7	11.1	304	7.5	9.6
305	8.9	7.9			
Females					
351	7.9	9.6	352	9.6	9.6
353	9.6	11.1	354	9.6	8.9
355	7.9	8.9			
IV					
Males					
401	8.2	9.6	402	8.2	8.6
403	9.6	11.1	404	8.6	11.4
405	10.0	9.3			
Females					
451	8.6	8.6	452	9.6	9.3
453	8.2	7.1	454	8.9	9.6
455	8.6	10.7			

CREATININE (MICROMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	27	37	102	24	40
103	38	44	104	42	38
105	30	49			
Females					
151	41	53	152	36	49
153	43	46	154	41	41
155	32	40			
II					
Males					
201	34	48	202	30	44
203	36	38	204	31	52
205	27	44			
Females					
251	28	43	252	39	32
253	29	29	254	26	49
255	30	32			
III					
Males					
301	32	38	302	20	33
303	41	45	304	39	43
305	8	43			
Females					
351	30	36	352	28	38
353	41	46	354	43	43
355	32	43			
IV					
Males					
401	36	46	402	31	31
403	38	34	404	38	33
405	38	34			
Females					
451	37	37	452	39	45
453	39	35	454	33	51
455	30	35			

SODIUM (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	139	143	102	140	142
103	146	145	104	148	151
105	148	140			
Females					
151	150	144	152	141	143
153	146	143	154	142	141
155	142	144			
II					
Males					
201	141	136	202	144	145
203	126	144	204	149	147
205	141	144			
Females					
251	145	144	252	147	142
253	145	145	254	142	145
255	139	147			
III					
Males					
301	146	147	302	147	144
303	146	147	304	146	156
305	146	142			
Females					
351	142	146	352	135	145
353	140	146	354	148	151
355	143	148			
IV					
Males					
401	140	146	402	144	143
403	147	143	404	146	147
405	141	142			
Females					
451	150	145	452	146	146
453	148	142	454	144	144
455	144	150			

POTASSIUM (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	6.6	5.8	102	6.7	5.9
103	6.6	6.9	104	8.2	8.2
105	6.5	6.7			
Females					
151	7.3	6.7	152	7.6	6.8
153	8.2	8.0	154	6.4	6.2
155	5.6	7.0			
II					
Males					
201	5.6	5.4	202	7.1	7.2
203	6.0	8.1	204	8.4	8.8
205	6.3	7.0			
Females					
251	6.3	6.7	252	6.0	6.3
253	6.1	7.4	254	7.4	6.9
255	7.4	7.1			
III					
Males					
301	6.3	7.6	302	6.4	6.9
303	6.9	7.8	304	6.4	7.7
305	5.6	7.0			
Females					
351	5.9	6.2	352	5.7	7.4
353	6.9	6.8	354	7.5	7.0
355	5.4	7.5			
IV					
Males					
401	7.0	7.0	402	5.9	6.2
403	7.9	7.1	404	7.6	7.0
405	7.7	5.8			
Females					
451	8.0	7.2	452	8.1	7.5
453	7.3	6.4	454	6.8	7.2
455	5.5	6.6			

CALCIUM (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	3.0	3.1	102	2.7	3.1
103	2.4	3.2	104	3.1	3.0
105	2.7	3.2			
Females					
151	2.6	3.4	152	3.0	2.8
153	2.9	3.0	154	2.9	3.1
155	2.8	3.3			
II					
Males					
201	2.8	3.0	202	2.8	3.3
203	2.8	2.9	204	2.5	3.5
205	2.7	3.1			
Females					
251	2.9	3.3	252	2.9	3.0
253	2.9	2.8	254	3.2	3.2
255	2.9	2.6			
III					
Males					
301	2.9	2.7	302	3.1	2.8
303	3.1	3.1	304	2.8	2.8
305	2.8	2.9			
Females					
351	2.8	2.7	352	3.0	2.7
353	3.0	3.2	354	3.2	2.9
355	2.7	2.9			
IV					
Males					
401	2.7	2.0	402	2.8	2.8
403	3.2	2.9	404	3.1	3.1
405	3.1	3.1			
Females					
451	3.1	3.2	452	3.2	3.1
453	3.0	3.0	454	2.7	3.2
455	2.8	2.8			

IRON (MICROMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	43.5	42.1	102	50.0	45.5
103	55.0	47.3	104	42.4	51.1
105	51.2	44.8			
Females					
151	56.9	56.1	152	44.2	35.6
153	65.4	47.4	154	54.4	36.5
155	51.1	42.2			
II					
Males					
201	52.5	44.1	202	57.4	58.9
203	54.1	49.1	204	68.2	64.3
205	47.7	49.7			
Females					
251	50.9	43.2	252	51.8	53.9
253	57.0	52.9	254	50.2	48.1
255	51.4	30.1			
III					
Males					
301	43.2	45.0	302	48.2	54.1
303	47.0	39.1	304	57.5	49.8
305	57.0	49.3			
Females					
351	55.0	48.9	352	51.5	25.6
353	49.6	45.9	354	60.5	48.3
355	43.0	39.5			
IV					
Males					
401	62.0	62.5	402	44.2	50.1
403	52.7	44.2	404	56.7	49.8
405	59.4	46.5			
Females					
451	60.1	46.0	452	55.2	48.2
453	56.1	38.6	454	50.4	37.7
455	35.1	38.4			

CHLORIDE (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	101	109	102	102	106
103	102	107	104	101	110
105	106	106			
Females					
151	107	106	152	103	101
153	101	106	154	106	107
155	104	108			
II					
Males					
201	102	104	202	103	109
203	101	108	204	108	108
205	105	111			
Females					
251	110	110	252	104	106
253	103	109	254	105	108
255	103	107			
III					
Males					
301	104	107	302	107	109
303	104	111	304	105	113
305	106	106			
Females					
351	105	107	352	104	108
353	104	110	354	112	110
355	101	109			
IV					
Males					
401	108	109	402	105	104
403	103	107	404	103	108
405	102	101			
Females					
451	108	109	452	108	110
453	108	106	454	102	105
455	108	109			

INORG. PHOSPHORUS (MMOL/L)

30-05-0387-90

Animal No.	Week 0	Week 4	Animal No.	Week 0	Week 4
I					
Males					
101	1.6	1.6	102	2.0	1.8
103	1.9	1.9	104	2.2	1.8
105	1.9	2.0			
Females					
151	2.0	2.0	152	2.1	1.8
153	2.2	2.1	154	2.1	2.2
155	1.6	1.9			
II					
Males					
201	1.9	2.2	202	2.0	2.2
203	1.7	1.9	204	2.4	2.5
205	2.1	2.0			
Females					
251	1.9	2.0	252	1.7	1.6
253	2.0	1.6	254	2.0	2.1
255	1.9	2.0			
III					
Males					
301	1.9	1.8	302	2.3	1.9
303	2.2	2.0	304	2.3	1.7
305	2.1	2.0			
Females					
351	1.8	1.8	352	2.0	1.7
353	2.0	1.8	354	2.4	2.1
355	1.8	2.0			
IV					
Males					
401	2.7	2.4	402	2.6	2.0
403	3.1	2.1	404	2.1	1.8
405	2.5	1.8			
Females					
451	2.1	1.7	452	2.3	1.7
453	1.9	2.1	454	2.3	2.1
455	2.1	1.6			

Organ weights(g) 30-05-0387-90

Terminal sacrifice, day 28

Anim.-no.	TERMINAL-WEIGHT	HEART	LIVER	KIDNEY L.	KIDNEY R.	ADREN. L.
I males						
101	504.	2.015	19.005	2.235	2.340	.124
102	537.	2.552	21.955	2.630	2.541	.182
103	499.	1.985	18.194	2.190	2.187	.101
104	545.	2.079	18.431	2.430	2.305	.086
105	544.	2.257	19.830	2.460	2.585	.097
I females						
151	449.	1.835	19.553	1.999	2.014	.129
152	520.	1.862	23.610	2.288	2.329	.123
153	444.	1.763	16.943	1.847	2.044	.118
154	465.	1.464	15.707	2.105	2.048	.126
155	552.	2.260	22.270	2.740	2.560	.073
II males						
201	482.	1.827	17.849	2.063	2.097	.097
202	506.	2.190	22.885	2.327	2.367	.123
203	573.	2.670	24.485	2.504	2.433	.108
204	556.	2.133	22.160	2.587	2.735	.097
205	553.	2.128	22.721	2.925	2.654	.107
II females						
251	455.	1.657	18.453	1.949	2.037	.170
252	542.	1.772	20.152	2.351	2.255	.164
253	514.	2.283	21.583	2.261	2.269	.130
254	518.	1.974	18.568	2.071	1.994	.099
255	501.	1.987	19.925	2.081	2.059	.124
III males						
301	582.	2.502	23.541	2.640	2.546	.097
302	564.	2.728	23.463	2.536	2.414	.071
303	499.	2.064	19.022	2.580	2.566	.125
304	499.	2.243	18.014	2.385	2.377	.158
305	521.	2.195	18.897	2.310	2.315	.104
III females						
351	449.	1.455	13.940	1.922	2.017	.169
352	502.	2.063	18.917	2.290	2.303	.119
353	461.	1.663	17.546	1.812	1.951	.082
354	482.	1.913	16.422	2.366	2.087	.131
355	455.	1.864	14.205	1.849	1.697	.128

Organ weights(g) 30-05-0387-90

Terminal sacrifice, day 28

Anim.-no.	TERMINAL-WEIGHT	HEART	LIVER	KIDNEY L.	KIDNEY R.	ADREN. L.
IV males						
401	558.	2.058	22.095	2.549	2.568	.047
402	554.	2.712	23.469	2.480	2.377	.107
403	615.	2.197	26.261	2.555	2.492	.112
404	518.	1.856	18.481	2.198	2.200	.081
405	629.	2.471	27.313	2.621	2.481	.127
IV females						
451	524.	2.283	21.387	2.403	2.522	.139
452	452.	1.803	14.271	1.798	1.771	.108
453	489.	1.930	17.337	1.990	1.934	.129
454	537.	1.905	20.821	2.340	2.261	.106
455	446.	1.585	15.089	1.719	1.931	.126

Organ weights(g) 30-05-0387-90

Terminal sacrifice, day 28

Anim.-no.	ADREN. R.	SPLEEN	PROST./UTERUS	TESTES/OVAR L.	TESTES/OVAR R.
I males					
101	.101	.609	-	1.374	1.369
102	.160	.443	-	1.010	1.185
103	.097	.561	-	1.396	1.324
104	.076	.696	-	1.164	1.232
105	.080	.737	-	1.267	1.213
I females					
151	.116	.552	1.308	.118	.102
152	.161	.788	2.319	.036	.043
153	.134	.746	1.695	.065	.050
154	.103	.697	1.914	.049	.051
155	.114	.791	1.187	.058	.073
II males					
201	.109	.488	-	1.088	1.180
202	.139	.655	-	1.083	.982
203	.085	.707	-	1.142	1.268
204	.096	1.044	-	1.065	1.144
205	.127	.799	-	1.364	1.241
II females					
251	.107	.617	1.406	.106	.112
252	.133	.896	2.045	.060	.034
253	.092	.740	1.690	.094	.081
254	.150	.848	1.494	.041	.062
255	.158	.729	1.011	.029	.058
III males					
301	.108	.522	-	.971	1.077
302	.098	.663	-	1.202	1.212
303	.092	.751	-	1.110	1.041
304	.214	.681	-	1.360	1.370
305	.092	.697	-	1.058	1.151
III females					
351	.078	.565	1.361	.066	.042
352	.094	1.563	2.613	.043	-
353	.114	.630	1.292	.028	.038
354	.135	.789	1.730	.059	.057
355	.124	.563	1.700	.032	.031

Organ weights(g) 30-05-0387-90

Terminal sacrifice, day 28

Anim.-no.	ADREN. R.	SPLEEN	PROST./UTERUS	TESTES/OVAR L.	TESTES/OVAR R.
IV males					
401	.081	.642	-	1.379	1.411
402	.158	.651	-	1.480	1.429
403	.104	.722	-	1.191	1.160
404	.116	.798	-	.855	.708
405	.102	.999	-	1.153	1.203
IV females					
451	.115	.896	1.350	.133	.128
452	.099	.626	1.213	.026	.024
453	.099	.931	2.253	.095	.037
454	.137	.791	2.082	.051	.043
455	.102	.678	1.665	.027	.031

Reports Code Table

N	Tissues within normal histiological limits
A	Autolysis precluding adequate evaluation
P	Paired organ missing
U	Tissue unsuitable for complete evaluation
*	Tissue unavailable for evaluation

1	minimal
2	mild
3	moderate
4	marked
()	focal
[]	locally extensive
<>	multifocal
P	Present
B	Neoplasm, Benign
M	Neoplasm, Malignant without Metastasis
C	Neoplasm, Malignant with Metastasis
X	Metastatic Site (+)
--	No data entered/not examined

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: Control SEX: MALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	101	102	103	104	105
Heart (Sudan red)	N	N	N	N	N
Kidney I (H.E.)			N		
Lympho-histiocytic infiltr.	(1)	-	-	-	-
Cortical fibrosis	-	-	-	(1)	(1)
Regeneration of tubules	-	(1)	-	(1)	(1)
Kidney I (Sudan red)	N	N	N		
Cortical fibrosis	-	-	-	(1)	(1)
Kidney II (H.E.)		N	N	N	
Lympho-histiocytic infiltr.	(1)	-	-	-	-
Regeneration of tubules	-	-	-	-	(1)
Liver (H.E.)					
Pericholangitis	-	2	-	2	2
Focal necrosis of hepatoc.	<3>	-	-	1	-
MPS-cell proliferation	2	2	1	1	2
Liver (Sudan red)					
Fatty infiltr.single hepatoc.	1	1	1	1	1
Skin (treated)	N	N		N	N
Epidermal hyperplasia	-	-	P	-	-
Skin (untreated)	N	N	N	N	N

24-Jan-1991

IBR

Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: Control SEX: FEMALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	151	152	153	154	155
Heart (Sudan red)	N	N	N	N	N
Kidney I (H.E.)					
Hyaline tubular casts	-	1	-	-	-
Lympho-histiocytic infiltr.	-	-	-	-	(1)
Cortical fibrosis	-	-	-	(1)	(1)
Fibrosis	-	-	<1>	<1>	-
Regeneration of tubules	1	-	<2>	<2>	(1)
Calcified tubular casts	<1>	-	2	-	-
Kidney I (Sudan red)	N	N	N		
Cortical fibrosis	-	-	-	(1)	(1)
Kidney II (H.E.)	N				
Hyaline tubular casts	-	2	2	-	-
Lympho-histiocytic infiltr.	-	-	-	-	(1)
Regeneration of tubules	-	-	-	<2>	(1)
Liver (H.E.)					
Pericholangitis	1	2	1	2	1
MPS-cell proliferation	-	-	(1)	(2)	(2)
Liver (Sudan red)	N				
Fatty infiltr.single hepatoc.	-	2	1	1	1
Diffuse fatty infiltration	-	1	-	-	-
Skin (treated)	N	N	N		
Epidermis, incomplete	-	-	-	P	P

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: Control SEX: FEMALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	151	152	153	154	155
Skin (untreated)	N		N	N	N
Epidermal hyperplasia	-	P	-	-	-

24-Jan-1991

Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg SEX: MALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	201	202	203	204	205
Liver (H.E.)					
Pericholangitis	1	2	1	2	2
MPS-cell proliferation	(2)	-	2	2	2
Sinusoidal leukocytosis	-	-	-	-	1
Skin (treated)		N			N
Epidermal hyperplasia	P	-	P	-	-
Epidermis, incomplete	-	-	-	P	-
Skin (untreated)	N	N	N	N	N

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Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg SEX: FEMALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	251	252	253	254	255
Liver (H.E.)					
Pericholangitis	1	1	1	1	1
MPS-cell proliferation	(1)	1	1	1	1
Skin (treated)					N
Hyperkeratosis	-	-	1	1	-
Epidermal hyperplasia	P	P	-	-	-
Skin (untreated)	N	N	N	N	N

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Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg SEX: MALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	301	302	303	304	305
Liver (H.E.)					
Pericholangitis	1	1	2	1	2
Focal necrosis of hepatoc.	-	-	-	1	-
MPS-cell proliferation	1	1	2	2	1
Sinusoidal leukocytosis	1	-	-	-	-
Skin (treated)	N	N		N	N
Hyperkeratosis	-	-	1	-	-
Skin (untreated)	N	N	N	N	N

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Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg SEX: FEMALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	351	352	353	354	355
Liver (H.E.)					
Pericholangitis	2	2	1	1	2
Focal necrosis of hepatoc.	-	-	-	-	<2>
MPS-cell proliferation	2	1	1	1	2
Sinusoidal leukocytosis	-	1	1	-	1
Skin (treated)	N	N	N		N
Hyperkeratosis	-	-	-	2	-
Epidermal hyperplasia	-	-	-	P	-
Skin (untreated)	N	N	N	N	N

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Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg SEX: MALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	401	402	403	404	405
Heart (Sudan red)		N	N	N	N
Lympho-histioc.infiltration	1	-	-	-	-
Kidney I (H.E.)				N	
Hyaline tubular casts	-	1	-	-	-
Cortical fibrosis	(1)	(1)	(1)	-	-
Calcified tubular casts	(1)	-	-	-	-
Lymph.-hist. infiltr.in pelvis	1	-	-	-	(1)
Kidney I (Sudan red)				N	N
Cortical fibrosis	(1)	(1)	(1)	-	-
Calcified tubular casts	(1)	-	-	-	-
Kidney II (H.E.)	N			N	
Hyaline tubular casts	-	1	1	-	-
Cortical fibrosis	-	-	-	-	(1)
Lymph.-hist. infiltr.in pelvis	-	-	-	-	(1)
Liver (H.E.)					
Pericholangitis	1	1	-	1	-
MPS-cell proliferation	2	2	-	1	1
Sinusoidal leukocytosis	1	1	1	1	-
Plant cell structure	-	-	2	-	-
Liver (Sudan red)					
Fatty infiltr.single hepatoc.	2	1	-	-	1
Diffuse fatty infiltration	1	-	1	1	-

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Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg SEX: MALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	401	402	403	404	405
Skin (treated)					
Hyperkeratosis	-	-	2	2	1
Epidermal hyperplasia	P	P	P	P	P
Skin (untreated)	N	N	N	N	N

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Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg SEX: FEMALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	451	452	453	454	455
Heart (Sudan red)	N	N	N	N	N
Kidney I (H.E.)	N				
Lympho-histiocytic infiltr.	-	(1)	-	(1)	-
Cortical fibrosis	-	-	(1)	-	(1)
Regeneration of tubules	-	(1)	(1)	<1>	-
Calcified tubular casts	-	1	-	-	1
Kidney I (Sudan red)	N	N		N	
Cortical fibrosis	-	-	(1)	-	(1)
Kidney II (H.E.)	N			N	
Lympho-histiocytic infiltr.	-	(1)	-	-	-
Regeneration of tubules	-	-	1	-	-
Calcified tubular casts	-	1	-	-	1
Liver (H.E.)					
Pericholangitis	1	1	1	1	1
Focal necrosis of hepatoc.	-	1	-	<3>	-
MPS-cell proliferation	1	1	1	1	1
Sinusoidal leukocytosis	1	-	1	1	1
Liver (Sudan red)			N	N	
Fatty infiltr.single hepatoc.	1	1	-	-	1
Skin (treated)		N	N		N
Hyperkeratosis	-	-	-	2	-
Epidermal hyperplasia	P	-	-	P	-

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Tabulated Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg SEX: FEMALE
WEEKS: ALL FATES: ALL

ANIMAL ID:	451	452	453	454	455
Skin (untreated)	N	N	N	N	*

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 101
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Focal necrosis of hepatoc., multifocal, moderate
MPS-cell proliferation, mild
Kidney I (H.E.): Lympho-histiocytic infiltr., focal , minimal
Kidney II (H.E.): Lympho-histiocytic infiltr., focal , minimal

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Skin (untreated);
Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 102
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, mild
MPS-cell proliferation, mild
Kidney I (H.E.): Regeneration of tubules, focal , minimal

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Kidney II (H.E.);
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 103
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): MPS-cell proliferation, minimal
Skin (treated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Kidney I (H.E.);
Kidney II (H.E.); Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 104
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, mild
Focal necrosis of hepatoc., minimal
MPS-cell proliferation, minimal
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Kidney I (H.E.): Cortical fibrosis, focal , minimal
Regeneration of tubules, focal , minimal

Tissues within normal histological limits:
Heart (Sudan red); Kidney II (H.E.); Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 105
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, mild
MPS-cell proliferation, mild
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Kidney I (H.E.): Cortical fibrosis, focal , minimal
Regeneration of tubules, focal , minimal
Kidney II (H.E.): Regeneration of tubules, focal , minimal

Tissues within normal histological limits:
Heart (Sudan red); Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 151
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (H.E.): Pericholangitis, minimal
Kidney I (H.E.): Regeneration of tubules, minimal
Calcified tubular casts, multifocal, minimal

Tissues within normal histological limits:
Liver (Sudan red); Heart (Sudan red); Kidney I (Sudan red);
Kidney II (H.E.); Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 152
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., mild
Diffuse fatty infiltration, minimal
Liver (H.E.): Pericholangitis, mild
Kidney I (H.E.): Hyaline tubular casts, minimal
Kidney II (H.E.): Hyaline tubular casts, mild
Skin (untreated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 153
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, focal , minimal
Kidney I (H.E.): Fibrosis, multifocal, minimal
Regeneration of tubules, multifocal, mild
Calcified tubular casts, mild
Kidney II (H.E.): Hyaline tubular casts, mild

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Skin (untreated);
Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 154
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, mild
MPS-cell proliferation, focal , mild
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Kidney I (H.E.): Cortical fibrosis, focal , minimal
Fibrosis, multifocal, minimal
Regeneration of tubules, multifocal, mild
Kidney II (H.E.): Regeneration of tubules, multifocal, mild
Skin (treated): Epidermis, incomplete, Present

Tissues within normal histological limits:
Heart (Sudan red); Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: Control ANIMAL ID: 155
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, focal , mild
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Kidney I (H.E.): Lympho-histiocytic infiltr., focal , minimal
Cortical fibrosis, focal , minimal
Regeneration of tubules, focal , minimal
Kidney II (H.E.): Lympho-histiocytic infiltr., focal , minimal
Regeneration of tubules, focal , minimal
Skin (treated): Epidermis, incomplete, Present

Tissues within normal histological limits:
Heart (Sudan red); Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 201
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, focal , mild
Skin (treated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 202
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (H.E.): Pericholangitis, mild

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 203
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, mild
Skin (treated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 204
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (H.E.): Pericholangitis, mild
MPS-cell proliferation, mild
Skin (treated): Epidermis, incomplete, Present

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 205
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, mild
MPS-cell proliferation, mild
Sinusoidal leukocytosis, minimal

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 251
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, focal , minimal
Skin (treated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 252
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Skin (treated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 253
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Skin (treated): Hyperkeratosis, minimal

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 254
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Skin (treated): Hyperkeratosis, minimal

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 50mg/kg ANIMAL ID: 255
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 301
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
.iver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Sinusoidal leukocytosis, minimal

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

24-Jan-1991

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 302
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 303
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, mild
MPS-cell proliferation, mild
Skin (treated): Hyperkeratosis, minimal

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 304
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (H.E.): Pericholangitis, minimal
Focal necrosis of hepatoc., minimal
MPS-cell proliferation, mild

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

24-Jan-1991

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 305
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, mild
MPS-cell proliferation, minimal

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 351
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (H.E.): Pericholangitis, mild
MPS-cell proliferation, mild

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 352
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, mild
MPS-cell proliferation, minimal
Sinusoidal leukocytosis, minimal

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 353
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Sinusoidal leukocytosis, minimal

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

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in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 354
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Skin (treated): Hyperkeratosis, mild
Epidermal hyperplasia, Present

Tissues within normal histological limits:
Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 150mg/kg ANIMAL ID: 355
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
.iver (H.E.): Pericholangitis, mild
Focal necrosis of hepatoc., multifocal, mild
MPS-cell proliferation, mild
Sinusoidal leukocytosis, minimal

Tissues within normal histological limits:
Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 401
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (Sudan red): Fatty infiltr.single hepatoc., mild
Diffuse fatty infiltration, minimal
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, mild
Sinusoidal leukocytosis, minimal
Heart (Sudan red): Lympho-histioc.infiltration, minimal
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Calcified tubular casts, focal , minimal
Kidney I (H.E.): Cortical fibrosis, focal , minimal
Calcified tubular casts, focal , minimal
Lymph.-hist. infiltr.in pelvis, minimal
Skin (treated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Kidney II (H.E.); Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 402
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, mild
Sinusoidal leukocytosis, minimal
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Kidney I (H.E.): Hyaline tubular casts, minimal
Cortical fibrosis, focal , minimal
Kidney II (H.E.): Hyaline tubular casts, minimal
Skin (treated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Heart (Sudan red); Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 403
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
.iver (Sudan red): Diffuse fatty infiltration, minimal
Liver (H.E.): Sinusoidal leukocytosis, minimal
Plant cell structure, mild
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Kidney I (H.E.): Cortical fibrosis, focal , minimal
Kidney II (H.E.): Hyaline tubular casts, minimal
Skin (treated): Hyperkeratosis, mild
Epidermal hyperplasia, Present

Tissues within normal histological limits:
Heart (Sudan red); Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 404
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (Sudan red): Diffuse fatty infiltration, minimal
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Sinusoidal leukocytosis, minimal
Skin (treated): Hyperkeratosis, mild
Epidermal hyperplasia, Present

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Kidney I (H.E.);
Kidney II (H.E.); Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 405
SEX: MALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record:	Related histopathology:
>Liver- focal yellowish discolored (diameter 1cm)	No corollary change detected

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): MPS-cell proliferation, minimal
Kidney I (H.E.): Lymph.-hist. infiltr.in pelvis, focal , minimal
Kidney II (H.E.): Cortical fibrosis, focal , minimal
Lymph.-hist. infiltr.in pelvis, focal , minimal
Skin (treated): Hyperkeratosis, minimal
Epidermal hyperplasia, Present

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 451
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Sinusoidal leukocytosis, minimal
Skin (treated): Epidermal hyperplasia, Present

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Kidney I (H.E.);
Kidney II (H.E.); Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 452
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, minimal
Focal necrosis of hepatoc., minimal
MPS-cell proliferation, minimal
Kidney I (H.E.): Lympho-histiocytic infiltr., focal , minimal
Regeneration of tubules, focal , minimal
Calcified tubular casts, minimal
Kidney II (H.E.): Lympho-histiocytic infiltr., focal , minimal
Calcified tubular casts, minimal

Tissues within normal histological limits:
Heart (Sudan red); Kidney I (Sudan red); Skin (untreated);
Skin (treated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR Project No.:30-05-0387-90
28-Day Repeated Dose Dermal Toxicity Test
with
" Lehmannblausulfat "
in Guinea Pigs

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 453
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
iver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Sinusoidal leukocytosis, minimal
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Kidney I (H.E.): Cortical fibrosis, focal , minimal
Regeneration of tubules, focal , minimal
Kidney II (H.E.): Regeneration of tubules, minimal

Tissues within normal histological limits:
Liver (Sudan red); Heart (Sudan red); Skin (untreated); Skin (treated)

= Histologic change related to necropsy record data

24-Jan-1991

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 454
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:

Liver (H.E.):	Pericholangitis, minimal
	Focal necrosis of hepatoc., multifocal, moderate
	MPS-cell proliferation, minimal
	Sinusoidal leukocytosis, minimal
Kidney I (H.E.):	Lympho-histiocytic infiltr., focal , minimal
	Regeneration of tubules, multifocal, minimal
Skin (treated):	Hyperkeratosis, mild
	Epidermal hyperplasia, Present

Tissues within normal histological limits:
Liver (Sudan red); Heart (Sudan red); Kidney I (Sudan red);
Kidney II (H.E.); Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

IBR

Individual Animal Data

PROJECT ID: 0387-90 GROUP: 300mg/kg ANIMAL ID: 455
SEX: FEMALE PATHOLOGIST: MES

ANIMAL FATE: Terminal sacrifice WEEKS ON TEST:4

Reference to necropsy record: Related histopathology:

>no specific findings

Microscopic Observations:
Liver (Sudan red): Fatty infiltr.single hepatoc., minimal
Liver (H.E.): Pericholangitis, minimal
MPS-cell proliferation, minimal
Sinusoidal leukocytosis, minimal
Kidney I (Sudan red): Cortical fibrosis, focal , minimal
Kidney I (H.E.): Cortical fibrosis, focal , minimal
Calcified tubular casts, minimal
Kidney II (H.E.): Calcified tubular casts, minimal

Tissues within normal histological limits:
Heart (Sudan red); Skin (treated)

Tissues unavailable for evaluation:
Skin (untreated)

= Histologic change related to necropsy record data

24-Jan-1991

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Project No.: 85-00-0387-90

CERTIFICATE OF ANALYSIS

PHOTOMETRIC ANALYSIS

(Lehmannblausulfat)

IBR Project-No.: 30-05-0387-90

CERTIFICATE OF ANALYSIS
PHOTOMETRIC DETERMINATION OF LEHMANNBLAUSULFAT
85-00-0387-90

IBR

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CERTIFICATE OF ANALYSIS
PHOTOMETRIC DETERMINATION OF LEHMANNBLAUSULFAT
85-00-0387-90

IBR

DECLARATION

We, the undersigned, hereby declare that the work was performed under our supervision and in accordance with the procedures. It is assured that the reported results faithfully reproduce the raw data obtained during the experimental work. To the best of our knowledge, no circumstances have been left unreported which may have affected the quality or integrity of the data or which might have a potential bearing on the validity and reproducibility of this study.

The study director accepts overall responsibility for the technical conduct of the study as well as for the interpretation, analysis, documentation and reporting of the results.

Scientific supervisor .....

Study director .....

17. 11 90
.....
Date

CERTIFICATE OF ANALYSIS
PHOTOMETRIC DETERMINATION OF LEHMANNBLAUSULFAT
85-00-0387-90

IBR

QUALITY ASSURANCE STATEMENT

The testing facilities utilized in this study have been inspected regularly in accordance with the principles of Good Laboratory Practice for the testing of chemicals as specified by national (BGB1. I, No. 13, § 19 a, March 22, 1990) and international (OECD, Paris, 1982) legislation.

Procedures relevant to studies of this type are inspected periodically. Inspections were conducted according to the standard operating procedures of the testing facility's quality assurance unit. The final report was audited in detail against the approved protocol and all pertinent raw data; the findings were reported to management and to study director on 20.11.1990.

i.A. K. Richard

(p.p. Quality Assurance Unit)

29.11.90

Date

CERTIFICATE OF ANALYSIS
PHOTOMETRIC DETERMINATION OF LEHMANNBLAUSULFAT
85-00-0387-90

IBR

GLP COMPLIANCE

To the best of my knowledge, this study was performed in accordance with the principles of Good Laboratory Practice for the testing of chemicals as specified by national (BGB1. I, No. 13, § 19 a, March 22, 1990) and international (OECD, Paris, 1982) legislation.

Study Director:

M. Egger

27. 11.90
Date

1. INTRODUCTION

1.1 Aims of the study

The test article was to be applied in a dermal toxicity test in guinea pigs as a solution in water. Photometric analysis was performed for concentration checks and stability testing.

1.2 Test article information

Test substance:	Lehmannblausulfat 1-Methoxy-2-amino-4-(2'-hydroxyethyl)-amino-benzene-sulfate (CAS Reg.-No.: not registered)
Samples:	Solutions of test article in water in concentrations of 5 %, 15 % and 30 %.
Samples received:	07.08.1990 (1. concentration check) 28.08.1990 (2. concentration check)
Sample storage:	at ambient temperature (25° C), protected from light

Measurements were performed directly after receiving the samples.

2. MATERIALS AND METHODS

2.1 Materials

Water was demineralized and purified to HPLC grade.
Quartz cuvettes were used throughout the study.
Photometric analyses were performed on a Kontron Uvikon 860 spectral photometer.

2.2 Methods

2.2.1 Photometric determination of Lehmannblausulfat

All experiments were carried out in accordance with IBR SOP/88/T/01. In brief, the procedure was as follows:

The spectrum of a fresh Lehmannblausulfat solution against solvent was recorded in the range 180nm to 900nm. The peak at 546nm was chosen for concentration measurements.

The reference standard was diluted to a concentration range of 0.2% to 5%, yielding corresponding OD(546nm) values from 0.04 to 1.03. In this range, the OD measured at 546nm gave a linear response to the increases in concentration.

Sample solutions in water were prepared according to the study protocol in the concentrations given

2.2.2 Stability testing of Lehmannblausulfat

All experiments were carried out in accordance with IBR SOP/88/T/01. In brief, the procedure was as follows:
The test article was prepared as a solution in water at a concentration of 5%. An initial spectrum between 180nm and 900nm was recorded. This procedure was repeated after 0.5, 1, 2, 3, 4 and 24 hours, respectively, on freshly prepared dilutions of the same solution.

3. RESULTS

3.1 Stability testing

Figure 1a shows the first of a series of UV spectra in the range from 180nm to 900nm taken at regular intervals after 30 and 60 minutes within the first 4 hours, whereas **Figure 1b** shows a spectrum after 24 hours (at 25°C). Peak checks were performed on every spectrum, and these values are presented in **Table 1**. A comparison of these values already indicate signs of chemical degradation within the first half hour.

Table 1

Results of stability testing of Lehmannblausulfat in a concentration of 5% water. The OD values were recorded in 0.5- and 1-hour intervals.

time	dilution factor	wavelength (nm)	absorbance	wavelength (nm)	absorbance
t=0h	0	466	0.933	549	1.198
t=0.5h	0	466	0.963	548	1.256
t=1h	0	464	1.014	548	1.377
t=2h	0	458	1.067	550	1.542
t=3h	0	454	1.140	550	1.722
t=4h	0	451	1.180	549	1.875
t=24h	5	418	3.370	547	8.085

Figure 1a

Initial UV spectrum of Lehmannblausulfat (5%) between 180nm and 900nm
Water was used as solvent and reference

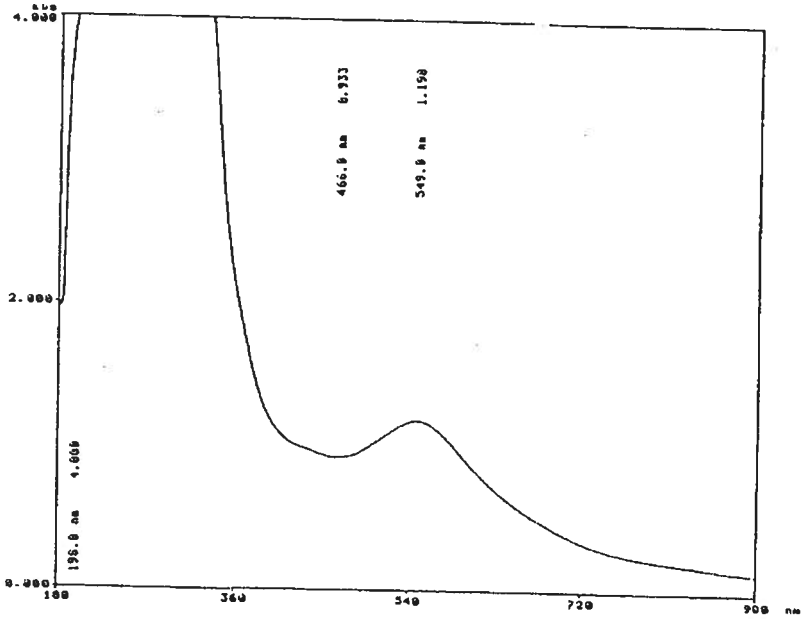
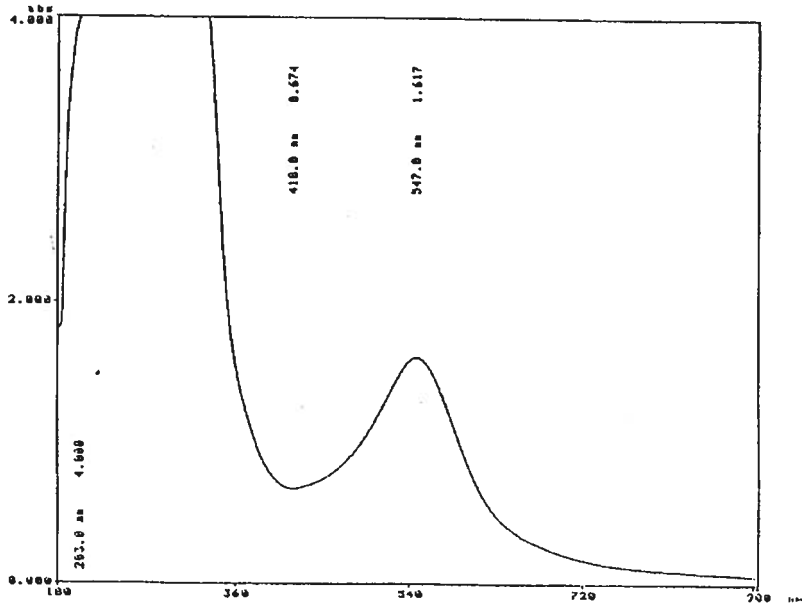


Figure 1b

UV spectrum of Lehmannblausulfat (5%) between 180nm and 900nm after 24 h at 25°C.
Water was used as solvent and reference



4. SUMMARY

The test article Lehmannblausulfat can be analyzed quantitatively with the aid of UV spectroscopy. The identity of samples of dosing solutions was confirmed by comparison to a reference standard of the test article.

However, the stability of the compound in aqueous solution is insufficient to allow analytical control measurements on aqueous samples after extended periods of time.

The concentration values obtained for solutions freshly prepared at the Bioanalytical Centre for validation purposes according to the study protocol are in good agreement with the required concentration levels.

In contrast, samples of solutions used in the dermal toxicity study, which were shipped to the Bioanalytical Centre for analytical controls, showed deviations above 10% (in one case, ca.42%) from the nominal values. This is clearly related to the insufficient stability of the test article in this vehicle.

ssniff Spezialdiäten GmbH · Postfach 2039 · 4770 Soest

ssniff
Spezialdiäten GmbH

Ferdinand-Gabriel-Weg 16
Postfach 2039
4770 Soest/Westfalen
Fernruf (02921) 73088
außerhalb der Bürozeiten: 62204
5662
Telex 84394 (MJK)
Telefax (02921) 74515

D E C L A R A T I O N

All our following products are delivered free of Aflatoxines to IBR Forschungs GmbH, Südkampen 31, 3o3o Walsrode 2

ssniff R	diet for rats
ssniff G	diet for guinea pigs
ssniff HH and HZ	diet for dogs
ssniff K	diet for rabbits
mümmel Z	diet for rabbits
ssniff MS 2	diet for mini pigs

The controls for residues are performed continually by the agricultural institute for investigation and research, Kiel (LUFA), completed by other official institutes.

Soest,

s s n i f f
Spezialdiäten GmbH

Geschäftsführende Gesellschafter: Wilhelm Keller, Thelle-Ochel, Soest Handelsregister: Amtsgericht Soest HRB 1497

Landwirtschaftliche Untersuchungs- und Forschungsanstalt Kiel
Postfach 30 67 · 2300 Kiel 1

IDR
Südkampen Nr. 31

3030 Walsrode 1

Landwirtschaftliche Untersuchungs- und Forschungsanstalt Kiel
der
Landwirtschaftskammer Schleswig-Holstein

2300 Kiel 1, 06.08.1990
Gutenbergstraße 75-77
Telefon (04 31) 169 04-0
Telegramm-Adresse: LUFA Kiel
Telex-Nr. 0292 634 lufak d
Telefax (04 31) 169 04 17

Gesch.-Z.: SO 10308
(bitte im Schriftverkehr angeben)
SO 140/ QVM 42
M 165/

Ihr Zeichen	Ihr Schreiben vom	Unser Zeichen
PF/vo	13.07.90	90/Schu/

Bezeichnung d. Probe (gem. Angabe d. Auftraggebers): ssniff G 4
Diät für Meerschweinchen
Charge 77079004

Probenahme am:		Erzeuger/Hersteller:	
Probenahme bei:		Herstellungsdatum:	
Probenehmer:		Partie-Nr.:	
Eingangsdatum:	16.07.1990	Größe der Partie:	
Verpackung:	Kunststoffdose	Schiff/LKW/Waggon:	
Siegel / Plombe:	ohne	Verkäufer:	
Gewicht d. Probe:		Käufer:	
Protokoll-Nr.:		Empfänger:	

Untersuchungsbefund

CHLORIERTE KOHLENWASSERSTOFFE:		
HCB (Hexachlorbenzol)	n.b.	<0,002 mg/kg
alpha-HCH	n.b.	<0,002 mg/kg
beta-HCH	n.b.	<0,002 mg/kg
gamma-HCH (Lindan)		0,012 mg/kg
delta-HCH	n.b.	<0,002 mg/kg
Quintozen	n.b.	<0,002 mg/kg
Heptachlor	n.b.	<0,002 mg/kg
Heptachlorepoxid	n.b.	<0,002 mg/kg
alpha-Chlordan	n.b.	<0,002 mg/kg
gamma-Chlordan	n.b.	<0,002 mg/kg
alpha-Endosulfan	n.b.	<0,002 mg/kg
beta-Endosulfan	n.b.	<0,002 mg/kg
Aldrin	n.b.	<0,002 mg/kg
Dieldrin	n.b.	<0,002 mg/kg
Endrin	n.b.	<0,002 mg/kg
p,p-DDE	n.b.	<0,002 mg/kg
o,p-DDT	n.b.	<0,002 mg/kg
p,p-DDD	n.b.	<0,002 mg/kg
p,p-DDT	n.b.	<0,002 mg/kg

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Landwirtschaftliche Untersuchungs- und Forschungsanstalt Kiel
Postfach 30 67 · 2300 Kiel 1

IDK
Südkampen Nr. 31

3030 Walsrode 1

Landwirtschaftliche Untersuchungs- und Forschungsanstalt Kiel

der

Landwirtschaftskammer Schleswig-Holstein

2300 Kiel 1, 06.08.1990
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Telegramm-Adresse: LUFA Kiel
Telex-Nr. 0292634 lufak d
Telefax (0431) 169017

Ihr Zeichen	Ihr Schreiben vom	Unser Zeichen
PF/vo	13.07.90	90/Schu/

Gesch.-Z.: SO 10308
(bitte im Schriftverkehr angeben)
SO 140/ QVM 42
M 165/

Bezeichnung d. Probe (gem. Angabe d. Auftraggebers): ssniff G 4
Diät für Meerschweinchen
Charge 77079004

Probenahme am:		Erzeuger/Hersteller:	
Probenahme bei:		Herstellungsdatum:	
Probenehmer:		Partie-Nr.:	
Eingangsdatum:	16.07.1990	Größe der Partie:	
Verpackung:	Kunststoffdose	Schiff/LKW/Waggon:	
Siegel / Plombe:	ohne	Verkäufer:	
Gewicht d. Probe:		Käufer:	
Protokoll-Nr.:		Empfänger:	

Untersuchungsbefund

Nitrit	<10 mg/kg	
Aflatoxin B1	nicht bestimmbar,	< 3 mcg/kg
	nicht nachweisbar,	< 1 mcg/kg
Blei (Pb)	1,1	mg/kg
Cadmium (Cd)	0,11	mg/kg
Quecksilber (Hg)	<0,01	mg/kg
Arsen (As)	<0,1	mg/kg

62 LANDWIRTSCHAFTSKAMMER SCHLESWIG-HOLSTEIN

(P. Kallweit)

(n.b. = nicht bestimmbar)

ssniff
Spezialdiäten GmbH
Wissenschaftliche Abteilung
— Labor —

Untersuchung

№ 3413

Herstellungs-/Eingangs-	datum	31.07.90
Chargen-Nr./Lieferant		66079031

ssniff G 4

Weender Analyse

Rohprotein	21,1	%
Rohfett	3,6	%
Rohfaser	14,2	%
Rohasche	8,3	%
H_2O	11,1	%
N-freie Extr.	41,7	%
Ca-Gehalt	1,27	%
P-Gehalt:	0,79	%

Spezialuntersuchungen:

Pellethärte nach Kahl: 17,1

Bemerkungen: 1.500 kg

IBR Forschungs GmbH, Südkampen

Soest, den 14. August 1990

ssniff
Spezialdiäten GmbH
Wissenschaftliche Abteilung
— Labor —

Untersuchung

Nº 3365

Herstellungs-/Eingangs-	datum	04.07.90
Chargen-Nr./Lieferant		77079004

ssniff G 4

Weender Analyse

Rohprotein	20,7	%
Rohfett	3,2	%
Rohfaser	14,2	%
Rohasche	8,3	%
H_2O	11,8	%
N-freie Extr.	41,8	%
Ca-Gehalt	1,41	%
P-Gehalt:	0,79	%

Spezialuntersuchungen:

Pellethärte nach Kahl: 17,3

Bemerkungen: 2.000 kg

IBR Forschungs GmbH, Südkampen

Soest, den 12. Juli 1990

LANDKREIS SOLTAU-FALLINGBOSTEL
Der Oberkreisdirektor
Wasseruntersuchungslabor

IBR-Forschungs GmbH
Südkampen 31

3030 Walsrode

Auskunft erteilt	Verwaltungsgebäude Soltau	Zimmer	Telefon
Frau Sandkühler	Winsener Str. 17	U 1	05191/85-2 24

Mein Zeichen: 66.37/66-33-2050/~~357~~ 417

Soltau, 11. September 1990
6635 09/15

H Y G I E N I S C H E W A S S E R A N A L Y S E

Entnahme durch : GA Walsrode Entnahme-Datum: 04.09.1990
Bezeichnung der Probe: Trinkwassereigenversorgungsanlage
Probenummer : ~~357~~ 417

BAKTERIOLOGISCHE UNTERSUCHUNG			Ergebnisse	Grenzwerte nach TVO
Koloniezahl (20 °C)	in	1 ml:		100
Koloniezahl (36 °C)	in	1 ml:		100
Escherichia coli	in	100 ml:		negativ
Coliforme Bakterien	in	100 ml:		negativ

HYGIENISCH-CHEMISCHE UNTERSUCHUNG				
Färbung, Trübung, Geruch		:	farblos, klar,	ohne Geruch
pH-Wert		:	7,0	6,5 - 9,5
Leitfähigkeit		µS/cm :	236	2.000
Kaliumpermanganat-Verbrauch	O_2	mg/l:	0,75	5
Ammonium		mg/l:	<0,04	0,5
Nitrat		mg/l:	<0,5	50
Nitrit		mg/l:	<0,02	0,1
Eisen, gesamt		mg/l:	0,08	0,2
Mangan, gesamt		mg/l:		0,05
Säurekapazität		mmol/l:		
Gesamthärte		mmol/l:		

Beurteilung:

Das Trinkwasser der Probe 357 reagiert chemisch neutral. Ammonium, Nitrat und Nitrit sind nicht nachweisbar. Kaliumpermanganat-Verbrauch und Leitfähigkeit sind unauffällig. Der Eisengehalt liegt unter dem Grenzwert der Trinkwasser-Verordnung.

Die Qualität des Trinkwassers ist bezüglich der untersuchten Parameter sehr gut.

Im Auftrag

stellvertretender Amtsarzt

3 1

Bezirksregierung Lüneburg
- 205.3-41401/3 -

GLP-Zertifikat

Bescheinigung

Hiermit wird bestätigt, daß
die IBR Forschungs GmbH
in 3030 Walsrode 2,
Südkampen Nr. 31

am 15.04.1988

von der für die Überwachung zuständigen Behörde nach Maßgabe der OECD-Richtlinien für nationale Inspektionen und Überprüfungen über die Einhaltung der Grundsätze der Guten Laborpraxis inspiziert worden ist.

Es wird hiermit bestätigt, daß Prüfungen in dieser Prüfeinrichtung nach den OECD-Grundsätzen für Gute Laborpraxis durchgeführt werden.

Certificate

It is hereby certified that
the IBR Forschungs GmbH
in 3030 Walsrode 2,
Südkampen Nr. 31

on 15.04.1988

was inspected by the competent authority in accordance with the OECD-Guidelines for National GLP Inspections and Study Audits regarding the compliance with the Principles of Good Laboratory Practice.

It is hereby certified that studies in this test facility are conducted in compliance with the OECD-Principles of Good Laboratory Practice.

Lüneburg, 27. 4. 1988

Im Auftrage

Seippel

Seippel
Pharmaziedirektor

BEZIRKSREGIERUNG LÜNEBURG 70