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HMX: 13 WEEK TOXICITY STUDY IN RATS BY DIETARY ADMINISTRATION

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D.J. Everett I.R. Johnson P. Hudson M. Jones

*31* July₄1985

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Contracting Officer's Technical Representative:

Jesse J. Barkley, Jr. U.S. Army Medical Bioengineering Research and Development Laboratory Fort Detrick, Frederick, Maryland 21701-5010

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Abstract

Rats were fed diets containing HMX for 13 weeks. Dose levels for males were 0, 50, 150, 450, 1350 or 4000 mg HMX/kg/day. Female rats received 0, 50, 115, 270, 620 or 1500 mg HMX/kg/day.

No deaths or clinical signs occurred attributable to dosing with HMX.

Reduced body weight gains and food consumptions were observed, more so at higher dose levels.

Haematological and clinical chemical observations were made only on top dose and control animals. There were slight but consistent reductions in Hb, PCV and possibly RBC. AP activity was increased and there was evidence of methaemoglobinaemia but other clinical chemical changes were inconsistent.

There were no changes at gross autopsy.

Histopathology revealed enlarged centrilobular cells with pale nuclei and dark cytoplasm in the livers of males dosed at 150 mg HMX/kg/day and above. Females given 270 mg HMX/kg/day and above showed changes in renal tubules. The renal effect was less apparent in males, IRI Report No. 2188

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# FOREWORD

"I, the undersigned, hereby declare that this work was performed under my supervision, according to the procedures herein described and that this report represents a true and accurate record of the results obtained."

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A.B. Wilson, B.V.Sc., M.R.C.V.S., D.A.B.T. Principal Investigator

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### QUALITY ASSURANCE AUTHENTICATION

The conduct of this study has been subjected to periodic inspections by the IRI Quality Assurance Unit. The dates of inspection are given below.

IRI Project No. 415669CR/2188

Report No. 2188

Date of Q.A. Inspection Date of Report to Management

15 December 1980 12 January 1981 9 February 1981 4 March 1981 16 March 1981

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16 December 1980 13 January 1981 10 February 1981 4 March 1981 19 March 1981

This report has been audited by the Quality Assurance Personnel according to the appropriate Standard Operating Procedure. The report is considered to describe accurately the methods and procedures used in the study and the original data generated during the study.

Andrew Waddel Signed: (Quality Assurance Manager)

Date: <u>14 Jan 1986</u>,

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### SUMMARY

Five groups of 20d and 209 rats of the Fischer 344 strain were dosed at concentrations of Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX) in the diet calculated to give dose levels of 50, 150, 450, 1350 or 4000 mg HMX/kg/day for male rats and 50, 115, 270, 620 or 1500 mg HMX/kg/day for female rats. One group of 203 and 209 rats received untreated diet and acted as contemporary controls. Study duration was 13 weeks, at the end of this period animals were killed and subjected to full necropsy.

Before dosing commenced and during Week 13 of dosing ophthalmoscopic examination was performed on all animals.

Haematology and clinical chemistry blood samples were taken during Weeks 5 and 12 of dosing. Urine samples were taken from the same animals in the same weeks.

Results may be summarised as follows:

- Only 3 premature deaths occurred during the Mortality: study, all from different treatment groups.
- None was observed which could be attributed Clinical Signs: to dosing with HMX.
- Body weight gains were reduced in male and Body Weights: female animals receiving HMX in dose related fashion.
- Food consumption trends were variable Food Consumption: throughout the study but treated groups consumed less food than untreated groups during dosing.
- No abnormalities were detected which could Opthalmoscopy: be attributed to dosing with HMX.

This fell within acceptable limits. Achieved Dosage:

Laboratory Investigations:

The following changes occurred: Reductions in Hb and PCV in male and female high dose animals in both Weeks 5 and 12. Reduced RBC counts in males and females in Week 12. Slight increase in methaemoglobin in male and female high dose rats in Week 12. Significant increase in AP levels in top dose males and females in Week 5, and (females only) in Week 12. Significant increase in

Laboratory BUN levels in Weeks 5 and 12 of females Investigations receiving 1500 mg HMX/kg/day. Increased (continued): albumin and total protein levels in top dose females in Week 12. Increased albumin levels in top dose males in Week 5.

> Reduced pH and SG with increased volume of urine in top dose female rats in Weeks 5 and 12. Fern-like crystals were seen in Week 12 in urine of top dose males and females.

- Terminal Studies: Two dose related lesions were seen: Toxic liver change, characterised by enlarged centrilobular cells with pale nuclei and dark cytoplasm, in significant numbers of males receiving 450, 1350 or 4000 mg HMX/kg/day. Tubular kidney change characterised by focal atrophy and dilatation in significant numbers of females receiving 270, 650 or 1500 mg HMX/kg/day.
- Organ Weights: The following changes were seen: Significantly reduced absolute and relative adrenal weights in all treated male groups with an increase in female groups. Relative brain weight increased in males and females receiving 4000 or 1500 mg HMX/kg/day. Absolute brain weights increased in top dose females. Absolute heart weights increased in male and female top dose rats.

Female treated rats showed a dose related increase in relative kidney weights.

Males showed reduction in absolute and relative spleen weights. Relative liver and lung weights increased in treated females. Females showed reductions in absolute spleen and ovary weights.

Conclusion: Significant toxic liver changes in males receiving 150 or more mg HMX/kg/day and tubular kidney changes in females receiving 270 or more mg HMX/kg/day. HMX administration tends to reduce red blood cell parameters and possibly caused methaemoglobinaemia.

#### INTRODUCTION

This study was designed to provide information on the toxic effects of the compound octahydro-1,3,5,7-tetranitro-1,3,5,7tetrazocine (HMX) and what doses could be used to give an indication of suitable dose levels for subsequent studies. HMX was administered via the diet at concentrations predicted each week to achieve dose levels of 50, 150, 450, 1350 or 4000 mg HMX/kg/day for male rats and dose levels of 50, 115, 270, 620 or 1500 mg HMX/kg/day for female rats continuously for 13 weeks. Dose levels were selected on the basis of results from previous studies.

The experiment was undertaken at the Elphinstone Research Centre of Inveresk Research International Limited within the Modular Animal Maintenance System (MAMS) complex. It was begun on 8 December 1980 and necropsies were completed on 19 March 1981.

All data generated and recorded during this study will be stored in the Scientific Archives of Inveresk Research International Limited.

#### MATERIALS AND METHODS

#### Test Substance

3.95 kg of HMX type B was received on 7 October 1980, a further 2 batches each of approximately 5 kg were received on 17 December 1980 and 2 February 1981. The compound was stored at ambient temperature in the dark.

### Method

Two hundred and eighty Fischer 344 rats, divided equally by sex, were obtained from Charles River U.S.A. via Charles River (U.K.) Limited, Manston, Kent, England on 5 December 1980. They were ordered in the weight range 40-60 g.

One hundred and twenty males and 120 females were allocated to treament groups and allowed to acclimatise to their new environment for 10 days before treatment began.

### Pre-Experiment Acceptance Testing

All animals were examined upon receipt for signs of disease.

Ten animals of each sex were selected at random and subjected to a macroscopic and microbial examination, together with a histopathological evaluation of main organs. Results indicated that, despite mild infestation by pinworm, the animals were acceptable to be used on study.

### Housing

Rats were housed in a barrier maintained animal room at a room temperature normally of  $21^{\circ}C + 2^{\circ}C$  and a target relative humidity of ca 50% (both automatically controlled), with ca 14 air changes/hour. At 12 h light/dark cycle was controlled by a time switch, light hours being 0700-1900 h. Room location was at Elphinstone Research Centre within the MAMS complex.

#### Caging and Cage Sanitation

Rats were housed one animal per cage in suspended polypropylene cages (overall dimensions ca 480 x 150 x 120 mm) with stainless steel wire grid tops and bottoms. Each cage had a polypropylene water bottle (total capacity 300 ml) with rubber washer and melamine cap.

Beneath each cage was a polypropylene tray containing absorbent paper. This paper was changed as required each week.

#### Diet and Water

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During the course of the study, tap water and a laboratory rodent diet (BP Nutrition UK Limited, Expanded Ground Maintenance Diet) were available to the rats <u>ad libitum</u>. Typical analyses for both diet and water are presented in Appendices 1 and 2.

### Animal Room Sanitation

Each morning, before other work in the room began, floors were mopped with a disinfectant solution (either 1% Tego from T.H. Goldschmidt and Company Limited, or 3% Hycogen from Hy-co Products (Scotland) Limited). Each afternoon, following completion of all other work, floors were swept then washed with a disinfectant solution. Once each week walls, ceiling, benches and racking within the animal room were washed with a disinfectant solution.

### Dose Levels, Treatment Groups and Animal Numbers

Dose levels were chosen on the basis of results from a 14 day dietary study conducted at IRI. (DAMD 17-80-C-0053.)

Treatment groups and dose levels were as follows:

Group	Dose Level mg HMX/kg/day (Males)	Animal Numbers (Males)	Dose Level mg HMX/kg/day (Females)	Animal Numbers (Females)
1	0	601-620	0	721-740
2	50	621-640	50	741-760
3	150	641-660	115	761-780
4	450	661-680	270	781-800
5	1350	681-700	620	801-820
6	4000	701-720	1500	821-840

### Distribution of Animals into Treatment Groups

On the day of arrival the animals were distributed at random into the treatment groups as follows:

Upon receipt the rats were placed in large holding cages. Male and female rats were divided into 7 body weight ranges of 5 g each. Twenty sequences of 6 cages were designated. Starting with the lowest weight range and then the highest, followed by the second lowest and so on, males were placed in the first cages of each of the 20 sequences, when these contained one animal each the second cages in the sequences were used and so on until 120 cages each contained one male rat.

This procedure was repeated using new cages and female rats. Each rat was ascribed to a treatment group by the use of another set of computer generated random number sequences. Thus any intergroup environmental differences were minimised.

#### Animal Identification

Each rat was given a unique earmark which identified it within the study and corresponded to that animal's study number.

### Route and Duration of Treatment

The test compound was administered orally via the diet for at least 91 consecutive days.

#### Diet Preparation

Fresh diets were prepared once each week. The concentration of test compound was adjusted each week to give as constant a mg/kg/day level as possible by prediction of mid-week body weight and weekly food consumption for the week in question.

Diets were prepared by direct admixture of the required amount of HMX to diet and blending for 20 min in a Winkworth change drum tumble mixer.

#### Dietary Sampling

Materials and methods are presented in Appendix 11.

A 100 g sample of diet from each group/sex was taken and retained immediately after diet preparation at the beginning of each study week. In addition, 4 samples of 100 g were taken from each group/sex at the beginning of Weeks 1, 2, 3, 4, 7, 10 and 13. The latter samples were analysed for HMX levels.

#### Observations

### Clinical Signs

All animals were checked in early morning and late afternoon on each day for dead or moribund animals. The onset and duration of all signs of ill health or reaction to treatment were recorded after daily examination of the

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animals. Each animal was given a detailed physical examination for clinical signs or external lesions once a week.

#### Deaths

Animals dying during study were given a detailed macroscopic examination and tissues listed under 'Post Mortem Studies' were preserved.

### Body Weight

The weight of each animal was recorded at weekly intervals commencing one week before the start of treatment up until the end of treatment. In addition, animals were also weighed on Day 4 of the first 4 weeks.

### Food Consumption

The quantity of food consumed by each animal was recorded once each week commencing one week before the start of treatment and up to the first day of autopsy. The amount of food scattered by each animal was also recorded.

#### Water Consumption

Water consumption was assessed visually for any intergroup differences.

#### Ophthalmic Examination

All animals were assessed before dosing commenced and during Week 13 of dosing. Animals' pupils were dilated with a midriatic (1% tropicamide) and ophthalmoscopy using an indirect ophthalmoscope was undertaken.

#### Laboratory Investigations

Blood samples were taken via orbital sinus under light ether anaesthesia from 10 males and 10 females from top and control groups during Weeks 5 and 12 of treatment.

#### Haematology

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The following parameters were measured on whole blood taken into tubes containing EDTA:

Red cell count (RBC) White cell count (WBC) Packed cell volume (PCV) Haemoglobin concentration (Hb) Methaemoglobin concentration Differential white cell count Reticulocyte count

Clotting time was assessed using the Hepato Quick test on samples obtained by tail snipping.

### Clinical Chemistry

The following parameters were measured on plasma samples obtained from whole blood taken into tubes containing heparin.

Aspartate aminotransferase (GOT, AST) Alanine aminotransferase (GPT, ALT) Alkaline phosphatase (AP) Lactate dehydrogenase (LDH) Blood urea nitrogen (BUN) Glucose Albumin Sodium Potassium Protein

### Urinalysis

Collections of individual urine samples were made over a 4 h period of food and water deprivation during Weeks 5 and 12 of dosing, on the same animals from which blood was taken.

The following measurements were made:

Glucose Blood Volume Protein Ketones Bile pigments Colour pH Specific gravity Microscopic examination of the spun deposit.

### Pharmacokinetic Sampling

Blood samples were obtained at post mortem by the removal of at least 3 ml whole blood via the caudal vena cava into heparinised tubes. Samples were taken from 5 male and 5

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female animals selected at random from each group. These samples were centrifuged and the plasma deep frozen and stored at IRI.

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### **Terminal Studies**

All animals which died or were sacrificed were necropsied. The gross dissection and necropsy was performed under the supervision of a pathologist. The necropsy is defined as external examination including body orifices, weighing of the following tissues:

> Brain Heart Kidney Ovaries Liver Lungs Testes Adrenals Spleen

and examination and fixation of the following tissues:

Brain Spinal cord Peripheral nerve (sciatic) Eyes Pituitary Thyroid Parathyroid Salivary glands (submaxillary) Heart Lungs Spleen Liver Pancreas Adrenals Lymph nodes (mesenteric cervical submaxillary bronchial) Kidneys Bladder Testes (plus epididymides) Prostate Ovaries (minus fallopian tubes) Uterus Fallopian tubes Stomach

Small intestine (duodenum jejunum ileum) Large intestine (caecum colon rectum) Skeletal mucle (thigh) Skin (abdominal) Mammary gland Any gross lesions e.g. tissue masses, suspected tumours (including surrounding normal tissue) Sternum Adipose tissue (perirenal) Nasal tubinate Trachea Thymus (where possible)

Samples of the above tissues were taken from all animals and placed in 10% neutral buffered formalin (except eyes which were preserved in Davidson's fluid).

The lungs were fixed in their entirety by perfusion with 10% neutral buffered formalin.

The calvarium was removed and the dorsal-nasal bone removed for examination of nasal tubinates before fixation. Liver lobes were sliced and kidneys cut transversley, the cut surfaces were examined before fixation.

Multiple, representative portions of large or variable tissue masses including surrounding unaffected tissue were fixed. Femoral bone marrow smears were prepared from all animals at sacrifice, air dried and fixed in absolute methanol for at least 5 min.

Carcasses of animals were discarded immediately following autopsy and placing in fixative of all tissues listed above.

### Processing of Fixed Tissues

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The fixation time was no less than 48 h and not more than 12 weeks.

Tissues were trimmed to a maximum thickness of 0.3 cm for processing.

Multiple portions of tumours or masses were submitted if these were large or variable in appearance. Surrounding normal tissue was included. Parenchymal organs, e.g. liver, were trimmed to allow the largest surface area possible for examination.

Mid-transverse sections through the entire cortex and medulla of each kidney were submitted.

Entire coronal (a transverse section parallel to the long axis of the body) sections of both right and left lungs including main-stem bronchi and bronchial lymph nodes were submitted.

Three cross sections of brain included:

- a) frontal cortex and basal ganglia,
- b) parietal and cortex and thalamus, and
- c) cerebellum and pons

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The spinal cord was sectioned in the thoraco-lumbar region.

Hollow organs were trimmed and blocked to allow a cross section slice from mucosa to serosa.

Tissues listed below were examined from the highest dose group and next lowest dose group and controls. Additionally liver and kidneys were identified as target organs in this preliminary analysis and were examined in all animals.

Tissues were cut at 4-6  $\mu$ m thickness and stained with haematoxylin and eosin (H and E).

Except where otherwise indicated, the following tissues were examined histologically:

Brain (cerebellum cerebrum stem) Spinal cord (thoraco-lumbar) Peripheral nerve (sciatic) Eyes Pituitary Thyroid Parathyroid (if possible) Salivary glands (submaxillary) Heart Lungs Spleen Liver Pancreas Adrenals

Lymph nodes (mesenteric cerival submaxillary bronchial) Kidneys Bladder Testes Prostate Ovaries Uterus Fallopian tubes (if possible) Stomach (glandular and non-glandular) Small intestine (duodenum jejunum ileum) Large intestine (caecum colon rectum) Skeletal muscle (thigh) Skin (abdominal) Mammary gland Any gross lesions Sternal marrow Adipose tissue (perirenal) Aorta Nasal tubinate Trachea Thymus (where feasible)

### Statistical Evaluation

Statistical evaluation of quantitative data was performed where it seem appropriate. Males were treated independently of females. The level of probability chosen as significant was P<0.05, but in any case the actual level is reported. For evaluation of mean differences a "two tail" distribution was used.

#### RESULTS

Dosing commenced:	15	December	1980
Duration of dosing:	13	Weeks	
Date of termination:	16	March 198	31

# Mortality

There were only 3 premature decedents in the study as follows:

One male receiving 150 mg HMX/kg/day in Week 9 of dosing. One control female which died at blood sampling during Week 13.

One female receiving 1500 mg HMX/kg/day in Week 1 of dosing.

### Clinical Signs

There was a number of clinical signs seen during the study which were not thought to be dose related. These included areas of alopecia, red or black encrusted eyes and yellow or brown staining of the fur and were present only in a few animals from treated and control groups alike. No clinical signs were observed which could have been attributed to dosing with HMX.

### Incidence of Palpable Masses

Only one animal developed palpable masses in the study: A male receiving 150 mg HMX/kg/day.

#### Body Weights

Group mean body weights are presented numerically in Table 1 and graphically in Figures 1 and 2.

### Males

There was a dose related reduction in group mean body weight in rats receiving HMX from Day 4 onwards. Body weights were statistically different from controls (P>0.05 for Group 2 and P>0.001 for other treated groups) in the first 4 weeks of study. Thereafter significance reduced at lower dose levels until termination when significance levels were P>0.05 for Groups 3 and 4, P<0.01 for Group 5 and P<0.001 for Group 6. There was a variable degree of statistical significance in treated groups during the study although Group 6 had statistically significantly reduced mean body weight (P>0.001) at each week from the start of the study.

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Body weight gains were 98, 94, 92, 89 and 85% of controls at the end of the study for Groups 2-6 respectively.

# Females

A similar situation occurred in females as in males, also with body weights of females receiving 1500 mg HMX/kg/day having a statistically significantly reduced body weight (P<0.001) each week from the beginning of the study.

Body weight gains were 101, 73, 87, 89 and 70% of controls for Groups 2-6 respectively.

### Food Consumption

Group mean food consumptions are presented in Table 2.

Food consumption was markedly reduced in Week 1 of study in both sexes of all groups receiving HMX, the food consumed by Group 6 male and female rats being 67 and 57% of that consumed by the respective controls in that week. This difference reduced as the study progressed until Week 12, in the case of males, and Week 10, in the case of females, with the treated groups eating the same as or more than the controls.

Total food consumption over the 13 weeks of treatment was, however, reduced in a dose related trend compared to control groups.

### Water Consumption

Visual assessment of water consumption revealed no intergroup differences.

#### Ophthalmic Examination

- (i) Observations before dosing; These were limited to occasional pitting, scarring or opacity of the cornea. Such abnormalities are typical of laboratory rats at this developmental stage.
- (ii) Results during Week 13 of treatment: No effects that could be attributed to dosing with HMX were observed.

#### Achieved Dosage

Achieved dosages are presented in Table 3.

The mean achieved dosage over the 13 weeks of treatment for each group receiving HMX fell within 3% of nominal. Palatability effects meant that significant variations from nominal values occurred in the first 3 weeks of the study (up to 30% above nominal).

### Analysis of HMX Concentrations in Formulated Diet

Results are presented in Table 4.

Apart from minor discrepancies most found levels in diet correlated well with theoretical values. There were, however, 2 exceptions. Firstly in Group 69 diet mixed on 15 December 1980, which was required to contain 12577 ppm HMX and was found to contain 4997 ppm HMX. Analysis of the archive sample revealed a concentration of 4386 ppm HMX. Because all the records concerned are in order this discrepancy was not readily explicable. Analysis of Groups 2 and 39 diets sampled on 29 December 1980 showed that there was a distinct possibility of the 2 diets having been interchanged, although, because again records are in order, it is not possible to state where this interchange took place.

### Laboratory Investigations

Laboratory investigations were undertaken on blood and urine samples taken from 10 males and 10 females in high and control dose groups during Weeks 5 and 12 of treatment.

Results for haematology are summarised in Tables 5 and 6 while individual values are presented in Appendices 3 and 4.

Results for clinical chemistry are summarised in Tables 7 and 8 while individual values are presented in Appendices 5 and 6.

Results of urinalysis are summarised in Tables 9 and 10 while individual values are presented in Appendices 7 and 8.

Haematology

 (i) Results during Week 5 of dosing (Table 5, Appendix 3). Significant reductions in haemoglobin (Hb) levels and packed cell volume (PCV) (P<0.001) in males and females receiving 4000 and 1500 mg HMX/kg/day respectively were seen. Other parameters fell within normal ranges except for isolated cases.

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(ii) Results during Week 12 of dosing (Table 6, Appendix 4). Significant reductions were seen in Hb, PCV and red blood cell (RBC) levels (P<0.01) in females receiving the high dose level of HMX, with corresponding reductions, though not significant, in the same parameters in males. Slight rises in methaemoglobin in both males and females receiving high dose of HMX were seen, significant (P<0.05) in males only. Female white blood cell (WBC) count was significantly raised (P<0.05) probably reflecting significant increases (P<0.05) in neutrophils.

Other parameters fell within normal ranges except for isolated cases.

### Clinical Chemistry

- (i) Results during Week 5 of dosing (Table 7, Appendix 5). There were increased alkaline phosphatase levels in males and a marginal increase in females (P<0.01 in males only) receiving 4000 or 1500 mg HMX/kg/day. There was also a reduced ALT level in males receiving 4000 mg HMX/kg/day (P<0.01). A significant increase was also seen in BUN levels of females receiving 1500 mg HMX/kg/day. Albumin levels were also increased in males receiving 4000 mg HMX/kg/day (P<0.001). Except for isolated cases other parameters were considered to fall within normal reference ranges.
- (ii) Results during Week 12 of dosing (Table 8, Appendix 6). Significant increases were seen in AP levels in males (P<0.001) and females (P<0.05) receiving the top dose level of HMX and also in albumin levels in females (P<0.001). The male control value for AP was rather lower than normally anticipated for animals of this age and thus the results should be interpreted with caution. Total protein levels of females receiving 1500 mg HMX/kg/day also showed a slight increase (P<0.05) in line with the raised albumin levels. BUN levels were also raised significantly (P<0.001) in females receiving 1500 mg HMX/kg/day. Other parameters were considered to be within normal ranges except for isolated cases.

### Urinalysis

 (i) Results during Week 5 of dosing (Table 9, Appendix 7). Females rats receiving 1500 mg HMX/kg/day showed a reduced pH and specific gravity (SG) with a corresponding increase in urinary volume. Males did not show this trend. Other parameters were considered to fall within normal ranges. (ii) Results during Week 12 of dosing (Table 10, Appendix 8). Female rats receiving 1500 mg HMX/kg/day showed a reduced pH and SG with a corresponding increase in volume. In addition to this effect fern-like crystals were noted in urine of males and females receiving 4000 or 1500 mg HMX/kg/day but not in controls.

Terminal Studies

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Gross and Histopathological Findings

Findings for individual animals are presented in Appendix 9.

No macroscopic lesions were observed which could be attributed to dosing with HMX. There were a number of lesions found on histopathological examination of the 2 highest dose and control groups but these were consistent with the age and strain of rats.

There were, however 2 lesions found which exhibited a dose related trend. These were found in liver and kidneys which were recognised as target organs and histopathologically examined in all other animals (see below).

Toxic changes in the liver were characterised by enlarged cells, mainly in centrilobular areas, with large, pale nuclei and dark, granular, eosinophilic cytoplasm. In some areas there was dilation of the sinusoids and small foci of necrosis.

This liver effect was most marked in males, all males receiving 450 or 4000 and 90% of males receiving 1350 mg HMX/kg/day exhibiting the condition.

Only one female receiving 270 mg HMX/kg/day showed the effect.

Tubular changes in kidneys were seen mostly in females receiving the higher dose levels of HMX and were characterised by focal atrophy and dilation of the tubules. Males also exhibited this condition but to a considerably lesser extent and one female control rat also showed this change.

	Т	oxic Liv	ver and	Tubular	Kidney Ch	nanges
Group	1	2	3	4	5	6
Males						
Dose Level (mg/kg/day)	0	50	150	450	1350	4000
No. Examined	20	20	19	20	20	20
Toxic Liver Change	0	0	2(11)	20(100)	18(90)	20(100)
Tubular Kidney Change	3(15)	0	0	0	2(10)	1(5)
Females						
Dose Level (mg/kg/day)	0	50	115	270	620	1500
No. Examined	20	20	20	20	20	19
Toxic Liver Change	0	0	0	1(5)	0	0
Tubular Kidney Change	1(5)	0	1(5)	4(20)	13(65)	10(50)

(Figures in brackets are % figures)

### Organ Weights

Group mean absolute and relative organ weights are presented in Tables 11 and 12 while individual absolute values are presented in Appendix 10.

### Males

Body weights of males were reduced in a dose related trend being statistically significant in males receiving 1350 (P<0.05) or 4000 mg HMX/kg/day (P<0.001) at termination. Consequently a number of organs showed changes in absolute weights not seen relative to body weight. Absolute adrenal weights in all treated groups were significantly reduced (P<0.001) while relative adrenal weights showed a reduction but at variable and dose independent significance leve.'s. There was a dose related increase in relative brain weight, significant in animals receiving 1350 (P<0.01) or 4000 (P<0.001) mg HMX/kg/day; thus increase was not shown by absolute values.

Absolute heart and kidney weights were also reduced significantly at the 2 highest dose levels but these changes were not seen in relative weights.

There was a dose related reduction in absolute spleen weight, significant in groups receiving 150, 450, 1350 or 4000 mg HMX/kg/day (P<0.001). This trend was also seen in relative spleen weights, the weights being significantly different from controls in animals receiving 50 (P<0.05), 150, 450 (P<0.01), 1350 or 4000 (P<0.001) mg HMX/kg/day.

Testes showed a dose related reduction, significant in all treated groups (P<0.001), compared to control animals. This trend was not seen relative to body weight.

#### Females

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Body weights were significantly reduced in females receiving 1500 mg HMX/kg/day (P<0.001) and so once more changes were seen in absolute weights which were not reflected relative to body weight. Relative adrenal weights in all treated groups were significantly different from controls but at variable levels of significance, this trend was also seen in absolute weights but significance was very variable.

Absolute brain weights were significantly increased in females receiving 115, 270, 620 (P<0.01) or 1500 (P<0.05) mg HMX/kg/day. Relative brain weights also showed a dose related increase in rats receiving 270 (P<0.01), 620 or 1500 (P<0.001) mg HMX/kg/day. Absolute heart weights showed a reduction, significant in rats receiving 620 (P<0.05) or 1500 (P<0.001) mg HMX/kg/day; this was not seen in relative weights. Absolute kidney weights were significantly increased in female rats receiving 115 and reduced in females receiving 1500 mg HMX/kg/day both (P<0.05) while relative kidney weights showed a dose related increase in females receiving 115 (P<0.05), 270 (P<0.01), 620 or 1500 (P<0.001) mg HMX/kg/day. Relative liver weights were increased in females receiving 115 (P<0.05), 620 or 1500 mg HMX/kg/day (P<0.01) this was not seen in absolute weights.

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Lungs showed a significant increase in weight in rats receiving 1500 mg HMX/kg/day (P<0.05) relative to body weight but not in absolute terms.

Females receiving 1500 mg HMX/kg/day showed reduction in absolute spleen (P<0.05) and ovary (P<0.001) weights not seen when expressed relative to body weight.

No other dose related effects were seen in any other organs.

#### DISCUSSION AND CONCLUSIONS

There was a treatment related reduction in growth rate in male and female rats receiving HMX but the significance reduced after the first 4 weeks of the study. The high statistical significances at the beginning of the study were probably due to unpalatability of the high concentrations of HMX in the diet. This theory is backed up by the food consumption figures which were very low at the start of treatment but improved throughout the study. Total food consumed was reduced in a dose related fashion mainly because of the low intake in the first 4 weeks of treatment.

Haematological examination revealed evidence of reductions in Hb, PCV and possibly RBC. The consistency of the observations suggests the effects were real and probably attributable to HMX. The alterations were not, however, very great and are unlikely to be of much biological significance per se. The increase in methaemoglobin at Week 12 could be attributable to HMX since its nitrate content could lead to methaemoglobin formation in broadly the same manner as sodium nitrate. The changes in leucocyte counts were neither large nor consistent and since rapid changes in these parameters can occur for a wide variety of reasons the evidence that they were the result of treatment of rats with HMX is rather tenuous.

Clinical chemical observations showed an increase in alkaline phosphatase activity. This could have been associated with the liver changes identified histopathologically although the liver changes in females were much less apparent than in males while generally speaking AP activity showed less evidence of a difference between the sexes.

The increase in BUN in female rats was very slight but could be consistent with the presence of renal damage. There was little evidence of either change in male rats. Increases in total protein and albumin occurred sufficiently consistently to suggest a relationship to dosing with HMX. While it is possible to hypothesise a relationship with renal and hepatic changes, there are insufficient data to speculate constructively on the nature of that link.

The increases in urine volume, lower pH and lower SG found on urinalysis of the females might be anticipated when the histopathological changes are taken into consideration. Neither effect occurred in male rats suggesting a difference between the sexes in response to dosing with HMX.

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When significant body weight changes occur it is extremely difficult to interpret organ weight changes (either absolute or relative). The majority of changes reflected to some degree the body weight trends, and thus the significance of the minor changes seen in spleen, adrenal, testes and ovary weights, is questionable. However, female brain weights were increased and while a change in proportionate body weight is not normally expected (brain weight tends to be related to age rather than body weight) the rise can be interpreted either as an effect of the compound or an effect of a lower than normal control group brain weight. Regrettably there are insufficient background data in this laboratory to support or refute the latter contention.

Histopathological evaluation indicated hepatic changes in male rats and renal changes in female rats. These seemed to correlate with AP activity increases (though both males and females displayed this) and the urine changes in female rats (increased volume, lower pH and lower SG). There was no evidence of toxic liver change in male rats at 50 mg/kg/day or of renal effects in the female rats at 115 mg/kg/day or of renal effects in the female rats at 115 mg/kg/day or less. The different target organs in the 2 sexes could be due to a difference in metabolism of HMX between them.

In conclusion, dosing of HMX to male and female F344 rats for 90 days via the diet results in a slight reduction in red cell parameters and possible methaemoglobinaemia. The most significant changes were toxic liver damage in male rats at doses of 150 mg HMX/kg/day and above and renal tubular damage in female rats at 270 mg HMX/kg/day and above. Other effects were of doubtful significance or most likely to be secondary to the hepatic and renal damage.

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Body Weights: Group Mean Values (g) HMX: 13 Week Toxicity Study in Rats

		2					I			
3 <b>3</b>	1 1	43	5đ	6ď	19	29	39	49	59	62
150		450	1350	4000	0	50	115	270	620	1500
108 <sup>20</sup>	0	111 <sup>20</sup>	111 <sup>20</sup>	110 <sup>20</sup>	96 <sup>20</sup>	97 <sup>20</sup>	98 <sup>20</sup>	100 <sup>20</sup>	97 <sup>20</sup>	97 <sup>20</sup>
119		117	112	102	105	66	92	90	85	82
130***	-	* 130***	124***	114***	112	106**	102***	102***	95***	***19
143		143	137	127	122	115	110	109	104	86
152*:	- 48	* 152***	146***	137***	125	120*	115***	113***	***601	103***
161		161	154	146	129	125	120	118	115	109
164***		* 164***	156***	149***	131	126*	122***	121***	115***	111***
170		172	164	155	135	128	12	122	117	111
176***		* 178***	170***	161***	138	132*	127***	124***	120***	116***
194***		* 193***	185***	176***	143	138	134**	131***	127***	118***
210**		208**	200***	193##1	150	145	141**	137***	133***	125***
223**		221**	214***	207***	153	150	147*	142***	139***	127***
234**		233**	227***	221***	157	153	151	145**	142***	132***
24219	-	243**	237***	232***	160	158	156	152*	148***	137***
251**	-	251**	247***	243***	165	162	160	154**	154**	143***
258**		256**	253***	249***	165	165	163	157*	156**	144***
269		268	264*	254***	165	170	169	161	160	145***
271*		270*	265**	257***	166 <sup>19</sup>	168	166	161	159	146***
163		159	154	147	70	71	51	61	62	49
94		92	89	85	1	101	73	87	89	70

\* Significantly different from control, P<0.05

\*\* Significantly different from control, P<0.01

\*\*\* Significantly different from control, P<0.001

Numbers in superscript denote survivors at end of week in guestion

HMX: 13 Week Toxicity Study in Rats Food Consumption: Group Mean Values (g/Rat/Week)

69	1500	5619	87	84	73	80	80	76	80	80	83	84	83	84	1030	85
59	620	62 <sup>20</sup>	84	88	75	68	82	85	85	93	92	95	88	92	1110	92
4 \$	270	69 <sup>20</sup>	84	16	79	68	83	82	84	91	16	97	91	63	1124	93
32	115	75 <sup>20</sup>	06	06	85	16	87	68	06	96	94	101	86	96	1182	98
29	50	87 <sup>20</sup>	92	95	85	94	92	88	89	96	93	66	97	63	1200	66
19	0	98 <sup>20</sup>	100	102	91	93	16	16	06	94	16	94	85	8919	1209	-
6ئ	4000	79 <sup>20</sup>		112	107	113	116	122	121	128	131	136	131	130	1537	92
53	1350	93 <sup>20</sup>		108	111	115	112	116	119	124	128	130	133	136	1540	92
<b>4</b> ઉ	450	100 <sup>20</sup>		117	109	118	117	119			127	130	134	125	1557	93
33	150	10420	121	117	113	118	115	118	118	122 <sup>19</sup>	127	129	130	125	1557	63
23	50	110 <sup>20</sup>		122	119	121	119	127	122	129	132	134	135	129	1620	97
1ð	0	118 <sup>20</sup>	127	131	127	128	125	125	132	131	131	138	132	127	1672	1
Treatment Period (weeks)		Ţ	2	m	4	S	9	7	80	6	10	11	12	13	Total Eaten (g) Weeks 1-13	% of Controls

Numbers in superscript denote survivors at end of week in question

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HMX: 13 Week Toxicity Study in Rats Achieved Dosage: Group Mean Values (mg/kg/day)

			DO	Dose Group	Group/Dose Level (mg/kg/day)	vel (mg,	/kg/day)				
Treatment Period (weeks)	2ð	35	4.5	53	6đ		29	39	44	ξ	69
	50	150	450	1350	4000		50	115	270	620	1500
1	 50	157	463	1304	3360		51	63	226	472	1082
2	 53	171	518	1570	4756	_	50	128	326	768	1963
e	 51	147	456	1310	4084		52	115	281	636	1526
4	 48	141	408	1292	3775	-	45	108	239	538	1273
5	 50	151	481	1398	4093		54	120	295	707	1670
9	 49	148	449	1356	4097	-	49	112	253	575	1444
۲ ا	 53	154	454	1399	4291		48	114	258	625	1433
80	 50	153	450	1403	4138	_	50	119	276	638	1534
6	 53	158	474	1446	4261		54	123	292	682	1494
10	 52	159	475	1445	4241		50	118	284	644	1555
11	 52	158	478	1432	4322		53	124	294	658	1592
12	 50	152	462	1386	3960		49	116	240	586	1644
13	48	147	425	1389	3939		49	113	289	631	1445
Mean Achieved Dosage Weeks 1-13	51.0	153.5	461.0	1394.6	4101.3		50.3	115.6	273.3	627.7	1511.9
s of Nominal	102	102	102	103	103		101	101	101	101	101

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# HMX: 13 Week Toxicity Study in Rats Analysis of HMX in Dietary Formulations

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Date		Concentrat	tion (ppm)	Deviation from	Concentra	tion (ppm)	Deviation from
,	Group	Nominal	Found	Nominal (%)	Nominal	Found	Nominal (%)
	2	420	409	2.6	415	438	5.5
	3	1250	1274	1.9	864	877	1.5
15 December 1980	4	3930	3936	0.2	2305	2309	0.2
Week 1	5	11520	11293	2.0	5151	5019	2.6
	6	33600	32925	2.4	12577	4997	*
	2	450	426	5.3	431	408	5.3
	3	1400	1419	1.4	1080	1149	6.4
22 December 1980	4	4345	4357	0.3	2916	2795	4.2
Week 2	5	12921	13166	1.9	6526	6721	3.0
	6	37538	36915	1.7	15833	16580	4.7
	2	480	482	0.4	467	964	*
	3	1389	1494	7.6	1062	540	*
29 December 1980	4	4288	4655	8.6	2527	2776	9.9
Week 3	5	12764	12959	1.5	5654	5929	4.9
	6	36500	34104	6.6	13065	13817	5.8
	2	506	549	8.5	474	533	12.4
	3	1482	1449	2.2	1114	1156	3.8
5 January 1981	4	4500	4532	0.7	2614	2487	4.8
Week 4	5	13331	13775	3.3	5850	6020	2.9
	6	38000	36757	3.3	13893	13607	2.1
······································	2	659	607	7.9	561	598	6.6
	3	1982	1811	8.6	1294	1272	1.7
26 January 1981	4	5732	5308	7.4	3076	3056	2.7
Week 7	5	17441	16966	2.7	7027	7011	0.2
	6	49325	46616	5.5	16565	15033	9.2
	2	715	698	2.4	606	590	2.6
	3	2158	2115	2.0	1377	1345	2.3
16 February 1981	4	6448	6218	2.7	3348	3297	1.5
Week 10	5	19105	16582	13.2	7372	7295	1.0
_	6	53864	52468	2.6	18289	17463	4.5
	2	729	716	1.8	618	661	7.0
	3	2214	2157	2.6	1377	1350	2.0
9 March 1981	4	6385	6437	0.8	3499	3553	1.5
Week 13	5	18942	18744	1.0	7678	7617	0.8

\* = See results section

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HMX: 13 Week Toxicity Study in Rats Haematology: During Week 5 Group Mean Values: Males

Dose mg/kg/ day	Tests Units	Hb 9/100 ml	RBC x 10 <sup>12</sup> /1	PCV B	MCH Pg	MCV f1	MCHC 9/d1	Rett	WBC × 10 <sup>9</sup> ∕1	WBC Neut Lymp Mono Eos x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1	Lутр x 10 <sup>9</sup> /1	Mono x 10 <sup>9</sup> /1	Eos x 10 <sup>9</sup> /1	Hepa sec	Met
Con	Ntumber	10	10	10	10	10	10	10		10	10	10	10	10	10
	Mean	16.4	7.3	47	23	65	35	3.6		0.8	6.3	0.0	0.1	31.7	0.8
	s.D.	0.4	0.3		T	m	-	1.2	6.0	0.3	0.8	0.0	0.1	3.0	0.4
4000	Number	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	Mean	15.6	7.3	45	22	62	35	3.5	7.2	1.2	6.0	0.0	0.0	32.8	1.0
	s.D.	0.4	0.4	T	٦	m	1	1.4	0.8	0.6	1.0	0.0	0.0	3.6	9.0
	Sig	* *		* *	*	*									

\* Significantly different from control, P<0.05
\*\*\* Significantly different from control, P<0.001</pre>

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TABLE 5 (continued)

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[	Γ						
Met	10	1.0	0.4	10	1.2	0.9	
Hepa sec	10	29.8	2.2	10	30.1	4.0	
Еов x 10 <sup>9</sup> /1	10	0.1	0.1	10	0.0	0.0	
WBC Neut Lymp Mono Eos x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1	10	0.0	0.0	10	0.0	0.0	
тутр × 10 <sup>9</sup> ∕1	10	6.0	6.0	10	5.4	0.3	*
Neut x 10 <sup>9</sup> /1	10	0.7	0.3	10	0.9	0.4	
WBC x 10 <sup>9</sup> /1	10	6.7	0.7	10	6.3	0.5	
Ret1 %	10	2.0	1.4	10	2.3	0.9	
MCHC g/dl	10	34	T	10	34	I	
MCV f1	10	66	e	10	64	2	-
мсн рд	10	23	1	10	22	I	
PCV 8	10	48	1	10	45	2	* * *
RBC  x 10 <sup>12</sup> /1	10	7.3	0.4	10	7.1	0.3	
НЬ 9/100 m1	10	16.5	0.3	10	15.6	0.6	* * *
Tests Units	Number	Mean	s.D.	Number	Mean	s.D.	Sig
bose mg/kg/ day	Con			1500			

\* Significantly different from control, P<0.05

\*\* Significantly different from control, P<0.001

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HMX: 13 Week Toxicity Study in Rats Haematology: During Week 12 Group Mean Values: Males

Tests Units	Hb 9/100 ml	RBC × 10 <sup>12</sup> /1	PCV *	MCH Pg	MCV f1	MCHC g/dl	Reti 8	₩ВС × 10 <sup>9</sup> /1	Neut x 10 <sup>9</sup> /1	Lутр × 10 <sup>9</sup> ∕1	WBC Neut Lymp Mono Eos $x 10^{9}/1 \times 10^{9}/1 \times 10^{9}/1 \times 10^{9}/1 \times 10^{9}/1$	Eos x 10 <sup>9</sup> /1	Hepa sec	Met
Number	- 10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	15.6	7.6	47	21	62	34	4.1	9.5	1.4	8.0	0.1	0.2	32.4	1.5
s.D.	0.8	0.5	2	1	e	1	2.1	2.3	0.4	2.2	0.1	0.3	2.9	1.0
Number	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Mean	15.2	7.3	45	21	62	34	3.8	9.3	1.0	8.2	0.1	0.0	32.8	2.3
s.D.	0.4	0.4	1	1	4	I	1.8	1.4	0.7	1.0	0.1	0.0	3.2	0.8
Sig														•

\* Significantly different from control, P<0.05

TABLE 6 (continued)

Females

r	r			T ·····			
we t	10	1.5	0.7	10	2.4	1.6	
Hepa sec	10	28.7	2.6	10	30.7	2.9	
Eos x 10 <sup>9</sup> /1	10	0.0	0.1	10	0.1	0.0	
Mono x 10 <sup>9</sup> /1	10	0.0	0.0	10	0.0	0.0	
WBC Neut Lymp Mono Eos x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1 x 10 <sup>9</sup> /1	10	5.7	1.5	10	7.0	1.7	
Neut x 10 <sup>9</sup> /1	10	0.6	0.3	10	1.0	0.4	*
₩ВС × 10 <sup>9</sup> /1	10	6.4	1.6	10	8.1	1.8	*
Ret1 8	10	2.9	1.7	10	3.4	1.6	
MCHC 9/d1	10	34		10	34	1	
MCV fl	10	64	1	10	65	2	*
MCH Pg	10	22	1	10	22	I	
PCV 8	10	46	2	10	44	1	**
RBC × 10 <sup>12</sup> /1	10	7.3	0.3	10	6.7	0.3	***
Hb 9/100 ml	10	15.9	0.8	10	14.8	0.4	:
Tests Units	Number	Mean	S.D.	Number	Mean	s.D.	Sig
bose mg/kg/ day	Con			1500			

\* Significantly different from control, P<0.05

\*\* Significantly different from control, P<0.01
\*\*\* Significantly different from control, P<0.001</pre>

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HMX: 13 Week Toxicity Study in Rats Clinical Chemistry: During Week 5 Group Mean Values: Males

dib 1/2			2 1				*
R TP 9/1			0.4				
Na mmo1/1	10	146	2	10	147	3	
I/UI LDH	10	357	85	10	417	164	
AP IU/1	10	712	85	10	840	64	*
ALT IU/1	10	72	7	10	63	9	*
AST IU/1	10	83	2	10	78	7	
G1u mmo1/1	10	8.14	0.78	10	7.72	0.71	
BUN mmo1/1	10	6.4	0.8	10	6.5	1.0	
Tests Units	Number	Mean	s.D.	Number	Mean	s.D.	Slg
Dose mg/kg/ day	Con			4000			

**\*\*** Significantly different from control, P<0.01

TABLE 7 (continued)

Females

	ŧ						
Alb 9/1	10	34	2	10	36	I	*
TP 9/1	10	59	2	10	62	2	*
K mmo1/1	10	4.3	0.3	10	4.3	0.3	
Na mmo1/1	10	145	2	10	146	2	
1/NI HQJ	10	261	46	01	254	60	
AP IU/I	10	635	52	10	676	73	
ALT IU/I	10	56	7	10	59	5	
AST IU/1	10	77	8	10	82	2	
Glu mmol∕l	10	7.97	0.58	10	7.98	0.61	
BUN mmo1/1	10	6.3	0.8	10	7.2	1.0	*
Tests Units	Number	Mean	s.D.	Number	Mean	s.D.	Sig
Dose mg/kg/ day	Con			1500			

\* Significantly different from control, P<0.05

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HMX: 13 Week Toxicity Study in Rats Clinical Chemistry: During Week 12 Group Mean Values: Males

Con Number Mean		Glu mmol/1	AST IU/1	ALT IU/1	AP IU/1	1/01 HQ1	Na mmo1/1	K mmo1/1	TP 9/1	Alb 9/1
Mean	10	10	10	10	10	10	10	10	10	10
	6.4	8.32	122	65	213	278	145	4.3	70	41
S.D.	0.4	1.36	27	19	18	65	e	0.3	2	I
4000 Number	10	10	10	10	10	10	10	10	10	10
Mean	6.7	7.73	104	48	415	286	147	4.0	69	42
S.D.	6.0	0.52	21	23	102	119	4	0.3	2	7
Sig					* * *			*		*

\* Significantly different from control, P<0.05
\*\*\* Significantly different from control, P<0.001</pre>

TABLE 8 (continued)

Females

	T			T			<u> </u>
Alb g/l	10	37	1	10	40	1	*
TP 9/1	10	61	2	10	64	I	* *
K mmo1/1	10	4.6	0.4	10	4.8	0.6	
Na mmo1/1	10	144	1	10	146	2	*
1/UI HQJ	10	470	126	10	417	174	
AP IU/1	10	467	80	10	553	61	*
ALT IU/1	10	62	34	10	57	11	
AST IU/1	10	06	23	10	84	20	
Glu mmol/l	10	8.25	1.19	10	7.86	0.96	
BUN mmol/1	10	6.5	0.8	10	7.7	0.5	*
Tests Units	Number	Mean	S.D.	Number	Mean	s.D.	Sig
Dose mg/kg/ day	Con			1500			

\* Significantly different from control, P<0.05

\*\* Significantly different from control, P<0.01</pre>

\*\*\* Significantly different from control, P<0.001

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# HMX: 13 Week Toxicity Study in Rats Urinalysis: During Week 5 Group Mean Values

Dose         PH         SG         Vol           (mg/kg/day)         Mean         8.8         1.054         0.8           Control         Mean         8.8         1.054         0.8           J         S.D.         0.3         0.024         0.3           J         S.D.         0.3         0.015         0.3           J         S.D.         0.6         0.015         0.3           J         S.D.         0.6         0.015         0.3           J         S.D.         0.6         0.016         0.6           Paan         8.79         1.0619         0.59           Paan         8.73         1.0613         0.59           Paan         8.73         1.0613         0.59           Paan         8.73         1.0613         0.59           Paan         8.73         1.0616         0.05           Paan         8.73         1.0616         0.59           Paan         8.73         1.0616         0.59           Paan         8.73         1.038         1.5           Paan         7.3         1.038         1.5           Paan         7.3         1.033			-		
Mean         8.8         1.054           S.D.         0.3         0.024           S.D.         0.3         0.024           Mean         8.6         1.060           S.D.         0.6         0.015           Mean         8.7         1.061           Mean         8.7         0.016           Mean         8.7         1.061           Mean         8.7         0.3           S.D.         0.4         0.016           Mean         7.3         1.038           S.D.         1.4         0.023	Dose (mg/kg/day)		Hd	SG	Vol (m1)
Mean         8.6         1.060           S.D.         0.6         0.015           Mean         8.79         1.0619           Mean         8.73         1.0616           S.D.         0.4         0.016           Mean         7.3         1.038           Mean         7.3         1.038           S.D.         1.4         0.023	Control	Mean	8.8	1.054	0.8
	3	S.D.	0.3	0.024	0.3
Mean         8.79         1.0619           S.D.         0.4         0.016           Mean         7.3         1.038           S.D.         1.4         0.023	4000	Mean	8.6	1.060	0.7
	S	S.D.	0.6	0.015	0.3
Mean 7.3 1.038	Control	Mean	8.7 <sup>9</sup>	1.061 <mark>9</mark>	0.0
S.D. 1.4 0.023	9	S.D.	0.4	0.016	
	1500	Mean	7.3	1.038	1.5
	\$	S.D.	1.4	0.023	0.9

All mean values derived from 10 individual values unless otherwise indicated by superscript

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# HMX: 13 Week Toxicity Study in Rats Urinalysis: During Week 12 Group Mean Values

Dose (mg/kg/day)		Hd	SG	Vol (ml)
Control	Mean	8.7	1.049	1.0
3	S.D.	0.7	0.016	
4000	Mean	8.1	1.049	1.0
3	S.D.	0.7	0.013	0.4
Control	Mean	8.1 <sup>9</sup>	1.051 <sup>8</sup>	0.6 <sup>8</sup>
9	S.D.	1.1	0.018	0.2
1500	Mean	6.6	1.019	2.7
ç	S.D.	0.5	0.004	

All mean values derived from 10 individual values unless otherwise indicated by superscript

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HMX: 13 Week Toxicity Study in Rats Absolute Organ Weights (g) Group Mean Values: Males

Dose mg/kg/day/ Sex	Body Weight	Adrenals	Brain	Heart	Klåneys	Liver	Lungs	Spleen	Testes
Mean	281.2	0.0224 <sup>37</sup>	1.863	0.892	0.965 <sup>40</sup>	10.653	1.323	0.638	2.018 <sup>40</sup>
S.D.	22.5	0.0033	0.040	0.066	0.067	1.511	0.123	0.059	0.139
Mean	281.5	0.019140	1.871	0.885	1.001 <sup>40</sup>	11.074 <sup>19</sup>	1.259	0.607	1.94340
S.D.	16.7	0.0032	0.061	0.060	0.071	1.205	0.115	0.033	0.094
Mean	272.9 <sup>19</sup>	0.019038	1.874 <sup>19</sup>	0.856 <sup>19</sup>	0.936 <sup>38</sup>	10.690 <sup>19</sup>	1.258 <sup>19</sup>	0.57919	1.91638
S.D.	17.3	0.0028	0.044	0.072	0.072	1.402	0.116	0.044	0.107
Mean	270.9	0.019939	1.865	0.860	0.935 <sup>40</sup>	10.323	1.327	0.572	1.904 <sup>39</sup>
S.D.	22.0	0.0036	0.059	0.077	0.085	1.137	0.132	0.053	0.102
Mean	266.4	0.018740	1.879	0.84 <sup>4</sup>	0.91040	10.082	1.287	0.554	1.87840
S.D.	22.3	0.0031	0.059	0.065	0.077	1.177	0.131	0.057	0.152
Mean	257.1	0.017839	1.875	0.817	0.88340	9.969	1.271	0.536	1.89140
S.D.	13.1	0.0026	0.042	0.055	0.050	1.001	0.175	0.047	0.086

\* Significantly different from control, P<0.05

\*\* Significantly different from control, P<0.01</p>

\*\*\* Significantly different from control, P<0.001

Means calculated from 20 individual values unless otherwise indicated by superscript

TABLE 11 (continued)

Females

Dose mg/kg/day/ Sex		Body Weight	Adrenals	Brain	Heart	Kidneys	Liver	Lungs	Spleen	Ovaries
0	Mean	165.8 <sup>19</sup>	0.021736	1.704 <sup>19</sup>	0.592 <sup>19</sup>	0.625 <sup>38</sup>	5.541 <sup>19</sup>	0.946 <sup>19</sup>	0.411 <sup>19</sup>	0.0273 <sup>38</sup>
	S.D.	11.2	0.0034	0.052	0.042	0.045	0.811	0.143	0.039	0.0054
503	Mean S.D.	166.7 8.5	0.0250 <sup>39</sup> 0.0044	1.739 0.103	0.604 0.043	0.645 <sup>40</sup> 0.043	5.717 0.521	0.911 0.065	0.418	0.0286 <sup>40</sup> 0.0061
115?	Mean	166.0	0.026440	1.771	0.590	0.65040	5.901	0.923	0.415 <sup>19</sup>	0.0298 <sup>40</sup>
	S.D.	8.6	0.0033	0.038	0.034	0.045	0.668	0.087	0.029	0.0067
2709	Mean	160.8	0.024 <sup>2</sup> 39	1.7719	0.573	0.633 <sup>40</sup>	5.646	0.969	0.411	0.0272 <sup>40</sup>
	S.D.	13.0	0.0064	0.043	0.050	0.059	0.796	0.130	0.050	0.0067
620 <i>°</i>	Mean	159.0	0.0231 <sup>38</sup>	1.760	0.558	0.639 <sup>40</sup>	5.813	0.964	0.413	0.0279 <sup>40</sup>
	S.D.	10.6	0.0060	0.055	0.046	0.053	0.748	0.118	0.041	0.0078
15009	Mean	146.1	0.0217 <sup>36</sup>	1.75 <mark>4</mark> 19	0.52319	0.60 <sup>1</sup> <sup>38</sup>	5.330 <sup>19</sup>	0.925 <sup>19</sup>	0.375 <sup>19</sup>	0.021538
	S.D.	13.2	0.0051	0.058	0.055	0.064	0.827	0.141	0.053	0.0062
•										

\* Significantly different from control, P<0.05</p>

\*\* Significantly different from control, P<0.01</pre>

\*\*\* Significantly different from control, P<0.001

Means calculated from 20 individual values unless otherwise indicated by superscript

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HMX: 13 Week Toxicity Study in Rats Relative Organ Weights (% of Body Weight) Group Mean Values: Males

Dose mg/kg/day/ Sex		Body Weight	Adrenals	Brain	Heart	Kidneys	Liver	sɓunŢ	Spleen	Testes
٤O	Mean	281.2	0.00804 <sup>37</sup>	0.666	0.318	0.344 <sup>40</sup>	3.783	0.470	0.227	0.720 <sup>40</sup>
	S.D.	22.5	0.00133	0.052	0.021	0.017	0.388	0.035	0.015	0.049
503	Mean	281.5	0.0067740	0.666	0.316	0.35640	3.936 <sup>19</sup>	0.447	0.215 <sup>5</sup>	0.69240
	S.D.	16.7	0.00112	0.037	0.020	0.016	0.334	0.039	0.011	0.044
1503	Mean	272.9 <sup>19</sup>	0.00655638	0.689 <sup>19</sup>	0.315 <sup>19</sup>	0.342 <sup>38</sup>	3.910 <sup>19</sup>	0.463 <sup>19</sup>	0.21319	0.704 <sup>38</sup>
	S.D.	17.3	0.00096	0.038	0.020	0.017	0.363	0.039	0.012	0.039
450 <i>đ</i>	Mean	270.9	0.0074 <sup>1</sup> 39	0.693	0.318	0.345 <sup>40</sup>	3.809	0.490	0.211	0.707 <sup>39</sup>
	S.D.	22.0	0.00145	0.052	0.020	0.021	0.241	0.039	0.014	0.045
13503	Mean	266.4	6.0070440	0.710	0.318	0.342 <sup>40</sup>	3.784	0.484	0.209	0.707 <sup>40</sup>
	S.D.	22.3	0.00131	0.055	0.020	0.020	0.294	0.049	0.025	0.054
40003	Mean	257.1	0.00697 <sup>39</sup>	0.730	0.318	0.344 <sup>40</sup>	3.884	0.494	0.209	0.737 <sup>40</sup>
	S.D.	13.1	0.00116	0.032	0.017	0.016	0.411	0.064	0.010	0.034
•										

\* Significantly different from control, P<0.05</p>

\*\* Significantly different from control, P<0.01</pre>

\*\*\* Significantly different from control, P<0.001</pre>

Means calculated from 20 individual values unless otherwise indicated by superscript

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TABLE 12 (continued)

Females

Dose mg/kg/day/ Sex		Body Weight	Adrenals	Brain	Heart	Kidneys	Liver	Lungs	Spleen	Ovaries
3 <b>0</b>	Mean	165.8 <sup>19</sup>	0.0132 <sup>36</sup>	1.032 <sup>19</sup>	0.357 <sup>19</sup>	0.378 <sup>38</sup>	3.336 <sup>19</sup>	0.570 <sup>19</sup>	0.248 <sup>19</sup>	0.0164 <sup>38</sup>
	S.D.	11.2	0.0021	0.064	0.019	0.018	0.367	0.071	0.023	0.0034
50%	Mean	166.7	0.0150 <sup>39</sup>	1.054	0.364	0.388 <sup>40</sup>	3.441	0.547	0.251	0.0171 <sup>40</sup>
	S.D.	8.5	0.0026	0.052	0.035	0.028	0.372	0.033	0.018	0.0034
115?	Mean	166.0	0.015840	1.068	0.357	0.39 <sup>±</sup> 40	3.55 <sup>3</sup>	0.557	0.248 <sup>19</sup>	0.0180 <sup>40</sup>
	S.D.	8.6	0.0018	0.053	0.018	0.020	0.331	0.050	0.017	0.0039
2709	Mean	160.8	0.014 <sup>3</sup> <sup>39</sup>	1.108 <sup>19</sup>	0.358	0.33440	3.508	0.605	0.255	0.0168 <sup>40</sup>
	S.D.	13.0	0.0035	0.094	0.018	0.020	0.275	0.083	0.023	0.0039
6209	Mean	159.0	0.014 <sup>8</sup> <sup>38</sup>	1.110	0.351	0.40240	3.650	0.608	0.258	0.0175 <sup>40</sup>
	S.D.	10.6	0.0037	0.067	0.022	0.030	0.327	0.067	0.017	0.0045
15002	Mean	146.1	0.014 <sup>836</sup>	1.20719	0.358 <sup>19</sup>	0.41138	3.63619	0.62 <sup>8</sup> 19	0.256 <sup>19</sup>	0.0147 <sup>38</sup>
	S.D.	13.2	0.0032	0.086	0.025	0.028	0.348	0.097	0.020	0.0039
4										

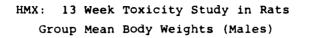
Significantly different from control, P<0.05</li>

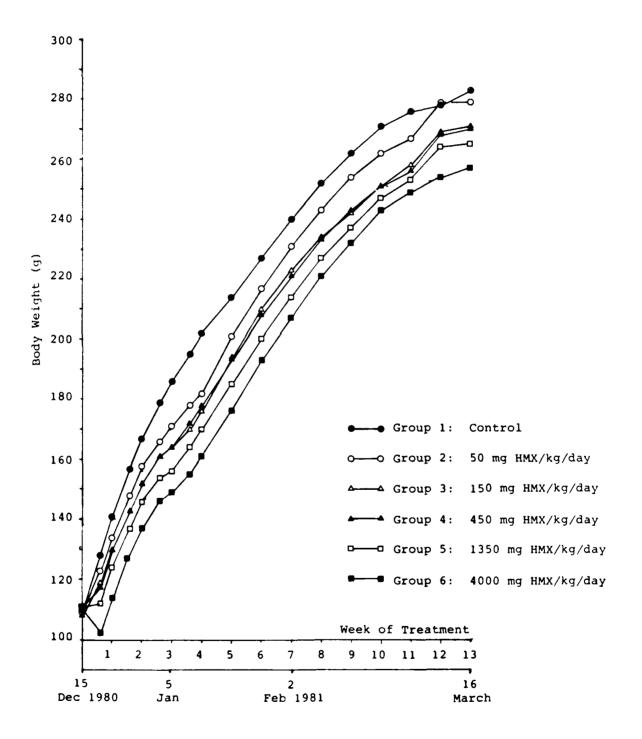
\*\* Significantly different from control, P<0.01</pre>

\*\*\* Significantly different from control, P<0.001</pre>

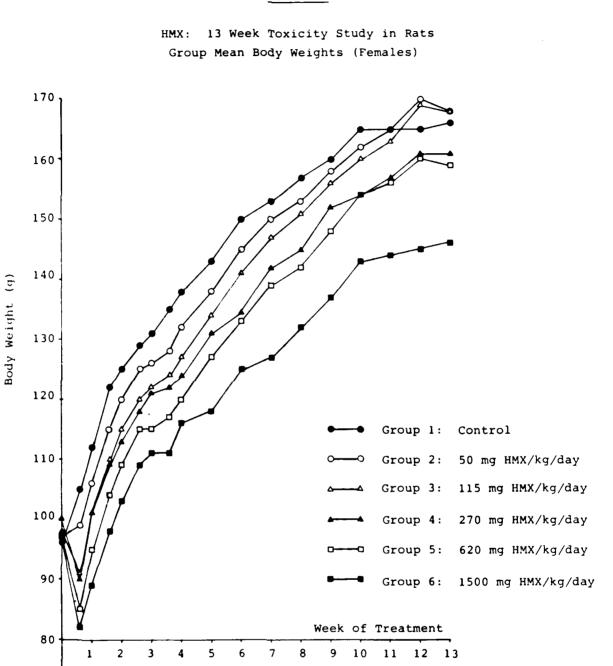
Means calculated from 20 individual values unless otherwise indicated by superscript







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3 Feb 1981

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March

15 Dec 1980

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Jan

## Diet Analysis

B.P. NUTRITION (U.K.) LTD.

Selenium

	CERTIFICA	L OF LABORATORY			1 DEC 1980
PRODUC		DUSE NO.1 (MODIFI	LUT EXPAN	DED FINE G	ROUNL'
BATCH N	0: 1021	PREMIX B	ATCH NO: P	120	-
DATE OF	MANUFACTURE	: 27TH NOVEMBER ;			
Found Analysi	\$	Contaminant	Found Analysia	I	Limit of Detection
8.7	%	Fluorine	5.3	mg/kg	10.0 mg/kg
3.4*	%	Nitrate as NaNO3	L1.0	mg/kg	1.0 mg/kg
15.4	%	Nitrite as NaNO2	1.4	mg/kg	1.0 mg/kg
2.9	%	Lead	∠1.0	mg/kg	1.0 mg/kg
4.6	٠,	Arsenic	0.11	mg/kg	0.2 mg/kg
0.88	%	Cadmium	0.25	mg/kg	0.2 mg/kg
0.61	*	Mercury	40.01	mg/kg	0.01 mg/kg

0.13

Total Aflatoxins NONE DETECTED ug/kg

mg/kg

Nutrient	Found Analys	is
Moisture	8.7	%
Crude Fat	3.4*	%
Crude Protein	15.4	%
Crude Fibre	2.9	%
Ash	4.6	%
Calcium	0.88	%
Phosphorus	0.61	%
1 idium	0.19	%
Chlorine	0.51	%
Potassium	0.92	*
Magnesium	0.16	%
Iron	173	რე/kg
Copper	12	mg/kg
Manganese	52	mg/kg
Zinc	36	mg/kg

Vitamin A	4500	iuAg
Vitamin E	70	mgikg
Vitamin C		mg/kg

\*repeat 3.5

Total P.C.B. NONE DETECTED 0.001 mg/kg mg/kg Total D.D.T. 0.005 mg/kg 0.001 mg/kg 0.001 Dieldrin 0.001 mg/kg mg/kg Lindane 0.004 mg/kg 0.001 mg/kg Heptachior NONE DETECTED 0.001 mg/kg mg/kg NONE DETECTED 0.02 mg/kg Malathion mg/kg **Total Viable**  $<1.0 \times 10^{3}$ Organisms per grm 1000/g Mesophilic  $2.5 \times 10^2$ per grm Spores 100/g Salmonellae Absent in NONE DETECTED Species per grm 20 grm Presumptive Absent in NONE DETECTED E. Coli per grm 10 grm Absent in E. Coli Type 1 NONE DETECTED per grm 10 grm Fungal Units NONE DETECTED Absent in per grm 10 grm Antibiotic Activity

ister. Signed 22nl Dec 1980 Dated

C & PODRIESTONENES DE D. C.C.M. H.D. C

**B.P. Nutrition (U.K.) Limited** Stepfield, Witham, Freev CHIR 16R

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0.02 mg/kg

1 ug/kg each of

B1,B2,G1,G2

460.0 -2 10 11 21 -17 0 2 **0**\*0 10.0 11 0.01 NIC. 14.Whre 24/3/81 **3**C F When the state of treventure of the survey of ManganesetMink IF 0403 Alluminium(At) (u]) ~? 0 M MM H/B/165 ගින් ගැනින් කිසින් للعتم تتدتحمال -4 JUN 1981 Ammunition of Nettogen Your Ref Althumond Netrogen anias atanagramme tuniter uside 10 Luchweise, Furmager Notrugen in Notrate Narugen in Narite Residuel Churche vereme evider D. sternational, Grotland. Lohur (Naren) 00pm Works & Chirler . ł I .! .' 1 -! , 1 I 1 territing and and an and the second second , T there was - - i -----• Ē ÷ ........... A support of the support • •• . The second secon ..... . = 15 u<mark>an</mark> Kanatan sebagai seta Analyse of a Sample of Water ŝ . . Room to the second , AND A DAMAGE --+ ļ Construction
 Const Autor 1: 1 - - -----:

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ŧ -Three revults indicate from the achect of the cheatcal analysis, a wholevoar water surrable for drinking and domentic purpones. e) -× ×. This charpen is very ferrit upped in appearance and is free from colour. The restriction is restrated and the water is addit in tharmiter with a low content of disposived and ide. The water is doft in the antials specifican structure of risk, iron and copper and is of a satisficatory statuand of organic quality. 1 ; ł H/R/ 14:3 Mugnesium Gulphate Magnesius Chloride Calcium Carbonate Cal- tue liutphate Fotessiue Nitrete Sudium Chlorida God. um Astrais : ` Silice (milligrammes per litre and millequivaleries per litre) 3 Mitterial Analysis of a Sample of Water : (after finitration of necessary) 1.414 Nume 1- ) Valer abin ł 96 n - 91 2 Anums 1 22 the and Laboration the Mary of the 3 3 3 Ŷ ¢ رال  $\geq$ 1.1.1 ť, ۰, ł distant in states of i () )) ? Caturos 1 s Comment ź Par. dt. Lativited Total 13 3 2 .==' 1 1 1 ×

## Water Analysis

APPENDIX 2

APPENDIX 2 (continued)

# ICLS

## <u>H/B/163</u>

# Organochlorine Pesticides

alpha - B.H.C.	NDLT	5 ng/1
gamma - B.H.C.	NDLT	5 ng/1
Heptachlor	NDLT	10 ng/1
Aldrin	NDLT	10 ng/1
Dieldrin	NDLT	20 ng/1
p.pD.D.T.	NDLT	10 ng/1
Polynuclear Aromatic Hydrocarbons		

Fluoranthene	NDLT	- 5	ng/1
Benzo (ghi) perylene	NDLT	1	ng/l
Benzo (k) fluoranthene	NDLT	1	ng/1
2,3 <u>o</u> - phenylenepyrene	NDLT	1	ng/l
Benzo (b) fluoranthene	NDLT	1	ng/1
Benzo (a) pyrene	NDLT	1	ng/l
Total PAH	NDLT	10	ng/l

Polychlorinated biphenyls

NDLT 200 ng/l expressed as AROCHLOR 1248

NDLT = Not detected, less than

Signed:

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P.S. WATERHOUSE, for: I.C.L.S. LABORATORIES LIMITED

# HMX: 13 Week Toxicity Study in Rats Haematology: During Week 5 Individual Values: Males

Dose mg/kg /day	Tests Units Grp S Anm	HB 9/100 ml	RBC x10 <sup>12</sup> /1	• • •	MCH PG	MCV Fl	MCHC 9/dl	Reti %	₩ВС ×10 <sup>9</sup> /1	Neut x10 <sup>9</sup> /1	Lymp x10 <sup>9</sup> /1	Mono x10 <sup>9</sup> /1	Eos x10 <sup>9</sup> /1	Hepa sec	Met %
	1 <b>A</b> 601 603 603 603 603 612 613 618 619 619 619			1 4 4 4 4 4 4 4 4 4 4 4 4 4	22 22 23 23 23 23 23 23 23 23 23 23 23 2	50 50 50 50 50 50 50 50 50 50 50 50 50 5	22222222222222222222222222222222222222	4 4 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	4-0/48/00	0001010000		0100000000	0.0000000000000000000000000000000000000	36.2 34.2 31.5 31.2 31.2 31.2 31.2 31.2 31.2 31.2	
	Mean S.D.	16.4 0.4	7.3 0.3	4 7 4 7 1	23 1	 65 3	35	3.6 1.2	7.1	0.8	6.3 0.8	0.0	0.1	31.7 3.0	0.8
4000	6 M 702 703 705 707 710 716 716 718 718 718 718		20.27.2 2.27.27.2 2.27.2.2.2 2.27.2.27.2 2.27.2.2.2.2	   4444444444   4800482000	22 22 22 22 22 22 22 22 22 22 22 22 22	65 65 65 65 65 65 65 65 65 65 65 65 65 6			0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	0.122840 0.02277 0.02777 0.02777 0.02777 0.02777 0.02777 0.02777 0.02777 0.02777 0.02777 0.02777 0.027777 0.027777 0.027777 0.027777777777	0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.0	0.1000000000000000000000000000000000000	0.0000000000000000000000000000000000000	35.2 31.2 31.2 35.7 35.7 35.7 35.7 35.7 35.7 35.7 35.7	. 6 . 0 . 0 . 0 . 0 . 0 . 0 . 0 . 0 . 0
8 7 1 1	Mean S.D.	15.6	7.3		 22 1	62 3	35 35 1	3.5 1.4	7.2	1.2	6.0 1.0	0.0	0.0	32.8	1.0 0.6

APPENDIX 3 (continued)

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Females

Eos Hepa Met 1 x10 <sup>9</sup> /1 sec %	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	0.0 30.1 1.2
моло x10 <sup>9</sup> /1	000000000000000000000000000000000000000	000000000000000000000000000000000000000	0.0
Lymp x10 <sup>9</sup> /1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	00 00 04 00 00 00 00 00 00 00 00 00 00 0	5.4 0.4
Neut x10 <sup>9</sup> /1	0.00 2.00 2.00 2.00 2.00 2.00 2.00 2.00	0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	0.0 0.3
₩ВС ×10 <sup>9</sup> /1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	00 0 0 0 0 0 0 0 0 0 0 0 0	6.3 0.5
Reti %	×4010021256	22. 24. 25. 26. 27. 27. 27. 27. 27. 27. 27. 27	2.3 0.9
9/d1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	×	34 1
MC V F I	67 67 67 68 68 68 68 68 68 68 68 68 68 68 68 68	00 00 00 00 00 00 00 00 00 00 00 00 00	64 2 
н 6 d	22 22 22 24 24 24 24 24 24 24 24 24 24 2	22 22 22 22 22 22 22 22 22 22 22 22 22	22 1
РС < %	0077887884444 0077887887888	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	45
RBC x10 <sup>12</sup> /1	7.55 7.75 8.75 7.67 7.91 7.91	0       	7.1 0.3
НЪ g/100 m1	16.6 15.2 15.2 15.3 15.4 16.4 16.6 16.6	16.5 15.4 15.4 15.6 15.4 15.4 15.4 15.4 15.4 15.4 15.4 15.4	15.6 0.6
Tests Units Grp S Anm	1 F 721 727 727 739 735 738 738 738	Mean S.D. 6 F 824 827 827 827 831 831 833 835 835 835 835 835 835	Mean S.D.
	с 0 0	1500	

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# HMX: 13 Week Toxicity Study in Rats Haematology: During Week 12 Individual Values: Males

X K t	3.5 2.0 2.9 2.9 2.9 2.5 2.9	1.0 2.1 2.5 2.5 2.5 2.5 2.1 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5 2.5	2.3 0.8
Hepa sec	34.2 35.2 35.2 35.2 35.2 25.8 32.2 25.8 32.2 25.8 32.2 25.8 32.2 25.8		32.8
Е05 x10 <sup>9</sup> /1		0.0	0.0
модо x10 <sup>-</sup> /1		0.0	0.1
۲۷۹۵ ×10/1	9		8.2 1.0
Neyt x10/1	00~7505000 0		1.0
WBC x10 /1	8.7 111.6 110.7 11.3 11.3 11.3 10.5 10.5 10.5 5.7	2.2 	9.3
Reti %	8 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~		3.8
MCHC g/dl	2888888888 2828888888 2828888888888888	44 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	34 1
MCV Fl	60 60 60 60 60 60 60 60 60 60 60 60 60 6	62 61 61 63 63 63 63 64 64 64	62 4
ысн рд	21 21 21 20 21 22 21 21 21 21 21 21 21 22 21 22 21 22 21 22 22	21 20 22 22 21 21 21 22 22 22 22 22 22 22 22	21
РС <	444444444 8444444444444444444444444444	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	45 1
RBC x10 <sup>12</sup> /1		0.5 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7	7.3 0.4
Hb g/100 x ml	14.6 15.5 15.5 15.5 16.1 16.1 16.1 16.1 16	15.6 15.0 15.0 15.0 15.0 15.1 15.1 15.8 15.8 15.8 15.2	15.2 0.4
Tests Units Grp S Anm	L <b>Σ</b> 601 603 603 612 612 612 612 613 613 613 613	Mean S.D. 6 M 702 6 M 703 703 703 703 716 716 716 718 719 719 719	Mean S.D.
Dose mg/kg /day	с 0 0	4000	

APPENDIX 4 (continued)

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X Xe t			1.6
Hepa sec	25.7 25.7 229.7 330.7 330.7 330.7 330.7 324.3 324.3 324.3 328.2 228.2	28.7 2.6 33.2 33.7 33.7 33.7 33.7 33.7 30.7 30.2 30.7 30.2	2.9
Eos x10 <sup>9</sup> /1		0.0000000000000000000000000000000000000	0.0
мопо x10 <sup>9</sup> /1	0000700070		
ل/10 <sup>9</sup> /1	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	1	1.7
Neut x10 <sup>9</sup> /1	0.0000.88114	00 010010101	•
₩ВС x10 <sup>9</sup> /1	00000000000000000000000000000000000000	6.4 10.5 10.5 10.6 10.6 9.7 9.0 9.1	1.8
Reti %	0 4 2 4 2 4 2 7 2 7 2 7 2 7 2 7 2 7 2 7 2	21 m 22 m	•
MCHC g/dl	4000000000 400000000 40040000000000000	4 4 4 4 4 4 4 4 4 4 4 4 4 4	-
MC V F I	665 66 66 66 66 66 66 66 66 66 66 66 66	0 4 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2
MCH Dg	22 22 22 22 22 22 22 22 22 22 22 22 22	22 22 22 22 22 22 22 22 22 22 22 22 22	
РС < %	44444444 447844444 447884444	4 14444444 4 14444444 4 14444444 4 14444444 4 14444444 4 14444444 4 14444444 4 14444444 4 1444444 4 14444444 1 14444444 1 1444444 1 1444444 1 1444444 1 1444444 1 1444444 1 1444444 1 1444444 1 14444444 1 14444444 1 14444444 1 144444444	
RВС d0 <sup>12</sup> /1		1.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	0.3
Hb 9/100 , ml	15.4 15.4 15.8 15.8 15.8 15.8 16.6 16.0 16.0		0.4
Tests Units Grp S Anm	1 F 721 722 727 729 730 735 737 738 738	Mean S.D. 6 F 824 826 826 831 831 834 835 835 835 835 837 837 837 837 837	s.D.
Dose mg/kg /day		1500	

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HMX: 13 Week Toxicity Study in Rats Clinical Chemistry: During Week 5

			Inc	Individual Values:	al Val		Males				
Dose mg/kg /day	Tests Units Grp S Anm	BUN mmol/ l	Glu mmol/ l	AST IU/I	ALT IU/1	AP IU/1	LDH LU/I	Na mmol/ 1	К mmol/ 1	TP g/l	Alb g/l
	1 M 601 M 601 603 605 609 612 613 613 619 619 619 620		7.91 9.27 9.29 7.18 7.57 8.23 8.23 8.23 8.23	88 77 87 88 87 85 85 85	65 81 81 81 81 80 73 80 80		403 408 3443 373 313 507 507 507 507 507 209 288		4 m m 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	65 65 65 65 65 65 65 65 65 65 65	88285555555
1         	Mean S.D.	6.4 0.8	8.14 0.78	83	72	712 85	357 357 85	 146 2	4.2 0.4	 62 2	 37 1
4000	6 M 702 6 M 703 703 707 710 714 714 719 719 719 719	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	8.29 7.65 8.29 8.37 7.72 7.72 7.84 7.84	73 90 84 77 77 79 79	663 588 57 57 70 70 70 70 70 70 70 70 70 70 70 70 70	817 817 807 817 817 897 897 898 819 811 988 988	403 4403 4483 4883 333 333 333 333 333 303 303 547 647	11111111111111111111111111111111111111	447474 47777 197777 19777 19777 1977777 197777 197777 19777777 197777 197777 197777 197777777 197777 1977777777	60 60 65 65 65 65 65 65 65	86664466466 86664666 866666666666666666
	Mean S.D.	6.5 1.0 + P	7.72 0.71  ANM 720	72 78 71 7 720,Repeat	63 8 6 6 1 1 1 1 1 1 0 5	840 64 Jes AST	417 164 and	147 147 3 ALT	4.1 0.3	63 2	39 1

APPENDIX 5 (continued)

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	lests Units Grp S Anm	8UN mmol/ 1	Glu / mmol/ 1	AST IU/l	ALT IU/1	AP IU/l	LDH IU/I	Na mmol/ l	K mmol/ l	тР g/l	41b 9/1
	L F 721 722 727 729 730 735 735 736 738 738	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	8.15 8.62 8.62 7.73 8.21 7.54 7.29 9.00	73 91 69 66 66 77 77 77 77 77 77 77	51 54 56 56 58 58 52 55 55 55 55 55	603 696 750 623 623 623 623 572 572 572 599 6269	244 244 268 268 268 253 253 254 249 2494 2494 2494	11111111111111111111111111111111111111	444044444 444444 44444 44444 44444 44444 4444	60 60 538 538 538 54 54 54 55 54 55 56 55 56 56 56 56 56 56 56 56 56 56	
	Mean S.D.	6.3 0.8	7.97 0.58	77 8	56 7	635 52	261 46	145 2	4.3 0.3	59 2	34
200	6 F 824 826 826 827 827 831 833 833 833 833 833 833 833 833 833	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	8.54 9.54 8.38 7.89 6.87 8.04 8.04 8.07 8.07 8.07 8.15	90 79 77 84 84 85 85 76	58 55 55 55 55 55 55 55 55 55 55 55 55 5	619 619 686 680 680 713 787 787 787 572 572 582 582	239 239 239 239 239 239 239 244 179	11111111111111111111111111111111111111	waaawaaaaa waaaaaaa waaaaaa	200 200 200 200 200 200 200 200 200 200	
	Mean S.D.	7.2	7.98 0.61	82 5	5 5 5	676 73	254 60	146 2	4.3 0.3	62 2	36 1

# HMX: 13 Week Toxicity Study in Rats Clinical Chemistry: During Week 12 Individual Values: Males

Dose mg/kg /day	Tests Units Grp S Anm	BUN mmol/ l	Glu mmol/ 1	AST IU/I	ALT IU/1	AP IU/1	LUH LU/I	Na mmol/ l	Na K mmol/mmol/ l l	тР g/l	A1b g/1
	L M 601+ M 601+ 603+ 609 615 613 618 619 619 619	00100000000000000000000000000000000000	8.07 7.82 7.74 9.755 7.17 7.78 7.78 8.00	124 133 133 128 128 133 133 133 134 101 124 124	79 79 59 73 73 73 73 73 73 73 73 73 73 73 73 73	214 214 214 217 217 217 194 190 231 231 251	278 278 278 244 228 283 228 228 228 258 258 263 263		447 mm 4444 1 4 4 1 4 4 4 4 4 4 4 4 4 4 4 4 4	690 600 600 600 600 600 600 600	1111000010 7777077077077077777777777777
       	Mean S.D.	5.4 0.4	8.32 1.36	122 27	 65 19	213 213 18	278 65	145	4.3 0.3	70	41
4000	6 M 702+ 6 M 703+ 703+ 707 716 716 718 718 719 719 719	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	7.64 7.64 7.64 7.27 7.18 7.18 7.45 7.45	142 142 105 105 96 96 96 101 133	105 105 350 350 322 322 356 369	224 324 324 432 453 453 525 525 566	228 2687 2687 2687 2687 2284 2293 2393 2393 2393 2393 2393 2393	157 157 157 157 157 157 157 157 157 157	4 m m 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	714 669 688 688 669	00-000-00 00-000-00 00-000-00 00-00-00 00-00-
	Mean S.D. A. + A	6.7 7.73 104 0.9 0.52 21 + ANM 605,620, ANM 601,603,6 ANM 601,603,702,Repeat V8	7.73 0.52 ANM 605 ANM 601	104 21 5,620, 1,603,7	73         104         48         415         286         147           52         21         23         102         119         4           605,620,703,Repeat         Values         AST         601,603,617,Repeat         Values         ALT           Repeat         Values         AP.ANM         603,Repeat         Values         ALT           801,603,702,Repeat         Values         AP.ANM         603,Repeat         Values         ALT	415 415 00 00 00 00 00 00 00 00 00 00 00 00 00	286 119 alues A alues A 603, Reg	• • •	4.0 0.3 0.3 Value	69	42

APPENDIX 6 (continued)

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Females

Dose mg/kg /day	Tests Units Grp S Anm	BUN mmol/ l	Glu mmol/ l	AST IU/l	ALT IU/1	AP IU/l	LDH LU/I	Na mmol/ l	K mmol/ l	IP g/l	Alb g/l
2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	L F 721+ 722 723+ 729 729 730 735 735 736 738 738	6.6 6.7 7.7 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7	8.48 8.48 6.46 7.87 7.87 7.87 10.59 8.48 8.48 8.48 8.48 8.48 8.48 9.48 9.4	68 105 138 138 138 138 138 105 64 92 92	147 32 32 32 55 61 55 35 35 35 35	489 331 489 589 589 589 566 472 472	433 433 433 453 453 423 423 423 423 423 423 423 423 423 42	1144 1445 1444 1444 1444 1444 1444 1444	N 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	6 6 6 0 1 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	22222222222222222222222222222222222222
	Mean S.D.	6.5 0.8	8.25 1.19	90 23	62 34	467 80	470 126	144	4.6 0.4	61 2	37 1
1500	6 F 824 826 826 823 823 831 831 834 834 835 835 835 835 835 835 835 835 835 835	00010000000000000000000000000000000000	8.84 5.69 6.95 8.36 7.95 7.95 7.89 8.72 8.72 8.72	124 128 124 124 124	55 55 59 59 59 78 78 78 78	542 542 543 543 543 543 562 6495 6493 619	463 463 323 323 323 323 328 328 413 413 348	148 148 1466 1446 1445 1445 1445 1445 1445 1445	44444444 2444444 2444444 244444 244444 244444 244444 244444 244444 244444 244444 2444444	00000000000000000000000000000000000000	0 0 1 0 0 % % % % % % % % % % % % % % %
	Mean S.D.	7.7 0.5	7.86 0.96	84 20	5 9 9	553 61	417 174	146 2	4.8 0.6	64 1	40
	5 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		ANM 721, ANM	721,727 727,735 836,837	7, Repeat 5, 834, Rej 7, Repeat	1 0	values AST eat Values Values LDH	T S ALT H	         	, , , ,	1

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HMX: 13 Week Toxicity Study in Rats Urinalysis: During Week 5 Individual Values: Males

wol Frot- Glucose
5 1 0
1 0.1
1.0 1
0.5 1
0.5 1
1.0 1
5
0.5 1 1
0
5 1
0.8
3
0.5 1
5 1
2
0
5
- <b>1</b> 
0.5 1
5 1
٦ 0
- 0
2
3

Note: All values shown in brackets were obtained from repeat samples

APPENDIX 7 (continued)

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	*	•	0	0	0	°	_	•	•	°	0			0	•	0	•	0	•	0	•	•	0			
	U	•	0	0	0	•		-	7	-	•			0	•	0	•	•	•	-	0	0	0			]
Хас	•	•	•	-	-	-		m	•	٦	-			0	0	1	0	I	2	2	1	7	-			1
MICROSCOPY	×	•	0	0	0	0		0	•	0	0			0	0	1 (0)	0	0	0	0	0	0	0			
MICI	3	•	0	0	0	0		0	0	7	0			0	0	0	0	0	0	0	0	0	0			]
	ъ С	-	-	-	I			-	-		-			1	٦	2	I	2	I	1	ı	1	-			1
	ធ	•	•	0	0	0		0	0	0	•			0	0	0	0	0	0	0	0	0	0	_		1
Colour		Я	ΡY	ΡY	ΡY	GY		к	DY	Y	Х			ΡΥ	ΡY	ΡY	ΡY	ΡY	ΡY	DΥ	ΡY	ΡY	Υ			
Blood pig-	ments	0	0	0	0	0		0	1 (0)	1 (0)	0			2 (0)	0	2 (0)	0	0	0	1 (0)	0	1 (0)	0			
Urobil	Inogen	0	0	0	0	0		0	0	0	0			0	0	0	0	0	0	0	0	0	0			
B1111-	rubin	0	0	0	0	0		0	0	0	0			0	0	0	•	0	0	0	0	0	0			
Ketones		0	0	0	0	0		0	0	0	0			0	0	0	0	0	0	0	0	0	0			
Glucose		0	0	0	0	0		0	0	0	0			0	0	0	0	0	0	0	0	0	0			
Prot-	UTP	7	-	-1	1	1		1	1	1	1			-		7	1		0	-	1	1	1			
10V I	1	0.5	0.5	0.5	0.5	0.5		0.5	0.5	0.5	0.5	0.5	0.0	1.0	3.0	1.5	1.0	1.0	3.0	0.5	2.0	1.0	0.5	1.5	6.0	
SG		1.052	1.043	1.050	1.044	1.051		1.070	1.082	1.084	1.074	1.061	0.016	1.027	1.023	1.030	1.029	1.025	1.024	1.086	1.027	1.032	1.074	1.038	0.023	
ЪН		0.6	8.5	8.5	0.6	9.0		0.6	0.6	8.5	8.0	8.7	0.4	6.0	7.0	8.0	5.5	6.0	8.0	9.0	6.0	8.5	9.0	7.3	1.4	
I.D. /Sex		7219	722	727	729	730	*735	736	737	738	739	Mean	s.D.	8249	826	827	828	831	832	834	836	837	839	Mean	s.D.	
Dose ma/ka/dav	fan /Eu /Eu	Control												1500								-				

\* = No urine sample produced on 3 successive occasions Note: All values shown in brackets were obtained from repeat samples

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HMX: 13 Week Toxicity Study in Rats

Urinalysis: During Week 12 Individual Values: Males

Dose	I.D.	Ha	US S	Vol	Prot-	Glucose	Ketones	B1114-	Urob11	Blood pig-	Colour		Σ	ICRO	MICROSCOPY		
mg/kg/day	/Sex	L	2	l e	ein				Inogen	ments		ы	CR 1	3	Я	с 0	A
Control	6013	0.6	1.052	0.5	T	0	1 (0)	0	0	3 (2)	λđ	1	0	0	0	3	
	603	0.6	1.045	0.5	1	0	0	0	0	I	ΡY	0	0	•	0	5	0
	605	0.6	1.022	2.0	F	0	0	0	0	1	ΡΥ	0	0	1	1	5	
	609	8.0	1.068	1.0	-	0	0	0	0	1 (0)	GY	0		0	0		1
	612	7.0	1.070	0.5	T	0	0	0	0	0	GY	0	0	0	0	0 3	
	615	9.0	1.050	1.0	-	0	0	0	0	0	GY	0	Ţ	-	0	2 0	
	617	0.6	1.066	0.5	-	0	0	0	0	0	ΡY	0	0	0	0	5	_
	618	9.0	1.026	1.5	1	0	0	0	0	0	ΡY	0	0		0	2	
	619	0.6	1.041	1.0	-	0	0	0	0	-	ΡY	0		0	0	2 1	0
	620	0.6	1.052	1.0	I	0	0	0	0	1	ΡΥ	0	0	0	•	2 0	<u> </u>
	Mean	8.7	1.049	1.0													
	s.D.	0.7	0.016	0.5						<u> </u>							
4000	7023	8.0	1.043	2.0	ľ	0	0	0	0	0	сX	•	2	0	0	0	•
	203	8.0	1.038	1.0	L	0	0	0	0	I	ΡY	0	1	0	0	3 0	
	705	8.0	1.052	0.5	I	0	1 (0)	o	0	0	ΡY	0	-	0	•	2	
	707	8.0	1.030	1.0	1	0	0	0	0	0	λď	0	1	0		2 0	•
	210	8.0	1.040	1.0	1	0	0	0	0	0	ΡY	0	5	0	0	-	
	714	0.6	1.064	0.5	1	0	0	0	0	0	ΡY	0	0	0	•	2 0	
	716	6.5	1.045	1.0	I	0	0	0	0	0	ΡY	I	7	0	0	2 0	
	718	8.0	1.052	1.0	1	0	0	0	0	0	γq	0	2	0	•	2 0	<u> </u>
	219	8.0	1.074	1.0	1	0	0	0	0	0	ΡY	0	1	•	•		
	720	9.0	1.049	1.0	-	0	0	0	0	0	ΡY	0				1 0	
	Mean	8.1	1.049	1.0										-			
	s.D.	0.7	0.013	0.4													
								.									

Note: All values shown in brackets were obtained from repeat samples

APPENDIX 8 (continued)

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Females

NSex         T         MI         ein         Indremain         Indremain	Dome	I.D.	HC	95 S	Vol	Prot-	Glucose	Glucose Ketones	B1111-	Urob11	Blood pig-	Colour		Σ	ICRO	MICROSCOPY	×	ļ
7219         6.0         1.043         0.5         1         0         0         0         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         1         0         0         1         0         0         1         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         1         0         0         1         0         0         1         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         1         0         0         1         0         1         0         1         0         1         0         1         0         1         0         1         1         1         1         1         1         1         1         1         1         1         1         1         1         1         1         1 </th <th>mg/kg/day</th> <th>/Sex</th> <th></th> <th></th> <th>1</th> <th>ein</th> <th></th> <th></th> <th>utanı</th> <th>Inogen</th> <th>ments</th> <th></th> <th>ы</th> <th>св</th> <th>3</th> <th>R</th> <th></th> <th>×</th>	mg/kg/day	/Sex			1	ein			utanı	Inogen	ments		ы	св	3	R		×
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Control	7219	6.0	1.043		T	0	0	0	0	0	Y	0	1	0	0		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		722	0.0	1.041		-	0	0	0	0	7	GY	0	2	0	0		
729         8.0         1.051         0.5         1         0         0         0         1         PY         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         1         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         0         1         0         1         0         0         1         0         1         0         0         1         0         1         0         1         0         1         0         1         0         1         1         0         1         1         0         1         1         0         1         1         0         1         1         0         1         1         <		727	8.0	1.030		-	0	0	0	0	0	ΡΥ	0	1	•	0		
•730       9.0       1.040       1.0       1       0       0 <t< td=""><td></td><td>729</td><td>8.0</td><td>1.051</td><td></td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>1</td><td>ΡΥ</td><td>0</td><td>1</td><td>0</td><td>0</td><td></td><td></td></t<>		729	8.0	1.051		1	0	0	0	0	1	ΡΥ	0	1	0	0		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		*730	0.6			T	0	0	0	0	0	ΡΥ	0	1	0	0		0
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\* = Insufficient sample on two occasions Note: All values shown in brackets were obtained from repeat samples

HMX: 13 Week Toxicity Study in Rats Clinical Signs, Gross and Histopathology for Individual Animals

Abbreviations Used:

KIE - Killed <u>in extremis</u>
FD - Found Dead
TK - Terminal Kill
NAD - No Abnormalities Detected
HE - Haematoxylin and Eosin

N.B. In all instances only those tissues showing abnormality are reported.

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	Number of	Sections Examined		Fat		Kidney	6unra	lieart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	lleum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenais	Bronchial L/N		Testes	Prostate	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
Death	ТК			Histopathology																																								
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: 415669CR <b>Group</b> :	Animal No: 601 Sex: O		Clinical History		NAD.															Necropsy Findings		NAD.																						If the second rest is a second rest is a second rest is a second rest.

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Animal No: 602

Group: 1 Control ъ Sex: Project No: 415669CR

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Time on Study (weeks)udy

Number of Sections Examined 벞 Cervical L/N Stomach Duodenum Jejunum Ileum Caecum Colon Spinal Cord Bone/Sternum Nasal Cavity Sciatic Nerve Trachea Thyroids Parathyroids Aorta Salivary Gl. S/M Lymph N. Pancreas Mes. Lymph N. Adrenals Bronchial L/N M<del>rrns/PrTubu</del> skin Mammary Gl. Eyes Brain Frestes Prostate Pitultary Aladder Fat Liver Kidney Lung Heart Spleen Thymus Muscle Rectum Histopathology ТК 14 NAD. Sample Necropsy Findings **Clinical History** NAD. NAD.

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	415669CR 41500p;	Animal No: 603 Sex: O		Clinical History		CRN														Necropsy Findings		toft testis larger than right.																			

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Time, on Study Death	-	14 TK		le Histopathology		NAD.																																		
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Crainer 1 Crainer		Animal No: 605 Sex: 0		Clinical History		NAD															Necropsy Findings		NAU.																	

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Death	Ϋ́		Histopathology		tubulat attopny and tubulat receneration.																																	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
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			Sample		Kidneys																																	
Provect No: 41566908 Group: 1 Control	606 Sex: 0		Clinical History		NAD.												Necrobsv Findings		NAD.																			

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	Number of			Liver	Kidney	fund	Heart	Spleen	Thymus	Muscle	Salivary GL.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	(Nucdenum			Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Strenning a Tuber	Tectes	Prostate	Pituitary	Bladder	Skin	namary 61.	Eyes Brain	Solnal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
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Death	ЪХ		Histopathology	tubular atrophy and tubular receneration.																												
Time on Study (Weeks)	14			Small foci tub epithelial req	•																											
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Project No: 415669CR Group: 1 Control	Animal No: 608 Sex: of	•	Clinical History	NAD.									Necropsy Findings	C4N																		
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	Number of	Sections Examined		Fat		Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Jetunum	lleum	Caecum	Calon	Rectum	Mes. Lymph N.		Uterus/P. Pulse	T	[lestes	Prostate	Picutary	Bladder	Mammary G?	Pvea	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	<u>.</u>	-
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: 415669CR Group:	Animal No: 609 Sex: O		Clintral History		NAD.													Necropsy Findings		Lungs darker than normal.																				

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Number of Sections Examined 뛷 spinal Cord Bone/Sternum Masal Cavity Sclatic Nerve Hronchial L/N <del>Nerns/PrTuluu</del> Trachea Thyroids Parathyroids Aorta Cervical L/N Stomach Jejunum Jejunum Caecum Caecum Mes. Lymph N. Adrenals Spleen Thymus Muscle Salivary Gl. S/M Lymph N. Pancreas Bladder Skin Mammary Gl. Eyes Prostate Pituitary Kidney festes Rectum Lung Heart Brain Fat Liver Histopathology Death ТX Time on Study (weeks) 14 NAD. Sample Group: 1 Control Sex: o Necropsy Findings **Clinical History** Project No: 415669CR 610 Animal No: NAD. NAD.

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Number of Sections Examined		Fat Liver	Kidney	fund	Heart	Spleen	Thymus	Muscle	Salivary GL.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta Cervical I./N	Stomach	Duodenum	Jejunum	lleum	Caecum	Colon	Hectum	Mes. Lymph N.	it created in the	Uterus/F.Tubeu		restes	Prostate	Pituitary	Bladder	Skin	Fires	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
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Project No: 415669CB Group: ] Control		Animal No: 615 Sex: O		Clinical History		NAD.													Necronsu Pindings	ACCIDENT FURTHER		NAD.									-									

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		lined			F	ŗ		H	<u>-</u>	·1-	-1-	1-	-	-	-	4	-	ᅼ	-	-1	4	-1	-1	-1	-1-	1	<u>-1</u>	<u>~</u> 1	╤┟	<u>+!-</u>		-1-	-1-	<u>- ا</u> ،	·1		<u>1</u> ~	1	<u>. La</u>	<u>u</u> =	-ic	<u>יזיכ</u> ש	<u>i_</u> 1.,
	Number of	Sections Examined		Fat	Liver	Kidnev	Lung	Heart	Spleen	Thomas	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Ducdenum	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Herno/Puture	fortor	Decetate	Pituitary	Bladder	Skin	Mammary Gl.	Eves	Brain	solnal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
(weeks) - 2	14 Trk			Histopathology			NAD.																																				
				Sample	2 duno		Z																																				
Project No: 415669CR Group: 1 Control	Animal No: 616 Sex: C			Clinical History			NAD.														Necropsy Findings			NAD.																			

i d15669CR Group: 1 Control 617 Sex: <b>đ</b> 14 The regension of the regulation of the regis of the regulation of the regulation of the regi			<b>P</b>	볓	-	_	1	Ţ			_				1~	J	1	7	1	-		5				-]~	]_	<b> </b> +		~		_	_		Ţ			Ţ	Ļ	0	Γ	
Group:     1     Time consistualy       Sex:     0     14       al History     Sample     NAD.		Number of	Sections Examin		Fat	Liver	A toney	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum		Colon	Rectum	Mac I umuh N	Adrenals	Bronchial L/N	Uterus/B. Bulaa	(Yustime	Testes	Prostate	Pitultary	Bladder	Skin Mammarv Cl	Pues	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
Group:     1     Time consistualy       sex:     0     14       al History     Sample     14       sign Findings     NAD.					КE																																					
Group: 1 Control Sex: of al History Sample Sample	Death	È	A1		Histopatholog																																					
Group: 1 Control Sex: of al History sy Findings	Time on Study (weeks)		<b>r</b>				NAU.																																			
Group: 1 Sex: of al History sy Findings					Sample																																					
	Group: 1	Sex:																		Necropsy Findings		NAD.																				

Project No:     610     21me (and study to be th)       Animal No:     613     Ser:     7       Animal No:     5     Semple     Histopy       Nu0.     Clunted History     Nu0.     Pistor       Nu0.     Nu0.     Nu0.     Pistor       Nu0.     Nu0.     Pistor     Pistor       Nu0.     Nu0.     Pistor     Pistor       Nu0.     Nu0.     Pistor     Pistor       Nu0.     Nu0.     Pistor     Pistor       Pistor     Pistor     Pistor       P	ſ		1		-	ĥ	Γ				_	_	Ţ	Ţ	Г	T	T	Γ			_				-	+   :	<u>ا</u>	Ţ		<u> </u>								<b>.</b>	
Image: sex of		Continue Printer		-				Spleen		Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	-	÷	Cervical 1./N	Stomach	Duodenum	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.		1		DEDELES	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Hone/Sternum	Nasal Cavity	Sclatic Nerve	
i 415669CR Group: 1 Control 618 Sex: J Clinical History Sample NAD. Necropsy Findings				ΛE																																			
: 415669CR Group: 1 Control 618 Sex: <b>đ</b> Clinical History Sample Necropsy Findings	Death	TK		Histopatholo																																			
: 415669CR Group: 1 Control 618 Sex: of Clinical History Necropsy Findings	Time on Study (Weeks)	14			NAD.																																		
: 415669CR Group: 1 618 Sex: J Clinical History Necropsy Findings				Sample																																			
	415669CR Group: 1	618 Sex: 0				.n.												Morroset Findinge	shurpur i Asdorran																				

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	Number of Sections Examined		Fat Liver	Kidney	Lung Heart	Spleen	Thymus Muscle	Salivary Gl.	Pancreas	Trachea	Parathyroids	Aorta Counter 1 / W	Stomach	Duodenum	Iteum	Caecum	Rectum	Mes. Lymph N.	Adrenals	and a territoria	Matru	Testes	Pituitary	Bladder	Skin Mammarv G	Eves	Brain	Spinal Cord	Nasal Cavity	Sciatic Nerve	
Time on Study Death	14 TK		Histopathology	NAD.																											
			Sample														_														
Drovert No. 416660CB Group: ] Control	Sex: 0		Clinical History	NAD										Necropsy Findings		NAD.															

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	Number of	Sections Examined		Fat	Liver	Kidney	fund	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyrotds	Parathyroids	AOTCA Cervica) 1./N	Stomach	Duodenum	Jetunum	lleum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	(Herns/P. Tubus		Testes	Prostate	Pltuitary	Bladder	Skin	Mammary GI.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
				λ																																								
Death	Х. H	11		Histopathology																																								
Time on Study		5 T				NAD																																						
				Sample																											-													
Protect No: 415669CB Group. 1 Control		26X:		Clinical History			NAU.														Necropsy ringings		NAD.																					

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	Number of Sections Examined	Ŧ		x r r r r r r r r r r r r r r r r r r r
			۷	
Death	TK		Histopathology	•
Time on Study	14			NAD.
mg HMX/kg/day	1		Sample	
2 50	Animal No: 621 Sex: J		Clinical History	NAD.

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Number of Sections Examined Э 2 Liver Kidneys Histopathology Death ТК Time on Study 14 NAD. Sample 50 mg HMX/kg/day Group: 2 Sex: d Necropsy Findings **Clinical History** Project No: 415669CR 622 Animal No: NAD. NAD.

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Э Number of Sections Examined Liver Kidneys Histopathology Death ŢΚ Time on Study 14 NAD. Sample 50 mg HMX/kg/day Group: 2 Sex: đ Necropsy Findings Clinical History Project No: 415669CR Animal No: 623 NAD. NAD.

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æ -~ Number of Sections Examined Liver Kidneys Histopathology Death ΤK Time on Study 14 NAD. Sample 50 mg HMX/kg/day 7 Sex: đ Necropsy Findings Group: **Clinical History** Project No: 415669CR 624 Animal No: NAD. NAD.

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Ħ  $\sim$ Number of Sections Examined l.iver Kidneys Histopathology Death ΤĶ Time on Study 14 NAD. Sample 50 mg HMX/kg/day 7 Sex: đ Necropsy Findings Group: **Clinical History** Project No: 415669CR 625 Acimal No: NAD. NAD.

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Project No: 115669(R. Group: 2 50 mg HM./Kg/day) Death Animal No: 626. See: of See: of Mean of Mean Mean of Me				
Image: 15669CR     Group:     Z     50 mg Hh/kg/day     Death       62b     Sax: 0     14     TK       Clinical History     Sample     Histopathology       Clinical History     Sample     MJD.	Γ	thed HF		
i H1569CR     Group:     2     50 mg HN./kg/day     Time, ugn, sgyudy       626     sex:     0     14     14       Clinical History     Sample     NAD.	Number of	Sections Exam		kidneys Kidneys
i 415669CR     Group:     2     50 mg HN./kg/day     Time,ggr, k5yudy       626     Sex:     0     14     14       Clinical History     Sample     NAD.			Y	
: 415669CR Group: 2 50 mg HM./kg/day 626 sex: d Clinical History Sample	Death	1 V	Histopatholog	· ·
: 415669CR Group: 2 50 mg HM/kg/c 626 Sex: 0 Clinical History Necropsy Findings	Time on Study 14			NAD.
: 415669CR Group: 2 50 mg 626 Sex: <b>đ</b> Clinical History Necropsy Findings	/kg/day		Sample	
	: 415669CR Group: 2 50 mg 626 Sex: O		Clinical History	

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	Number of Sections Examined			Liver Kidneys	 	 							
			۷										
Death	ТК		Histopathology		-								
<b>Time</b> workstudy	14			NAD.									
50 mg HMX/kg/day			Sample	Liver	 								
Project No: 415669CR Group: 2 50 mg HM	Sex: 0		Clinical History	NAD.			Necropsy Findings	Liver - nodule of liver tissue on surface of central lobe and forming adhesion with diaphragm.					

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볓 Number of Sections Examined ~ l.iver Kidneys Histopathology Death ТΚ Time on Study 14 NAD. Sample 50 mg HMX/kg/day Group: 2 Sex: d Necropsy Findings **Clinical History** Project No: 415669CR 628 Animal No: NAD. NAD.

Number of Sections Examined 뉟 4 2 Liver Kidneys Histopathology Death ΤX Time on Study **1**4 NAD. Sample yeng HMX/kg/day 2 Sex: đ Group: Necropsy Findings **Clinical History** Project No: 415669CR 629 Animal No: NAD. NAD.

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Number of Sections Examined H ----l.iver Kidneys Histopathology Death тк Time on study 14 NAD. Sample 50 mg HMX/kg/day Group: 2 Sex: o Necropsy Findings Clinical History Project No: 415669CR 630 Animal No: NAD. NAD.

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Э 2 Number of Sections Examined Liver Kidneys Histopathology Death ТĶ Time on Study 14 NAD. Sample 50 mg HMX/kg/day Group: 2 Sex: d Necropsy Findings **Clinical History** Project No: 415669CR 631 Animal No: NAD. NAD.

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HE Number of Sections Examined Liver Kidneys Histopathology Death ТK Time on Study 14 NAD. Sample 50 mg HMX/kg/day Group: 2 Sex: d Necropsy Findings **Clinical History** Project No: 415669CR 632 Animal No: NAD. NAD.

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	Number of Sections Examined			Liver Kidneys					
Death	TK		Histopathology		-				
Time on Study	14			NAD.					
mq HMX/kq/dav			Sample						
Project No: 415669CR Group: 2 50 mg HM	Sex: d		Clinical History	NAD.			Necropsy Findings	NAD.	

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ANALYSIN STREET STREET

Death Time on Study

-	5	븰	Π		TT	
	Number of Sections Examined			Li ver Kidneys		· · · · · · · · · · · · · · · · · · ·
	TK		Histopathology	oci		
(weeks) /	1.4			Clear cell foci.		
X/kg/day			Sample	Liver		
Project No: 415669CR Group: 2 50 mg HMX/kg/day	4-		Clinical History	NAD.	Necropsy Findings	NAD.

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	P	뷮	44	ШТ	ΠΠ	Π	Ш	Ш			
	Number of Sections Examined		Liver Kidneys	 					 	<u> </u>	
Death	TK	Histopathology	oci.	-							
Time on Study	14		Clear cell foci.								
X/kg/dav		Sample	Liver	 					 		
Project No: 415669CR Group: 2 50 mg HMX/kg/dav	Sex: đ	Clinical History	NAD.			Necropsy Findings	NAD.				

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50 mg HMX/kg/day Group: 2 sev: d Project No: 415669CR Animal No: 636

Death

Time werkstudy

ſ	pa	끮			TT	
	Number of Sections Examined			Liver Kidneys		
_			y			
	TK		Histopathology	-		
(WEEKS)	14					
x/kg/day			Sample			
Froject No: 410669CK Group: 2 50 mg HMX/Kg/day	Animal No: 636 Sex: O		Clinical History	Lesion on bridge of nose from week 12- 13.	Necropsy Findings	NAD.

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Ĵł:

Number of Sections Examined Liver Kidneys Histopathology Death ТΚ Time on Study 14 NAD. Sample 50 mg HMX/kg/day 2 sex: đ Necropsy Findings Group: **Clinical History** Project No: 415669CR 637 Animal No: NAD. NAD.

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Number of Sections Examined Э Liver Kidneys Histopathology Death ТK Time on Study 14 NAD. Sample 50 mg HMX/kg/day Group: 2 Sex: d Necropsy Findings **Clinical History Project No: 415669CR** 638 Animal No: NAD. NAD.

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Э Number of Sections Examined -Liver Kidneys Histopathology Death ТĶ T1me weeks udy 14 NAD. Sample 50 mg HMX/kg/day 7 Sex: đ Necropsy Findings Group: **Clinical History** Project No: 415669CR 639 Animal No: NAD. NAD.

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HE Number of Sections Examined -1 Liver Kidneys Histopathology Death ΤK Time on Study 14 NAD. Sample 50 mg HMX/kg/day 2 Sex: o Necropsy Findings Group: Clinical History Project No: 415669CR 640 Animal No: NAD. NAD.

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	HE G	1	-1-1	П	Π	Π	Π	Π		Ш	$\square$	Π	Π	Π	Π	Π	Π	
	Number of Sections Examined		Liver Kidneys															
Time on Study Death	ТК	Histopathology	NAD.			-												
1X/kg/dav		Sample																
Project No: 415669CR Group: 3 150 mm HMX/km/dav	Sex: O	Clinical History	NAD.					Necropsy Findings	NAD.									

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Æ Number of Sections Examined Liver Kidneys Histopathology Death ТΚ Time on Study 14 NAD. Sample Group: 3 150 mg HMX/kg/day Sex: d Necropsy Findings **Clinical History Project No: 415669CR** 642 Animal No: NAD. NAD.

Æ 22 Number of Sections Examined Liver Kidneys Histopathology Death ΤĶ Not examined. Time on Study 14 Sample Lungs Group: 3 150 mg HMX/kg/day Lungs - irregular dark red patches. Sex: o Necropsy Findings **Clinical History** Project No: 415669CR 643 Animal No: NAD.

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믳 Number of Sections Examined 20 Liver Kidneys Histopathology Death ТĶ Slight toxic change. Time on Study .14 Sample Liver Group: 3 150 mg HMX/kg/day Sex: o Necropsy Findings Clinical History **Project No: 415669CR** Animal No: 644 NAD. NAD.

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Group: 3 150 mg HMX/kg/day Project No: 415669CR

Death

Time on Study

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Ined	뷮		44	Π	Π	Π	ШП	Π					Π	Π	
Number of Sections Examined			Liver Kidneys										-		
		уу													
FD		Histopathology			-										
1weeks)			Autolytic.	Autolytic.											
iou mg HMX∕kg∕day		Sample	Liver	Kidneys		<u></u>									
Animal No: 645 Sex: 0		Clinical History	2 masses V/L abdomen from week 6-9.					Necropsy Findings	Abdomen filled with red fluid. Two masses attached to abdominal wall -	Mass 1 - 45 x 30 x 30 rum, multilobed with varying consistency from very firm to soft. Colour varies from dark red to white.	Mass 2 - 12 x 10 x 4 mm attached to Mass 1, pale pink in colour.	Thymic lymph node dark red and enlarged.	Brain - very friable.		

Number of Sections Examined 볓 Liver Kidneys Histopathology Death ТK Time on Study 14 NAD. Sample 3 150 mg HMX/kg/day Sex: d Group: Necropsy Findings **Clinical History Project No: 415669CR** 646 Animal No: NAD. NAD.

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	Number of Sections Examined		Liver Kidneys															
Death	ТК	Histopathology				-												
Time on Study	.14		Slight toxic change.															
150 mg HMX/kg/day	• •	Sample	Liver				·					_						
Project No: 415669CR Group: 3 150 mg H	Sex: đ	Clinical History	NAD.					Necropsy Findings										

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Ŧ 2 Number of Sections Examined Liver Kidneys Histopathology Death ΤĶ Time weeks budy .14 NAD. Sample 3 150 mg HMX/kg/day Sex: đ Necropsy Findings Group: Clinical History Project No: 415669CR Animal No: 648 NAD. NAD.

106

Number of Sections Examined 뷮 2 Liver Kidneys Histopathology Death ТΚ Time on Study 14 NAD. Sample 3 150 mg HMX/kg/day Sex: o Necropsy Findings Group: **Clinical History** Project No: 415669CR 649 Animal No: NAD. NAD.

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븾 ~ Number of Sections Examined Liver Kidneys Histopathology Death ТК Time on Study 14 NAD. Sample Group: 3 150 mg HMX/kg/day Sex: đ Necropsy Findings Clinical History Project No: 415669CR Animal No: 650 NAD. NAD.

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103

H 2 Number of Sections Examined Liver Kidneys Histopathology Death ΤK Time on Study 14 NAD. Sample 3 150 mg HMX/kg/day Group: Necropsy Findings **Clinical History** Project No: 415669CR 651 Animal No: NAD. NAD.

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2 Number of Sections Examined 뉟 Liver Kidneys Histopathology Death ТΚ Time on Study 14 NAD. Sample Group: 3 150 mg HMX/kg/day Sex: o Necropsy Findings **Clinical History** Project No: 415669CR 652 Animal No: NAD. NAD.

ł	Ţ	뷮			Π			
	Number of Sections Examined		Liver Kidneys					
<b></b>		Хb						
Death	ТК	Histopathology						
Time on Study	14		NAD.					
150 mg HMX/kg/day	•	Sample						
Project No: 415669CR Group: 3 150 mg Hi	Sex: o	Clinical History	NAD.		Necropsy Findings	NAD.		

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Number of Sections Examined Æ Liver Kidneys Histopathology Death ТĶ Time on Study 14 NAD. Sample 3 150 mg HMX/kg/day Sex: d Necropsy Findings Group: **Clinical History** Project No: 415669CR 654 Animal No: NAD. NAD.

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CONTROL STATIST

Number of Sections Examined ΗE ~  $\sim$ L1 ver K1dneys Histopathology Death ΤK Time on Study 14 NAD. Sample Liver Group: 3 150 mg HMX/kg/day Sex: đ Liver - 10 mm diameter swelling on median lobe. Necropsy Findings **Clinical History** Project No: 415669CR 655 Animal No: NAD.

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Number of Sections Examined HΕ Liver Kidneys Histopathology Death ΤK Time on Study J 4 NAD. Sample Group: 3 150 mg HMX/kg/day Sex: o Necropsy Findings **Clinical History** Project No: 415669CR Animal No: 656 NAD. NAD.

볓 22 Number of Sections Examined Liver Kidneys Histopathology Death ТΚ Time on Study 14 NAD. Sample 3 150 mg HMX/kg/day Group: Sex: of Necropsy Findings **Clinical History** Project No: 415669CR 657 Animal No: NAD. NAD.

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Number of Sections Examined Ä 2 Liver Kidneys Histopathology Death ΤK Time on Study 14 NAD. Sample Group: 3 150 mg HMX/kg/day Sex: đ Necropsy Findings **Clinical History** Project No: 415669CR 658 Animal No: NAD. NAD.

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3 150 mg HMX/kg/day Group: 3 Sex: đ Project No: 415669CR

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Number of Sections Examined Æ 2 Liver Kidneys Histopathology ТК Time on Study 14 NAD. Sample Liver Necropsy Findings Liver - lobulation prominent. Clinical History 629 Animal No: NAD.

띛 Number of Sections Examined 22 Liver Kidneys Histopathology Death ΤK Time on Study 14 NAD. Sample Group: 3 150 mg HMX/kg/day Sex: đ Necropsy Findings **Clinical History** Project No: 415669CR Animal No: 660 NAD. NAD.

118

Number of Sections Examined Э Liver Kidneys Histopathology Death ТK Slight toxic change. Time on Study 14 Sample Liver 450 mg HMX/kg/day Group: 4 Sex: 0 Necropsy Findings **Clinical History Project No: 415669CR Animal No: 661** NAD. NAD.

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	Number of Sections Examined		Liver Kidneys																	
Death	TK	Histopathology	change.		-															
Time on Study	.14		Slight toxic change.														ŗ			
450 mg HMX/kg/dav		Sample	Liver																	
Project No: 415669CR Group: 4 450 md H	Sex: đ	Clinical History	Black encrusted right eye from week 8-10.					Necropsy Findings	NAD											

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	Number of Sections Examined		_	Liver Kidneys	 													
Death	ТК		Histopathology	change.		•												
Time weeks)udy	14			Slight toxic change.						-								
4X/kg/day	,	-	Sample	Liver										_				
Project No: 415669CR Group: 4 450 mg HMX/kg/day	Sex: đ		Clinical History	NAD.				Necropsy Findings	NAD.									

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벌 20 Number of Sections Examined Liver Kidneys Histopathology Death ТK Slight toxic change. Time on Study .14 Sample Liver 450 mg HMX/kg/day Group: 4 Sex: 0 Necropsy Findings **Clinical History** Project No: 415669CR Animal No: 664 NAD. NAD.

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Death Time on Study Group: 4 450 mg HMX/kg/day Project No: 415669CR

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Number of Sections Examined			Liver Kidneys																	
тк		Histopathology	change.			-	ı													
1.4			Slight toxic change.																	
		Sample	Liver																	
Animal No: 665 Sex: 0		Clinical History	NAD.								Necropsy Findings	NAD.								
Anta			NA	_								NA								

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Project No: 415669CR Group: 4 450 mg HMX/kg/day Animal No: 666 Sex: 0

Death

Time on Study

	<u></u>	14-			
Number of Sections Examined	ų	Liver 2			
ΤK	Histopathology		-		
14			Toxic change.		
	Sample				
AnimalNo: 666 Sex: o <sup>0</sup>	Clinical History			Necropsy Findings	Liver - mottled.

450 mg HMX/kg/day Group: 4 Sex: đ Project No: 415669CR 667

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Ä 22 Number of Sections Examined Liver Kidneya Histopathology Death ΤK Toxic change. Not examined. Time on Study 14 Sample Liver rungs Left eye red rimmed from week 9-11. Necropsy Findings Clinical History Lungs redder than normal. Animal No:

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Ŧ 4 Number of Sections Examined Liver Kidneys Histopathology Death ТK Slight toxic change. Time on Study 14 Sample Liver Group: 4 450 mg HMX/kg/day Sex: o Necropsy Findings Clinical History Project No: 415669CR 668 Animal No: NAD. NAD.

126

Number of Sections Examined Ŧ Liver Kidneys Histopathology Death ТΚ Slight toxic change. Time on Study 14 Sample Liver Group: 4 450 mg HMX/kg/day Sex: 0 Necropsy Findings Clinical History Project No: 415669CR 669 Animal No: NAD. NAD.

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	Number of Sections Examined			Liver Kidneya								····								
			×																	
Death	TK		Histopathology	change.			•													
Time on Study	14			Slight toxic change.	Not examined.															
450 mg HMX/kg/day			Sample	Liver	Lungs								_						-	
Project No: 415669CR Group: 4 450 md HM	Sex: o		Clinical History	NAD.						Necropsy Findings	Lungs darker than normal.									

Number of Sections Examined 22 Liver Kidneys Histopathology Death ТК Slight toxic change. Time on Study 1.4 Sample Liver 4 450 mg HMX/kg/day Group: Necropsy Findings Clinical History Project No: 415669CR Animal No: 671 NAD. NAD.

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Number of Sections Examined Ŧ 2 Liver Kidneys Histopathology Death ТĶ Slight toxic change. Time on Study 14 Sample Liver 4 450 mg HMX/kg/day Sex: d Necropsy Findings Group: Clinical History Project No: 415669CR 672 Animal No: NAD. NAD.

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Ę Number of Sections Examined Liver Kidneys Histopathology Death ТK Slight toxic change. Time weeks)udy 14 Sample Liver 450 mg HMX/kg/day Group: 4 Sex: đ Necropsy Findings **Clinical History** Project No: 415669CR Animal No: 673 NAD. NAD.

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	Number of Sections Examined		Liver Kidneys	<b></b>		<b></b>	
Death	тк	Histopathology	Toxic change, two areas of necrosis.	·			
Time on Study	-14		Toxic change,				
450 mg HMX/kg/day		Sample	Liver				
Project No: 415669CR Group: 4 450 mg Hh	Animal No: 674 Sex: C	Clinical History	NAD.			Necropsy Findings	NAD.

22 볓 Number of Sections Examined Liver Kidneys Histopathology Death ТК Toxic change. Time on Study 14 Sample Liver Group: 4 450 mg HMX/kg/day Sex: đ Necropsy Findings **Clinical History** Project No: 415669CR Animal No: 675 NAD. NAD.

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42 Number of Sections Examined 볓 Liver Kidneya Histopathology Death ΤK Slight toxic change. Time on Study 14 Sample Liver Group: 4 450 mg HMX/kg/day Sex: d Necropsy Findings **Clinical History** Project No: 415669CR Animal No: 676 NAD. NAD.

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134

Number of Sections Examined HE 22 Liver Kidneys Histopathology Death TΚ Slight toxic change. Time on Study 14 Sample Liver 450 mg HMX/kg/day 4 Eyes red rimmed from week 12-13. Sex: o Necropsy Findings Group: **Clinical History** Project No: 415669CR 677 Animal No: NAD.

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벌 22 Number of Sections Examined Liver Kidneys Histopathology Death ΤK Slight toxic change. Time on Study 14 Sample Liver Group: 4 450 mg HMX/kg/day Sex: d Necropsy Findings **Clinical History** Project No: 415669CR 678 Animal No: NAD. NAD.

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	٢	Ined		441111	Π	
		Sections Examined		Liver Kidneys		
	Time OckStudy Death	J4 TK	Histopathology	Slight toxic change.		
L			Sample	Liver	 	
	: 415669CR	Animal No: 679 Sex: 0	Clinical History	Lesion on bridge of nose from week 12-13.	Necropsy Findings	NAD.

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Æ Number of Sections Examined Liver Kidneys Histopathology Death ΤK Slight toxic change. Time on Study 14 Sample Liver Group: 4 450 mg HMX/kg/day Sex: 0 Necropsy Findings Clinical History Project No: 415669CR 680 Animal No: NAD. NAD.

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	Number of Sections Examined		Fat			<u>,</u>	Spleen	Thymus	Muscle	Salivary GL.	o/m Lymph N. Pancreas	Trachea	_	Parathyroids	Aorta Carutan 1 /N		Duodenum	Jejunum []	lleum			Mes. Lymph N.    Adrenals	Bronchial L/N	and the second		festes	Prostate Pituitary	Bladder	skin	Nry GL.		Brain []	Spinal Cord 2	Bone/Sternum [] Nagal Cautru []	Sciatic Nervo		<u>_</u>
Time on Study Death	TK		Histopathology		Areas toxic change, mainly centrilobular.				<u> </u>			<u>_</u>	<u></u>			2.2					2			<u>.</u>	<u>*</u>					2	E3			<del>X</del> <del>X</del>			
HMX/kg/day			Sample		LIVEL																														_		
: 415669CR Group: 5 1350 mg	Animal No: 681 Sex: đ		Clinical History	NAD													Necropsy Findings		NAD.																		

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Group: 5 1350 mg HMX/kg/day Project No: 415669CR

Death

Number of Sections Examined 볓 Trachea Thyroids Parathyroids Aorta Cervical L/N Stomach Stomach Jejunum Ileum Caecum Spinal Cord Hone/Sternum Nasal Cavity Sclatic Nerve Thymus Muscle Sallvary Gl. S/M Lymph N. Pancreas Mes. Lymph N. Adrenals Bronchial L/N Prostate Pltuitary Hladder Skin Mammary Gl. Eyes うけんし していしん Spleen Fat Liver Kidney Lung Heart Rectum festes Brain Areas toxic change, mainly centrilobular. Histopathology ТΚ Time on Study (Weeks) 14 Sample Liver ъ Necropsy Findings **Clinical History** Sex: 682 Animal No: NAD. NAD.

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	Number of	Sections Examined		<u> </u>	Kidney		Soleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N. Pancreas	Trachea	Thyroids	Parathyroids	Aorta Cervical 1 /N	Stomach	Duodenum	Jejunum	1leum		Colon		Advensie	bronchial L/N	Iterra/B. Build		festes	Prostate	Pituitary	191400er	Mammary Gl.	Eves	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sclatic Nerve	
Time on Study Death (weeks)		14 TK		Histopathology		Areas toxic change.																																
HMX/kg/day				Sample		Liver																																
Project No: 415669CR Group: 5 1350 mg H	Sex: O			Clinical History		NAD.											Necropsy Findings			NAU.																		

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	Number of	Sections Examined		Fat	Liver	Kidney	- rrmd	Celeon	spreen	Thymus	Muscle	Salivary GL.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Je)unum	lleum		Bectum		Mes. Lymph N. Adrenalc	uvereliate Uverebial T/M	BEUNCHIAL L/N	******	Testes	Prostate	Pituitary	ßladder	Skin	Mammary Gl.	Eyes	Brain	spinal Cord	Hone/Sternum	Masal Cavity	Sciatic Nerve		
				Å																																								
Death		TK		Histopathology		ande – mild.																																						
Time on Study (weeks)		14				Areas toxic change																													-					-			_	
mq HMX/kq/dav				Sample		Liver																																						
Project No: 415669CR Group: 5 1350 mg Hv	<b>f</b> o			Clinical History		NAD.															Necropsy Findings		NAD.																					

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	Number of Sections Examined		Fat	Liver	Kidney	5un 1	Heart	spleen	Sunyfit.	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids		Cervical L/N	Prodente	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N		festes	Prostate	Pltuitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
Time on Study Death	14 TK		Histopathology		Areas toxic change - mild.																																				
mg HMX/kg/day			Sample		Liver																																				
Project No: 415669CR Group: 5 1350 mg H	Animal No: 685 Sex: đ		Clinical History		NAD.														Necronsy Findings		NAD.																				

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	Number of Sections Examined	-	Fat		 <u> </u>	Thymus	Salivary Gl.	S/M Lymph N.	Pancreas	-	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum []	Ileum	raecum rolon	Rectum	ymph N.	Adrenals	Bronchial L/N	Internal Particular	Taktos	Prostate	Pituitary [	Rladder [	17 GI.	Eyes	Solnal Cord	Bone/Sternum	Nasal Cavity	Sclatic Nerve	
Time on Study Death	TK		Histopathology	Areas toxic change, mainly centrilobular.																													
ma HMX/kg/dav			Sample	Liver									_														 						
Crown 5 1350 md HW	Sex: 0		Clinical History	NAD										Necropsy Findings		NAD																	

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	Number of Sections Examined	-	Fat Liver			Thymus	Muscle	Salivary Gl.	Pancreas			Aorta	ALL/N	Stomach	Ducidenum []	Jejunum []	Caecum	Colon	Rectum	Hes. Lymph N.		Bronchial L/N	1	restes	Prostate	Pituitary	Bladder	Skin	Mammary GL.	Eyes			Bone/Sternum   Nasal Cavity	Scintic Nerve		
ļ	<u>.</u>			- mild.		<u> </u>	2	<u></u>	<u> </u>	T	<u>+ c</u>		0	2	<u>a</u>		<u>- U</u>	2	2	<u> </u>	<u> </u>	<u>n 1</u>	3		<u>.</u>	<u>a</u>	<u>e</u>	<u> </u>	2.0	<u>a</u> :	<u> </u>	<u> </u>	<u>2_</u>			
Death	ΤK		Histopathology	Areas toxic change, mainly centrilobular																																
Time on Study	14			Areas toxic ch																																
X/kq/day		-	Sample	Liver											-																					
Distribution of the second crown: 5 1350 mg HMX/kg/day	Sex: 0		Clinical History	NAD.											Necropsv Findings	- 1																				

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	Number of	Sections Examined		Fat	Kldnev	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum 110:	Liver,	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Total Land		lestes	Prostate		Bladder skin		Fues	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sclatic Nerve	
		_		۶۲ ۲																				_																
Death	TK			Histopathology																																				
Time on Study (Weeks)	14				UAN			2																									_							
mg HMX/kg/day				alquino												_																								
: 415669CR Group: 5 1350	Animal No: 688 Sex: o		Clinical History		NAD.													Necropsy Findings		NAD.																				

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	Number of	Sections Examined		Fat	Liver	Lund	Heart	Spleen	Thymus	Muscle	Salivary Gl	S/M Lymph N. Pancreas		Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	lileum.	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Uterus/P.Tube		restes	Pitultary	Bladder	Skin	Manmary Gl.	Eyes		Bone/Sternum	Nasal Cavity	Sclatic Nerve	
·				~		trilobular - mild.																																
Death	È	J.K		Histopathology		Areas toxic change, mainly centrilobular	•																															
Time on Study (weeks)		14				Areas toxic ch																						- 74										
HMX/kg/day				Sample		Liver																																
Project No: 415669CR Group: 5 1350 mg Hh	Animal No: 689 Sex: C			Clinical History		NAD.													Necropsy Finaings	NAD																		

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	Number of	Sections Examined		Fat	Liver	Kidney	bund	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyrolds	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	[leum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterna/Permine		Testes	Prostate	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve
				~																																							
Death	TK			Histopathology		carll food turbular dilation	UTAL ULIACTON.																																				
Time on Study	14	•				could foot tob	Smatt toot cut																							<u>.</u>													
mq HMX/kq/day				Sample			stauets																																				
Project No: 415669CR Group; 5 1350 mg HM				Clinical History			NAD.														Necropsy Findings			NAD.																			

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	Number of Sections Examined		Fat	Liver	Lung	Heart	Spleen	Thymus	Salivary G	S/M Lymph N.	Pancreas	Trachea	Parathvroids	Aorta	Cervical L/N	Stomach	Duodenum	Ileum	Caecum	Colon	Adrenals	Bronchial L/N	Uterus/P.Bullio		Prostate	Pituitary	Bladder	Skin Version Cl	Fund	Brain	Spinal Cord	Hone/Sternum	Masal Cavity	Sciatic Nerve	
Death	ТК		Histopathology		toxic change, mainly centrilobular.																														
Time on Study	14				Areas toxic cr								_							_	 														
НМХ∕kg∕day			Sample		12/17																														
5 1350 muj	Animal No: 691 Sex: d		Clinical History	NAD.												Necropsy Findings		NAD.																	

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Group: 5 1350 mg HMX/kg/day Sex: 0 Project No: 415669CR Animal No: 692

Death ¥ Time on Study (weeks)udy 1 4

Number of

С.

Animal No: 692 Sex: O		14 TK	Sections Examined HE	면법
Clinical History	Sample	Histopathology	Fat Liver	
			Kidney	-
Scabs on right of nose from week 8-14.	Liver	Toxic change, mainly centrilobular - mild.	Lung	4
			Spleen	- ]
			Thymus	-
			Muscle	-
			Salivary Gl.	_
			S/M Lymph N. Pancreas	-  -
			Trachea	T-
			Thyroids	4
			Parathyroids	7
			Aorta Comical 1 /	Ţ.
			Stomach	L
Necronsv Findings			Ducdenum	
			Jejunum	]
-			lleum	_].
Baid patch on nose.			Caecum	
			Rectum	
			Aes. Lymph N.	_
			Adrenals	~
			Bronchial L/N	_
			Uterus/P.Tule	<b>1</b>
			festes	Ļ
			Prostate	
			Pituitary	_
			Bladder	
			Skin	_]
			Mammary GI.	
			Brain	,]_
			sotnal Cord	
			Bone/Sternum	
			Nasal Cavity	
			Sciatic Nerve	
	<b></b>			

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	Number of Sections Examined		Liver				Muscle	רי קינו.	S/M Lymph N.	Pancreas		Paratheroide	_	Cal L/N		Duodenum	Jejunum	lleum		Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterna/ Primau	Testes	Prostate	Pituitary	Bladder	Skin	Hammary GI.	Eyes		Bone/Sternum [	Nasal Cavity	Sciatic Nerve	
				ular - mild.	atronh (ad tuhulos																															
Death	ТК	Histopathology		Toxic change, mainly centrilobular	staine mainly atr	ital necrosis.																														
Time on Study (weeks)	14			Toxic change,	One testis cor	Some interstitial necrosis.																														
mg HMX/kg/day		Sample		Liver	Tectes																															
Project No: 415669CR Group: 5 1350 mg HI	Nnimal No: <sup>693</sup> Sex: C	Clinical History		NAD.												Necropsy Findings		Left testis smaller than right.																		

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	ine	-	-		<u> </u>	-  -	12	1-1	-	-1	-1	-1	1	<u>d -</u>	1 9	<u>d -</u>	4-	٦	0	-1	-1	-1	<u>-</u> !	<u> </u>	<u>ملت</u> ز		<u>1~</u>	-	_	-1			~!-	<u>- 1</u>	<u>~ </u>		<u>ب</u> ل	<u>.</u>	1
	Number of Sections Examined		Pat	kidney	Lung	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Desthursday	Paratnyrolds	Committee 1 - Ve	stomach	Duodenum	Jejunum	lleum	Caecum	Colon	Kectum	Mes. Lymph N.	Adrenals	Bronchial L/N	And the second	festes	Prostate	Pituitary	Bladder	skin	Mammary Gl.	Eyes		Spinal Cord	Bone/Sternum Nasal Cavity	Sciatic Nerve		_
		1			obular.																																		
Death	ΤK		Histopathology		Toxic change, mainly centrilobular.	ial gland.	•																																
Time on Study (Weeks)	14				Toxic change,	Cystic preputial gland.			_																							_							
ng HMX/kg/day			Sample	-	LIVEL	Skin																																	
Project No: 415669CR Group: 5 1350 mg HM	Animal No: 694 Sex: C		Clinical History		. DAN												Necropsy Findings		NAD.																				

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	lined	Ŧ		· [-	۲ŀ	<u>.</u>  -	-	-		-	[-]	2	<b>-</b>	4-	1-	Ц	4	-1-	1-	<u>.</u>	<u>-</u>	_	~	<u>+!</u> ~ 8		<u>l-</u>	-1	_1-		<u>'</u>	<u>!</u>	Eł			
	Sections Examined		Fat Liver	Kidney	Lung	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N. Pancreas	Trachea	Thyroids	Parathyroids	Cervical L/N	Stomach	Ducdenum	Je)unum	[] eum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N		festes	Prostate	Pituitary	Bladder	Mammary GL.	Eyes	Brain	Spinal Cord	Nasal Cavity	Sciatic Nerve	
Time on Study Death	14 TK		Histopathology	reludolistado ulaire obredo cisce	TOALC CHANGE, MALINE CONCLUSION TO TACTURE																														
HMX/kg/day	1		Sample		19/17																														
Project No: 415669CR Group: 5 1350 mg HM	Sex: 0		Clinical History		NAU.											Necropsy Findings			MAU.																

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	Number of Sections Examined		Pat	Kidney	Lung	Solaen	Thymas	Muscle	Salivary Gl.	S/M Lymph N.	rancreas	Trachea	Parathurolde	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	[]eum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Brends/P. Puber		DESTES	Pitultary	Bladder	skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum		SCIALIC NELVE	
			бо		lobular.																																	
Death	тĸ		Histopathology		Toxic change, mainly centrilobular.																																	
Time on Study (Weeks)	14			-	Toxic change,																																	
mg HMX/kg/day			Sample	-	LIVEL													_																				
Project No: 415669CR Group: 5 1350 mg H	Animal No: 696 Sex: đ		Clinical History		NAU.												Necropsy Findings		NAD.																			

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	Number of	Dections Examined		Fat Liver	 		Heart	Spleen	Thymus	Muscle	Salivary Cl.	S/M Lymph N.			Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum J	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	P Tulot	Testes	e	Pituitary	Bladder [	Skin	Mammary GI.	Eyes	Spinal Cord	Bone/Sternum	Nasal Cavity	SCIALIC NELVE	
Death	ТК			Histopathology		, mainly centrilobular.		r atropny and tubular epithetiai																															
Time on Study	14					Toxic change,		Focus tubular	regeneration.																														
HMX/kg/day				Sample		Liver		Kidneys																											 				
Project No: 415669CR Group: 5 1350 mg HM	647 Sex: 0			Clinical History															Necropsy Findings																				
roject l	ADIMAL NO:					NAD.															NAD.																		

Death

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Number of Sections Examined		Pat	Kidney	fund	Heart	uaarde	Muscle	Salivary GL.	S/M Lymph N.	Pancreas	Trachea	Parathyroids	Aorta	Cervical L/N	Diodenie	Jejunum	Ileun	Caecum	Rectum	Mes. Lymph N.	Adrenals Bronchial I /N	Uternar F. Tuben	Marine -	festes	Prostate	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Hasal Caviry	Sciatic Nerve		
14 TK		Histopathology	Movic change mainly centrilchular	The change matrix centritionial.	Congested.																														
		Sample	L tuer			Lymph Nodes																													
Animal No: 698 Sex: 0		Clinical History	QAZ												Necropsy Findings		Left bronchial lymph nodes enlarged.																		

Project No: 415669CR Group: 5 1350 mg HMX/kg/day Animal No: 699 Sex: đ

Death

Time on Study (Weeks) 14

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Number of Sections Examined ¥ Trachea Thyroids Parathyroids Aorta Cervical L/N Stomach Duodenum Jejunum Jejunum Caecum Colon Rectum Salivary Gl. S/M Lymph N. Pancreas Mes. Lymph N. Adrenals Bronchial L/N <del>Merus/F.Tulm</del> Testes Prostate Pituitary Hladder Skin Mammary Gl. Eyes Spleen Thymus Muscle THE PARA Fat Liver Kidney Lung Heart Toxic change, mainly centrilobular. Histopathology Sample Liver Necropsy Findings **Clinical History** NAD. NAD.

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Spinal Cord Bone/Sternum Nasal Cavity Sciatic Nerve

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	Number of Sections Examined		Fat Liver	Kidney Lung	Heart	anet u	Muscle Salivary Gl.	S/M Lymph N. Pancreas	Trachea	Thyroids	Parathyroids Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Caecum	Colon	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/ Prubod	Testes	Prostate	Pituitary	Bladder	SKIN Mammarv Gl.	Evea	Brain	Spinal Cord	Bone/Sternum Nasal Cavity	Sciatic Nerve	
Death	ΤK		Histopathology	Toxic change, mainly centrilobular.	Many macrophages containing brown staining																											
Time on Study (weeks)	14			Toxic change,	Many macropha	material.	_																						<u> </u>			
mo HMX/kg/dav			Sample	Liver	Bronchial	Lymph Nodes																										
Provert No: 415669CB Group : 5 1350 mg H	Sex: O		Clinical History	NAD.										Necropsy Findings		Bronchial lymph nodes slightly enlarged.																

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	Number of Sections Examined		Fat	Liver Kidney	lieart	Spleen	Thymus Muscle	Salivary Gl.	S/M Lymph N. Pancreas	Trachea	Thyroids Parathyroids	Aorta	Cervical L/N	Stomach Ducdenum	Jejunum	Ileum	Caecua	Recture	Mes. Lymph N.	Adrenals	Bronchial L/N	Uteras/P. Pubes	Tactac	Prostate	Pituitary	Bladder	SKIN Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Sciatic Nerve	
		-	Y	trilobular.																													
Death	TK		Histopathology	Areas toxic change, mainly centrilohular.		ion.																											
Time on Study (Weeks)	14			Areas toxic ch		Slight congestion.																											
mg HMX/kg/day			Sample	Liver		Lungs																											
Project No: 415669CR Group: 6 4000 mg H	Animal No: 701 Sex: of		Clinical History	NAD.										Necropsy Findings		[unds redder than normal	minds reader citati normat.																

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	Ined	Ë			~ <del> </del>	-		-1-		-1	4.	44	-	<u>-</u> 1:	-	4-		<u>-</u>  ·	-1-	<u>-</u> ك	<u>.</u> ∙I∼:	_		<u>1</u> ~	-1-		1-1	0	<u>~</u>	<u>~  -</u>	-1-	þ	<u>i-</u>	
	Number of Sections Examined		Pat Liver	Kidney	Lung Heart	Spleen	Thymus	salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Parathyroids	Aorta	Cervical L/N	Ducdenie	Je junum	lleum	Caecum	Colon	Mes. Lumph N.	Adrenals	Bronchial L/N		Testes	Prostate	Bladder	skin	Mammary Gl.	Eyes	Brain Ceisal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
	•••																																	
Death	TK		Histopathology	reludotivatoro ulaira operato otvot occur reludotivatoro	ange, matury o																													
Time on Study (Weeks)	14				Areas LOXIC CII		NAD.																											
HMX/kg/day			Sample	1011	плег		Eves																									_		
Project No: 415669CR Group: 6 4000 mg HM			Clinical History		Red stains round right eye, black encrustations round nose from week	13-14.										Necropsy Findings		Red staining round right eye. Black	CILLERCELION LOUND NOSC.															

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	Number of	Sections Examined		Fat		Lung	Heart	Spleen	Thymus	Muscle	Salivary GL.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Corridor 1 1 1	Stomach	Duodenum	Jejunum	lleum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	and a second	Testes	Prostate	Pltultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	NASAL CAVILY	SCIALIC NELVE	
				۸۲ ۸۲		bular areas.																																			
Death	ΞK	4		Histopathology		Toxic change, mainly centrilobular areas.																																			
Time on Study (Weeks)	14	F 1				Toxic change,																																			
MX/kg/day				Sample		Liver																																		-	
: 415669CR Group:	No: 703 Sex: d			Clinical History															Necropsy Findings																						
roject	Animal No:					NAD.															NAD.																				

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	Number of Sections Examined		Fat Liver	Kidney Lung	Heart Spleen	Thymus Muscle	S/M Lympn N. Pancreas	Trachea	Parathyroids	Aorta	Cervical L/N	Duodenum	Jejunum	Leum	Colon	Rectum	Mes. Lymph N. Adrenals	Bronchial L/N	Uterus/Pr@ubus		Destes	Pituitary	Bladder	Skin	Mammary GL.	Eyes Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
			Y	ntrilobular.	ular epithelial																										
Death	ΤK		Histopathology	Areas toxic change, mainly centrilobular.	Focus tubular atrophy and tubular epithelial																										
Time on Study (weeka)	14			Areas toxic c	Focus tubular	regeneration.																									
ma HMX/kg/dav	<u>·</u>		Sample	Liver	Kidneys																				_						
Privat No. 41566000 Group: 6 4000 mg HM	Sex: đ		Clinical History	NAD.								Macronev Findinge	churphir i ledotnau		- ACN																

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	Number of Sections Examined	Pat Liver	Kidney	Heart	Spleen	Thymus Muscle	Salivary Gl.	S/M Lymph N. Pancreas	Trachea	Thyroids	Parathyroids	Cervical L/N	Stomach	Duodenum	Jejunum	Caecum	Colon	Rectum	Mes. Lymph N.	Morenais Bronchial L/N	Uterna/F. Pubeo		Testes	Pituitary	Bladder	Skin	Manmary GI.	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Scintic Nerve	 
		X	lar and peri-																														
Death	TK	Histopathology	Areas toxic change, centrilobular and																														
Time on Study (weeks)	14		Areas toxic ch	portal.													-		Ţ									<u> </u>					
q∕dav		Sample	Liver																		***										-		
Project No: 415669CR Group: 6 4000 mg/kg/dav	705 Sex: 0	Clinical History	NAD.											Necropsy Findings		NAD.																	

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Den 볓 Number of Sections Exami Bronchial L/N Uteras/P.Pubas Brain Spinal Cord Bone/Sternum Nasal Cavity Sciatic Nerve Trachea Thyroids Parathyroids Aorta Aorta Cervical L/N Cervical L/N Duodenum Jejunum Salivary Gl. S/M Lymph N. Pancreas Mes. Lymph N. Prostate Pituitary Bladder Skin Mammary Gl. Eyes Adrenals Spleen Thymus Muscle I leum Caecum Colon Rectum Kidney Pat Liver 'estes Heart bung Histopathology Death ТĶ Areas toxic change. Time on Study (weeks) 14 Sample Liver 4000 mg HMX/kg/day 9 ъ Necropsy Findings Group: **Clinical** History Sex: Project No: 415669CR Animal No: 706 NAD. NAD.

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Number of Sections Examined	T			<u> </u>	Muscle	<u> </u>	S/M Lymph N.	Trachea		sbids	Cervical L/N	Stomach	Duodenum	[ ] leun	Caecum	Colon	Mos Iverh v	-	T/N	and a state		restes	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain []	Spinal Cord 2	Nasal Cavity	Sciatic Nerve 2	<u></u>
	A KE	toxic change, centrilobular and peri-																														
Death TK	Histopathology	ange, centrilob																														
Time on Study (weeks) 14		Areas toxic ch	portal.																													
HMX/kg	Sample	Liver																														
Project No: 415669CR Group: 6 4000 mg H Animal No: 707 Sex: 0	Clinical History											Necropsv Findings																				

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	Number of Sections Examined		Pat	Kidney	Heart	Spleen	Thymus	Muscle	Salivary GL.	Pancreas	Trachea	Thyroids	Parathyroids	Carvical 1/N	Stomach	Duodenum	Jejunum	[leum	Caecum	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/Fylubac	festes	Prostate	Pituitary	Skin	ry 61.	Eyes	Brain [	Spinal Cord	Bone/Sternum	MASAL CAVITY	SCIALIC NELVE 2	
			ЭУ																																	
Death	ΤK		Histopathology	ande																																
Time on Study (Veeks)	14			Areas toxic change																																
mg HMX/kg/day			Sample	Liver																																
: 415669CR Group: 6 4000	Animal No: 708 Sex: d		Clinical History	Lesion on bridge of nose from week 12-13.												Necropsy Findings		Bald patch on bridge of nose.																		

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		i ned	Ĕ		<u>-</u>	• <u>†</u> •	-	-	-	-1-	-1-	-1-	<u>-</u>	19			d.	4	-	<u>-</u>		1	-1	<u>- 1</u>	<u>~lo</u>	1	7	-	<u>-</u> ŀ	-1-	-	0	<u>~!-</u>	Ŀ		9	-1	
	Number of	Sections Examined		Pat	Kidnev	Lung	Heart	Spleen	Thymus		Salivary GL	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Jetunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Bronchial L/N	Uterna/B. Bub		Testes	Prostate Dituitati	Bladder	skin	Mammary Gl.	Eyes Brain		Bone/Sternum	Nasal Cavity	Sciatic Nerve	
	<b>T</b>			Уę		ular and peri-																																
Death		тк		Histopathology		Areas toxic change, centrilobular and peri-																																
Time on Study (Weeks)		14				Areas toxic ch	portal.								-																							
HMX/kg/day				Sample		Liver																																
Project No: 415669CR Group: 6 4000 mg H	100 E	Sex:		Clinical History		NAD.												Necrobsy Findings			. MAU.																	

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	Number of Sections Examined		-Fat Ituer	<u> </u>	<u> </u>	Spleen	Muscle	Salivary Gl.	S/M Lymph N. Pancreas	Trachea	Parathyroids	Aorta	Cervical L/N	Stomach	Jejunum	Ileum	Caecum	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N		Testes	Prostate	Pituitary	Bladder	Mammary G1.		Brain	Spinal Cord	Bone/Sternum Nasal Cavity	Sclatic Nerve		LL
Death	ТК		Histopathology	Areas toxic change, mainly centrilobular.										_																				
Time on Study (weeks)	14		-	Areas toxic chang																													<u>.</u>	
HMX/kg/dav			Sample	Liver																			<u> </u>											
Proiect No: 415,669CB Group: 6 400 mg HMX	Sex: đ		Clinical History	encrustations round nose	12-13. Red stains round right eye in	• • • •									Necropsy Findings		NAD.																	

DODA BELEVER, WAARAN SARASA

Group: 6 4000 mg HA Sex: đ	HMX/kg/day	Time on Study (Weeks) 14	Death		Number of
		4	TK		Sections Examined
	Sample		Histopathology		Fat
	Liver	Toxic change, n Periportal.	Toxic change, mainly centrilobular but Periportal.	it some	Liver Kidney Lung Heart
					Spleen Thymus Muscle Salivary Gl.
		- <u>-</u>			S/M Lymph N. Pancreas Trachea Thyroids
					Parathyroids Aorta Cervical L/N Stomach Duodenum
					Jejunum Tleum Caecum Colon
					Rectum Mes. Lymph N. Adrenals Bronchial L/N U <del>trins/F.Tube</del> o
					Prostes Frostate Pituitary Bladder Skin Ammary Gl.
		<del> </del>			Eyes Brain Spinal Cord Bone/Sternum Masal Cavity Sciatic Nerve Sciatic Nerve

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	Number of Sections Examined		Pat	Kidney	Lung Heart	Spleen	Chymus an	Muscle Salivarv Gl.	S/M Lymph N.	Pancreas	Trachea	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	leuma Ileuma	Caecum	Colon	Rectum	Mes. Lymph N.	HADRENGIS	Herns/Premoto	Wat we	festes	Prostat <del>a</del> Pituitarv	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord Bona/Starnum	Nasal Cavity	Sciatic Nerve	
Death	TK		Histopathology		Toxic change, centrilobular and periportal.																														
Time on Study (weeks)	14				Toxic change,											_			_																
x/kg/day			Sample		Liver																								-						
Project No: 415669CR Group: 6 4000 mg HMX/kg/day	Sex: o		Clinical History		NAD.											Necropsy Findings		NAD.																	

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	Number of	Pections Examined	Fat	Li ver Kidnev	fund	Heart	Spleen	Thymus	Saltwarr ()	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids		Stomach	Duodenum	Jejunum	lleum	Color	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	UTER SASTE VERSES	Testes	Prostate	Pituitary	Bladder	 iry Gl.	Eyes	Brain	Spinal Cord	Nasal Cavity	Sclatic Nerve	
Death	TK		Histopathology		inge.																															
Time on Study	14			Areae touto cho	ALEAS LOXIC CHANGE.																															
mg HMX/kg/day			Sample	Liver																																
: 415669CR Group: 6 4000	Animal No: 713 Sex: of		Clinical History	NAD.													Necropsy Finalngs		NAD.																	

io: 415669CR Group: 714 5552 - 관	Project No:
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	Number of Sections Examined		Pat	 >	Lung Heart	Spleen	1	مايد ب	Salivary Gl.	Pancreas	Trachea	Thyroids	Parathyroids    Aorta	cal L/N	Stomach	Duodenum	Je)unum	Treum Taorim	Colon	Rectum	Mes. Lymph N.	Wonchield 1 / 1 / 1	- 1	Т	Testes	Pituitarv	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum [] Nacal Cauteu []	Sciatic Nario	
			>	and periportal.																															
Death	ТК		Histopathology	centrilobular and																															
Time on Study (weeks)	14			Toxic change,																															
mg HMX/kg/day			Sample	Liver																								-							
Project No: 415669CR Group: 6 4000 mg HM	Animal No: 714 Sex: of		Clinical History	NAD.												Necropsy Findings		NAD.																	

715     Sax:     0     14     π       Clintcal History     Sample     Histopathology     Para       Invertiging     Sample     Foxic change, centrilobular and periportal.     Para       Necropsy Findings     Para     Para     Para       Necropsy Findings     Para     Para     Para       Para     Para     Para     Para       Para <th>,</th> <th>Inn / Av / VIII</th> <th>(Weeka)</th> <th></th> <th></th> <th></th> <th></th>	,	Inn / Av / VIII	(Weeka)				
Sample     Mistopathology     Pt.       Liver     Toxic change, centrilobular and periportal.     Reart Stand       Provens     National Stand     Pteriportal.       Provens     Pteriportal.     Pteriportal.       Pteriportal.     Pteriportal.     Pteriporteriportal.       Pteriportal.	Animal No: 715 Sex: d		14	ТК		Number of Sections Exami	Led T
Liver Toxic change, centrilobular and periportal. Liver Cump to the second sec	Clinical History	Sample		Histopathology		Fat	뵈~
And the second and periperation of the second and periperation		1 tuer		a bue veludalitation		Liver Kidney	
Spient Strang discrete Strang		TAATT	I TOXIC CHANGE, C	d nue rennontititue:	her thorral.	Lung	FF
Mayea Mayaa Mayaa						Spleen	-
Sallvary Gl. Sallvary Gl. Sallvary Gl. Sallvary Gl. Phyroids Pryroids Perting Science Discrete Protein Science Color Rectum Rect						Thymus	-
Standard Contractions Standard N. Penetress Protecte						Muscle	
Pancreas Treches Treches Treches Parethyroid						Salivary GL.	
Traches Traches Traches Traches Traches Provide Norta Constraint Constraint Constraint Provide Namery GL Provide Provi						Pancreas	-1-
Thread the temperature of tempe						Trachea	-   -
Parachyroida Parachyroida Aercta Aercta Aerca Stomach Jejuuum Jejuuum Iteum Colon Rectum Rectum Rectum Rectum Retenals Arrenals A						Thyroids	1~
Acrea Ac			_			Parathyroids	4
Cervical L/N Cervical L/N Ducdenum Lejunum Caecum Res. Lymph N. Adrenals Internolal L/N Resters Prostate Pituitary Riader Skin Spinal Cord Spinal Cord Spinal Cord						Aorta	-
Protection Percent						Cervical L/N	_
Duckenum Duckenum Jeyunum Iteun Rectum Rectum Rectum Merensfirmtune Iteuttary Iteuttary Rith Return Brain Spinal Cord Bone/Sternum None/Sternum			_			Stomach	4
Andread and a straight N. Andread and A. Andread andre	Necropsy Findings					Duodenum	4
Arthur 113 113 114 114 114 114 114 114 114 114						Jejunum Tiour	4.
ymph N. 11s 11s 11al L/N 7. 7. 7. 7. 61. 7. 61. 7. 61. 7. 61. 7. 61. 7. 61. 7. 61. 7. 61. 7. 61. 7. 7. 61. 7. 7. 61. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7.						Caecum	
ymph N. Jas L/N Affal L/N						Colon	<u> </u> _
ymph N. His L/N Hial L/N HF. Futures ite ary r r y Gl. Cord Cord Cord Cord						Rectum	-
is ital L/N MFr.Pulson is is is is is is is is is is is is is						Mes. Lymph N.	0
vie Tulues vie tulues ite ite ite vy Gl. y Gl. cord fernum cavity c Nerve						Adrenals	2
AF Tutes it it it it it it cord for cord cord for cord cord for for for for for for for for for for						Bronchial L/N	_
ary ite ary r y Gl. Cord iternum cavity c Nerve						(Herus/P. Tubos	4
tte ary r y Gl. Cord ternum cavity c Nerve							4
ite ary r r r cord cavity c Nerve						Testes	~
ary r y Gl. Cord ternum Cavity c Nerve						Prostate	<u> </u> _
y Gl. Cord Cavity Cavity C Nerve						Pitultary	-
y Gl. Cord iternum Cavity c Nerve						Bladder	
y Gl. Cord iternum Cavity c Nerve						Skin	_
Cord iternum Cavity c Nerve						Mammary Gl.	_
Cord iternum Cavity C Nerve						Eyes	~
						Brain	_
						Spinal Cord	~
						Bone/Sternum	<u>_</u>
Sciatic Nerve						Nasal Cavity	0
						Sciatic Nerve	F
							L

Histopatho		Sample		<b>Clinical History</b>	Clinica	
τĸ	14			Sex: đ	716	Animal No: 716
Death	Time on Study (Weeks)	4000 mg HMX/kg/đay	4000 mg F	Group: 6	415669CR	Project No: 415669CR

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Number of Sections Examined			Liver	Luna	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/P.T.Moo		Testes	Prostate	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
	]			some peri-														-																								
TK		Histopathology		change, mainly centrilobular but																																						
14				Toxic change,	portai.																																					
		Sample		Liver																																	-					
Animal No: 716 Sex: O		Clinical History		NAD.														Necropsy Findings		U KI																						

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	Number of	Sections Examined		Fat Liver	Kidney	Heart	Spleen	Thymus	Salivary Gl.	S/M Lymph N.	Traches	Thyroids	Parathyroids	Cervical L/N	Stomach	Duodenum	Jejunum	Caecum	Colon	Rectum	Mes. Lymph N. Adrenals	Bronchial L/N	Uterus/F. Pube	marius	Testes	Pituitary	Bladder	Skin	Puese	Brain	Spinal Cord	Bone/Sternum	Sciatic Nerve		
				Y	oular, but some																														
Death	TK			Histepathology	Toxic change, mainly centrilobular, but	·																													
Time on Study (weeks)	14				Toxic change,	periportal.																													
HMX/kg/dav				Sample	Liver																												-		
Project No: 415669CR Group: 6 4000 mg H	Sex: 0			Clinical History	NAD						-					Necropsy Findings		NAD.																	

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Project No:	415669CR	Group: 6	4000 mg	нмх/кө
Animal No:	718	Sex: 0		

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	Number of Sections Examined		Pat	Kidney			Thymus	Salivary Gl.	S/M Lymph N. Pancress	Trachea	Thyroids	Parathyroids	Cervical L/N	Stomach	Duodenum	Ileum	Caecula	Colon Rectin	Mes. Lymph N.	Adrenals	Bronchial L/N		Testes	Prostate	Picuteary	Skin	Mammary Gl.	Eyes	Sainal Cord	Bone/Sternum	Nasal Cavity	Scintic Nerve	
			٨	d periportal.	•																												
Death	TK		Histopathology	Toxic change, centrilobular and periportal.																													
Time on Study (weeks)	14			Toxic change, (		-																											
HMX/kg/day			Sample	Liver																													
Project No: 415669CR Group: 6 4000 mg HM	<b>f</b> 0		Clinical History	NAD.											Necropsy Findings		NAU.																

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	Number of	Sections Examined		Fat		kidney	fund	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Paratuyrolds	Morta Carvical 1/N	Ctomode 4/1	Ducdenim	Tetunum		Carcum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterno/F.Tubec		restes	Prostate	Pituitary	Bladder	Skin	Nammary GL.	eyes eret	orain	Spinal Cord	Bone/Sternum	Nasal Cavity	Scintic Nerve		
						ular, with foci																																						
Death	ŢΚ	41		Histopathology		mainly centrilob	periportal.																																					
Time on Study	14	14				Texte change,	periportal.																																				 	
MX/ku/dav				Sample		1.iver																																						
Project No: 415669CR Group: 6 4000 mg HMX/ku/day				Clinical History			• • • • • • • • • • • • • • • • • • • •														Necropsy Finaings		NAD.																					

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Death	TK	
Time on Study (Weeks)	14	
<b>Group</b> : 6 4000 mg HMX/kg/day	Sex: ð	
Project No: 415669CR	Animal No: 720	

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Number of Sections Examined		Fat Liver	Kidney Lung Heart	Spleen Thymus	Muscle	Salivary Gl. S/M Lymph N.	Pancreas	Trachea	Parathyroids	Aorta	Stomach	Duodenum	Jejunum	Caecum	Colon	Rectum Mag	Mes. Lymph N.   Adrenals	Bronchial L/N	Uterns/P.Subes	restes	Prostate	Pitultary	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Nasal Cavity R	Sciatic Nerve	
		γ	Toxic change, mainly centrilobular but some foci periportal.																											
TK		histopathology	nainly centrilob																											
14			Toxic change, n periportal.																											
	Cample		Liver																											
Animal No: 720 Sex: 0	Clinical History	- 1									Vortige: Cipelo	Nectobsy Findings	NAD.																	
Anim			z							_			N,																	 

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	Number of Sections Examined	Fat	Liver Kidnev	Lung	Heart Spleen	Thymus	Muscle Salivary Gi	S/M Lymph N.	Pancreas	Trachea Thuroida	Parathyroids	Aorta	Cervical L/N	Duodenum	Jejunum	Ileun	Colon	Rectum	Mes. Lymph N.	Adrenals Bronchial L/N	Uterus/F.Tubes	Ovaries		Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
Death	FD	Histopathology																														<u></u>	
Time, Glekstudy	£1		Controcted	rongested.	NAD.	NAD.																											
		Sample	Tunde	spinu	Trachea	Uterus																	-										
Project No: 415669CR Group: 1 Control	Animal No: 721 Sex: 9	Clinical History	Died at blood sameling	DIEN at DIOOD Sampling.										Necropsy Findings		Red staining round right eye.	lungs dark red.		Traches - frothy exudate.	Uterus dilated.													

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	Number of	Sections Examined		Fat	Liver	Lung	Heart	Spleen	Thymus	Salfware Cl	S/M Lymph N.	Pancreas	Trachea	Thyroids	Paratnyroids Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	I leum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F. Tubes	Toot of	Pretito	Pitultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	NASAL CAVITY	Sciatic Nerve
				y								-	-																									
Death	ΤK	۷T		Histopathology																																		
Time, Que Study	14					NAD.																																
				Sample																																		
l Control	•								-																													
Group:	Sex:			<b>Clinical History</b>													Etadiana	Nectobsy Findings	l																			
: 415669CR	722			Clinic													Norton	Nectob																				
roject No:	nimal No:					NAU-														NAD.																		

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			뵈	-	ŀ	<u>r</u>	2	F			-1		-1	-1	-1	2	<u>-</u> L:	<u>-</u>	-1-	<u>.</u>	<u>-</u> 1-	1:	1-	<u>.</u>	<u>1-</u>	4-	<u> -</u>		_	~	4-	1-	<u>. -</u>	1-	<u>.</u>	<u> </u> ~	-	ſ	1-			1	
	Sections Fund			Fat	Liver	Kidney	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyrolds	Parathyroids	AOFTA	Cervical L/N	Stomach	Duodenum	unum an		Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	Tuetes	Dituitary	Bladdor	Skin	Mammarv Gl.	Eves	Brain	Cainel Cond	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
Time, Bb kStudy Death	14 TK			Histopathology		NAD.																																					
				Sample																																							
Project No: 415669CR Group: 1 Control	Animal No: 723 Sex: Y			Clinical History		Encrustations round eyes from week 10-11.														Necrosty Findings	sourpur J Asda Law																						

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	Section Fundad	SECTION EXAMIN		4			Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Parathurofde		Cervical L/N	Stomach	Duodenum	Jejunuma	Ileum	Calecum	Colon	Rectum	Mes. Lymph N.	Aurendis	Bronchial L/N	samu . J/snaph	UVALIES Toatoc	Pituitary	Bladder	Diaunet		2	Eyes	 Spinal Cord	Bone/Sternum	NASAL CAVICY	Sciatic Nerve	
	-	-1		ъду																																			
Death	ТК			Histopathology	nt. NAD.																																		
Time, QD <sub>k</sub> Study	14				Unly one present.													=										-											
				Sample	Ovary																																		
Droject No: 41566905 Group : 1 Control	724			Clinical History	NAD.													Necronsy Findings		al the control locate that loft	RIGHT UVARY LARGEL UNAN TELL.																		

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	Number of	Sections Examined				 Kidney	1		Spleen	Thymus	Muscle	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum			Rectum	Mae (timbh N	Adrenals	Bronchial T/N	Uterus/F. Tubes	÷	T	T	Pituitary []	Bladder	Skin Skin	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity 7	Sciatic Nerve	
Death		TK			Histopathology																					-															
Time, Riekstudy		14			<u> </u>	NAD																																			
					Sample																												<u>.</u>								
Project No: 4156690R Group: 1 Control		A :xes cz/ :ON TENTUR			Clinical History	NAD.														Necropsy Findings		NAD.																			

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	Number of Sections Examined		Fat	Kidney	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S∕M Lymph N. Pancreas	Tractor	Thvroids	Parathyroids	Aorta	Cervical L/N	Ducdoour	Jetunun	Ileum	Calecum	Colon	Rectum	Mes. Lymph N. Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	90100	Dituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Colotio Neury	SCIALIC NELVE	
				infiltration.																																		
Death	ТК		Histopathology	Two foct periportal lymphocyte infiltration	on footduuf - Theorem																																	
Time, weekstudy	14			Two foci perip					_																													
			Sample	Liver																												_						
Project No: 415669CR Group: 1 Control	Animal No: 726 Sex: 9		Clinical History	Encrustations round right eve from	week 9-11.												Necropsy Findings		NAD.																			

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Project No: 415669CR Group: 1 Control Animal No: 727 Sex: Q

Time<sub>(w</sub>Pb<sub>k</sub>Study Death 14 TK

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Number of Sections Examined		Fat	Liver	Kidney	5und	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	<b>Parathyroids</b>	Aorta	Cervical L/N	Stomach	Duodenu	Jejunum	ITeum	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	DIUNCHIAL L/N	Ovaries	Tostac	Prestate	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
		Абс																										_													
TK		Histopathology																																							
14				NAD.	-																																				
		Sample		Lungs	1																																				
Animal No: 727 Sex: Q		Clinical History		NAD.														Necropsv Findings			wungs darker red than normal.																				

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	Number of	Sections Examined		Fat	Liver	Kidney	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	Testes	Prestate	Pitultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Scintic Nerve	
				λ																																							_	
Death		TK		Histopathology																																								
Time, QQAXStudy		14				NAD.																																						
				Sample		Lungs																																						
Project No: 415669CR Group: 1 Control	778			Clinical History		NAD.															Necropsy Findings		Lungs redder than normal.																					

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	Number of	Sections Examined		Fat		Kidney	Heart	Spleen		Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trache	Thyroids	Parathyrolds	Aorta	Cervical L/N	Stomach	Duodenum	l Jenne	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	Testec	Prostate	Pituitary	Bladder	Skin Keesen Ci	- TO A TOMMAN	Eyes		Spinal Cord	Hone/Sternum	Colatic Nervo	SCHOLDE NET VELVE	
Death		τĸ		Histopathology																																						
Time, gbkStudy		14				NAD.																																				
	1		J	Sample																																						
<b>Group</b> :   Control		Sex: Q		History												i				Findings															·							
41566900		729		Clinical History																Necropsy Findings																						
Protect No:	rujere m.	Animal No:				NAD.																NAN	• • • • •	-													-					<b></b> .

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	Number of	Sections Examined		Fat	Liver	Lund	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F. Tubes	Ovaries			Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
				~																																							
Death		ТК		Histopathology																																							
Time, QBekStudy		14																																							<u>.</u>		
				Sample																																							
roject No: 415669CR Group: 1 Control		UNIMAL NO: 730 SEX: Y		Clinical History	Dicht eve half closed and red rimmed	in week 13.														Necropsy Findings		NAD.																					

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	Number of Sections Examined			_	<u> </u>	Spleen	Thymus	- 5 2			Trachea U	abids	Aorta	L L/N	Stomach	Duodenum	Ileum	Cafecum	Colon	Rectula	Mes. Lymph N. 1	N/ 1			Tostoc	5	Bladder 1	Skin	Mammary Gl.	Eyes 2		Bone/Sternum 1	Nasal Cavity I	Sclatic Nerve 2	
Death	ТК		Histopathology																																
Time, QBekstudy	14			NAD.																													-		
			Sample																																
Project No: 415669CR Group : 1 Control	Animal No: 731 Sex: Q		Clinical History	NAD.												Necropsy ringings																			

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1 Control	0
Group:	Sex.
415669CR	117
Project No:	Animal No:

Death	TK
Time <sub>(w</sub> gb <sub>k</sub> Study	14

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	Number of Sections Examined		Fat	Jav 11	Kidney	bung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries			FILUTEARY	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
, ,	14 TK		Histopathology		NAD.																																							
			Sample																																									
115669CR	Animal No: 732 Sex: 9		Clinical History		NAD.															Necropsy Findings		NAD.																						

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	Number of Sections Examined		Fat	Kidney	Spleen	Thymus Muscle	Salivary Gl. IS/M Lymph N.	Pancreas	Trachea	Parathyroids	Aorta	Cervical L/N Stomach	Duodenum	Jejunum	Calecum	Colon	Rectum	Mes. Lymph N. Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries		Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brdin Frisi Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
			Ъ	lar epithelial																												
Death	TK		Histopathology	atrophy and tubular epithelial	a																											
Time, Qbkstudy	14			Focus tubular a regeneration.	Cystic follicle.			_																								
			Sample	Kidneys	Thyroid	1		-		-														_								
Project No: 415669CR Group: 1 Control	Animal No: 733 Sex: 9		Clinical History	NAD.									Necropsy Findings		NAD.																	

Project No: 415669CR Group : 1 Control	734
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Group :	1	Control	Time, Que Study	Death	
Sex:	•		14	ТК	_

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Number of	Sections Examined		Fat	- Liver	kidney			Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	CETVICAL L/N	Ducdenim	Jetunum	Ileum	Cafecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/r.Tubes	Uvaries		Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	MASAL LAVITY	Sciatic Nerve	-
ΨK			Histopathology																																						
14					NAD.																																				
			Sample																													_									•
			Clinical History																Necropsy Findings																						
Animal No:					NAD.														_		NAD.																				

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	Number of	Sections Examined		Fat	Liver	Kidney	Lung	Heart	Spleen	Thymus	Muscle	Salivary GL.	S/M LYEDD N.	Trachos	Thyroids	Parathyroids	Aorta	Cervical L/N	Duodenum	Jejunum	Ileun	Cafecum	Colon	Rectum	Mes. Lymph N.	Adrenats	Bronchial L/N Uterus/F.Tubes	Ovaries	Testec		Pituitary	Bladder	SKIN Mammarv Gl.	Eves	Brain		Bone/Sternum	Nasal Cavity	Sciatic Nerve	
				thology																																				
Death	E	TK		Histopathology																																				-
T1me, Qlekstudy	V	14				NAD.																																		-
				Sample																																				
Project No: 415669CR Group : 1 Control		Animal No: / JS Sex: Y		Clinical History		NAD.													Necropsy Findings		NAD.																			

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	1 Control	0•
ſ	Group:	Sex:
	415669CR	736
:	Project No: 415669CR	Animal No:

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Death

Time, QBkStudy

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Number of Sections Frankad			<b>_</b>	Kidney		Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas		-	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum U	Jejunum []	Ileum	Cafecum	Colon	Rectum 1	Mes. Lymph N.	Adrenals 2		r. Tubes				Picuicary L			Fires	Brain			Nasal Cavity h	Sciatic Nerve	
ТК		Histopathology																																				- <b>-</b>		
14				NAD.	NAD								-												-															
		Sample		Lungs	Ovaries																																			
Animal No: 736 Sex: 9		Clinical History		NAD.														Necropsy Findings		[ungs - grev batches on all lobes		Left ovary surrounded by bubble of clear	fluid																	

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	Number of	Sections Examined		rat	fund Lund	Heart	Spleen	Thymus	Muscle	Salivary GI. S/M Lvmph N.	Pancreas	Trachea	Thyrolds	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum		Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Orer ton	Totoc	Prostate	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Nasal Cavity	æ	
				У																																	
Death		ТК		Histopathology																																	
Time, Que Study		14			NAD.						-																										
				Sample	Ovaries			-																													
Project No: 415669CR Group: 1 Control	737 584.	Sex		Clinica' History	NAD.												Necropsy Findings		Left ovary larger than right.																		

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	Number of	Sections Examined		Fat Liver	Kidnev	Lund	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchlal L/N	Uterus/r.Tubes	Totto	Duration	Pituitarv	Rladder	Skin	Mammarv Gl.	Fves	Brain	Crinel Cord	Bone/Sternim	Nasal Cavity		SCIALIC NELVE	
				y		_																																					
Death		TK		Histopathology																																							
Time, Wek Study		14				NAD.																								-													
				Sample																								_															
Project No: 415669CR Group: 1 Control	738 Sex:			Clinical History		Black encrustations round eyes in week 13.														Necropsy Findings																							

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	Number of	Sections Examined		Fat	Liver	V door	Lund	Heart	Spleen	Thymus	Muscle	Salivary Gi.	S/M Lymph N.	Pancreas	Trachea	inyrotus Parathurnide	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum		Rectum	Mae Timph N	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	Tostos	Pirufearv	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
study Death	X	41		Histopathology																																						
Time, webkstudy	PI						NAD.				_												-															_				
				Sample																	-																					
Project No: 415669CR Group : 1 Control	719 544.			Clinical History			NAD.													Necropsy Findings		NAD.																				

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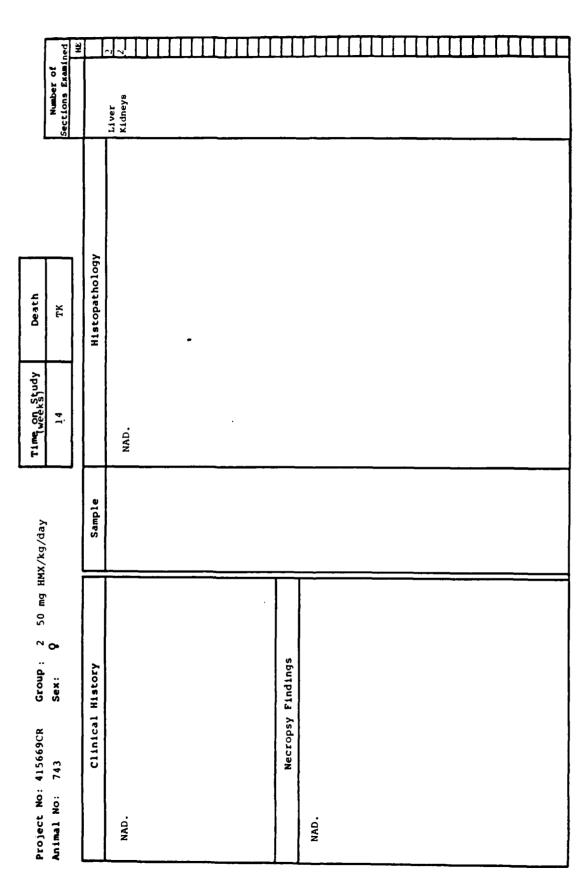
Death	ТК
Time, Qlk Study	14

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Number of Sections Examined		Fat	Liver	Kidney	toort	Coleon	spiteen	Thymus	Muscle		TO ATEATING		rancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	StomAch	Duodenum	Tetinin		Ileum	I leum Cafecum	Ileum Cafecum Colon	I leum Cafecum Colon Rectum	Jejuna Ileum Cafecum Colon Rectum Mes, Lymph N.	Lieum Cafecum Colon Rectum Mes. Lymph Adrenais	ure Junuar Calecum Colon Rectum Mes. Lymph N. Adrenals Bronchial L/N	lleum Cdecum Cdecum Colon Rectum Mes. Lymph N. Adrenals Bronchial L/N Uterus/F.Tubes	leum Cafecum Cafecum Rectum Mes. Lymph Adrenals Bronchal L Uterus/F.Tu	lejuum Cdecum Cdecum Colon Rectum Mes. Lymph Mareals Bronchial L Uterus/F.Tu Ovaries	Terum Cafecum Cafecum Rectum Mes. Lymph Adrenals Bronchial Uterus/F.Tu Ovaries	leum Cafecum Cafecum Rectum Mes. Lymph Mes. Lymph Mes. Lymph Bronchial L Uterus/F.Tu Vuterus Pressie Ptuitary	leum Cafecum Cafecum Colon Rectum Mes. Lymph Marenais Bronchial L Uterus/F.Tu Uterus/F.Tu Varies Presses Pltuitary Bladder	Terum Cafecum Cafecum Rectum Mes. Lymph Mes. Lymph Mes. Lymph Mes. Lymph Vertual Provide Provide Provide Provide Provide Provide Provide Stin Stin	Ileum Cdecum Cdecum Colon Rectum Mes. Lymph Mes. Lymph Mes. Lymph Mereals Partes Pituitary Pituitary Bladder Skin Skin Mammary Gi,	I contract Cafecum Cafecum Mest. Lymph Mest. Lymph Adrenals Adrenals Bronchial L Uterus/F.Tu Ovaries Prester Pleuitary Pleuitary Bladder Skin Skin Skin Skin Skin	Ileum Cafecum Cafecum Restum Mes. Lymph Adrenals Bronchial L Uterus/F.Tu Vuerus/F.Tu Vuerus/F.Tu Vuerus/F.Tu Bladder Skin Mammary GI. Eyes	Ileum Cafecum Cafecum Rectum Mes. Lymph Mes. Lymph Mes. Lymph Mes. Lymph Mes. Lymph Varies Prests Prests Plusitary Bladder Stain Brain Solnal Cord	Ileum Cdecum Cdecum Rectum Mes. Lymph Mes. Lymph Mes. Lymph Mernals, F.Tu Uterus/F.Tu Ovaries Pituitary Blader Skin Skin Brain Spinal Cord Spinal Cord	Julium Colon Colon Rectum Mes. Lymph N Mars. Lymph N Mars. Lymph N Horenais Bronchial L/ Uterus/F.Tub Ovaries Pituitary Bladder Skin Bladder Skin Brain Spinal Cord Bone/Sternum Nasal Cord
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Sex: Q		cal History																		Necropsy Findings																						
740		Clinical																		Necrop																						
Animal No:				NAD.																				NAD.	NAD.	NAD.	NAD.	NAD.	NAD.	NAD.	. GAN	. GAN	. UAD .	NAD.	GAN	GAN	GAN	NAD.	. GAN	. CAN	. CAN	GAN

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	Number of Sections Examined		Liver Kidneys													
Death	TK	Histopathology			•											
Time on Study	14		NAD.													
X/kg/dav		Sample														
Project No: 415669CR Group; 2 50 mg HMX/kg/dav	Sex: Q	Clinical History	NAD.				Necropsy Findings	NAD.								

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	Number of Sections Examined	_		Liver Kidneys													1	<b>-</b>							1	4 <b>4</b>	•	-			
Death	ТК		Histopathology					•																							
Time on Study	14			NAD.							•					-															
mq HMX/kg/đav	•		Sample																							 				_	
50	Sex: 9		Clinical History	Right eye red encrusted from week 10-	11.									Necronsy Findings	chutnut i Jedottaw	NAD.															



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	Number of Sections Examined			Liver Kidneys			
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			Histopathology				
Death	ТК		stopa				
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study							
Time on Study	14						
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day			Sample				
X/kg/					 	 	
mg HMX/kg/day							
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Group :	Sex:		Hist			Find	
9CR			<b>Clinical History</b>			Necropsy Findings	
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t No:	No:			•			
Project No: 415669CR	Animal No:			NAD.			NAD.

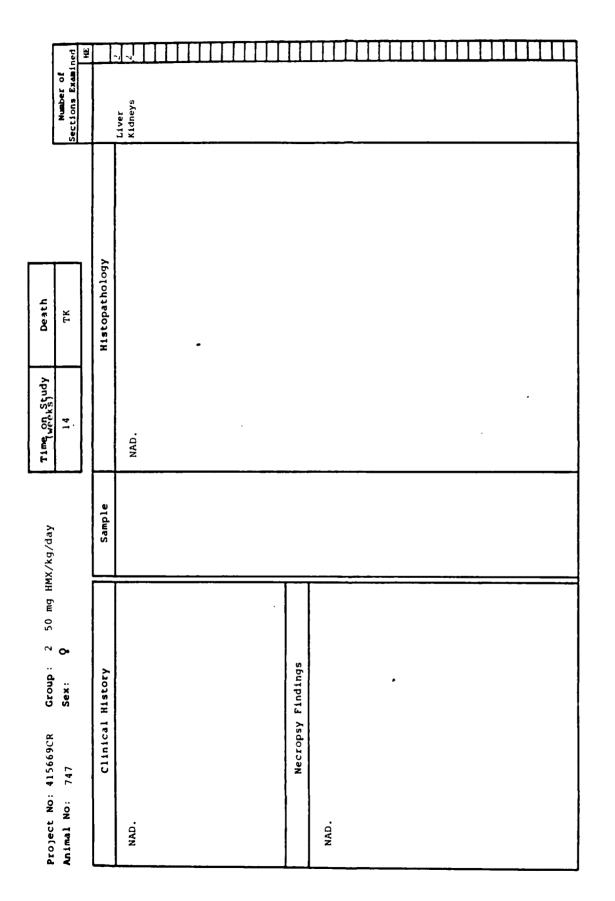
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	Number of Sections Examined			Liver Kidneys														
			Y															
Death	ТК		Histopathology															
Time on Study	1.4			NAD.														
x/kg/day			Sample															
Project No: 415669CR Group: 2 50 mg HMX/kg/day	Sex: 9		Clinical History	Right eye red encrusted in week ll.					Necropsy Findings	NAD.								

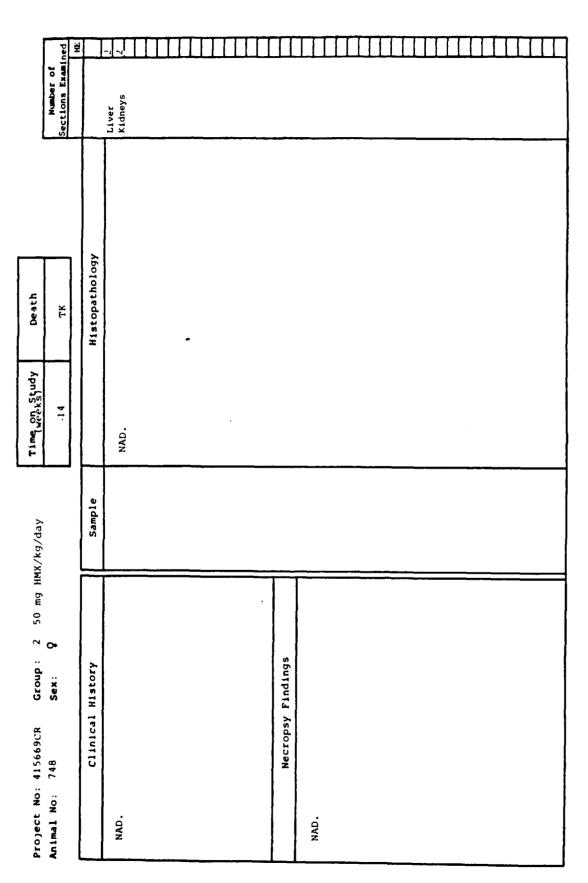
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	Number of Sections Examined		Kidneys
		~	
Death	ΤK	Histopathology	•
Time on Study	.14		NAD.
HMX/kg/day		Sample	
Project No: 415669CR Group: 2 50 mg HM	Sex: Q	Clinical History	NAD. NAD.

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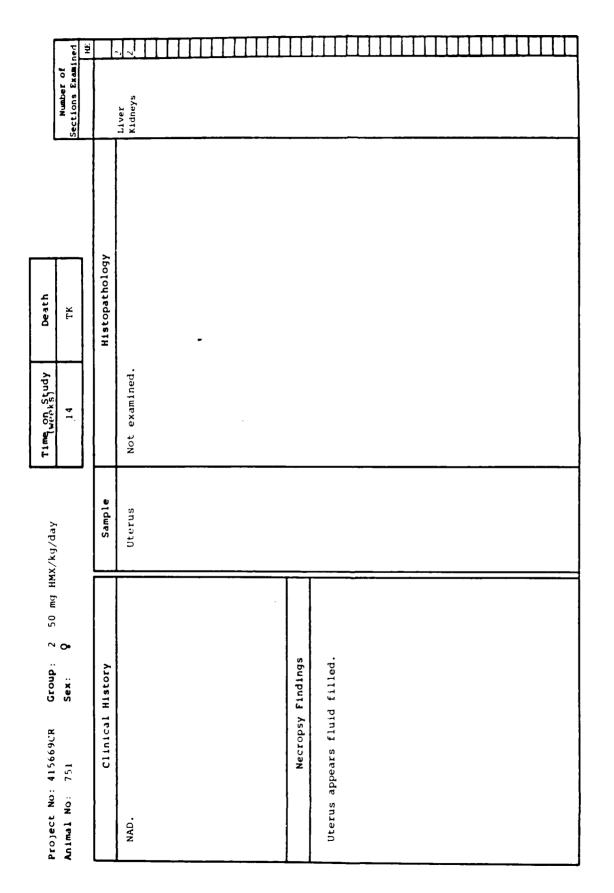
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	Number of	Sections Examined			Liver Kidneys														- 1						
Death		TK		Histopathology					-																
Time on Study		.14				NAU.							-												
50 mg HMX/kg/dav	Inn /fry /w			Sample																					
		Animal No: 749 Sex: Y		Clinical History		NAD.							Necropsy Findings		NAD.										

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Number of Sections Examined Æ Liver Kidneys Histopathology Death ΤK Time on Study .14 NAD. Sample Group: 2 50 mg HMX/kg/day Sex: 9 Black encrusted left eye from week 7-13. Necropsy Findings **Clinical History** Sex: **Project No: 415669CR** Animal No: 750 NAD.



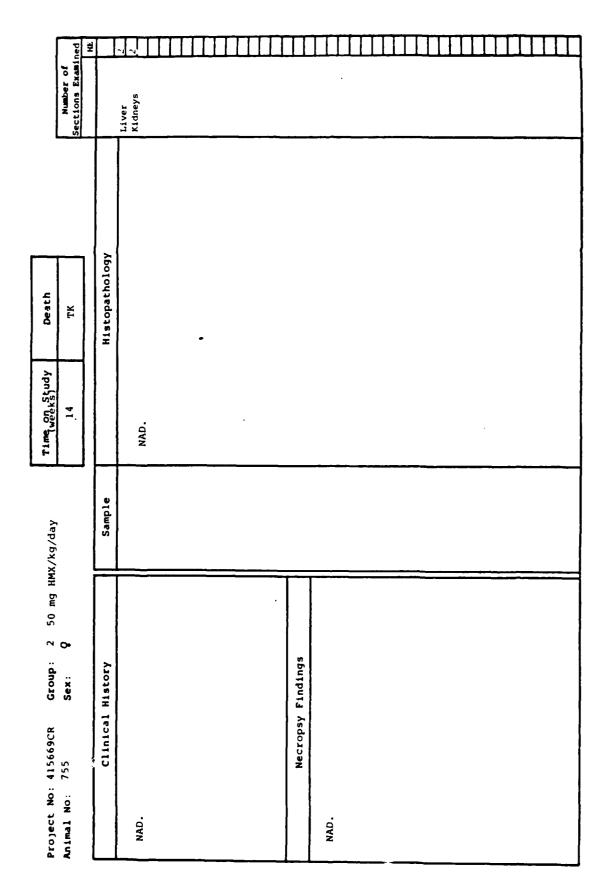
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	Number of Sections Examined			Liver Kidneys			 				 	 					
		-	y	Two well defined areas of large macrophages, polymorphs, lymphocytes and RBCs. Possible thrombus.													
Death	ТК		Histopathology	Two well defined areas of large macrophages polymorphs, lymphocytes and RBCs. Possible thrombus.		•											
Time on Study	14			Two well defin polymorphs, ly thrombus.													
mg HMX/kg/day		-	Sample	Liver										- <u>-</u>			
50	Sex: Q		Clinical History	NAD.					Necropsy Findings	C A Z							

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	Number of Sections Examined			Liver Kidneys								<u> </u>	 						
Death	TK		Histopathology				•												
Time on Study	, 14			Not examined.															
X/kg/dav	•		Sample	Ovaries															
Project No: 415669CR Group; 2 50 mg HMX/kg/dav	Sex: Q		Clinical History	Flaky skin on hind feet from week 12- 13.						Necropsy Findings	Left ovarian bursa dilated with clear	. Luid.							

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	Number of Sections Examined			Liver Kidneys	<u> </u>						<u> </u>	1															
			۷																								
Death	ТК		Histopathology					•																			
Time on Study	14			NAD.																							:
(/kg/day			Sample																						_		
Project No: 415669CR Group: 2 50 mg HMX/kg/day	Sex: 9		Clinical History	Dark encrusted right eve from week 9-12.									Necropsy Findings		NAD.												

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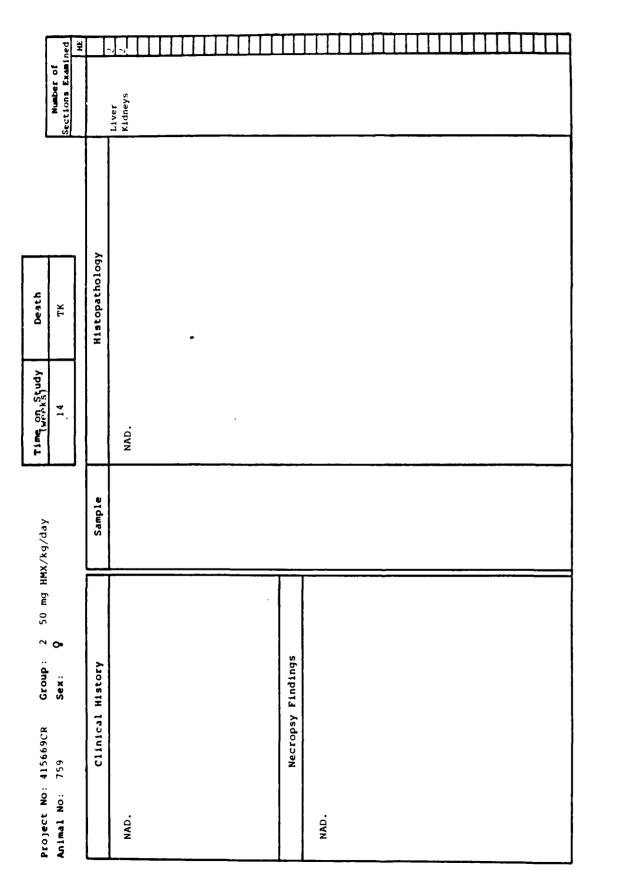
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	Number of Sections Examined	Ŧ		Liver <u>5</u> Kidneys 2					11	- <b>-</b>	<u> </u>	<u></u>	_ <b>1</b> _			<u> </u>							
-			Y																				
Death	ТК		Histopathology				•																
Time on Study	14			NAD.																			
X/kg/day			Sample																				
Project No: 415669CR Group: 2 50 mg HMX/kg/day	Sex: Q		Clinical History	NAD.							Necropsy Findings	NAD	• 700										

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	Number of Sections Examined			Liver Kidneys								 							
Death	TK		Histopathology																
Time on Study	1 d			NAD.															
mg HMX/kg/day		-	Sample																
50	Sex: 9		Clinical History	NAD.						Necropsy Findings	NAD.								

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	Number of Sections Examined	Ŧ		Liver 2		1.	_1.	1.1			<u> </u>	<b>I</b>	<u> </u>			1		<b>I</b>	<u> </u>	_ <b>_</b>						L	 - J -	<u> </u>
			Y																									
Death	TK		Histopathology					•																				
Time on Study	L4			NAD.																								
X/kg/day			Sample																									
Project No: 415669CR Group: 2 50 mg HMX/kg/day	Sex: Q		Clinical History	NAD.									Necropsy Findings		NAD.													



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	Number of Sections Examined			Kidneys
		2	λf	
Death	TK		Histopathology	-
Time on Study	۶ I.			Q
mq HMX/kq/day			Sample	
50	Sex: 9		Clinical History	NAD. NAD.

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Number of Sections Examined		s Alago and a state and a sta
ly Time on Study Death 14 TK	Sample H1stopathology	LAD.
ng HMX/kg/đay	Sa	
Project No: 415669CR Group: 3 115 mg Animal No: 761 Sex: Q	Clinical History	NAD. NAD.

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	Number of Sections Examined			Liver Klåneys										
			Y											
Death	ТK		Histopathology			-								
Time on Study	14			NAD.										
115 mg HMX/kg/day			Sample											
	Sex: 9		Clinical History	NAD.				Necropsy Findings	NAD.					

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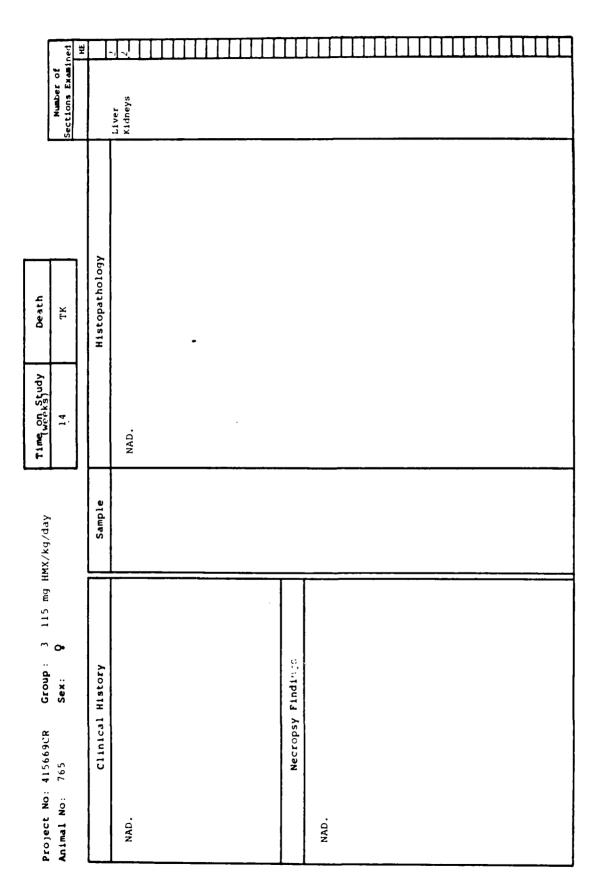
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	Number of Sections Examined			Liver Kidneys															
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Death	TK		Histopathology				-												
Time on Study	1.4			NAD.															
mg HMX/kg/day	•		Sample										_						-
115	Sex: 9		Clinical History	NAD.							Necropsy Findings	NAD.							



Number of Sections Examined ΗE Liver Kidneys Histopathology Death ΤK Time on Study .14 NAD. Sample Group: 3 115 mg HMX/kg/day Sex: 9 Necropsy Findings **Clinical History** Sex: Project No: 415669CR 766 Animal No: NAD. NAD.

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	Number of Sections Examined		Kidneys	
Death	тк	Histopathology		
		H1s	•	
Time on Study	.14		NAD.	
5 mg HMX/kg/day		Sample		
15 mg HM	I			
	•		s a	
Group :	Sex:	History	Finding	
415669CR	767	Clinical History	Necropsy Findings	
<b>Project No: 415669CR</b>	Animal No:		NAD.	

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	Number of Sections Examined		Liver Kidneys			
		hology				
Death	ΤK	Histopathology		•		
Time on Study	.14		NAD.			
5 mg HMX/kg/day		Sample			·	
11	Sex: Q	Clinical History	NAD.		Necropsy Findings	NAD.

	hed			П
	Number of Sections Examined		Kidneys	
<b></b>	T1	ду		
Death	тк	Histopathology	-	
Time on Study	14		NAD.	
ma HMX/kg/dav		Sample		
115	Sex: 9	Clinical History	NAD. NAD.	

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	Number of Sections Examined			Liver Kidneys					
			Y						
Death	TK		Histopathology		-				
Time on Study	14			NAD.					
5 mg HMX/kg/day			Sample						
11	Sex: Q		Clinical History	NAD.		Necropsy Findings	NAD.		

	ned	Э			Π	Π	Π	П		Π	$\prod$	$\prod$		Π	Π	Π	Π	Π	Π
	Number of Sections Examined			Liver Kidneys															
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Death	ТК		Histopathology				-												
Time on Study	1 đ			NAD.								_							
115 mg HMX/kg/day	•		Sample																
	Sex: Q		Clinical History	NAD.						Necropsy Findings	NAD.								

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	Number of Sections Examined		Liver Kidneys	 		
		1Y				
Death	ΤK	Histopathology				
Time on Study	14		Not examined.			
mg HMX/kg/day		Sample	Ovaries			
Project No: 415669CR Group: 3 115 mg HM)	Sex: 9	Clinical History	NAD.	Necropsy Findings	Right ovary surrounded by bubble of clear fluid.	

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	Number of Sections Examined		Liver Kidneys
[		λБо	
Death	TK	Histopathology	•
Time on Study	14		
mg HMX/kg/day		Sample	
115	Sex: Q	Clinical History	NAD. NAD.

Death ТK Time on study 14 115 mg HMX/kg/day ~ **o** Group : Sex: Project No: 415669CR 174

Number of Sections Examined ÷ Liver Kidneys Histopathology NAD. Sample Necropsy Findings Clinical History Animal No: NAD. NAD.

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	Number of Sections Examined			Liver Kidneys								
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£			Histopathology									
Death	ŢΚ		lstopa		_							
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Time on Study	14											
Time .	-			NAD.		·						
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/day			Sample									
5 mg HMX/kg/day					 			 	 			
15 mg												
	•	I										
Group :	Sex:		lstory				Necrossy Findings					
			Clinical History				Pace F					
<b>Project No: 415669CR</b>	775		Clin	:			Neur					
r No:	 No											
Project	Animal No:			NAD.				NAD.				

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	Number of Sections Examined			Liver Kidneys											
			Y												
Death	ТК		Histopathology			-									
Time on Study	1.4			NAD.									-		
mg HMX/kg/day			Sample								 			 	
Project No: 415669CR			Clinical History	NAD.				Necropsy Findings	NAD.						

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	Number of Sections Examined		Líver Kídneys			
Death	ТК	Histopathology		•		
T1me on Study	14		NAD.			
5 mg HMX/kg/dav		Sample				
11	Sex: Q	Clinical History	NAD.		Necropsy Findings	NAD.

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Project No: 415669CR Group: 3 115 mg HMX/kg/day Animal No: 778 Sex: 9

Death

Time on Study

Э Number of Sections Examined Liver Kidneys Histopathology ТК Not examined. 14 Ovaries Sample Right ovarian bursa dilated with clear fluid. Necropsy Findings Clinical History Animal No: 778 NAD.

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			Y																		
Death	ΤK		Histopathology	-			•														
<b>Time</b> ton <sub>k</sub> Study	14			NAD.																	
mg HMX/kg/day			Sample																		-
115	Sex: 9		Clinical History	NAD.							Necropsy Findings	NAD.									

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	Number of Sections Examined		Liver Kidneys
Time on Study Death	1.4 T'K	Histopathology	Foci tubular atrophy and tubular epithelial regeneration. Some tubules dilated and contain eosinophilic material.
5 mg HMX/kg/day		Sample	Kidneys
11	Sex: 9	Clinical History	NAD. NAD.

/day Time_vonkStudy Death I a TK Sections Example of Namber of Namber of Namber of Namber of Namber of Namber of Liver 1.1 regeneration. Some tubular epithelial Kidneys cosinophilic material.	
/day Sample Kidneys	
Бя/Хж	
Project No: 415669CR     Group: 4     270 mg HMX/kg/day       Animal No: 781     Sex: 9     Samp       Animal No: 781     Sex: 9     Samp       NAD.     Clinical History     Samp       NAD.     NaD.     NaD.     NaD.	

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Number of Sections Examined 별 Liver Kidneys Histopathology Death ТК **Time** weeksbudy 1.4 NAD. Sample 4 270 mg HMX/kg/day **Q** Group : Sex : Necropsy Findings **Clinical History** Project No: 415669CR 782 Animal No: NAD. NAD.

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	Number of Sections Examined		Liver Kidneys
[]		Кро	
Death	тк	Histopathology	-
Time on Study	14		NAD.
IX/kg/day		Sample	
Project No: 415669CR Group: 4 270 mg HMX/kg/day	Sex: 9	Clinical History	NAD. NAD.

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	Number of Sections Examined		Liver Kidneys
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Death	ΤK	Histopathology	
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Time on Study	₹.		
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mg HMX/kg/day		Sample	
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Group :	Sex:	Histo	Lindin 1
9CR		Clinical History	Necropsy Findings
Project No: 415669CR	784	CII	Sec.
ct No:	Animal No:		
Proje	Anima		NAD.

	led	냋	[			П			
	Number of Sections Examined			Liver Kidneya					
			Y						
Death	ТК		Histopathology	-	-				
Time on Study	14			Not examined.					
mg HMX/kg/dav			Sample	Ovaries					
270 1	Sex: 0		Clinical History	NAD.		Necropsy Findings	Left ovary smaller than right.		

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	Number of	Sections Examined			Liver Kidneys											<b>.</b>						<u> </u>				<u> </u>	_						 		
Death	2 E			Histopathology						-																									
Time on Study	-	5			NAD.																														
HMX/kg/day			Sample																																
270 mg	Sex: 9			Clinical History	NAD.												Necropsy Findings		NAD.																

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	Number of Sections Examined			Liver Kidneys
			Y	Small foci tubular atrophy and tubular epithelial regeneration. Some tubules dilated and contain eosinophilic material.
Death	тк		Histopathology	ular atrophy an generation. Som osinophilic mate
Time on Study	14			Small foct tuk epithelial reg and contain ec
MX/kg/day			Sample	Kidneys
Project No: 415669CR Group: 4 270 mg HMX/kg/day			Clinical History	NAD. NAD.

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	Number of Sections Examined			Liver Kidneys															
			y																
Death	TK		Histopathology			-													
Time on Study	14			NAD.	. <u> </u>														
270 mg HMX/kg/day			Sample																
	Sex: 9		Clinical History	NAD.					Necropsy Findings	NAD.									

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	Number of Sections Examined		Liver Kidneys
Death	ТК	Histopathology	-
Time on Study	.14		NAD.
270 mg HMX/kg/day		Sample	
	Sex: 9	Clinical History	NAD. NAD.

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	Number of Sections Examined	-		
	Nu Section			Liver Kidneys
			y	d tubular
Death	TK		Histopathology	tubular atrophy and tubular regeneration.
Time on Study	.14			Small foci tul epithelial rec
270 mg HMX/kg/day			Sample	Kidneys
70 mg HI				
4	•			
Group :	Sex:		History	Findings
415669CR	790		Clinical History	Necropsy Findings
<b>Project No: 415669CR</b>	Animal No:			NAD.

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ſ	ned HE		
	Number of Sections Examined HE		Liver Kidneys
Time on Study Death	.14 ТК	Histopathology	NAD.
270 mg HMX/kg/day		Sample	
	Sex: 9	Clinical History	NAD. NAD.

ſ	peu	Ŧ		
	Number of Sections Examined			K 1 dney s
			λt	
Death	ΤK		Histopathology	-
Time on Study	14			
270 mg HMX/kg/day			Sample	
	Sex: 9		Clinical History	NAD. NAD.

[	ined	2	
	Number of Sections Examined		Liver Kidneys
<b>[</b> ]		logy	
Death	ΤK	Histopathology	-
T1me on Study	4٤		Ada
270 mg HMX/kg/day		Sample	
Project No: 415669CR Group: 4 270 mg H	Sex: 9	Clinical History	NAD. NAD.

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볓 Number of Sections Examined Liver Kidneys Histopathology Death ТΚ Time on Study 14 NAD. Sample 270 mg HMX/kg/day - O Group: Sex: Necropsy Findings **Clinical History** Project No: 415669CR 794 Animal No: NAD. NAD.

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		길보	Π		Π	Π	$\square$		Π	ΓΠ	Π	$\prod$	Π	Π	Π	Π	T	Π
	Number of Sections Evention			Liver Kidneys				 										
Time on Study Death	14 TK		Histopathology	NAD.			-											
HMX/kq/dav			Sample															
270 mg	Sex: 9		Clinical History	NAD.					Necropsy Findings	NAD.								

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	Number of Sections Examined			Liver Kidneys	 		
			бу				
Death	ТК		Histopathology		-		
Time on Study	.14			Not examined.			
mg HMX/kg/day			Sample	rungs			
270	Sex: 9		Clinical History	NAD.		Necropsy Findings	Lungs redder than usual.

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**EXTERNO** 

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Group: 4 270 mg HMX/kg/day

Nation N

Number of Sections Examined E. Liver Kidneys Histopathology Death ТĶ Time on Study 14 NAD. Sample 270 mg HMX/kg/day Group: 4 Sex: 9 Necropsy Findings Clinical History Sex: Project No: 415669CR Animal No: 798 NAD. NAD.

ſ	Ţ	•		
	Number of Sections Examined		Liver Kidneys	
Death	TK	Histopathology		
Time on Study D	.14	Hist	LAD.	
270 mg HMX/kg/day		Sample		
	•	Clinical History	NAD.	

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	f Ined	보	┝┷			
	Number of Sections Examined			Liver Kidneys		
			Y	sinusoids in centrilobular		
Death	ТК		Histopathology			
T1me <sub>weeks</sub> tudy	14			Slight dilation of areas.		
270 mg HMX/kg/day			Sample	Liver		
	•		Clinical History	NAD.	Necropsy Findings	Liver slightly mottled.

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	Number of	Sections Examined		Fat	Kidney	Lung	Heart	Spleen	e Liston	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Anta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileun	Caecum	Bectum	Maccum	Arenale	N/ 1 [F] I /N	Uterus/F.Tubes	Ovaries	Testee	Pfruffarv		Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
				Х																																			
Death		TK		Histopathology	-	Area dilated tubules in cortex.																																	
Time, Bakstudy		14				Area dilated																							_								-		
(/kg/day				Sample		Kidneys																											_						
דרסייבר ארי אוקאניים (גרסטים: 5 20 mg HMX/kg/day		Animal No: 801 Sex: 7		Clinical History		NAD.												Necronsy Findings			NAU.																		

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Group: Project No: 415669CR

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Time, QB KStudy 5 620 mg HMX/kg/day O

Death

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Number of Sections Frantana		Ī	Liver		Heart	Spleen		Miscle	Salivary GL.	S/M Lymph N.	Pancreas	Trachea	Thyroids	yrolds	Aorta Corrigo 1 7 / 1		Stomach L			Cafecum 1	Colon 1	Rectum	Mes. Lymph N. 1	Adrenals 2	Bronchial L/N 1	Uterus/F.Tubes	۵ 		Pitultary 1	Bladder 1	Skin	Mammary Gl. 0	Eyes 2	Brain 3	Spinal Cord 2		NASAL LAVITY 0	Sciatic Nerve 2	
	_	λ		•																			-																
τĸ		Histopathology		dilated tubules in cortex.		s Incenti.																																	
14				Foci dilated	Cvet in corners litere	char III cothn																	_						-										
		Sample		Klaneys	Ovarv	1																														_			
Animal No: 802 Sex: 9		Clinical History															Necropsy Findings			UVATIAN DUTSAE - SLIGHT CYSTIC dilation.																			

1	Γ	pe	뷮	-	-	7	~		[	-]-	-]-		-[-	<u> </u> _	~	4	_	0	]	]	_	_			_].	,	~	·[~	5	4	4	_	_		_	~	_]	~	_	_		
	Number of	Sections Examined		Fat	Liver	Kidney	Lung	Heart	spieen	SUBVATION CONTRACTION CONTRACTICON CONTRACTIC		Salivary GL.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Caecum	Colon	Kectul	Mes. Lymph N.	Adrenals Preschiel I /N	Itens/F. Tubes	Ovaries	Testes	Presses	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	SCIATIC Nerve	
Death		TK		Histopathology																																						
Time, QBkSs udy		14				NAD.																																				
HMX/kg/day				Sample																																						
620 mg		Animal No: 803 Sex: V		Clinical History		Scabs on right of nose from week 9-11.														Necropsy Findings		Can																				

620 mg HMX/kg/day	
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Group:	Sex:
415669CR	804
Project No:	Animal No:

Death

Time, Que Study

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Number of	Sections Examined		Fat	LIVEL	Kidney		Sulsen	Thymus	BTJCTH	Salivary Gl.	N UTEN N	Pancreas	Trachea	Thyroids	Farachyrolds	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	I Leun	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Overlee	Totto	Para ta	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
ΤK			Histopathology																																						
14					NAD.			 	-															_											_	-					
Inn /fry /vem			Sample																																						
Animal No: 804 Sex: 9			Clinical History		NAD.													Necronsy Findings	shiithiit i ledataan		NAD.				-																

805 Sex: 9		14	ŢK	Number of Sections Examined	of tamined
Clinical History	Sample		Histopathology	Fat	뛷
				Liver	-
Growth in right hind foot from week 12-13.	Kidneys	Area tubular atrophy.	trophy.	Kidney	~
				5 mm	<u>~  </u>
					<u>• i-</u>
				Thuman	-1-
				Muscle	<u>-1-</u>
				Saltvarv G	<u> </u>
				N drawing M/S	<u> -</u>
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				Control	<u>ا۔</u> ج
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Nectonsy Findings		-			4:
shiithiit J Asdornau				nuodenum 104	4
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		-			<u>_l</u> .
				Colon	_
				Rectum	-
				Mes. Lymph N.	
		-		Adrenals	5
				Bronchial L/N	
				Uterus/F.Tubes	ubes ]
				Ovaries	2
				Testec	4
				Prestate	4
				Pituitary	
				R ladder	1-
				Chin	4-
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				manuary ut.	-1-
				Fyes	<u>, ]</u> ,
				Brain	~
				Spinal Cord	5
				Bone/Sternum	
				Nasal Cavity	
				Sciatic Nerve	ve 2
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	Number of	Sections Examined		Fat	Liver	Kidney	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Paratnyroids	Correction 1 / M	Stomach	Duodenum	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F. Tubes	Ovaries		Pituitary	Diaddor	Diauurei	Mammarv Gl.	Fine 1 41.	cyes Brain	spinal Cord	Bone/Sternum Nasal Cavity	Sciatic Nerve		
Death	Ψ×			Histopathology			arropny in correx.															-																				
Time, QBkS5 udy	14						Areas cubular acr																																			
mg HMX/kg/dav				Sample		Vidnoss	VIUNEYS																																		_	
620	806 Sav. 0			Clinical History																Necropsv Findings		NAD																				

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	Number of	Sections Examined HE	Fat	L.	Kidney	•	Heart	<u> </u>	Thymus	Muscle	 ż	Pancreas			Paratnyroids	-	Duodenum	Jejunuma []	Ileum	Cafecum []	Colon 1	Rectum 1	Mes. Lymph N.	Adrenals	Bronchial L/N	l samil. 1/smash			Picuitary 1	Bladder		iry Gl.	Eyes 2	Brain 3	Spinal Cord	Bone/Sternum	Nasal Cavity 1	Sciatic Nerve	
	<u> </u>	<u></u>			-											<u>, .</u>			-	<u>u</u>	0				<u></u>				<u>+</u>			<u>L</u>	<u></u>	<u></u>	<u></u>	8	<u>z</u>	<u>.</u>	
Death	ΤK		Histopathology		rosis																																		
Time, weeks udy	14				Small area nerrosis																																		
mg HMX/kg/day			Sample		Duodenum																					- <u></u>													
620	807 Sex: Q		Clinical History		NAD												Necropsy Findings																						

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	Number of	Sections Examined		Fat	Liver	Lung	Heart	Spleen	Thymus and the second	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Paratnyroids	Carutaal 1 /N	Stomach	Duodenum	Jetunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries		Presete	Pltultary	Bladder	SKIN	Mammary GI.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
				Y		tubular regeneration.																_																			
Death	ЧĻ	V11		Histopathology		σ	dildton.	Peyer's patch hyperplastic.																																	
T1me <sub>(w</sub> gg <sub>k</sub> Study	1 4					Foci tubular a	Focus tubular dilation.	Peyer's patch	1	NAD.																															
mq HMX/kq/day				Sample		Kidneys		Ileum		Ovaries																															
620	ROR Sex: Q			Clinical History		NAD.												Necropsy Findings		Ileim - Dever's matches wrominent	TTOM TELET & DUCHES DIONITHENC.	Ovaries - right larger than left	Control taking target clight tere!																		

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at ned	벌	F	r	<u>·</u> È	• •	<u>-  </u>	-1	-	-1	-1	-1	-1	<u>-</u> [·	-1-	-1-	19		1-	4-	-	_		-1	<u>-</u> !	~!			<u>v I</u> c		-	1-	-	-1	-	~	2		_	<u>~</u> 1	
Number of Sections Examined	Fat	Liver	Kidnev		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	rear c	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyrolds	Parathyroids		Stomach	Ducdenum	Jetunum	Ileum	Catecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Otterus/r. Thur	Totto		Pitultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
Time <sub>(MBb</sub> KStudy Death 14 TK	Histopathology			NAD.																																				
HMX/kg/day	Sample																					_	-																	
Project No: 415669CR Group: 5 620 mg HM Animal Po: 809 Sex: 9	Clinical History			NAD.														Necronsy Findings	churpur ledonow	NAD.																				

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	Number of	Sections Examined		Fat	Liver	Lung Valuey	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N. Pancreas	Trachea	Paratheroide	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Carecum	Colon	Rectum	Mes. Lymph N.	AGTENALS	Bronchial L/N	Ovaria	Tostac	Prestate	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	MASAL LAVILY	SCIATIC Nerve	
				Y																																	-			
Death		TK		Histopathology		trophy.																																		
Time, Queks; udy		14				Foci tubular atrophy.							 																											
mg HMX/kg/day				Sample		Kidneys																																		
620	810 Sex: 9			Clinical History		NAD.												Necropsy Findings		NAD.																				

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Number of Sections Examined HE	Fat Liver	Kidney Lung	Heart Spleen	Thymus Muscle	Salivary Gl. S/M Lymph N. Pancreas	<b>Trachea</b> Thyroids	Parathyroids Aorta	Cervical L/N Stomach	Jejunum	Ileum Caecum	Colon Rectum	Mes. Lymph N. Adrenals	Bronchial L/N	Uterus/F.Tubes Ovaries	Testec	Prestate	Pituitary	Bladder	Mammary Gl.	Eyes	Brain Griferi Cond	Spinal Cord	Nasal Cavity	Sciatic Nerve	
Death TK	Histopathology																								
Time, Bekstudy 14	HIS	NAD.																							
HMX/kg/day	Sample																								
Project No: 415669CR Group: 5 620 mg HMX Animal No: 811 Sex: 9	Clinical History	NAD.							Necropsy Findings	NAD.															

5 620 mg HMX/kg/day	
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Group:	Sex:
415669CR	812
<b>Project No: 415669CR</b>	Animal No: 812

Death	TK
Time, Qlakstudy	14
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Sample Histopathology Fat Liver Kidney Fat	
Histopathology Fat NAD. Histopathology Fat Liver Lung Hart Speen Thymus Hascle Sallvary Gl. Sallvary Gl. Sallvary Gl. Sallvary Gl. Sallvary Gl. Sallvary Gl. Sallvary Gl. Sallvary Gl. Stonath Hernary Cl. Bronchial L/M Hernary Gl. Bronchial L/M Hernary Gl. Spinal Cord Brone/Sternum	
NAD. Liver NAD. Liver Lung Heart Salivary Gl. Salivary Gl. Salivary Gl. Salivary Gl. Salivary Gl. Salivary Gl. Salivary Gl. Salivary Gl. Salivary Gl. Salivary Gl. Bronchial L/N Natrens/F.Thubes Districtes Fluutary Strain Sciatic Nerve	_
NAD. Kidney Lung Lung Lung Lung Rywus Miywus Miywus Miywus Salivary Cl. Salivary Cl. Salivary Cl. Salivary Cl. Salivary Cl. Salivary Cl. Salivary Cl. Salivary Cl. Scatta KN Nucerus/F. Tubes Reconchial L/N Uterus/F. Sual Cord Bone/Sternum	-
Heart Spleen Thywus Muywus Muywus Muywus Muywus Muywus Muywus Pancreas Trachea Thyroids Pancreas Parchea Tryroids Parchea Parc	
Spien Thymus Muscle Sallvary Gl. S/M Lymph N. Pancreas Trachea Trachea Trachea Trachea Aorta Aorta Aorta Aorta Colon Recum Mereals Bronchial L/N Uveris Provis Stinal Cord Brain Spinal Cord Brain Spinal Cord Brain Sciati Carity Sciati Carity	
Thymus Muscle Salivary Gl. SAlivary Gl. SAlivary Gl. SAlivary Gl. SAlivary Gl. SAlivary Gl. SAlivary Gl. Sathods More Strum Marenals Duodenum Duodenum Duodenum Duodenum Duodenum Duodenum Marenals Duodenum Duode	
Muscle Sallvary Gi. Sallvary Gi. Santuary Gi. Shronda Throids Pancreas Trachea Throids Pancreas Aorta Cervical L/N Stomach Duchenum Jejunum Ceccum Ceccum Colon Rectum Merveris Pitutary Pitutary Pitutary Pitutary Pitutary Pitutary Pitutary Pitutary Pitutary Pitutary Pitutary Pitutary Spinal Cord Brain Spinal Cord	
Salitary Gi. S/A Lymph N. Pancreas Trachea Trachea Trachea Aorta Aorta L/N Stomach Duodenum Jejunum Lieun Cocon Rectun Meronkial L/N Uterns/F.Tubes Uvaries Dirutary Brons/F.Tubes Uvaries Present Brain Spinal Cord Bons/Sternum Nasit Cord	_
-Ymph N. -Ymph N. - cal L/N - cal L/N - cal L/N - cal L/N - in - Lymph N. - in - Lymph N. - in - Lymph N. - in - cal L/N - in - cal L/N - cal L/N	
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ry Gl. ry Gl. 1 Cord Sternum Cavity 1 CNELY	
ry Gl. 1 Cord Sternum Cavity 1 CNerve	
ary Gl. 1 Cord Sternum . Cavity . La Nerve	
n 11 Cord Sternum . Cavity .11 Nerve	
Brain Spinal Cord 2 Bone/Sternum 1 Nasal Cavity 1 Sciatic Nerve 7	
Spinal Cord 2 Bone/Sternum 1 Nasal Cavity 1 Sciatic Nerve 7	
Bone/Sternum 1 Nasal Cavity 1 Sciatic Nerve 2	
Sciatic Nerve 2	

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	Number of	Sections Examined		Fat	Kidney	Lung	reat c	apreen	spart.	Saltvary G	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	lleum	Caecum	Colon	Meetum Mee 1.mach M	Atonala	Renchial 1./N	Uterus/F. Tubes	Ovaries	Totoc	Prostate	Pituitary	Bladder	MAMMAYY C)	Eves	Brain	Sninal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
Death		TK		Histopathology																																				
Time, Que KStudy De		14 T		Histo	Foci tubular atrophy.																																			
HMX/kg/day	<u>.</u>		J	Sample	Kidneys																																			
620 mg		Animal No: 813 Sex: Y		Clinical History	Red encrustations round right eye from	week 10-11.													Necropsy Findings		NAD.																			

 415669CR	Group:	ა <b>(</b>	620 n	бш	HMX/k
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Ined	볖			2	F	-	-	-	-	Ŀ	<u>-1</u> .	1	1~	-	5	-	4	-	-1	-1		-1	-1	<u>-l-</u>	<u>.</u>		4	4	_	~	<u>.</u> ].	-1	~!~	<u> ~</u>	-		h	$\Box$
Number of Sections Examined		Fat	Kidney	Fung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Tracnea	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Calecum	Colon	Rectum	Mes. Lymph N.	Rronchial 1./N	litenis/F. Tubes	Ovaries	Tastac	Prostate	Pitultary	Bladder	Skin	- Annuary 41.	Eyes Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
14 TK		Histopathology																																				
-				NAU.									_				_				_																	
		Sample					·																															
Animal No: 814 Sex: Q		Clinical History															Necropsy Findings		NAD.																			

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	i ined	벞	-		h	1	F	1-	1-	<u>' -</u>	-		-	-1	2	<u>-</u> [.		d-	<u> </u> -	-	-	-		_	-1	~	-	_	2	朻	<u> -</u>			0	~1	-	~	-	<u>.</u>	<u>.                                    </u>	
	Number of Sections Examined		Fat	Liver	Kidnev	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	AULU	Cervical L/N	Diodenim	Jetunum	Ileum	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	UVALIES T-11	Presto	Pitultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Sciatic Nerve		
Time, Blekstudy Death	14 TK		Histopathology		Ford flibbling at working and flibbling and flipbling	recentration.																																			
HMX∕kg/ḋay			Sample		Kidnevs																														-						
: 415669CR Group: 5 620 mg	Animal No: 815 Sex: 💡		Clinical History		NAD.														Necropsy Findings		NAD.																				

HMX/kg/day	
620 mg h	
S	0
Group :	Sex.
415669CR	816
oject No:	Imal No.

Death

Sex: 9 14 TX 3. 14 TX 3. Semple 14 145.079 145.01099 14.0000 14.000 14.000 14.000 14.000 14.000 14.00000 14.00000 14.00000 14.00000 14.00000 14.00000 14.00000 14	, a	뷛		-1-	٦L						7	T	ן	J,	]	Ţ	Ţ	Ţ	]		Ţ	_]	<u> </u>	٦,	1	1		Ţ					L		6	
B16     Sexi: 9     14       Clinical History     Sample     Areas tubular       Kidneys     Areas tubular     Regeneration.	Number of Sections Examine			 ~		Spleen	-	-	Pancreas	Trachea	-	Parathyroids	-		Stomach	Duodenum	Jejunum	Treche	Caecum	Loton	Kectum	Mes. Lymph N.			r.Tubes		Dituitary	Disadow 1	Brauer Skin	Mammarv Gl.	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity		·
B16     Sexi: 9     14       Clinical History     Sample     Areas tubular       Kidneys     Areas tubular     Regeneration.			y	lar epithelial	_																															
B16     Sexi: 9     14       Clinical History     Sample     Areas tubular       Kidneys     Areas tubular     Regeneration.	ΤK		Histopatholog	atrophy and tubu																																
816 Sex: 9 Clinical History Kid Necropsy Findings	14				. not the tanget																		-													
816 Sex: Clinical History Necropsy Findings		-	Sample	Kidneys																																
	816 Sex:		Clinical History	4D.								•				Necropsy Finaings		AD.																		

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	Number of Sections Examined		Fat	L1 Ver	Lung	Heart	Spleen	Thymus	Muscle	Salivary GL.	S/M Lymph N.	Traches	Thyroids	Parathyroids	Aorta	Cervical L/N	Duodenum	Jetunum Jetunum	Ileum	Calecum	Colon		Mes. Lympn N. Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	Tostac	Pituitarr.	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Masal Lavity	SCIATIC Nerve	
			Å		Small foci tubular atrophy and tubular epithelial			<u> </u>																														
Death	TK		Histopathology		ular atrophy and																																	
T1me, QBkStudy	14				Small foci tub	regeneration.																																
{/kg/day	 ; ,		Sample		Kidneys																																	
Project No: 415669rp Group: 5 620 mg HMX/kg/day	819 Sex: 9		Clinical History		Scab to right of vaginal opening in	week 7.												Necropsy Findings																				

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	Number of	Sections Examined			Kidney	Fung	Heart	Spleen	Thymus	Muscle	S/M Lymph N.	rancreas	Thurotde	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum			Mes. Lymph N.		Uterus/F.Tubes	-	Totto		Pitultary [	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Sciatic Nerve		
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Death	Ĭ	11		Histopathology	ant ant the	חומד בהזרווב																																	
T1me <sub>(.QDbKS</sub> tudy		r -			Cmall foot turb	SWALL LUCE LUD																						-											
g/day	1			Sample	v i drouc	vraneys																														_			
Project No: 415669CR Group: 620 mg HMX/kg/day	830 <b>522</b> . 0			Clinical History		. MAU.												Necropsy Findings		NAD.																			

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	Number of	Sections Examined		Fat	Liver	vaney	Lung	Soleen	Thumus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	rafacily tutus	Cervical L/N	Stomach	Duodenum	Jejunum	I leum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	UVALIES Toatoc	Duratate	Pitultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	NASAL LAVITY	SCIALLC NELVE	
Time, weekstudy Death		14 TK		Histopathology		NAD.								-																		01	<u> </u>			5		Ζ	2	
mg HMX/kg/day				Sample		Eyes																																		
1500				Clinical History		Eyes black encrusted from week 9-13.													Necropsy Findings		Eyes - red encrusted.																			

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	Number of	Sections Examined	Fat.	Liver	Kidney	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	AOLLA	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	orerus/r.inpes	UVALIES Toatoo		Pitultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	-
Death	ŢΥ		Histopathology																																							
Time, Que Study	1 4				NAD.																																					
mg HMX/kg/day			Sample																																							
1500			Clinical History		NAD.															Necropsy Finaings		NAD.																				
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	Number of	Sections Examined		Fat 11	Lung	Heart	Spleen	Thymus	Saltwarr Cl	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach		[]eum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries		Pitultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
Death	FD			Histopathology			ric.																																
Time, QR KStudy D	1			Hist	Sections autolytic.		congested and autolytic.																																
mg HMX/kg/day		_		Sample			sbung																																
1500	Sex: 9			Clinical History		encrusted patch at top of left hind leg	In week I.										Necronsv Findings			Yellow staining round nose and mouth.		ted. subcutaneous tissue tequened.	[ungs = irreqular dark red natches on all	- TITESATIAT ANT LEA PARCHES ON	10003														

**CARENTER SECONDER** 

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	Number of	Sections Examined		Fat		<del>ہ</del> ۔۔	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Trachea	5	olds	Aorta Cervical 1./N	•	Duodenum	Jejunum	Ileum	Caecum	Celon	Rectum	Mes. Lymph N.	1	Bronchial L/N		T	T	Pitultary	Bladder	Skin	Mammary GL	Eyes Brain		Spinal Cord	Bone/Sternum Nacal Cantty	Sciatic Nerve		
						ur epithelial																																		
Death	a E	4		Histopathology		atrophy and tubular epithelial																																		
Time, Bhek\$\$udy		t 				Foci tubular a	eration.																																	
mq HMX/kq/day				Sample		Kidnevs																																		
1500		Animal No: 824 Sex: Y		Clinical History														Necronsy Findings																						

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6 1500 mg HMX/kg/day O Group: Project No: 415669CR

Death

Time, weekstudy

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	Sections Purchase		Fat Liver		kaney	5un T	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyrcids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	Tostas	Presses	Pituitary	Bladder	skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
			λť																																								
	TK		Histopathology																																								
(WEEKS)	14				NAD.								-																														
HMX/kg/day			Sample										-																														
1500 mg	825		Clinical History		Encrustations round eves from week 10-11.	blood in cade black encrueted note in	PLOUD III CAYE, DIACA ENCLUSION NOSE III	MCEK II.												Necropsv Findings																							

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	Fat Liver	Kidney	Lung Heart	Spleen	Thymus	Muscle	Salivary UL.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Duccentin	Jejunum	Ileum	Calecum	Colon	Rectum	Mes. Lympn N. Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	100100	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum Nasal Cavity	Sciatic Nerve		
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	Histopathol																																		
			NAU.																			•											_		
	Sample																																		
	Clinical History		NAD.											Nacarati Pindinas	shutnut i Asdoloan		NAD.																		
		Sample Histopathology Fat	Clinical History Sample Histopathology Fat Liver	Sample Histopathology Fat Liver Kidney NAD. Lang	Clinical History Sample Histopathology Fat Liver Kidney Lung Heart Spleen	Clinical History Sample Histopathology Fat Liver Kidney Lung Heart Spleen Thymus	Clinical History Sample Histopathology Fat Kidney Lung Heart Spieen Thymus WAD.	Clinical History Sample Histopathology Fat Liver Kidney Lung Heart Spleen Thymus Muscle Salivary Gl.	Clinical History Sample Histopathology Fat Liver Kidney Lung Heart Spleen Thymus Muscle Salivary Gl. SALVmph N.	Clinical History Sample Histopathology Fat Liver Kidney Lung Heart Spieen Thymus Muscle Salivary Gl. SA Lymph N. Pancreas	Clinical History Sample Histopathology Fat Kidney Kidney Kidney Kidney Lung Heart Spleen Thymus MAD. Salivary Gl. Sylvery Gl. Sylvery Gl. Sylvery Gl. Sylvery Gl. Sylvery Silvary Gl. Sylveres Trachea	Clinical History Sample Histopathology Fat Liver Kidney Liver Kidney Liver Kidney Liver Seleen Thymus Muscle Salivary Gi. SAlivary Gi. SALIVARALIVI SALIVARA	Clinical History Sample Histopathology Fat Liver Kidney Liver Kidney Liver Kidney Liver Kidney Liver Kidney Liver Kidney Lung Heart Spieen Thymus MaD. Rancreas Trachea Trachea Trachea Trachea Trachea Trachea Trachea Trachea Trachea Corta	Clinical History Sample Histopathology Fat Liver Kidney Liver Kidney NAD. NAD. NAD. Practice Spleen Thyse Heart Clinical Histopathy Clinical Kines Parathyroids Parathyroids Parathyroids Parathyroids Corrected L/N	Clinical History Sample Histopathology Fat Liver Kidney Liver Kidney Liver Kidney Liver Kidney Lung Reart Soleen Typela Panceas Trachas Parceas Trachas Parceas Trachas Parceas Trachas Parceas Trachas Parceas Trachas Parceas Trachas	Clinical History Sample Histopathology Fat Liver Kidney Luver Kidney Luver Kidney Luver Kidney Luver Kidney Heart Seleen Thyroids Parathyroids Acta L/N Necropsy Findings	Clinical History     Sample     Histopathology     Fat       Ridney     Histopathology     Fat       Ridney     Lung     Lung       NAD.     NAD.     Heart       Spleen     Thymus       Ruscle     Spleen       Thymus     Sconach       Docleman     Jeunan       Jeunan     Jeunan	Clinical History     Sample     Histopathology     Fat       Canadia     Nab.     Histopathology     Fat       Carrier     Sample     Sample     Sample       Nab.     Nab.     Sample     Sample       Nab.     Nab.     Sample     Sample       Nab.     Nab.     Sample     Sample       Carrier     Sample     Sample     Sample       Nab.     Nab.     Sample     Sample       Carrier     Sample     Sample     Sample       Necropsy Findings     Sample     Sample     Sconach       Necropsy Findings     Sample     Sample     Sample	Clinical History Sample Histopathology Fat Clinical History Sample Histopathology Fat Kidney Kidney Lung Peart Spient Pearting P	Clinical History     Sample     Histopathology     Fat       Reconstruction     Fat     Ender       NAD.     Histopathology     Fat       NAD.     NAD.     Ender       Spleen     Spleen     Ender       Traches     Traches     Traches       Traches     Traches     Traches       Necropsy Findings     Dodema     Dodema       Recoms     Sconsol     Eccus       Recons     Eccus     Clon	Clinical History Sample Histopathology Ret Cliver Kidney Liver Kidney Lang Histopathology Ret Kidney Lung Histopathology Ret Kidney Lung Histopathology Cliver Kidney Liver Ki	Clinical History Sample Histopathology Fat Clinical History Sample Histopathology Fat NAD. Histopathology Fat Salivary Gl. Salivary Gl. S	Clinical History     Sample     Histopathology     Fat       Clinical History     Sample     Histopathology     Fat       Intervention     NAD.     NAD.     Liver       Patron     Kidney     Histopathology     Fat       Patron     Kidney     Naple     Naple       Patron     Kidney     Histopathology     Fat       Patron     Kidney     Histopathology     Fat       Patron     Kidney     Naple     Naple       Patron     Kidney     Naple     Naple       Patron     Kidney     Naple     Naple       Patron     Kidney     Naple     Naple       Patron     Kidney     Sconch L/N     Sconch L/N       Patron     Necropsy Findings     Patron     Sconch L/N       Patron     Ketum     Patron     Patron       Patron     Ketum     Patron	Clinical History Sample Histopathology Ret Liver Sample NAD. Histopathology Ret Ridney Hart Spleen Typus Heart Typ	Clinical History     Sample     Histopathology     Etc.       NAD.     Sample     MAD.     Etc.       NAD.     NAD.     Etc.     Etc.       Name     NAD.     Etc.     Etc.       Name     Etc.     Etc.     Etc.       Name     Etc.     Etc.     Etc.       Necropsy Findings     Etc.     Etc.     Etc.       Necropsy Findings     Etc.     Etc.     Etc.       Necropsy Findings     Etc.     Etc.     Etc.       Otoen     Etc.     Etc.     Etc.       Statistic     Etc.     Etc.     Etc.       Statistic     Etc.     Etc.     Etc.       Statistic     Etc.     Etc.     Etc.       Etc.     Etc.     Etc.     Etc.	Clinical History Sample Histopathology Re Clinical History Sample Histopathology Re MAD. NAD. Recent Saluery Cli Saluery Cli S	Clinical History Sample Histopathology Fat Utive Sample Histopathology Itive Sample Reserved a Sample Nab. NAD. NAD. NAD. Nab. Nab. Nab. Nab. Nab. Nab. Nab. Nab	Clinical History Sample Histopathology Fat Liver Spleen International MAD. Histopathology Fat School MAD. NAD. NAD. NAD. NAD. NAD. NAD. NAD. N	Clinical History     Sample     Histopathology     Part       Clinical History     Sample     Histopathology     Part       NAD.     NAD.     NAD.     Standard       Name     NAD.     Standard     Standard       NAD.     NAD.     Standard     Standard       NAD.     NAD.     Standard     Standard       NAD.     NAD.     Standard     Standard       Nacca     Standard     Standard     Standard       Nacca     Standard     Standard     Standard       Nacca     Standard     Standard     Standard       Nacca     Standard     Standard     Standard       Naccasy Findings     Standard     Standard     Standard       Neccosy Findings     Standard     Standard     Standard	Clinical History Sample Histopathology Rate Clinical History Sample Histopathology I and NAD. Histop	Clinical History     Sample     Histopathology     Pack       Cunical History     Sample     Histopathology     Pack       NAD.     NAD.     NAD.     Exect States       NAD.     NAD.     Exect States     Exect States       NAD.     Exect States     Exect States     Exect States       NAD.     Exect States     Exect States     Exect States       NAD.     Exect States     Exect States     Exect States       NAD.     Exect States     Exect States     Exect States       NAD.     Exect States     Exect States     Exect States       NAD.     Exect States     Exect States       NAD.     Exect States <t< td=""><td>Clinical History     Sample     Histopathology     Ket       Cinical History     Sample     Histopathology     Extension       NAD.     NAD.     Extension     Extension       Process     Extension     Extension     Extension       Process     Extens</td><td>Clinical History Gample Histopathology React React Nuo. Band Histopathology React React Standard React Standard</td><td>Clancel History Sample Histopathology Rt Liver Kidny K</td><td>Clinical History     Sample     Mistopathology     Per tiver       Rush     Nuclear     Nuclear     Per tiver       Rush     Nuclear     Per tiver     Per tiver       Rush     Per tiver     Per tiver       Rush     Per tiver     Per tiver</td></t<>	Clinical History     Sample     Histopathology     Ket       Cinical History     Sample     Histopathology     Extension       NAD.     NAD.     Extension     Extension       Process     Extension     Extension     Extension       Process     Extens	Clinical History Gample Histopathology React React Nuo. Band Histopathology React React Standard React Standard	Clancel History Sample Histopathology Rt Liver Kidny K	Clinical History     Sample     Mistopathology     Per tiver       Rush     Nuclear     Nuclear     Per tiver       Rush     Nuclear     Per tiver     Per tiver       Rush     Per tiver     Per tiver       Rush     Per tiver     Per tiver

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	Number of Sections Examined	Fat	Kidney	Heart	Spleen	Thymus Muscle	Salivary Gl.	S/M Lymph N. Pancreas	Trachea	 	Parathyroids	Cervical L/N	Stomach	Duodenum	Jejunum	Catecum	Colon	Rectum	Mes. Lymph N.	Bronchial L/N	Uterus/F.Tubes	5	Totos	Prestate	Pltuitary	Bladder	Skin Mammary G	Find the state	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
		2	ırge, pale																										-					
Death	ТK	Histopathology	li packed with large,																															
Time, Qlakstudy	14		Area of alveoli	macrophages.	NAD.																													
mq HMX/kq/dav	•	Sample	sɓunŋ		Uterus																													
1500	827 Sex: Q	Clinical History	Blood in cage in weeks 11 and 13.	12.										Necropsy Findings	1	Uteru - both horns dilated with clear	. Tund.																	

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: No: 415669CR Group: 6 1500 mg HMX,	
Project No:	And and No.

Death

Time weekstady

6 1500 mg HMX/kg/day	
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Group :	Sex:
415669CR	828
: ON	No:
Project No:	Animal No:

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Number of Sections Examined		Fat	LIVER	Lung	Heart	Splee	Thymus	unscre	Salivary GL.	Pantreas	Traches	Thurnide	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Catecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	_				Skin		Rumary GL.			Bona/Charmer			SCIATIC Nerve	_
ТК		Histopathology																																						
14			NAD																																					
		Sample																			Ξ.																			
No: 828 Sex: 💡		Clinical History														Necroney Findings	Southur 1 Astornam																							
Animal No:			NAD.																NAD.										<u>.</u>			_						_		

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Number of Sections Examined HE	Fat	r r r r r r r r r r r r r r r r r r r	
		ar epithelial	
Death TK	Histopathology	tubular dilation and tubular epithelial teration.	
Time <sub>(u</sub> gb <sub>k</sub> §\$udy 14		Foci tubular d regeneration.	_
mg HMX/kg/day	Sample	Kidneys	
Project No: 415669CR Group: 6 1500 mg Hh Animal No: 829 Sex: 9	Clinical History	NAD. NAD.	

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	Number of Sections Examined		Fat	<u>ب</u> ب	Lung	Spleen	Thymus	Salivary Gl.	S/M Lymph N.	Traches	· · · ·	Parathyroids	AOFCA	Stomach	Duodenum	Jejunum	Ileum	Calecum	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	F.Tubes	Ovaries		2	Bladder	Skin	Mammary Gl.	Eyes	Spinal Cord	Nasal Cavity	Sciatic Nerve	
			λ																															
Death	TK		Histopathology	dilation.																														
Time <sub>(w</sub> gg <sub>k</sub> Study	14			Focus tubular dilation.																														
mg HMX/kg/dav			Sample	Kidnevs																														
1500	830 Sex: 9		Clinical History	UAN VAN											Necropsy Findings			• CW																

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	Number of	Sections Examined	Fat	Liver	Kidney	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N. Pancreas	Trachea	Thyrolds	Parathyroids	Aorta	Cervical L/N Stomach	Duodenum	Jejunum	Ileum		Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Tottot	Provide state	Pituitary	Bladder	Skin	Fves	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	SCIATIC Nerve	
/ Death	TK		Histopathology		tubular atrophy and tubular	regeneration.																															
Time, QB kS fudy	14				Small foci t		NAD												<u></u>																<u> </u>		
mg HMX/kg/day			Sample		Kidneys		Ovaries																														
1500	Animal No: 831 Sex: Q		Clinical History		NAD.												Necropsy Findings		Left overy smaller than right.																		

415669CR Group: 832 Sex:

Death

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	Number of Sections Examined	-	Fat Liver	<u> </u>		The second	Salivary Gl.	S/M Lymph N. Pancreas	 Thyroids Parathyroids	Aorta	Cervical L/N	Stomach Duodenum	Jetunum	<u></u>	Catecum	Colon	Nettum	Actenals	L L/N	Uterus/F.Tubes		Tostac	Pituitarv	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum Nasal Cavity	Sciatic Nerve		
			Å																														
	ТК		Histopathology	foci tubular dilation.	ч.																												
(WEEKS)	14			Small foci tub	Area congestion.																									_			
mg HMX/kg/day			Sample	Kidneys	Liver																											_	
1500	Sex: Q		Clinical History	NAD.								Stadi-	Nectopsy Finantias	Turned darker red than normal	rando adver tea chan share																		

Group: Sex: Project No: 415069CR 833 Animal No:

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Death ЧĽ Time, Que KStudy 14 6 1500 mg HMX/kg/day Q

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	Sections Frantined			rat 1.1 ver		Tupe Tupe		rearc	uaarde	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	Testes	Prestate	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		
	TK			Histopathology																																									
- ISUSSAI	14					LOCUS CUDUIAL														<u> </u>																									
App/by/vi				sample		channed						-																																	
ECOLECC NO: 4120096CK ALAND: A TOOD WA WAY VALAR	Animal No: 833 Sex: 9			Clinical History		NAU.															Necropsy Findings		NAD.																						

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	Number of Sections Examined		Fat	Kidney	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Trachea	Thyroids	Parathyroids	AOTCA	Cervical L/N	Duodenum	Jejunum	Ileum	Caecum	Colon	Kectum	Mes. Lymph N.	Bronchial 1./N	Uterus/F.Tubes	Ovaries	Totto	Prostate	Ficutoary	Bladder	Free to the to the total to the total to the total tot	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	Pancreatic Mass
			λ																																		
Death	TK		Histopathology		•																																
Time, QlaxStudy	14			Culenia ticeno	hard the stand																																
mg HMX/kg/day			Sample	Macc from	Pancreas																																
<b>Project No: 415669CR Group</b> : 6 1500 mg Hh	Animal No: 834 Sex: Q		Clinical History	Right eve black oncructed right of face	swollen in week 13.												Necropsy Findings		Tip of tail missing.		Right eye - slight corneal opacity.		Pancreas - 2 mm diameter red mass.														

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	Number of	Sections Examined		Fat	- Liver	Kidney	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Outer us/ r	Tostic	Prostate	Pitultary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve		-
Time, Quek\$tudy Death	14 TK			Histopathology		Area lymphocyte infiltration.																																						
MX/kg/day				Sample		Muscle			4																													_						
Project No: 415669CR Group: 6 1500 mg HMX/kg/day	835 Sex: 9			Clinical History		Black encrusted nose and forelegs in	week 1.		Blood in cage from week I-2.												Necropsy Findings		NAD.																					

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	Number of	Sections Examined		Fat	LI VET	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	Pancreas	Trachea	inyroids Parathuroide	Acte	Carutaal 1./N	Stomach	Duodenum	Jejunum	lleum	Calecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/r.iupes	Tottoe	Processo	Pltuitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum Nacal Cavity	Colletto Mound	SCINIC MELAE	
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Death	τĸ			Histopathology		atrophy.																																			
Time, QAkStudy	14					Foci tubular		ryst.											-																						
mg HMX/kg/dav				Sample		Kidneys		UVALY																																	
1500				Clinical History		Black encrusted eyes in week 13.													Pindian.	Nectopsy runnings		Left ovary - clear fluid filled sac 3 mm	diameter.																		

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	Number of Sections Examined		Fat Liver	Kidney Lunq	Heart	Thymus	Muscle	Salivary GL.	Pancreas	Trachea	Parathyroids	Aorta	Cervical L/N	Stomach	Jejunum	Ileum	Caecum	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Ovaries	Testec	Presso	Pituitary	Bladder	Mammary G1.	•	Brain	Spinal Cord	Bone/Sternum Nasal Cavity	Sciatic Nerve	
Time, BbkStudy Death	14 TK		Histopathology	Foci tubular dilation and tubular atrophy.																													
mg HMX/kg/day			Sample	Kidneys		<u></u>																											:
1500	837 Sex: 9		Clinical History	Right eye red encrusted in week 13.					=						Necropsy Findings		- man																

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6 1500 mg HMX/kg/day **Q** Group: Sex: **Project No: 415669CR Animal No: 838** 

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	Number of Sections Examined		Fat Liver	Kidney	Lung	Heart	Spleen	Thymus Muscle	Salivary Cl	S/M Lymph N.	Pancreas	Traches	Thyroids	Faraunyroids	Aorta Countral r /w	CELVACEL E/1	Stomach			ICaecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F. Tubes	Ovaries	Tautos	Press	Pituitary	Bladder	Skin	Mammary G1.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
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	TK		Histopathology		atrophy.	4 ( ) B		atrophy.																																
(WEEKS)	14				Foci tubular atrophy.	clicht conger	SILIGHT CONGESTION.	Focus acinar atrophy.		NAD.		_																												
IX/kg/day			Sample		Kidneys		sbunn	Pancreas		Trachea																														
project No: 415669rb Group: 6 1500 mg HMX/kg/day	838		Clinical History		NAD.													Necropsy Findings		Lungs darker than normal.		Froth in trachea.																		

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	Number of	Sections Examined		Fat		Kidney	Fund	Heart	Spleen	Thymus	Muscle	Salivary GL.	S/M Lymph N.	Pancreas	Trachea	Thyroids	Parathyrolds	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum	Ileum	Caecum	Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries	Toston	Presto	Pituitary	Bladder	Skin	Mammarv Gl.	Eves	Brain		Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
Time, QB KS fudy Death	14 TK			Histopathology		NAD.																																							
mg HMX/kg/day	•	-		Sample					-														-																						
1500	Sex: 9			Clinical History		NAD.															Necropsy Findings		NAD.																						



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	Number of	Sections Examined		Fat	Liver	Lung	Heart	Spleen	Thymus	Muscle	Salivary Gl.	S/M Lymph N.	ralicteds	Tracnea	Parathyroids	Aorta	Cervical L/N	Stomach	Duodenum	Jejunum		Colon	Rectum	Mes. Lymph N.	Adrenals	Bronchial L/N	Uterus/F.Tubes	Ovaries Tostoc	Ducatata	Pituitary	Bladder	Skin	Mammary Gl.	Eyes	Brain	Spinal Cord	Bone/Sternum	Nasal Cavity	Sciatic Nerve	
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Death	τĸ	4 T		Histopathology		atropny.																																		
Time, Que Study	14				Pool Auturlan	roci tubular atropny.																																		
MX/kg/day	-			Sample	vidno	vtaueys		_																																
Project No: 415669CR Group: 6 1500 mg HMX/kg/day	Sex: Q			Clinical History															Necropsy Findings																					

APPENDIX 10

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HMX: 13 Week Toxicity Study in Rats Absolute Organ Weights (g) Individual Values: Males

mg/kg/ An dav/ N	,		Adrei	enals			K1dn	Kidneys				Tea	Testes
- <u></u>	No.	Body Weight	Ч	R	Brain	Heart	ч	24	Liver	Lungs	Spleen	ц	ĸ
93	601	288	0.022	0.020	1.83	1.04	0.93	0.95	10.16	1.51	0.78	1.98	1.95
	602	305	0.020	0.017	1.87	0.87	1.00	1.01	11.41	1.40	0.68	2.08	2.04
	603	294	0.026	ru U	1.92	0.94	0.94	0.97	10.15	1.18	0.62	2.67	2.02
Ŭ	604	262	0.022	ی م	1.84	0.90	0.95	10.01	10.32	1.21	0.57	1.82	1.81
	605	255	0.028	0.022	1.84	0.81	0.88	16.0	11.18	1.36	0.65	1.92	2.00
	606	263	0.024	0.027	1.85	0.85	0.91	0.96	12.46	1.31	0.59	2.03	1.92
	607	289	0.021	0.021	1.91	0.92	0.99	1.01	10.74	1.36	0.76	2.08	2.12
	608	285	0.020	0.014	1.77	0.86	0.98	0.98	10.14	1.55	0.60	1.94	1.94
<u> </u>	609	278	0.028	0.026	1.87	0.84	0.99	0.94	10.23	1.23	0.61	2.02	2.03
<u> </u>	610	285	0.024	0.020	1.80	0.88	0.95	0.95	10.23	1.34	0.63	2.03	1.97
	611	299	0.026	0.024	1.89	16.0	1.00	0.97	12.03	1.47	0.70	2.10	2.02
	612	257	0.023	0.020	1.90	0.79	0.87	0.88	9.28	1.14	0.55	2.00	1.96
<u> </u>	613	319	0.022	rJ	1.85	0.96	1.02	1.01	12.50	1.43	0.70	2.17	2.14
	614	328	0.023	0.024	1.93	0.95	11.11	1.15	14.50	1.39	0.71	2.19	2.10
	615	282	0.026	0.026	1.86	0.87	1.01	0.97	9.76	1.31	0.61	1.96	1.88
<u> </u>	616	275	0.027	0.021	1.84	0.98	0.99	0.93	10.41	1.35	0.60	2.06	2.00
<u> </u>	617	234	0.019	0.020	1.64	0.76	0.82	0.79	8.01	1.11	0.55	1.81	1.85
	618	277	0.022	0.016	1.85	0.89	0.94	1.94	9.81	1.21	0.64	2.05	1.99
	619	290	0.025	0.022	1.91	0.91	1,03	1.04	11.63	1.40	0.64	2.05	2.02
	620	259	0.018	0.024	1.88	06.0	66.0	1.03	8.10	1.20	0.63	2.01	1.98
<u>-</u>	Mean	281.2	0.0	0224	1.863	0.892	0.965	65	10.653	1.323	0.638	2.018	8
~	s.D.	22.5	0.0	0033	0.040	0.066	0.067	67	1.511	0.123	0.059	0.139	61

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a = Damaged at autopsy

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**Reality** 

Weight     L       295     0.02       297     0.02       297     0.02       264     0.01       267     0.02       269     0.01       269     0.01       269     0.01       269     0.01       269     0.01       269     0.01       269     0.01       269     0.01       263     0.01       263     0.01       263     0.01       263     0.01       263     0.01       263     0.01       263     0.02       263     0.01       263     0.02       263     0.02       264     0.02       213     0.02       213     0.02       213     0.02       314     0.02       267     0.02       313     0.02       313     0.02		·	Adre	renals			Kidneys	leys				Теа	Testes
621         295         0.021         0.015         1.85         0.93         1.02         1.01           622         297         0.021         0.019         0.020         1.93         0.92         1.09         1.04           623         276         0.019         0.020         1.181         0.92         1.09         1.04           623         264         0.022         0.017         1.86         0.93         0.97         0.97           625         267         0.022         0.018         1.90         0.91         0.91         0.91           626         267         0.021         1.73         0.74         0.91         0.91           628         276         0.013         0.015         1.97         0.85         1.06         1.03           629         266         0.019         0.015         1.95         0.99         0.92         0.92           630         293         0.022         0.019         1.95         0.99         0.92         0.92           631         284         0.021         0.019         1.93         0.97         0.91         0.92           631         284         0.022         0.019 </th <th></th> <th></th> <th>ы </th> <th>ĸ</th> <th>Brain</th> <th>Heart</th> <th>Ч</th> <th>R.</th> <th>Liver</th> <th>Lungs</th> <th>Spleen</th> <th>ц</th> <th>æ</th>			ы 	ĸ	Brain	Heart	Ч	R.	Liver	Lungs	Spleen	ц	æ
297 $0.021$ $0.019$ $1.031$ $1.93$ $0.92$ $1.09$ $1.04$ 276 $0.019$ $0.020$ $1.81$ $0.86$ $1.05$ $1.09$ 264 $0.022$ $0.017$ $1.86$ $0.89$ $0.92$ $0.97$ 267 $0.022$ $0.018$ $1.90$ $0.91$ $0.97$ $0.91$ 276 $0.022$ $0.019$ $1.73$ $0.74$ $0.91$ $0.91$ 276 $0.027$ $0.019$ $1.73$ $0.74$ $0.91$ $0.91$ 276 $0.013$ $0.015$ $1.97$ $0.85$ $1.06$ $0.92$ 276 $0.013$ $0.015$ $1.76$ $0.83$ $1.06$ $0.92$ 276 $0.013$ $0.015$ $1.76$ $0.83$ $1.06$ $0.92$ 278 $0.013$ $0.015$ $1.97$ $0.87$ $0.93$ $0.92$ 284 $0.021$ $0.019$ $1.88$ $0.91$ $0.92$ $0.92$ 278 $0.022$ $0.019$ $1.82$ $0.91$ $0.92$ $0.92$ 278 $0.022$ $0.018$ $1.88$ $0.92$ $0.92$ $0.92$ 278 $0.022$ $0.018$ $1.88$ $0.92$ $0.92$ $0.92$ 278 $0.019$ $0.022$ $1.98$ $0.92$ $0.92$ $0.92$ 278 $0.019$ $0.022$ $1.98$ $0.92$ $0.92$ $0.92$ 278 $0.019$ $0.023$ $0.023$ $0.022$ $0.92$ $0.92$ 278 $0.019$ $0.023$ $0.023$ $0.023$ $0.92$ <td< td=""><td></td><td></td><td>0.021</td><td>0.015</td><td>1.85</td><td>0.93</td><td>1.02</td><td>1.01</td><td>11.71</td><td>1.22</td><td>0.60</td><td>1.98</td><td>1.90</td></td<>			0.021	0.015	1.85	0.93	1.02	1.01	11.71	1.22	0.60	1.98	1.90
276 $0.019$ $0.020$ $1.81$ $0.86$ $1.05$ $1.09$ $264$ $0.022$ $0.017$ $1.86$ $0.89$ $0.92$ $0.97$ $267$ $0.022$ $0.018$ $1.90$ $0.91$ $0.91$ $0.91$ $0.91$ $267$ $0.022$ $0.010$ $1.73$ $0.74$ $0.91$ $0.91$ $276$ $0.027$ $0.019$ $1.97$ $0.85$ $0.96$ $0.99$ $276$ $0.027$ $0.015$ $1.76$ $0.85$ $1.06$ $0.92$ $276$ $0.021$ $0.015$ $1.76$ $0.83$ $1.00$ $0.92$ $276$ $0.021$ $0.015$ $1.97$ $0.85$ $1.06$ $0.92$ $276$ $0.021$ $0.015$ $1.97$ $0.87$ $0.92$ $0.92$ $263$ $0.021$ $0.019$ $1.82$ $0.91$ $1.06$ $1.03$ $263$ $0.022$ $0.019$ $1.88$ $0.92$ $0.92$ $278$ $0.022$ $0.018$ $1.88$ $0.93$ $1.02$ $278$ $0.019$ $0.022$ $1.94$ $0.92$ $0.92$ $278$ $0.019$ $0.022$ $1.94$ $0.93$ $1.03$ $278$ $0.019$ $0.022$ $0.018$ $1.86$ $0.92$ $278$ $0.019$ $0.022$ $1.94$ $0.92$ $0.92$ $213$ $0.022$ $0.018$ $1.86$ $0.92$ $0.92$ $214$ $0.019$ $0.022$ $0.018$ $1.86$ $0.92$ $214$ $0.021$ $0.022$ $0.018$	62	_	0.021	0.019	1.93	0.92	1.09	1.04	11.50	1.21	0.60	1.94	1.94
264 $0.022$ $0.017$ $1.86$ $0.89$ $0.92$ $0.97$ $1.00$ $288$ $0.020$ $0.018$ $1.90$ $0.91$ $0.91$ $0.91$ $0.91$ $267$ $0.022$ $0.010$ $1.73$ $0.74$ $0.91$ $0.91$ $0.91$ $269$ $0.018$ $1.92$ $0.85$ $1.06$ $0.91$ $0.91$ $266$ $0.013$ $0.015$ $1.76$ $0.85$ $1.06$ $1.03$ $276$ $0.022$ $0.015$ $1.76$ $0.83$ $1.00$ $0.92$ $276$ $0.013$ $0.015$ $1.76$ $0.83$ $1.00$ $0.92$ $263$ $0.020$ $0.015$ $1.95$ $0.90$ $1.05$ $1.00$ $284$ $0.021$ $0.017$ $1.88$ $0.91$ $0.92$ $0.92$ $283$ $0.022$ $0.017$ $1.88$ $0.91$ $0.92$ $0.92$ $273$ $0.022$ $0.019$ $1.88$ $0.91$ $0.92$ $0.92$ $273$ $0.022$ $0.019$ $1.88$ $0.92$ $0.92$ $0.92$ $278$ $0.019$ $0.022$ $1.84$ $0.87$ $0.92$ $0.92$ $278$ $0.019$ $0.022$ $1.84$ $0.92$ $0.92$ $0.92$ $278$ $0.019$ $0.022$ $1.84$ $0.92$ $0.92$ $0.92$ $213$ $0.022$ $0.018$ $1.88$ $0.92$ $0.92$ $0.92$ $214$ $0.023$ $0.023$ $0.019$ $1.92$ $0.92$ $0.92$ $214$ $0.023$ <td< td=""><td>62</td><td></td><td>0.019</td><td>0.020</td><td>1.81</td><td>0.86</td><td>1.05</td><td>1.09</td><td>11.68</td><td>1.28</td><td>0.62</td><td>1.91</td><td>1.90</td></td<>	62		0.019	0.020	1.81	0.86	1.05	1.09	11.68	1.28	0.62	1.91	1.90
288         0.020         0.018         1.90         0.91         0.97         1.00           267         0.022         0.010         1.73         0.74         0.91         0.91           269         0.018         0.017         1.92         0.85         0.96         0.99           276         0.027         0.019         1.97         0.85         1.06         1.03           276         0.027         0.015         1.75         0.83         1.00         0.92           276         0.021         0.019         1.97         0.85         1.06         1.03           284         0.021         0.019         1.82         0.91         0.92         0.92           283         0.022         0.017         1.88         0.97         0.97         0.97           284         0.021         0.019         1.82         0.97         0.97         0.97           263         0.019         0.017         1.93         0.97         0.97         0.97           278         0.019         0.017         1.93         0.97         0.97         0.97           278         0.019         0.022         0.184         0.87         <	62		0.022	0.017	1.86	0.89	0.92	0.97	10.76	1.16	0.58	1.93	1.89
267 $0.022$ $0.010$ $1.73$ $0.74$ $0.91$ $0.91$ $269$ $0.018$ $0.017$ $1.92$ $0.85$ $0.96$ $0.99$ $276$ $0.027$ $0.019$ $1.97$ $0.85$ $1.06$ $1.03$ $276$ $0.020$ $0.015$ $1.97$ $0.83$ $1.00$ $0.92$ $266$ $0.013$ $0.015$ $1.97$ $0.83$ $1.00$ $0.92$ $284$ $0.020$ $0.017$ $1.82$ $0.91$ $0.93$ $0.92$ $284$ $0.021$ $0.017$ $1.88$ $0.91$ $0.97$ $0.87$ $263$ $0.019$ $0.017$ $1.88$ $0.91$ $0.97$ $0.87$ $263$ $0.019$ $0.017$ $1.88$ $0.91$ $0.97$ $0.87$ $263$ $0.019$ $0.017$ $1.88$ $0.97$ $0.97$ $0.87$ $278$ $0.019$ $0.017$ $1.93$ $0.95$ $0.92$ $0.90$ $278$ $0.019$ $0.012$ $1.01$ $1.03$ $1.01$ $278$ $0.016$ $0.018$ $1.86$ $0.95$ $0.90$ $0.88$ $278$ $0.016$ $0.018$ $1.86$ $0.93$ $1.01$ $214$ $0.022$ $0.018$ $1.86$ $0.93$ $1.01$ $214$ $0.022$ $0.018$ $1.86$ $0.93$ $1.01$ $214$ $0.022$ $0.018$ $1.86$ $0.93$ $1.01$ $214$ $0.022$ $0.019$ $1.92$ $0.93$ $1.01$ $214$ $0.022$ $0.019$ $1.$	62		0.020	0.018	1.90	0.91	0.97	1.00	ŋ	1.38	0.60	1.95	1.94
269       0.018       0.017       1.92       0.85       0.96       0.99         276       0.027       0.019       1.97       0.85       1.06       1.03         266       0.013       0.015       1.76       0.83       1.00       0.92         293       0.020       0.015       1.76       0.83       1.00       0.92         293       0.021       0.019       1.82       0.91       0.92       0.92         293       0.021       0.017       1.88       0.97       0.97       0.97         263       0.022       0.017       1.88       0.97       0.97       0.97         264       0.022       0.018       1.88       0.97       0.90       0.93         278       0.019       0.022       1.93       0.95       0.90       0.96         278       0.019       0.022       1.86       0.95       0.90       0.93       1.01         264       0.019       0.023       1.98       0.95       0.90       0.98       1.01         214       0.024       0.023       1.98       0.95       0.90       0.93       1.01         264       0.019	62		0.022	0.010	1.73	0.74	0.91	0.91	9.54	1.17	0.60	1.71	1.86
276 $0.027$ $0.019$ $1.97$ $0.85$ $1.06$ $1.03$ $266$ $0.013$ $0.015$ $1.76$ $0.83$ $1.00$ $0.92$ $293$ $0.020$ $0.015$ $1.95$ $0.90$ $1.05$ $1.00$ $293$ $0.021$ $0.019$ $1.82$ $0.91$ $0.93$ $0.92$ $284$ $0.021$ $0.017$ $1.88$ $0.91$ $0.93$ $0.92$ $263$ $0.019$ $0.017$ $1.88$ $0.97$ $0.87$ $0.97$ $263$ $0.022$ $0.018$ $1.88$ $0.90$ $1.06$ $1.03$ $278$ $0.019$ $0.022$ $1.918$ $0.90$ $1.06$ $1.03$ $278$ $0.019$ $0.022$ $1.84$ $0.85$ $1.03$ $1.01$ $278$ $0.019$ $0.022$ $1.84$ $0.95$ $0.90$ $0.88$ $214$ $0.019$ $0.022$ $1.84$ $0.85$ $1.03$ $1.01$ $213$ $0.023$ $0.018$ $1.86$ $0.95$ $0.90$ $0.88$ $214$ $0.016$ $0.018$ $1.86$ $0.95$ $0.90$ $0.88$ $214$ $0.023$ $0.023$ $1.92$ $0.93$ $1.01$ $1.01$ $213$ $0.022$ $0.019$ $1.86$ $0.93$ $1.02$ $1.01$ $214$ $0.023$ $0.019$ $1.90$ $0.93$ $1.01$ $1.10$ $213$ $0.021$ $0.019$ $1.95$ $0.93$ $1.01$ $1.00$ $213$ $0.021$ $0.019$ $1.85$ $0.76$ <	62		0.018	0.017	1.92	0.85	0.96	0.99	10.43	1.30	0.62	1.92	1.96
266         0.013         0.015         1.76         0.83         1.00         0.92           293         0.020         0.015         1.95         0.90         1.05         1.00           284         0.021         0.019         1.82         0.91         1.05         1.00           283         0.021         0.017         1.82         0.91         0.93         0.92           263         0.019         1.88         0.87         0.97         0.87           263         0.022         0.018         1.88         0.90         1.03           263         0.022         0.018         1.88         0.90         1.03           278         0.022         0.018         1.88         0.90         1.03           278         0.019         0.022         1.84         0.85         1.01           264         0.023         1.86         0.95         0.90         0.88           214         0.023         1.92         0.93         1.01         1.01           213         0.023         0.019         1.86         0.93         1.07           314         0.021         0.019         1.95         0.93         1.1	62		0.027	0.019	1.97	0.85	1.06	1.03	10.52	1.17	0.57	1.92	1.87
293       0.020       0.015       1.95       0.90       1.05       1.00         284       0.021       0.019       1.82       0.91       0.93       0.92         263       0.019       0.017       1.88       0.87       0.97       0.87         263       0.019       0.017       1.98       0.95       0.97       0.92         263       0.022       0.018       1.88       0.90       1.03       0.97         278       0.022       0.018       1.88       0.90       1.06       1.03         278       0.019       0.022       1.84       0.85       1.03       1.01         278       0.019       0.022       1.84       0.85       1.03       1.01         278       0.016       0.184       0.85       1.03       1.01         264       0.023       1.84       0.85       0.90       0.88         314       0.023       0.015       1.85       0.93       1.07         313       0.021       0.019       1.96       0.93       1.07         313       0.021       0.019       1.85       0.93       1.01       1.00         267       <	62	<u>~</u>	0.013	0.015	1.76	0.83	1.00	0.92	9.9	1.49	0.60	1.82	1.83
284       0.021       0.019       1.82       0.91       0.93       0.92         263       0.019       0.017       1.88       0.87       0.97       0.87         263       0.019       0.017       1.88       0.87       0.92       0.90         264       0.022       0.018       1.93       0.95       0.92       0.90         278       0.019       0.022       1.84       0.85       1.03       1.01         278       0.016       0.018       1.86       0.95       0.90       1.06         278       0.016       0.018       1.86       0.95       0.90       0.88         279       0.016       0.018       1.86       0.93       1.01         214       0.023       0.023       1.92       0.93       1.07         314       0.023       0.019       1.92       0.93       1.11       1.12         313       0.021       0.019       1.85       0.93       1.10       1.00         267       0.021       0.019       1.85       0.76       1.01       1.00	63	-	0.020	0.015	1.95	06.0	1.05	1.00	10.85	1.31	0.63	2.15	2.02
263       0.019       0.017       1.88       0.87       0.97       0.87         263       0.022       0.017       1.93       0.95       0.90       0.90         294       0.022       0.018       1.93       0.95       0.92       0.90         294       0.022       0.018       1.88       0.90       1.06       1.03         278       0.019       0.022       1.84       0.85       1.03       1.01         278       0.019       0.022       1.84       0.85       1.03       1.01         278       0.016       0.018       1.86       0.95       0.90       0.88         264       0.016       0.023       1.92       0.93       1.08       1.07         314       0.023       0.015       1.85       0.96       1.11       1.12         313       0.020       0.019       1.90       0.93       1.12       1.10         267       0.021       0.019       1.85       0.76       1.01       1.00	63		0.021	0.019	1.82	16.0	0.93	0.92	12.65	1.25	0.66	1.94	1.87
263       0.022       0.017       1.93       0.95       0.92       0.90         294       0.022       0.018       1.88       0.90       1.06       1.03         278       0.019       0.022       1.84       0.85       1.03       1.01         278       0.019       0.022       1.84       0.85       1.03       1.01         278       0.016       1.84       0.85       1.03       1.01         264       0.016       1.86       0.95       0.90       0.88         299       0.024       0.023       1.92       0.93       1.01       1.01         314       0.023       0.015       1.85       0.96       1.11       1.12       1.12         313       0.020       0.019       1.90       0.93       1.12       1.10         267       0.021       0.019       1.85       0.76       1.01       1.00	63		0.019	0.017	1.88	0.87	0.97	0.87	10.21	1.09	0.53	1.85	1.90
294       0.022       0.018       1.88       0.90       1.06       1.03         278       0.019       0.022       1.84       0.85       1.03       1.01         264       0.016       0.018       1.86       0.95       0.90       0.88         299       0.023       1.86       0.93       1.08       1.07         314       0.023       0.195       1.85       0.96       1.11       1.12         313       0.020       0.019       1.90       0.93       1.12       1.10         313       0.021       0.019       1.95       0.93       1.12       1.10         267       0.021       0.019       1.85       0.76       1.01       1.00	- - - - - - - - - - - - - - - - - - -		0.022	0.017	1.93	0.95	0.92	06.0	10.05	1.18	0.60	2.11	2.17
278       0.019       0.022       1.84       0.85       1.03       1.01         264       0.016       0.018       1.86       0.95       0.90       0.88         299       0.024       0.023       1.92       0.93       1.08       1.07         314       0.023       0.015       1.85       0.96       1.11       1.12         313       0.020       0.019       1.90       0.93       1.12       1.10         267       0.021       0.019       1.85       0.76       1.01       1.00			0.022	0.018	1.88	06.0	1.06	1.03	12.08	1.16	0.63	2.02	1.96
264     0.016     0.018     1.86     0.95     0.90     0.88       299     0.024     0.023     1.92     0.93     1.08     1.07     1       314     0.023     0.015     1.85     0.96     1.11     1.12     1       313     0.020     0.019     1.90     0.93     1.12     1       267     0.021     0.019     1.85     0.76     1.01     1.00     1	63		0.019	0.022	1.84	0.85	1.03	1.01	11.69	1.14	0.62	1.96	2.05
299     0.024     0.023     1.92     0.93     1.08     1.07       314     0.023     0.015     1.85     0.96     1.11     1.12       313     0.020     0.019     1.90     0.93     1.12     1.10       267     0.021     0.019     1.85     0.76     1.01     1.00	63		0.016	0.018	1.86	0.95	0.90	0.88	8.68	1.13	0.56	1.92	1.87
314         0.023         0.015         1.85         0.96         1.11         1.12           313         0.020         0.019         1.90         0.93         1.12         1.10           267         0.021         0.019         1.85         0.76         1.01         1.00	- 63		0.024	0.023	1.92	0.93	1.08	1.07	12.62	1.35	0.61	2.08	2.13
313         0.020         0.019         1.90         0.93         1.12         1.10           267         0.021         0.019         1.85         0.76         1.01         1.00	63		0.023	0.015	1.85	0.96	1.11	1.12	12.09	1.48	0.68	1.93	1.89
267 0.021 0.019 1.85 0.76 1.01 1.00	e3	_	0.020	0.019	1.90	0.93	1.12	1.10	12.11	1.36	0.63	1.99	1.97
	64		0.021	0.019	1.85	0.76	1.01	1.00	12.30	1.34	0.59	1.90	1.85
Mean 281.5 0.0191 1.871 0.885 1.001 11.074			0	1610	1.871	0.885	1.0	01	11.074	1.259	0.607	1.943	13
S.D. 16.7 0.0032 0.061 0.060 0.071 1.205				0032	0.061	0.060	0.0	71	1.205	0.115	0.033	0.094	94

a = Omitted from mean due to erroneous data

Q 33

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Dose	Antmal	A DO	Adrei	nals			Kidneys	еув				Testes	tes
day/ Sex	No.	Weight	ы	æ	Brain	Heart	ы	ж	Liver	Irungs	Spleen	ц	æ
1503	641	287	0.021	0.021	1.95	\$6.0	06.0	0.94	10.10	1.22	0.64	2.06	2.01
	642	305	0.020	0.019	1.87	0.91	1.00	1.01	14.84	1.27	0.66	2.04	2.04
	643	302	0.014	0.017	1.94	0.93	1.09	1.01	11.74	1.44	0.55	2.02	2.00
	644	269	0.021	0.019	1.86	0.94	0.97	0.92	9.83	1.43	0.58	2.10	2.06
	646	265	0.015	0.016	1.85	0.74	0.94	0.94	11.48	1.25	0.56	1.83	1.84
	647	275	0.018	0.018	1.84	0.85	0.86	0.88	9.81	1.50	0.56	1.97	2.03
	648	292	0.025	0.024	1.91	1.00	1.12	1.10	10.90	1.40	0.64	2.05	1.86
	649	271	0.018	0.017	1.90	0.84	16.0	0.87	9.89	1.15	0.63	1.87	1.81
	650	269	0.020	0.019	1.89	0.83	0.95	0.93	10.23	1.26	0.51	1.97	1.94
	651	276	0.019	0.020	1.88	0.80	0.92	0.89	11.01	1.29	0.57	1.96	1.96
	652	265	0.020	0.020	1.87	0.89	0.95	0.95	11.23	1.11	0.57	1.90	1.89
	653	278	0.023	0.020	1.92	0.82	0.99	1.01	12.22	1.22	0.60	1.92	1.98
	654	258	0.021	0.014	1.83	0.76	0.94	0.89	9.71	1.20	0.55	1.70	1.72
	655	278	0.019	0.017	1.88	0.85	0.94	0.98	10.89	1.30	0.59	1.88	1.98
	656	290	0.025	0.022	1.85	0.95	1.02	0.92	11.95	1.25	0.62	1.85	1.83
	657	256	0.020	0.019	1.91	0.84	0.84	0.87	10.01	1.08	0.58	1.78	1.84
	658	264	0.018	0.013	1.82	0.81	0.88	0.86	8.80	1.13	0.56	1.90	1.82
	629	239	0.016	0.016	1.77	0.73	0.82	0.86	9.46	1.16	0.49	1.71	1.75
	660	247	0.020	0.018	1.87	0.83	0.86	0.85	9.01	1.25	0.55	2.01	1.93
	Mean	272.9	0.0	0610	1.874	0.856	0.936	36	10.690	1.258	0.579	1.916	16
	s.D.	17.3	0.0	0028	0.044	0.075	0.072	72	1.402	0.116	0.044	0.107	07

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Dose mg/kg/	Animal	Body	Adre	enals	Brain	Heart	Kidneys	eys	Ltver	Lungs	Spleen	Ter	Testes
day/ Sex	•0v	weight	ы	a			<u>ц</u>	æ				ы 	æ
4503	661	272	0.012	0.011	1.88	0.85	0.89	0.86	10.07	1.44	0.57	1.83	1.88
	662	275	0.019	0.019	1.92	0.84	0.88	06.0	10.72	1.17	0.56	1.89	1.89
	663	317	0.023	0.021	1.90	1.03	1.12	1.08	12.33	1.50	0.67	2.03	2.08
	664	281	0.020	0.020	1.94	0.92	0.98	1.06	10.95	1.47	0.63	2.03	2.06
	665	286	0.017	0.019	1.90	06.0	0.98	0.87	10.35	1.31	0.63	1.87	1.91
	666	281	0.018	0.019	1.88	0.80	0.94	0.90	10.33	1.37	0.59	1.94	1.94
	667	267	0.021	0.021	1.79	0.82	0.89	06.0	9.29	1.61	0.56	1.68	1.81
	668	268	0.021	0.019	1.84	0.87	0.94	0.93	10.18	1.37	0.58	1.84	1.74
	669	290	0.022	0.025	1.91	0.82	0.99	0.97	10.07	1.29	0.64	1.91	1.89
	670	272	0.025	0.025	1.89	0.92	0.92	16.0	9.66	1.29	0.53	2.01	2.00
	671	222	0.016	0.014	1.81	0.70	0.76	0.76	8.04	1.08	0.46	1.84	1.70
	672	261	0.022	0.020	1.71	0.89	1.00	1.05	9.84	1.27	0.57	1.93	1.87
	673	268	0.018	0.020	1.87	06.0	0.92	0.95	10.68	1.32	0.62	1.96	1.98
	674	290	0.024		1.92	0.89	1.02	0.99	12.66	1.44	0.63	2.08	2.03
	675	288	0.022	0.021	1.90	0.89	1.06	1.04	11.29	1.28	0.53	1.97	1.90
	676	261	0.018	0.021	1.93	0.95	0.99	1.02	11.32	1.29	0.54	1.95	1.90
	677	243	0.026	0.027	1.77	0.83	0.80	0.85	9.54	1.32	0.49	1.77	1.77
	678	225	0.022	0.018	1.83	0.69	0.82	0.81	8.17	1.06	0.55	1.83	1.75
	679	281	0.020	0.012	1.84	0.85	0.91	0.89	10.69	1.38	0.54	q	1.98
	680	269	0.021	0.019	1.87	0.84	0.91	0.94	10.28	1.27	0.54	1.96	1.86
	Mean	270.9	0.6	0.0199	1.865	0.860	0.935	35	10.323	1.327	0.572	1.904	04
	s.D.	22.0	0.0	.0036	0.059	0.077	0.085	85	1.137	0.132	0.053	0.102	02
	a = Damé	Damaged at autopsy	topsy										
	b = Omit	Omitted from mean	I.	robably (	probably erroneous data	data							

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APPENDIX	

Dose ma/ka/	Antmal	Rode	Adre	Adrenals			Kidı	Kidneys				Te	Testes
day/	No.	Weight	ц 	×.	Brain	Heart	ц 	æ	Liver	Lungs	Spleen	L	æ
13505	681	289	0.018	0.016	1.89	0.89	0.85	06.0	10.57	1.39	0.58	1.99	1.93
_	682	281	0.019	0.018	1.85	0.88	16.0	16.0	9.72	1.19	0.57	1.91	1.85
	683	260	0.018	0.017	2.03	0.82	06.0	0.88	10.34	1.13	0.45	1.94	1.83
	684	268	0.025	0.019	1.94	0.85	0.95	0.92	9.67	1.53	0.51	1.98	1.94
	685	287	0.019	0.020	1.88	0.87	1.02	1.02	12.46	1.34	0.62	1.95	1.94
	686	280 <sup>a</sup>	0.023	0.021	1.84	0.86	0.98	0.96	11.34	1.37	0.56	2.08	1.92
	687	221	0.016	0.016	1.76	0.66	0.75	0.73	7.99	1.35	0.66	1.71	1.64
	688	224	0.022	0.022	1.81	0.83	0.82	0.86	9.17	1.15	0.49	1.75	1.74
	689	297	0.016	0.017	1.95	0.97	1.02	0.98	10.61	1.43	0.64	1.98	1.88
	690	297	0.020	0.020	1.84	0.89	1.00	0.95	10.18	1.34	0.63	2.12	2.00
	691	259	0.018	0.018	1.90	0.76	0.81	0.82	8.47	1.20	0.51	1.85	1.86
	692	258	0.027	0.023	1.90	0.89	96.0	0.92	10.43	1.47	0.52	1.99	1.92
	693	247	0.015	0.011	1.88	0.81	0.88	0.86	8.90	1.16	0.53	1.86	1.20
_	694	292	0.020	0.018	1.90	0.88	1.02	0.98	11.57	1.34	0.59	1.76	1.90
	695	243	0.017	0.016	1.82	0.84	0.82	0.87	9.41	1.13	0.51	1.77	1.83
	696	254	0.024	0.020	1.89	0.85	0.89	0.84	9.59	1.15	0.53	1.89	1.75
	697	261	0.017	0.018	1.80	0.80	0.82	0.86	9.02	1.18	0.49	1.89	1.92
	698	264	0.018	0.016	1.90	0.82	0.95	0.93	10.57	1.16	0.54	2.01	1.97
	669	259	0.015	0.017	1.89	0.78	0.94	0.88	9.48	1.26	0.54	1.85	1.76
	700	286	0.021	0.016	1.90	0.92	0.97	1.07	12.14	1.47	0.60	2.02	2.02
	Mean	266.4	0.(	0.0187	1.879	0.844	0.910	10	10.082	1.287	0.554	1.878	78
	S.D.	22.3	0.0	1031	0.059	0.065	0.077	17	1.177	0.131	0.057	0.152	52

a = PM room weight missing - MAM weight used

Balance

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mg/rg/ day/         Mitmat         Body           day/         No.         Weight           Sex         701         253           40003         701         253           702         284         703         258           703         703         258         701           703         703         258         701           705         705         265         71           705         705         265         703									-			
701 702 703 704 705 705		•		Brain	Heart	•	6	Liver	Lungs	Spleen		(
701 702 703 704 705		4	×			Ŀ	X				н	<b>e</b> .
		0.018	0.017	1.86	0.74	0.85	0.80	9.25	1.83	0.55	1.81	1.84
	_	0.020	0.019	1.92	0.85	0.90	0.90	9.69	1.25	0.58	2.13	2.08
<u></u>		0.017	0.017	1.92	0.84	0.90	0.93	10.52	1.17	0.58	1.85	1.84
		0.019	0.016	1.88	0.93	0.96	0.96	11.22	1.56	0.59	1.87	1.87
		0.018	0.015	1.85	0.83	0.93	0.87	10.26	1.29	0.55	2.00	1.94
		0.016	0.017	1.91	0.81	96.0	0.93	10.44	1.33	0.60	1.94	1.93
		0.020	0.018	1.86	0.80	0.87	0.82	9.54	1.35	0.52	1.96	1.93
708 25		0.022		1.85	0.84	16.0	06.0	8.89	1.21	0.50	1.94	1.89
		0.014	0.012	1.82	0.80	0.83	0.88	9.37	1.21	0.55	1.83	1.80
		0.019	0.016	1.81	0.76	0.85	0.81	9.08	1.06	0.48	1.87	1.83
		0.019	0.021	1.91	0.92	0.97	0.89	11.07	1.39	0.62	1.97	1.98
		0.017	0.018	1.79	0.76	0.86	0.82	11.77	1.11	0.50	I.78	1.70
713 25		0.018	0.011	1.88	0.73	0.87	06.0	11.18	1.32	0.51	1.87	1.81
		0.024	0.019	1.88	0.79	0.83	0.78	8.11	1.10	0.48	1.95	1.94
		0.021	0.019	1.91	0.84	0.89	16.0	11.12	1.15	0.50	1.83	1.83
	242	0.021	0.021	1.91	0.79	0.85	0.88	9.89	1.28	0.45	1.97	1.91
		0.015	0.014	1.91	0.82	0.89	0.89	9.75	1.25	0.54	1.84	1.80
		0.020	0.017	1.81	0.75	0.87	0.89	8.99	1.15	0.49	1.82	1.78
719 25		0.019	0.018	1.90	0.85	0.85	0.80	8.67	1.16	0.53	2.02	1.90
	266	0.018	0.016	1.92	0.88	0.96	0.97	10.57	1.25	0.59	1.94	1.83
Mean 25	257.1	0.01	0178	1.875	0.817	0.883	33	9.969	1.271	0.536	1.891	1
S.D. 1	13.1	0:00	0026	0.042	0.055	0.050	50	1.001	0.175	0.047	0.086	و

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a = Damaged at autopsy

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N.C.

Females

Dose mq/kq/	Animal	Body	Adren	nals			Kidneys	leys				Ovaries	ies
day/ Sex	.ov	Weight	г	р <u>с</u> ,	Brain	неагс	-1	ĸ	LIVEL	sbung	spieen	ч	a
50	722	167	a	0.021	1.69	0.59	0.63	0.44	5.02	1.02	0.44	0.022	0.023
	723	167	0.030	0.029	1.73	0.64	0.68	0.68	5.89	0.85	0.41	0.035	C'0'0
	724	166	0.026	0.025	1.74	0.59	0.62	0.64	5.01	0.86	0.38	0.024	0.040
	725	159	0.022	0.024	1.75	0.55	0.56	0.58	4.69	0.79	0.37	0.024	0.035
	726	146	0.018	0.017	1.61	0.52	0.56	0.54	4.57	0.72	0.36	0.023	0.021
	727	162	0.017	0.020	1.76	0.59	0.68	0.65	5.12	1.18	0.45	0.029	0.027
	728	161	0.025	0.022	1.68	0.60	0.62	0.60	5.00	1.16	0.39	0.027	0.028
	729	183	0.025	0.024	1.76	0.61	0.69	0.71	5.78	0.95	0.49	0.028	0.024
	730	144	0.018	0.018	1.66	0.51	0.59	0.57	4.63	0.72	0.40	0.028	0.029
	731	186	0.016	0.019	1.74	0.66	0.68	0.68	6.85	1.18	0.46	0.028	0.027
	732	159	0.019	0.019	1.70	0.55	0.57	0.57	5.40	0.83	0.38	0.022	0.026
	733	168	0.023	0.024	1.60	0.57	0.63	0.64	6.15	1.09	0.37	0.029	0.026
	734	185	0.018	0.019	1.71	0.62	0.71	0.70	7.29	1.06	0.41	0.027	0:030
	735	160	0.025	2.020	1.71	0.64	0.61	0.60	5.40	0.92	0.36	0.019	0.027
	736	160	a	0.025	1.64	0.58	0.63	0.59	6.95	16.0	0.48	0:030	0.030
	737	169	0.026	0.023	1.74	0.55	0.63	0.60	5.07	0.84	0.41	0.043	0.022
	738	175	0.020	0.020	1.71	0.62	0.61	0.62	6.00	0.99	0.40	0.025	0.027
	739	171	0.020	0.020	1.66	0.60	0.61	0.59	5.64	0.97	0.40	0.023	0.019
	740	163	0.021	0.023	1.79	0.65	0.63	0.62	4.82	0.93	0.44	0.026	0.024
	Mean	165.8	0.0	0.0217	1.704	0.592	0.625	25	5.541	0.946	0.411	0.0	0.0273
	s.D.	11.2	0.0	0.0034	0.052	0.042	0.045	45	0.811	0.143	0.039	0.0	0.0054

Not a constrained

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a = Damaged at autopsy

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Dose			Adrei	renals			Kidneys	eys				Ovaries	ies
mg/kg/ day/ Sex	An Ima I No.	Body Weight	ы	<u>م</u>	Brain	Heart	Ч	×	Liver	Lungs	Spleen	ч	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
505	741	181	0.029	0.027	1.80	0.61	0.73	0.72	6.40	1.02	0.47	0.043	0.041
	742	157	0.025	0.024	1.81	0.59	0.64	0.64	5.29	0.82	0.40	0.037	0.022
	743	171	0.024	0.025	1.78	0.62	0.70	0.69	6.59	0.94	0.43	0.028	0.021
	744	162	0.025	0.023	1.79	0.59	0.71	0.72	6.56	0.90	0.39	0.023	0.031
	745	167	0.025	0.021	1.81	0.58	0.62	0.61	5.10	0.96	0.44	0.024	0.030
	746	167	0.015	0.019	1.77	0.59	0.67	0.67	5.22	0.88	0.42	0.025	0.020
	747	161	0.027	0.031	1.80	0.58	0.66	0.67	6.36	0.93	0.44	0.033	0.036
	748	171	0.029	0.025	1.77	0.64	0.64	0.65	5.02	0.92	0.42	0.028	0.029
	749	171	0.025	0.025	1.70	0.60	0.61	0.60	5.60	0.99	0.39	0.031	0.030
	750	171	0.020	0.021	1.75	0.54	0.58	0.58	5.86	0.77	0.35	0.032	0.026
	751	165	0.026	0.026	1.81	0.60	0.69	0.65	5,58	0.86	0.41	0.033	0.027
	752	156	0.031	0.025	1.60	0.62	0.61	0.60	5.38	0.86	0.40	0.026	0.027
	753	166	0.024	0.021	1.74	0.58	0.68	0.65	6.04	0.88	0.41	0.036	0.032
	754	179	0.029	0.027	1.77	0.68	0.70	0.68	5.69	1.01	0.48	0.023	0.034
	755	166	0.025	0.030	1.67	0.60	0.62	0.62	5.97	0.94	0.40	0.025	0.023
	756	158	0.029	0.022	1.75	0.57	0.64	0.64	6.11	0.88	0.40	0.026	0.029
	757	169	0.026	0.025	1.70	0.55	0.62	0.62	5.31	0.91	0.40	0.020	0.023
	758	169	0.040	đ	1.74	0.57	0.58	0.55	4.86	1.00	0.40	0.037	0.026
	759	180	0.026	0.022	1.84	0.65	0.66	0.65	5.45	06.0	0.53	0.037	0.031
	760	146	0.018	0.017	1.68	0.72	0.62	0.61	5.94	0.85	0.38	0.017	0.020
	Mean	166.7	0.0	.0250	1.739	0.604	0.645	<b>t</b> 5	5.717	0.911	0.418	0.0	0.0286
	S.D.	8.5	0.0	.0044	0.103	0.043	0.043	13	0.521	0.065	0.040	0.0	0.0061

a = Damaged at autopsy

Dose Dose	l em t ut	Body	Adrer	nals			Ridneys	leys				Oval	Ovaries
day/ day/ Sex	No.	Weight	د 	æ	Brain	Heart	<u>ل</u>	~	Liver	Lungs	Spleen	ц	ĸ
1159	761	152	0.026	0.025	1.72	0.51	0.57	0.60	4.86	0.78	0.37	0.027	0.031
	762	173	0.022	0.020	1.74	0.59	0.66	0.69	5.02	0.96	0.43	0.030	0.028
	763	166	0.029	0.029	1.78	0.57	0.67	0.65	6.09	0.88	0.45	0.045	0.046
	764	166	0.025	0.025	1.76	0.58	0.64	0.59	5.24	0.98	0.38	0.020	0.016
	765	163	0.024	0.025	1.80	0.57	0.70	0.67	5.53	0.95	0.39	0.029	0.044
	766	153	0.021	0.021	1.81	0.59	0.61	0.62	5.11	0.82	0.42	0.021	0.020
	767	151	0.027	0.020	1.70	0.58	0.61	0.62	4.87	0.86	0.43	0.029	0.029
	768	182	0.033	0.030	1.78	0.66	0.74	0.69	6.25	1.01	0.48	0.034	0.029
	769	162	0.027	0.025	1.71	0.58	0.60	0.56	5.72	0.86	0.38	0.024	0.029
	770	171	0.029	0.023	1.78	0.58	0.67	0.65	6.53	0.97	0.44	0.030	0.028
	171	173	0.025	0.027	1.75	0.64	0.66	0.67	6.65	0.90	0.41	0.020	0.034
	772	170	0.029	0.028	1.82	0.66	0.70	0.74	6.17	0.99	0.43	0.023	0.043
	773	157	0.027	0.028	1.79	0.56	0.64	0.62	6.48	1.07	rđ	0.025	0.030
	774	163	0.033	0.028	1.75	0.60	0.65	0.67	6.31	0.93	0.40	0.032	0.031
	775	169	0.028	0.026	1.78	0.60	0.68	0.68	6.90	0.77	0.38	0.029	0.028
	776	160	0.025	0.025	1.81	0.57	0.61	0.56	5.45	0.85	0.42	0.029	0.023
	777	168	0.029	0.026	1.72	0.57	0.61	0.61	5.36	1.05	0.45	0.030	0.036
	778	174	0.023	0.024	1.78	0.59	0.69	0.65	6.37	0.88	0.40	0.034	0.030
	179	180	0.032	0.029	1.82	0.58	0.70	0.68	6.60	16.0	0.42	0.031	0.033
	780	167	0.032	0.025	1.81	0.61	0.68	0.69	6.53	1.04	0.40	0.027	0.033
	Mean	166.0	0.0	1264	1.771	0.590	0.650	50	106.3	0.923	0.415	0.0	0.0298
	s.D.	8.6	0.0	1033	0.038	0.034	0.045	45	0.668	0.087	0.029	0.0	0.0067

a = Omitted from mean due to erroneous data

Dose ma/ka/	Animal	Bodv	Adre	enals			Kidneys	leys				Ovaries	ies
day/ Sex	No.	Weight	ц.	œ.	Brain	Heart	-1	æ	Liver	Lungs	Spleen	ц	ĸ
2709	781	162	0.032	0.034	1.79	0.59	0.65	0.67	6.02	0.92	0.41	0.035	0.036
	782	165	0:030	0.027	1.72	0.62	0.68	0.68	5.63	0.93	0.49	0.027	0.029
	783	169	0.029	0.023	1.83	0.61	0.68	0.68	6.22	0.88	0.44	0.026	0.031
	784	164	0.039	0.030	1.75	0.59	0.67	0.66	5.62	1.02	0.38	0.031	0.036
	785	167	0.021	0.021	1.75	0.53	0.58	0.58	4.88	0.95	0.39	0.012	0.030
	786	164	0.028	0.029	1.82	0.59	0.68	0.67	5.74	0.94	0.44	0.034	0.032
	787	158	0.020	0.020	1.76	0.59	0.60	0.56	5.87	1.27	0.40	0.017	0.025
	788	169	0.029	0.023	1.76	0.62	0.69	0.67	5.65	46.0	0.47	0.021	0.034
	789	152	ĸ	0.024	1.73	0.56	0.60	0.63	5.27	0.86	0.40	0.024	0.026
	790	120	0.012	0.009	1.71	0.45	0.46	0.48	3.66	0.82	0.25	0.013	0.011
	167	156	0.024	0.021	1.83	0.53	0.61	0.62	5.30	1.00	0.40	0.021	0.022
	792	159	0.028	0.025	,a	0.54	0.63	0.63	5.26	1.28	0.44	0.021	0.028
	193	160	0.020	0.023	1.74	0.57	0.60	0.58	5.59	6.03	0.37	0.028	0.020
	794	142	0.020	0.020	169	0.48	0.58	0.58	4.59	0.81	0.36	0.029	0.030
	795	172	0.029	0.036	1.79	0.66	0.69	0.71	6.63	1.18	0.42	0.029	0.029
	796	179	0.028	0.017	1.82	0.63	0.72	0.77	6.49	0.98	0.42	0.028	0.032
	797	163	0.018	0.016	1.78	0.58	0.65	0.62	6.13	0.92	0.42	0.032	0.027
	798	153	0.023	0.023	1.81	0.57	0.62	0.61	5.55	0.94	0.44	0.027	0.030
	662	161	0.015	0.017	1.75	0.58	0.62	0.60	5.62	0.89	0.43	0.027	0,023
	800	180	0.030	0.027	1.81	0.57	0.67	0.64	7.42	0.92	0.45	0.042	0.034
	Mean	160.8	0.0	.0242	1.771	0.573	0.633	33	5.646	0.969	0.411	0.0	0.0272
	s.D.	13.0	0.0	.0064	0.043	0.050	0.059	59	0.796	0.130	0.050	0.0	0.0067
				1									

a = Damaged at autopsy

b = Omitted from mean due to erroneuous data

(continued)
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APPENDIX

Dose mg/kg/	Animal	Body	Adren	nals		:	Kidneys	eys				Ovaries	ea
day/ Sex	No.	Welght	ц.	ĸ	Brain	неагс	<u>ب</u>	æ	Liver	rungs	spleen	г	ĸ
6209	801	163	0.011	0.015	1.75	0.55	0.68	0.65	6.25	10.0	0.45	0.032	0.027
	802	172	0.02 <sup>a</sup>	0.02 <sup>a</sup>	1.77	0.62	0.61	0.61	7.29	1.17	0.45	0.04ª	0.03 <sup>a</sup>
	803	160	0.032	0.030	1.84	0.61	0.67	0.68	6.20	1.00	0.42	0.026	0.040
	804	158	0.027	0.024	1.76	0.55	0.62	0.59	6.20	0.83	0.38	0.028	0.019
	805	153	0.019	0.011	1.69	0.48	0.57	0.54	4.59	0.83	0.39	0.016	0.024
_	806	164	0.024	0.022	1.82	0.55	0.60	0.62	6.30	06.0	0.43	0.037	0.035
	807	148	0.033	0.030	1.77	0.55	0.65	0.62	5.55	0.98	0.42	0.033	0.036
	808	160	A	0.022	1.78	0.50	0.67	0.65	5.02	0.89	0.42	0.021	0.036
	608	166	0.019	0.019	1.85	0.55	0.65	0.65	5.33	1.08	0.39	0.028	0.025
	810	148	0.020	0.017	1.67	0.59	0.60	0.56	5.91	0.94	0.39	0.032	0.023
	811	143	0.017	0.020	1.68	0.49	0.60	0.56	5.31	0.77	0.32	0.012	0.020
	812	159	0.026	0.024	1.81	0.56	0.64	0.66	5.72	1.02	0.41	0.020	0.026
	813	147	0.031	0.030	1.79	0.56	0.67	0.73	5.11	1.06	0.41	0:030	0.028
	814	147	0.014	0.014	1.79	0.48	0.54	0.55	4.70	1.05	0.34	0.015	0.019
	815	151	0.022	0.022	1.65	0.55	0.65	0.64	5.59	1.01	0.41	0.030	0.021
	816	173	0.033	0.028	1.73	0.61	0.70	0.69	6.35	1.18	0.47	0.030	0.038
	817	168	0.027	0.026	1.75	0.59	0.66	0.66	6.52	96*0	0.47	0.025	0.027
	818	182	0.029	0.027	1.78	0.63	0.75	0.75	6.88	1.05	0.48	0.032	0.034
	819	149	0.026	0.019	1.73	0.53	0.11	0.60	4.91	0.77	0.39	0.022	0.018
	820	168	٩	0.028	1.78	0.61	0.71	0.68	6.52	0.88	0.42	0.032	0.048
	Mean	159.0	0.0	1231	1.760	0.558	0.639	39	5.813	0.964	0.413	0.0	0.0279
	s.D.	10.6	0.0	0.0060	0.055	0.046	0.053	53	0.748	0.118	0.041	0.0	0.0078

 $a \approx Accidentally recorded to incorrect number of d.p.$ 

b = Damaged at autopsy

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No.         Meridy below bel	Dose		-Fog	Adrer	renals			Kidneys	sya				Ovaries	les
821         1130         0.022         0.022         1.64         0.48         0.56         0.53         0.71         0.14         0.020           822         141         0.016         0.017         1.67         0.47         0.54         0.56         4.69         1.22         0.155         0.029           824         162         0.025         0.022         1.87         0.47         0.54         0.56         5.66         0.98         0.42         0.029           825         155         0.026         0.03         1.77         0.50         0.65         5.66         0.98         0.71         0.023           827         1135         0.019         1.74         0.55         0.65         5.70         0.98         0.71         0.013           829         121         0.016         0.117         0.51         0.51         0.51         0.014         0.025           829         121         0.016         0.014         1.70         0.43         0.52         0.54         4.07         0.93         0.013           820         121         0.016         0.014         1.74         0.52         0.50         5.46         0.93         0.23	mg/kg/ day/ Sex	.oN	weight	ц	×	Brain	Heart	ц	<u>م</u>	Liver	rugs	Spleen	ы	æ
822         141         0.016         0.017         1.67         0.47         0.54         0.56         0.98         0.42         0.024           824         162         0.025         0.022         1.82         0.577         0.66         0.69         5.66         0.98         0.422         0.024           825         144         0.025         0.024         182         0.577         0.655         0.66         6.36         0.98         0.42         0.024           827         1135         0.023         0.019         1.74         0.55         0.603         5.18         0.38         0.019           829         1131         0.015         0.018         1.74         0.55         0.50         3.82         0.39         0.39         0.39           829         121         0.016         0.014         1.70         0.53         0.53         5.70         0.99         0.34         0.019           820         152         0.016         0.174         0.53         0.53         0.51         0.91         0.93         0.019           821         152         0.016         0.174         0.53         0.53         0.51         0.93         0.018 </td <td>15009</td> <td>821</td> <td>061</td> <td>0.022</td> <td>0.022</td> <td>1.64</td> <td>0.48</td> <td>0.56</td> <td>0.52</td> <td>5.53</td> <td>0.71</td> <td>0.34</td> <td>0.020</td> <td>0.019</td>	15009	821	061	0.022	0.022	1.64	0.48	0.56	0.52	5.53	0.71	0.34	0.020	0.019
162         0.025         0.022         1.82         0.57         0.66         0.69         5.66         0.98         0.42         0.024           155         0.026         1.76         0.57         0.65         0.66         6.36         0.96         0.38         0.017           144         0.024         1.77         0.50         0.65         0.63         4.61         0.86         0.37         0.017           135         0.015         0.104         1.74         0.55         0.60         6.34         4.61         0.86         0.38         0.014           131         0.015         0.174         0.55         0.60         0.63         0.54         4.07         0.93         0.014           131         0.015         1.74         0.45         0.53         0.53         4.61         0.95         0.37         0.014           121         0.016         1.79         0.41         0.52         0.53         4.81         0.97         0.91         0.014           122         0.026         0.73         0.41         0.53         0.53         4.81         0.97         0.91         0.014         0.023         0.014           170		822	141	0.016	0.017	1.67	0.47	0.54	0.56	4.69	1.22	0.35	0.019	0.019
		824	162	0.025	0.022	1.82	0.57	0.66	0.69	5.66	0.98	0.42	0.029	0.024
144 $0.024$ $1.77$ $0.50$ $0.65$ $0.55$ $0.63$ $5.18$ $0.88$ $0.38$ $0.017$ 135 $0.023$ $0.019$ $1.74$ $0.55$ $0.63$ $4.61$ $0.85$ $0.37$ $0.013$ 133 $0.015$ $0.018$ $1.74$ $0.55$ $0.63$ $0.52$ $0.38$ $0.014$ $0.027$ 121 $0.016$ $0.015$ $1.774$ $0.46$ $0.53$ $0.54$ $4.07$ $0.93$ $0.34$ $0.014$ 121 $0.016$ $0.014$ $1.770$ $0.43$ $0.52$ $0.59$ $5.46$ $0.97$ $0.013$ 144 $0.022$ $0.014$ $1.70$ $0.52$ $0.53$ $0.53$ $0.51$ $0.07$ $0.023$ $0.018$ $0.018$ 170 $0.023$ $0.021$ $1.79$ $0.53$ $0.53$ $4.81$ $0.93$ $0.018$ 170 $0.023$ $0.014$ $0.53$ $0.53$ $0.516$		825	155	0.026	л.	1.76	0.57	0.65	0.66	6.36	0.96	0.38	0.024	0.025
135 $0.023$ $0.019$ $1.74$ $0.55$ $0.60$ $0.63$ $4.61$ $0.85$ $0.37$ $0.011$ 144 $0.028$ $0.024$ $1.78$ $0.54$ $0.63$ $0.62$ $5.70$ $0.95$ $0.38$ $0.019$ 133 $0.015$ $0.018$ $1.74$ $0.46$ $0.53$ $0.53$ $5.70$ $0.93$ $0.34$ $0.014$ 121 $0.016$ $0.014$ $1.70$ $0.43$ $0.52$ $0.50$ $3.82$ $0.87$ $0.37$ $0.019$ 152 $0.027$ $0.026$ $1.79$ $0.61$ $0.52$ $0.59$ $5.89$ $0.91$ $0.37$ $0.018$ 144 $0.027$ $0.026$ $1.79$ $0.61$ $0.52$ $0.53$ $5.46$ $0.97$ $0.34$ $0.026$ 170 $0.040$ $0.024$ $1.73$ $0.47$ $0.53$ $0.53$ $4.81$ $0.83$ $0.34$ $0.026$ 170 $0.025$ $0.024$ $1.79$ $0.61$ $0.52$ $0.53$ $4.81$ $0.83$ $0.34$ $0.026$ 170 $0.025$ $0.021$ $1.74$ $0.53$ $0.74$ $0.69$ $7.21$ $1.00$ $0.48$ $0.020$ 171 $0.022$ $0.014$ $1.74$ $0.53$ $0.68$ $0.65$ $5.29$ $0.93$ $0.914$ 172 $0.022$ $0.014$ $1.74$ $0.53$ $0.68$ $0.67$ $0.92$ $0.74$ $0.91$ 172 $0.022$ $0.014$ $1.80$ $0.61$ $0.53$ $0.68$ $0.67$ $0.92$ $0.74$ <		826	144	0.024	es	1.77	0.50	0.65	0.59	5.18	0.88	0.38	0.017	0.023
		827	135	0.023	0.019	1.74	0.55	0.60	0.63	4.61	0.85	0.37	0.011	0.019
133 $0.015$ $0.018$ $1.74$ $0.46$ $0.53$ $0.54$ $4.07$ $0.93$ $0.34$ $0.014$ 121 $0.016$ $0.015$ $1.70$ $0.43$ $0.52$ $0.50$ $3.82$ $0.91$ $0.37$ $0.021$ 152 $0.022$ $0.014$ $1.70$ $0.52$ $0.58$ $0.59$ $5.89$ $0.91$ $0.37$ $0.019$ 144 $0.027$ $0.026$ $1.79$ $0.61$ $0.622$ $0.59$ $5.46$ $0.91$ $0.37$ $0.02$ 146 $0.024$ $1.73$ $0.47$ $0.53$ $0.53$ $4.81$ $0.93$ $0.34$ $0.026$ 170 $0.040$ $0.024$ $1.73$ $0.47$ $0.53$ $0.53$ $4.81$ $0.97$ $0.34$ $0.020$ 171 $0.023$ $0.021$ $1.90$ $0.53$ $0.69$ $0.714$ $0.63$ $0.021$ $0.041$ 172 $0.023$ $0.021$ $1.80$ $0.63$ $0.69$ $0.70$ $6.34$ $0.97$ $0.34$ $0.021$ 172 $0.023$ $0.021$ $1.80$ $0.63$ $0.64$ $5.28$ $0.74$ $0.23$ $0.041$ 172 $0.022$ $0.019$ $1.74$ $0.53$ $0.66$ $0.64$ $5.28$ $0.91$ $0.017$ 132 $0.016$ $0.022$ $0.014$ $1.80$ $0.55$ $0.56$ $5.44$ $0.77$ $0.38$ $0.011$ 148 $0.022$ $0.016$ $0.55$ $0.56$ $5.44$ $0.77$ $0.38$ $0.016$ 142 $0.021$		828	144	0.028	0.024	1.78	0.54	0.63	0.62	5.70	0.95	0.38	0.019	0.023
		829	133	0.015	0.018	1.74	0.46	0.53	0.54	4.07	0.93	0.34	0.014	0.014
		830	121	0.016	0.015	1.70	0.43	0.52	0.50	3.82	0.87	0.27	0.021	0.022
144 $0.027$ $0.026$ $1.79$ $0.61$ $0.62$ $0.59$ $5.46$ $0.97$ $0.34$ $0.025$ 146 $0.026$ $0.024$ $1.73$ $0.47$ $0.53$ $0.53$ $4.81$ $0.83$ $0.33$ $0.018$ 170 $0.040$ $0.024$ $1.73$ $0.47$ $0.53$ $0.53$ $4.81$ $0.83$ $0.33$ $0.018$ 170 $0.040$ $0.024$ $1.73$ $0.47$ $0.53$ $0.53$ $4.81$ $0.83$ $0.33$ $0.018$ 172 $0.023$ $0.021$ $1.80$ $0.63$ $0.69$ $0.70$ $6.34$ $0.97$ $0.48$ $0.020$ 172 $0.025$ $0.025$ $1.74$ $0.53$ $0.68$ $0.64$ $5.28$ $0.92$ $0.31$ $0.017$ 132 $0.022$ $0.014$ $1.80$ $0.54$ $0.52$ $4.37$ $0.74$ $0.31$ $0.017$ 132 $0.021$ $1.74$ $0.55$ $0.56$ $5.29$ $1.28$ $0.37$ $0.017$ 148 $0.016$ $0.014$ $1.80$ $0.55$ $0.56$ $5.29$ $1.28$ $0.37$ 151 $0.022$ $0.016$ $0.51$ $0.55$ $0.56$ $5.44$ $0.77$ $0.38$ $0.016$ 142 $0.022$ $0.016$ $0.55$ $0.56$ $5.44$ $0.77$ $0.38$ $0.016$ 142 $0.022$ $0.022$ $1.74$ $0.55$ $0.68$ $0.65$ $0.79$ $0.79$ $0.37$ 146.1 $0.022$ $0.016$ $0.52$ $0.68$ $0.$		831	152	0.022	0.014	1.70	0.52	0.58	0.59	5.89	0.91	0.37	0.019	0.027
146         0.026         0.024         1.73         0.47         0.53         0.53         4.81         0.83         0.33         0.018           170         0.040         0.024         1.90         0.58         0.74         0.69         7.21         1.00         0.48         0.020           170         0.040         0.024         1.90         0.58         0.74         0.69         7.21         1.00         0.48         0.020           172         0.025         1.74         0.53         0.68         0.64         5.28         0.92         0.38         0.017           132         0.016         1.74         0.53         0.68         0.64         5.28         0.37         0.37         0.017           132         0.016         1.74         0.55         0.56         5.29         1.28         0.37         0.017           148         0.016         1.76         0.55         0.56         5.29         1.28         0.37         0.017           154         0.016         1.74         0.55         0.56         5.44         0.77         0.38         0.016           146.1         0.022         0.016         0.55         0.56		832	144	0.027	0.026	1.79	0.61	0.62	0.59	5.46	0.97	0.34	0.025	0.029
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$		833	146	0.026	0.024	1.73	0.47	0.53	0.53	4.81	0.83	0.33	0.018	0.030
172         0.023         0.021         1.80         0.63         0.69         0.70         6.34         0.97         0.48         0.020           148         0.025         0.025         1.74         0.53         0.68         0.64         5.28         0.97         0.48         0.020           132         0.022         0.019         1.74         0.53         0.68         0.64         5.28         0.97         0.38         0.017           132         0.022         0.019         1.74         0.53         0.54         0.52         4.37         0.74         0.31         0.017           154         0.016         1.74         0.51         0.55         0.56         5.44         0.37         0.016           142         0.021         0.016         1.76         0.55         0.56         5.44         0.77         0.38         0.016           141         0.022         0.022         1.74         0.55         0.68         0.65         5.44         0.77         0.38         0.016           146.1         0.022         0.022         1.74         0.55         0.68         0.65         5.44         0.77         0.38         0.020      <		834	170	0.040	0.024	1.90	0.58	0.74	0.69	7.21	1.00	0.48	0.020	0.037
148         0.025         0.025         1.74         0.53         0.68         0.64         5.28         0.92         0.38         0.041           132         0.022         0.019         1.74         0.46         0.54         0.52         4.37         0.74         0.31         0.017           154         0.016         0.014         1.80         0.51         0.55         0.56         5.29         1.28         0.37         0.017           142         0.021         0.016         1.76         0.50         0.55         0.56         5.44         0.77         0.38         0.016           142         0.022         0.016         1.76         0.50         0.55         0.56         5.44         0.77         0.38         0.016           151         0.022         0.022         1.74         0.55         0.68         0.65         5.56         0.45         0.020           146.1         0.0217         1.754         0.523         0.601         5.330         0.925         0.375         0.020           146.1         0.0051         0.058         0.064         0.827         0.141         0.053         0.00		835	172	0.023	0.021	1.80	0.63	0.69	0.70	6.34	0.97	0.48	0.020	0.022
132         0.022         0.019         1.74         0.46         0.54         0.52         4.37         0.74         0.31         0.017           154         0.016         0.014         1.80         0.51         0.55         0.56         5.29         1.28         0.37         0.017           142         0.021         0.016         1.76         0.55         0.56         5.44         0.77         0.38         0.016           151         0.022         0.174         0.55         0.68         0.65         5.56         0.85         0.016           1         146.1         0.022         1.74         0.523         0.601         5.330         0.925         0.375         0.020           1         146.1         0.0217         1.754         0.523         0.601         5.330         0.925         0.375         0.020           1         146.1         0.0051         0.058         0.055         0.661         5.330         0.925         0.375         0.020		836	148	0.025	0.025	1.74	0.53	0.68	0.64	5.28	0.92	0.38	0.041	0.013
154         0.016         0.014         1.80         0.51         0.55         0.56         5.29         1.28         0.37         0.017           142         0.021         0.016         1.76         0.50         0.55         0.56         5.44         0.77         0.38         0.016           151         0.022         0.012         1.74         0.55         0.68         0.65         5.56         0.45         0.020           1         146.1         0.0227         1.74         0.523         0.601         5.330         0.925         0.45         0.020           1         146.1         0.0217         1.754         0.523         0.601         5.330         0.925         0.375         0.020           1         146.1         0.0217         1.754         0.523         0.601         5.330         0.925         0.375         0.023           1         13.2         0.0051         0.058         0.055         0.064         0.827         0.141         0.053         0.00		837	132	0.022	0.019	1.74	0.46	0.54	0.52	4.37	0.74	0.31	0.017	0.019
142         0.021         0.016         1.76         0.50         0.55         0.56         5.44         0.77         0.38         0.016           151         0.022         0.022         1.74         0.55         0.68         0.65         5.56         0.85         0.45         0.020           1         146.1         0.0217         1.754         0.523         0.601         5.330         0.925         0.375         0.02           1         146.1         0.0217         1.754         0.523         0.601         5.330         0.925         0.375         0.02           1         13.2         0.0051         0.058         0.055         0.064         0.827         0.141         0.053         0.00		838	154	0.016	0.014	1.80	0.51	0.55	0.56	5.29	1.28	0.37	0.017	0.018
151         0.022         0.022         1.74         0.55         0.68         0.65         5.56         0.85         0.45         0.020           1         146.1         0.0217         1.754         0.523         0.601         5.330         0.925         0.375         0.02           .         13.2         0.0051         0.058         0.055         0.064         0.827         0.141         0.053         0.00		839	142	0.021	0.016	1.76	0.50	0.55	0.56	5.44	0.77	0.38	0.016	0.017
1         146.1         0.0217         1.754         0.523         0.601         5.330         0.925         0.375           .         13.2         0.0051         0.058         0.055         0.054         0.053		840	151	0.022	0.022	1.74	0.55	0.68	0.65	5.56	0.85	0.45	0.020	0.030
· 13.2 0.0051 0.058 0.055 0.064 0.827 0.141 0.053		Mean	146.1	0.0	1217	1.754	0.523	0.6	51	5.330	0.925	0.375	0.0	215
		s.b.	13.2	0.0	1051	0.058	0.055	0.0	54	0.827	0.141	0.053	0.0	062

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a = Damaged at autopsy

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## APPENDIX 11

HMX: 13 Week Toxicity Study in Rats Analysis of HMX in Formulated Diets

### Materials

1,3 Dinitrobenzene (Organic Analytical Standard Grade) BDH Chemicals Ltd, Poole, England.

Acetonitrile (HPLC Grade) Rathburn Chemicals Ltd, Walkerburn, Scotland.

### Method

A suitable weight of diet (2.5 g or 5 g) was weighed accurately into clean glass 8 oz jars. To this was added 1 ml of internal standard solution (dinitrobenzene in acetonitrile at a suitable concentration) and 50 ml of acetonitrile as extracting solvent. The jars were shaken mechanically for 1 h then left to settle, preferably overnight. A suitable aliquot was transferred to a sample vial and analysed by HPLC.

Standard solutions of HMX were prepared by adding a known amount of HMX (equivalent to that of the group being analysed) to a sample of untreated diet. These were treated with internal standard solution and extracting solvent as described for the formulated diet samples.

Three quality control samples were included with each batch of test samples and standards. For this purpose a solution of HMX in acetonitrile was prepared by an independent analyst and these solutions used by the analyst to spike blank diet samples in exactly the same way as the standards.

### HPLC Conditions

Instrument:	Hewlett Packard 1084B with variable wave- length detector and automatic sampler.
Column:	100 x 5 mm stainless steel packed with ODS Hypersil (5 $\mu)$ .
Solvent:	Acetonitrile:Water (40:60 v/v).
Flow:	1.5 ml/min.













Oven Temperature:	40 <sup>°</sup> C.
Wavelenth:	228 nm.
Attenuation:	2 <sup>5</sup> -2 <sup>8</sup> .
Chart Speed:	0.5 cm/min.

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# APPENDIX 12

Methods and Units used in Laboratory Investigations

Haematology

Parameters	Method	Units
Haemoglobin: (Hb)	Drabkin, D.L. and Austin, J.H. J. Biol. Chem., <u>98</u> , 719, (1932).	g/dl
Total Red Blood Cell Count: (RBC)	Coulter Counter, Coulter Electronics Ltd.	$\times 10^{12}/1$
Packed Cell Volume: (PCV)	Modified Strumia, M.M. <u>et al</u> , Amer. J. Path., <u>24</u> , 101 <del>6, (1</del> 954).	8
Absolute Values:		
Mean Cell Volume: (MCV)		fl
Mean Cell Haemoglobin: (MCH)	Haematological Slide Rule	þà
Mean Cell Haemo- globin Concen- tration: (MCHC)		g/dl
Reticulocyte Count:	Visual appraisal using new methylene blue vital staining.	ક
Total White Blood Cell Count: (WBC)	Coulter Counter, Coulter Electronics Ltd.	x 10 <sup>9</sup> /1
Differential White Cell Count:	Visual appraisal of stained film. (May-Grunwald and Giemsa Stain.)	x 10 <sup>9</sup> /1
Hepato Quick: (Boehringer)	Tryding, N.u.a., Farmakoterapai, <u>25</u> , 27, (1969).	sec

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Clinical Chemistry				
Parameters	Method	Units		
Urea: (BUN)	Karmen, A., J. Clin. Invest., 34, 131, (1955). Adapted for centrifugal analysis.	mmol/1		
Glucose:	Barthelmai, W. and Czok, R., Klin. Wochschr., <u>40</u> , 585, (1962).	mmol/1		
Aspartate Trans- aminase: (GOT) or (AST)	Enzyme Commission of the German Society for Clinical Chemistry. Z. Klin. Chem. Klin. Biochem., <u>10</u> , 281, (1972). Adapted for centrifugal analysis.	10/1		
Alanine Trans- aminase: (GPT) or (ALT)	Enzyme Commission of the German Society for Clinical Chemistry. Z. Klin. Chem. Klin. Biochem. <u>10</u> , 281, (1972). Adapted for centrifugal analysis.	IU/1		
Lactate Dehydro- genase: (LDH)	Enzyme Commission of the German Society for Clinical Chemistry. Z. Klin. Chem. Klin. Biochem., <u>10</u> , Jg., 281-291, (1972). Adapted for centrifugal analysis.	IU/1		
Sodium: (Na)	I.L. flame photometer	mmol/1		
Potassium: (K)	I.L. flame photometer	mmol/1		
Total Protein:	Henry, R.J., Sobel, C. and Berkman, S., Anal. Chem., <u>29</u> , 1491, (1957). Adapted for centrifugal analysis.	g/l		
Albumin:	Rodkey, F.L., Clin. Chem., <u>11</u> , 478, (1965); Dow, D. and Pinto, P.V.C., Clin. Chem., <u>15</u> , 1006, (1969).	g/l		
Alkaline Phosphatase: (AP)	Enzyme Commission of the German Society for Clinical Chemistry. Z. Klin. Chem. Klin. Biochem., 10, 251, (1972). Adapted for	<b>T</b> 11 / 1		
	centrifugal analysis.	IU/1		

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### Urinalysis

Parameter

M.	~+	h.	bo
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Boehringer BM8 Test Strips pH: Specific Gravity: Refractometer Protein: Boehringer BM8 Test Strips Glucose: Boehringer BM8 Test Strips Ketones: Boehringer BM8 Test Strips Blood: Boehringer BM8 Test Strips Bilirubin: Boehringer BM8 Test Strips Urobilinogen: Boehringer Test Strips Microscopy: Urine samples centrifuged at 1,000 rpm for 10 min and spun deposit examined for: epithelial cells (E) crystals (CR) white blood cells (W) erythrocytes (R) organisms (O) casts (C) abnormal constituents (A) For the sake of clarity only the initials E, CR, W, R, O, C and A are used in the tables of results. Scoring for qualititative urine tests is: NB 0 = negative1 = trace amount2 = small amount3 = large amount Colour: Y = yellowG = greenP = pale

D = dark

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## PERSONNEL INVOLVED IN PROJECT 415669CR

Principal Investigator: A.B. Wilson, B.V.Sc., M.R.C.V.S. Project Leader: C.J. Perry, B.Tech. Project Management S.R. Maddock, B.Sc. I.R. Johnson, H.N.D., M.I.Biol. Animal Services Manager: A. Dick, F.I.A.T. D.G. Brown, A.I.A.T. Senior Technician: Technician-in-Charge: E. Bell A.J. Spencer, B.V.M.S., Veterinary Officer: M.R.C.V.S., Ph.D. Ophthalmoscopist: R.J. Greenough, B.Sc., M.I.Biol. W.J. Maule, F.I.M.L.S. Haematologists: P. Hudson, F.I.M.L.S. J.R. Cowie, F.I.M.L.S., Ch.F. Clinical Chemists: P. Hudson, F.I.M.L.S. M.S. Henderson, B.Sc., Ph.D. Dispensary Supervisor: A.T. Soden Test Substance Formulator: J.N. Done, B.Sc., Ph.D. Dietary Analysis Supervisor: M. Jones, B.V.M.S., M.R.C.V.S. Pathologist: A.W. Waddell, B.Sc., Ph.D. Quality Assurance: E.M. Baxendine, B.Sc. N. McLachlan, B.Sc.

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