8.1.

REPORT

ACUTE ORAL TOXICITY STUDY IN THE JAPANESE QUAIL

WITH

TERBUTHYLAZINE

NOTOX Project 240007
NOTOX Substance 74376

STATEMENT OF GLP COMPLIANCE

NOTOX B.V., 's-Hertogenbosch, The Netherlands

The study described in this report has been correctly reported and was conducted in compliance with the most recent edition of:

The OECD Principles of Good Laboratory Practice

which are essentially in conformity with:

The United States Environmental Protection Agency (FIFRA). Title 40 Code of Federal Regulations Part 160.

The United States Environmental Protection Agency (TSCA). Title 40 Code of Federal Regulations Part 792.

Japanese Ministry of Agriculture, Forestry and Fisheries (59 NohSan, Notifications No. 3850).

Study Director
Dr. E. Heijink

Date: 30 November 1998

Management
W.J.A.M. Frieling DVM

Date: 30 November 1998

QUALITY ASSURANCE STATEMENT

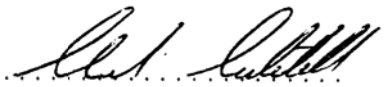
NOTOX B.V., 's-Hertogenbosch, The Netherlands

This report was audited by the NOTOX Quality Assurance Unit to ensure that the methods and results accurately reflect the raw data.

The dates of Quality Assurance inspections and audits are given below. During the on-site inspections procedures applicable to this type of study were inspected.

DATES OF QAU INSPECTIONS/ AUDITS	REPORTING DATES
on-site inspection (s)	
3 September 1998	7 September 1998
protocol inspection (s)	
29 July 1998	29 July 1998
report audit (s)	
5 October 1998	5 October 1998

Head of Quality Assurance: C.J. Mitchell B.Sc.



Date: 1-12-98

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SUMMARY

This study was performed to assess the acute oral toxicity of TERBUTHYLAZINE to the Japanese quail when administered as a single oral dose.

The study carried out was based on the OECD 401 guideline and the relevant EPA guidelines.

Treatment

TERBUTHYLAZINE was administered by oral gavage, using corn oil as a vehicle, to five birds of each sex at 2, 11, 64, 357 and 2000 mg/kg body weight. A control group of five birds of each sex was dosed with vehicle (5 ml/kg). Birds were observed at periodic intervals on the day of dosing and daily thereafter; body weight was determined at start of the study (day 1) and weekly thereafter. Food consumption was measured from days 1-4, 4-8, 8-11 and 11-15. Macroscopic examination post-mortem was performed at termination (day 15).

Results

No mortality occurred.

Quick breathing, hunched posture and/or lethargy were observed among birds receiving 11, 357 or 2000 mg/kg. Treatment-related fluid faeces was observed in females receiving 11 mg/kg and above and in males receiving 64 mg/kg and above. All clinical signs had disappeared by day 4 of treatment.

No differences were noted in body weights or body weight gain between birds of treated and control groups.

A reduction in mean food consumption was noted for males and females receiving 357 or 2000 mg/kg body weight over the first 4 days of observation.

No treatment-related abnormalities were found in the birds at macroscopic post-mortem examination.

Conclusions

Under the conditions of this study, the oral LD_{50} values of TERBUTHYLAZINE in Japanese quail in the sexes combined, or for the individual sexes were established as exceeding 2000 mg/kg body weight.

PREFACE

GENERAL

Title	Acute oral toxicity study in Japanese quail with TERBUTHYLAZINE.
Sponsor	OXON Italia SpA Via Sempione 195 I-20016 PERO (MI) Italy
Study Monitor	Mrs. Dr. M. Ciccotelli
Testing Facility	NOTOX B.V. Hambakenwetering 3 5231 DD 's-Hertogenbosch The Netherlands
Study Director	Dr. E. Heijink
Coordinating Biotechnician	I.F. van Dreumel
Necropsy	W.J.A.M. Frieling DVM
Study Schedule	
Start pilot study	25 August 1998
Start main study	3 September 1998
End main study	17 September 1998

TEST SUBSTANCE

The sponsor is responsible for the completeness and GLP Compliance of all test substance data.

Identification	TERBUTHYLAZINE
Description	White powder
Batch	88495015
Purity	97.7%
Test substance storage	At room temperature in the dark
Stability under storage conditions	Stable
Expiry date	01 July 2000
Specific Gravity	1.188 g/cm^3
Vehicle	Corn oil, specific gravity 0.92
Rationale for vehicle	Based on trial formulations performed at NOTOX.
Stability in vehicle	Corn oil :not indicated

PREPARATION OF TEST FORMULATION

The test substance was suspended in a suitable vehicle. Adjustment was made for the specific gravity of vehicle. The test formulation was homogenised to a visually acceptable level by stirring. The test formulation was dosed within 4 hours after preparation. If considered necessary, homogeneity during treatment was maintained using a magnetic stirrer. Concentration of test substance in vehicle was varied to allow constant dosage volume in terms of ml/kg body weight.

PURPOSE AND RATIONALE

The objective of this study was to assess the toxicity of Terbuthylazine when administered to Japanese quail in a single oral dose, followed by an observation period of either 14 days or for the duration of toxic symptoms (with a maximum of 21 days). The study was intended to derive a median lethal dose (LD50), if possible.

This study should provide a rational basis for risk assessment in birds. The oral route was selected as it is a possible route of bird exposure in the field.

DEFINITIONS

LD50 is the median lethal concentration, i.e. the dose of the test substance that is estimated to result in a 50% mortality of the birds in response to a single oral dose.

Lethal threshold dose is the lowest dose tested that causes death in a small number of the treated animals after a single oral administration.

GUIDELINES

The protocol was reviewed and agreed thereafter by the Article 14-functionary and the Ethical Committee of NOTOX as required by the Dutch Act on Animal Experimentation.

The study procedures described in the report were based on the following guidelines:

OECD Guidelines for Testing of Chemicals, Section 4, Health Effects. Acute oral toxicity. No 401, February 1987.

Environmental Protection Agency - Code of Federal Regulations 40, Environmental Effects Testing Guidelines. Avian acute oral toxicity test. Part 797.2175, July 1991. *

Environmental Protection Agency - FIFRA Pesticides Assessment Guidelines, Subdivision E, Hazard Evaluation Wildlife and Aquatic Organisms. Avian single-dose oral LD50 test. Paragraph 71-1, October 1982. *

Environmental Protection Agency - FIFRA Accelerated Reregistration Phase 3 Technical Guidance, Subdivision E. Acute LD50 test for Waterfowl and Upland Game Birds. Guideline Ref. No. 71-1, December 1989. *

Environmental Protection Agency - Office of Prevention, Pesticides and Toxic Substances, Ecological Effects Test Guidelines, Public Draft Guideline. Avian acute oral toxicity test. Paragraph 850.2100, April 1996. *

* With the exception that the study was performed with Japanese quails.

ARCHIVING

NOTOX B.V. will archive the following data for at least 10 years: protocol, report, test substance reference sample and raw data. No data will be withdrawn without the sponsor's written consent.

METHODS

TEST SYSTEM

Test system	Japanese quail (Coturnix coturnix japonica; Temminck and Schlegel, 1849) Healthy birds will be purchased from H. and E. Küberich, Geesdorf, Germany. Birds were from the same hatch and phenotypically indistinguishable (except for size) from wild birds. Recognized by international guidelines (EPA, OECD) as a recommended test system.
Number of birds per dose group	5 males, 5 females.
Total number of birds	30 males and 30 females.
Age at start of treatment	8 weeks.
Body weight at start of treatment	Males : 166 - 209 g Females: 173 - 217 g
Identification	Leg bands.
Allocation	Birds were randomly assigned to treatment groups, using a computer-generated algorithm.
Acclimatisation	16 days under laboratory conditions. During this period no mortality was recorded.

HUSBANDRY

Laboratory Conditions	Air-conditioned room with about 15 air changes per hour and controlled environment: a temperature of 15 to 27°C, relative humidity 45-70%, and a lighting regimen of 8 hours artificial fluorescent light/16 hours dark. Light intensity 50-60 lux.
Accommodation	Housing in stainless steel wire mesh, battery type cages (dimensions: 90 x 55 x 25 cm^3); 5 birds per cage (of the same dose group).
Diet	Free access to a standard commercial quail diet, SDS, Special Diet Services, Witham, Essex, United Kingdom. A certificate of nutrient and contaminant analysis of diet was included in the report.
Water	Free access to tap water. Results of chemical and contaminant analysis by BCO Anaytical Services BV, Breda, The Netherlands, were examined and archived.

TREATMENT

Method	Oral by gavage.
Frequency	Once, at day 1.
Dose levels	Group 1: 0 mg/kg body weight (vehicle control) Group 2: 2 mg/kg body weight Group 3: 11 mg/kg body weight Group 4: 64 mg/kg body weight Group 5: 357 mg/kg body weight Group 6: 2000 mg/kg body weight Dose levels were based on the observations in the dose range finding study. The results of this study were reported and evaluated in Appendix 1.
Dose volume	5 ml/kg body weight.
Fasting	Prior to dosing food was withheld for 15 to 20 hours. Immediately after dosing, food was provided. Water was freely available.

OBSERVATIONS

Mortality	On day of dosing: continuously during the first 1 to 2 hours after dosing, and subsequently every 2 hours (at least three times). During remainder of study period: twice a day.
Clinical signs	On day of dosing: continuously during the first 1 to 2 hours after dosing, and subsequently every 2 hours (at least three times). During remainder of study period: once a day. Mortality and clinical signs were recorded in the computer under NOTOX project 240029. All symptoms were recorded and graded according to fixed scales: Maximum grade 3: grading slight (1) to severe (3) Maximum grade 1: presence is scored (1)
Body weights	Day 1 (day of dosing), day 8 and day 15.
Food consumption	Food consumption was monitored from days 1-4, 4-8, 8-11 and 11-15 and until the end of the study if extended.

PATHOLOGY

All birds were sacrificed by carbon dioxide asphyxiation and subjected to necropsy. Descriptions of all internal macroscopic abnormalities were recorded. Gross necropsies included general inspection of the gastro-intestinal tract, liver, kidney, heart and spleen.

INTERPRETATION OF THE RESULTS

The study was evaluated based on the Standard Evaluation Procedure for Avian Single-Dose Oral LD50, EPA-Hazard Evaluation Division, June 1985.

The LD_{50} values, the associated 95% confidence interval and the slope of the dose mortality curve were not calculated since no mortality occurred.

The following statistical methods were used to analyse body weight:
- If the variables could be assumed to follow a normal distribution, the Dunnett-test (many-to-one t-test) based on a pooled variance estimate was applied for the comparison of the treated groups and the control groups for each sex.
- The Steel-test (many-to-one rank test) was applied instead of the Dunnett-test if the data could not be assumed to follow a normal distribution.

Group means were calculated for continuous data and medians were calculated for discrete data (scores) and indicated in the summary tables.

Test statistics were calculated on the basis of exact values for means and pooled variances. Individual values, means and standard deviations may have been rounded off before printing. Therefore, for example, two groups may display the same printed means for a given parameter, yet display different test statistics values.

RESULTS

MORTALITY

No mortality was recorded.

OBSERVATIONS

Clinical signs

The following clinical findings were noted:

0 mg/kg:	Fluid faeces in all birds during first hour after dosing.
2 mg/kg:	Fluid faeces in all birds during first hour after dosing, no test substance-related findings were noted.
11 mg/kg:	Fluid faeces in all females during 0-3 hours after dosing. Fluid faeces and quick breathing in all males during first hour after dosing.
64 mg/kg:	Fluid faeces in all birds during 0-5 hours after dosing. One female had a wound on the right leg on day 1, which was considered not to be related to treatment with the test substance.
357 mg/kg:	Fluid faeces in all birds during 0-7 hours after dosing. One female showed quick breathing during the first hour after dosing. Hunched posture was observed in two males and two females on day 1.
2000 mg/kg:	Fluid faeces in all birds during 0-7 hours after dosing. Quick breathing was observed in one female during the first hour after dosing. Two males showed hunched posture and lethargy and had recovered from these signs by day 2 or 4 of treatment.

Despite the absence of a clear dose relationship, the observations quick breathing, hunched posture and lethargy were considered to be related to treatment with the test compound.

Fluid faeces was observed in birds of the control group during the first hour after dosing. This is regularly seen in birds following administration of a formulation after fasting for 15 to 20 hours. In the 2 mg/kg group, fluid faeces lasted equally long as in the control group and was not considered to be an adverse effect of the test substance. In the 11 mg/kg group for the females and in the 64, 357 and 2000 mg/kg groups for both sexes, fluid faeces was present for a longer period of time, and was considered to be attributable to treatment with the test substance.

Body weights

No differences were noted in body weights or body weight gain between birds of treated and control groups.

Food consumption

In the 2000 mg/kg body weight group, a reduction in mean food consumption was noted for both males and females over the first 4 days of observation. A comparable reduction was revealed for the females of the group receiving 357 mg/kg body weight, whereas a slight reduction in mean food consumption was observed for the males in this group. No changes in food consumption were noted for the lower treatment groups as compared to the control group.

PATHOLOGY

Macroscopic examination of the birds post-mortem revealed:

0 mg/kg:	No findings.
2 mg/kg:	No findings.
11 mg/kg:	Enlarged atrium and nodules on the liver in one male.
64 mg/kg:	No findings.
357 mg/kg:	No findings.
2000 mg/kg:	Black discolouration of testes in one male.

These incidental findings were considered to have occurred by chance and not attributable to treatment with the test substance.

CONCLUSION

Under the conditions of this study, the oral LD_{50} values of TERBUTHYLAZINE in Japanese quail in the sexes combined, or for the individual sexes were established as exceeding 2000 mg/kg body weight.

APPENDIX 1

SUMMARY REPORT OF DOSE RANGE FINDING STUDY

SUMMARY REPORT OF DOSE RANGE FINDING STUDY

In this report a summary is provided of the dose range finding study, which was performed to set dose levels for the main study. The data were collected under NOTOX project 240018.

Treatment

Three groups of one male and one female each were treated with Terbuthylazine at dose levels of 20, 200 or 2000 mg/kg body weight by oral gavage. The dose volume was 5 ml/kg body weight. Birds were checked for mortality, clinical signs and body weights in a similar way as described for the main study, except that the study continued for 8 days.

Results

No mortality was recorded.

The following clinical signs were observed at all dose levels on day 1: ventro-lateral recumbency, hunched posture, quick breathing, ptosis and fluid faeces. At dose levels of 200 and 2000 mg/kg uncoordinated movements were noted in addition. Birds treated at 20 or 200 mg/kg had recovered from these findings by day 2. In the highest treatment group, signs remained present in both birds up to day 4.

No effects on body weights were seen at day 8 of observation.

Conclusions

Based on these results it was decided to conduct a full study with dose levels selected to be 0, 2, 11, 64, 357 and 2000 mg/kg body weight.

APPENDIX 2

FIGURES AND TABLES

FIGURE 1A

BODY WEIGHT GAIN

MALES

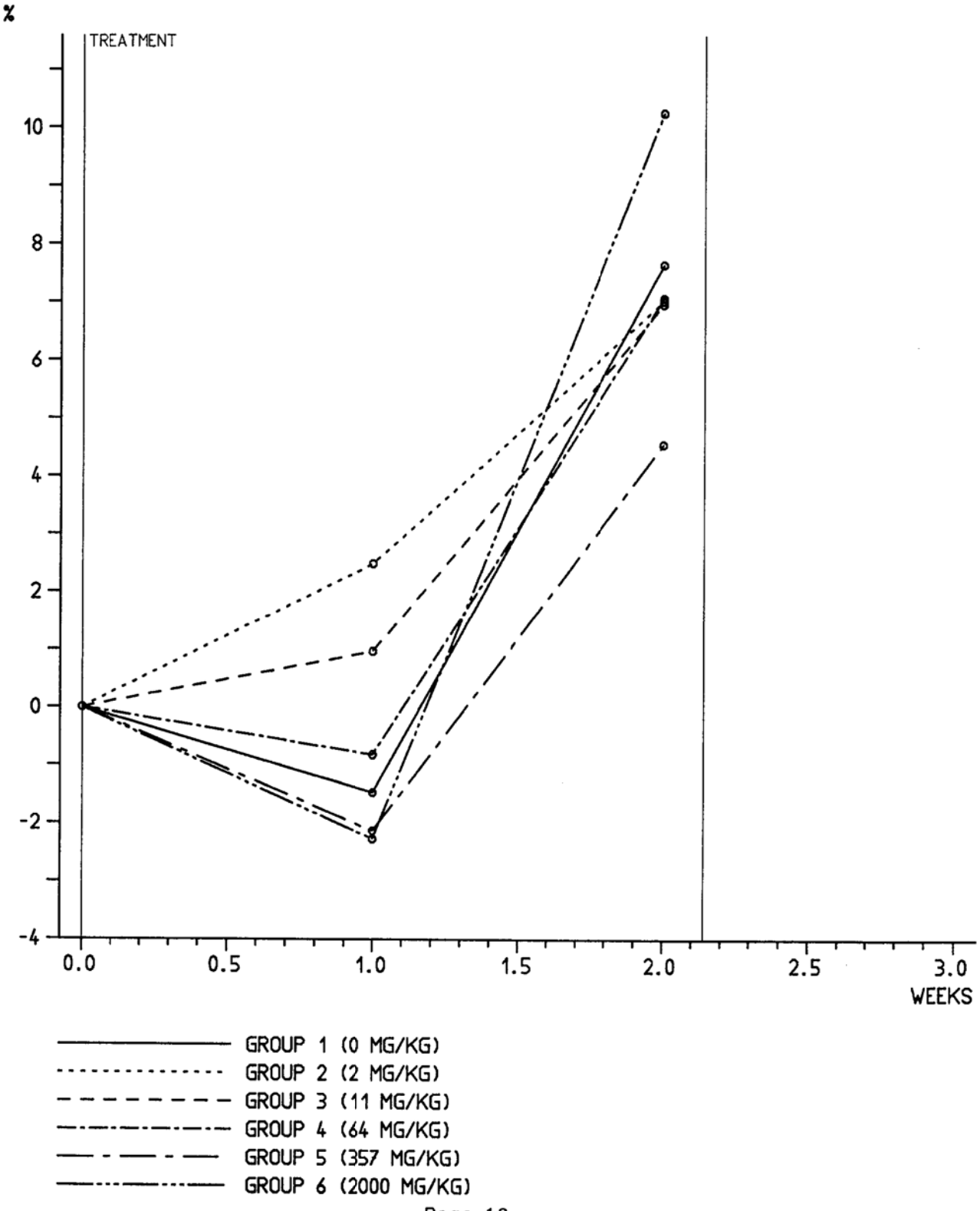

FIGURE 1B

BODY WEIGHT GAIN
FEMALES

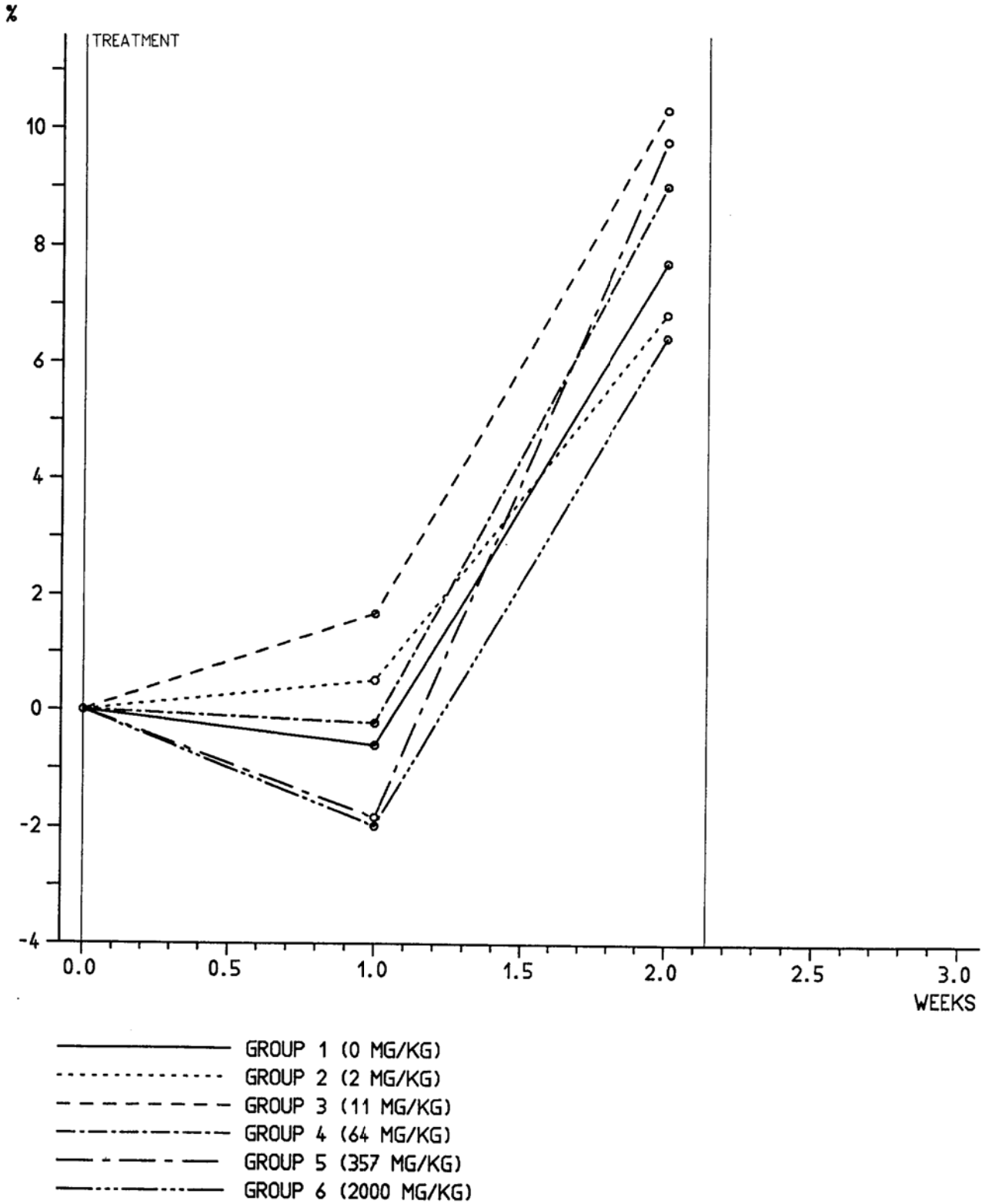

TABLE 1

MORTALITY
MALES

NUMBER OF DECEDENTS AFTER TREATMENT

Test day	1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Hours after treatment	0	1	3	5	7														
Group 1 (0 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 2 (2 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 3 (11 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 4 (64 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 5 (357 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 6 (2000 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

FEMALES

NUMBER OF DECEDENTS AFTER TREATMENT

Test day	1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Hours after treatment	0	1	3	5	7														
Group 1 (0 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 2 (2 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 3 (11 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 4 (64 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 5 (357 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 6 (2000 MG/KG)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

TABLE 2

CLINICAL SIGNS (SUMMARY)
MALES

Test day Time after treatment. Hours:		10	11	13	15	17	2	3	4	5	6	7	8	9	10	11	12	13	14	15
GROUP 1 (0 MG/KG)	GRADE																			
FLUID FAECES	(1)	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 2 (2 MG/KG)																				
FLUID FAECES	(1)	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 3 (11 MG/KG)																				
QUICK BREATHING	(1)	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
FLUID FAECES	(1)	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 4 (64 MG/KG)																				
FLUID FAECES	(1)	5	5	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 5 (357 MG/KG)																				
HUNCHED POSTURE	(1)	-	-	1	2	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
FLUID FAECES	(1)	5	5	5	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 6 (2000 MG/KG)																				
LETHARGY	(1)	-	-	-	1	2	1	-	-	-	-	-	-	-	-	-	-	-	-	-
	(2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	(3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HUNCHED POSTURE	(1)	-	1	2	2	2	1	1	-	-	-	-	-	-	-	-	-	-	-	-
FLUID FAECES	(1)	5	5	5	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Number of animals / - = not observed / . = observation not performed

TABLE 2

CLINICAL SIGNS (SUMMARY)
FEMALES

Test day / Time after treatment. Hours:		1 0	1 1	1 3	1 5	1 7	2	3	4	5	6	7	8	9	10	11	12	13	14	15
GROUP 1 (0 MG/KG)	GRADE																			
FLUID FAECES	(1)	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 2 (2 MG/KG)																				
FLUID FAECES	(1)	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 3 (11 MG/KG)																				
FLUID FAECES	(1)	5	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 4 (64 MG/KG)																				
WOUND (LEG RIGHT)	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	(2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	(3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
FLUID FAECES	(1)	5	5	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 5 (357 MG/KG)																				
HUNCHED POSTURE	(1)	-	1	2	2	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-
QUICK BREATHING	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
FLUID FAECES	(1)	5	5	5	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GROUP 6 (2000 MG/KG)																				
QUICK BREATHING	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
FLUID FAECES	(1)	5	5	5	5	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Number of animals / - = not observed / . = observation not performed

TABLE 3

BODY WEIGHTS (GRAM) SUMMARY
MALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 1 WEEK 1	MEAN ST.DEV. N	192 9.8 5	189 13.0 5	191 15.2 5	190 25.2 5

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN ST.DEV. N	193 7.9 5	196 13.0 5

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 8 WEEK 2	MEAN ST.DEV. N	190 16.0 5	194 12.0 5	193 14.1 5	188 22.9 5

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN ST.DEV. N	189 18.6 5	191 10.4 5

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 15 WEEK 3	MEAN ST.DEV. N	207 12.7 5	202 13.8 5	205 17.3 5	202 20.5 5

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN ST.DEV. N	202 21.9 5	216 15.4 5

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

TABLE 3

BODY WEIGHTS (GRAM) SUMMARY
FEMALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 1 WEEK 1	MEAN	195	197	200	196
	ST.DEV.	16.0	9.0	5.1	11.9
	N	5	5	5	5

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN	195	196
ST.DEV.	9.6	8.4
N	5	5

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 8 WEEK 2	MEAN	194	199	203	196
	ST.DEV.	12.7	19.5	6.5	9.4
	N	5	5	5	5

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN	191	192
ST.DEV.	9.1	5.3
N	5	5

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 15 WEEK 3	MEAN	210	212	221	214
	ST.DEV.	13.1	29.9	3.9	13.2
	N	5	5	5	5

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN	214	208
ST.DEV.	9.5	3.5
N	5	5

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

TABLE 4

BODY WEIGHT GAIN (%) SUMMARY
MALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 8 WEEK 2	MEAN ST.DEV. N	-1 3.6 5	2 2.7 5	1 0.9 5	-1 2.5 5

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN ST.DEV. N	-2 6.3 5	-2 1.7 5

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 15 WEEK 3	MEAN ST.DEV. N	8 1.4 5	7 6.4 5	7 1.6 5	7 5.2 5

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN ST.DEV. N	5 8.0 5	10 4.0 5

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

TABLE 4

BODY WEIGHT GAIN (%) SUMMARY
FEMALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 8 WEEK 2	MEAN ST.DEV. N	-1 2.6 5	1 5.9 5	2 0.8 5	0 3.0 5

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN ST.DEV. N	-2 1.9 5	-2 2.8 5

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAY 15 WEEK 3	MEAN ST.DEV. N	8 3.0 5	7 11.3 5	10 1.5 5	9 3.9 5

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN ST.DEV. N	10 2.2 5	6 3.1 5

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

TABLE 5

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAYS 1-4 WEEK 1	MEAN	20	20	22	21
	ST.DEV.	---	---	---	---
	N (CAGE)	1	1	1	1

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN	18	14
	ST.DEV.	---	---
	N (CAGE)	1	1

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAYS 4-8 WEEKS 1/2	MEAN	18	19	20	18
	ST.DEV.	---	---	---	---
	N (CAGE)	1	1	1	1

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN	19	21
	ST.DEV.	---	---
	N (CAGE)	1	1

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAYS 8-11 WEEK 2	MEAN	24	24	23	25
	ST.DEV.	---	---	---	---
	N (CAGE)	1	1	1	1

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN	25	26
	ST.DEV.	---	---
	N (CAGE)	1	1

TABLE 5

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
MALES

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAYS 11-15 WEEKS 2/3	MEAN	24	22	19	23
	ST.DEV.	---	---	---	---
	N (CAGE)	1	1	1	1

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN	24	26
	ST.DEV.	---	---
	N (CAGE)	1	1

MEAN OF MEANS OVER TREATMENT		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
	MEAN	21	21	21	22

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN	21	22

TABLE 5

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES

TREATMENT		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAYS 1-4 WEEK 1	MEAN	24	21	22	19
	ST.DEV.	---	---	---	---
	N (CAGE)	1	1	1	1

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN	14	14
	ST.DEV.	---	---
	N (CAGE)	1	1

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAYS 4-8 WEEKS 1/2	MEAN	19	18	20	18
	ST.DEV.	---	---	---	---
	N (CAGE)	1	1	1	1

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN	18	18
	ST.DEV.	---	---
	N (CAGE)	1	1

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAYS 8-11 WEEK 2	MEAN	26	25	26	24
	ST.DEV.	---	---	---	---
	N (CAGE)	1	1	1	1

		GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
	MEAN	26	24
	ST.DEV.	---	---
	N (CAGE)	1	1

TABLE 5

FOOD CONSUMPTION (G/ANIMAL/DAY) SUMMARY
FEMALES

		GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
DAYS 11-15 WEEKS 2/3	MEAN ST.DEV. N (CAGE)	25 --- 1	24 --- 1	23 --- 1	23 --- 1

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN ST.DEV. N (CAGE)	24 --- 1	23 --- 1

MEAN OF MEANS OVER TREATMENT	GROUP 1 0 MG/KG	GROUP 2 2 MG/KG	GROUP 3 11 MG/KG	GROUP 4 64 MG/KG
MEAN	23	22	23	21

	GROUP 5 357 MG/KG	GROUP 6 2000 MG/KG
MEAN	20	20

TABLE 6

CLINICAL SIGNS
MALES
GROUP 1 (0 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
1	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

GROUP 2 (2 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
11	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
12	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
13	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
14	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
15	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- = sign not observed / . = observation not performed / + = animal dead

TABLE 6

CLINICAL SIGNS
MALES
GROUP 3 (11 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
21	BREATHING																				
	QUICK BREATHING.....	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
22	BREATHING																				
	QUICK BREATHING.....	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
23	BREATHING																				
	QUICK BREATHING.....	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
24	BREATHING																				
	QUICK BREATHING.....	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
25	BREATHING																				
	QUICK BREATHING.....	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

GROUP 4 (64 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
31	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
32	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
33	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
34	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
35	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- = sign not observed / . = observation not performed / + = animal dead

TABLE 6

CLINICAL SIGNS
MALES
GROUP 5 (357 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
41	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
42	POSTURE																				
	HUNCHED POSTURE.....	(1)	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
43	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
44	POSTURE																				
	HUNCHED POSTURE.....	(1)	-	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
45	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

GROUP 6 (2000 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
51	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
52	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
53	BEHAVIOR																				
	LETHARGY.....	(3)	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	POSTURE																				
	HUNCHED POSTURE.....	(1)	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
54	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
55	BEHAVIOR																				
	LETHARGY.....	(3)	-	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-
	POSTURE																				
	HUNCHED POSTURE.....	(1)	-	1	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- = sign not observed / . = observation not performed / + = animal dead

TABLE 6

CLINICAL SIGNS
FEMALES
GROUP 1 (0 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
6	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
9	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

GROUP 2 (2 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
16	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
17	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
18	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
19	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
20	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- = sign not observed / . = observation not performed / + = animal dead

TABLE 6

CLINICAL SIGNS
FEMALES
GROUP 3 (11 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
26	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
27	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
28	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
29	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

GROUP 4 (64 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
36	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
37	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
38	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
39	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
40	SKIN / FUR / PLUMAGE																				
	WOUND (LEG RIGHT).....	(3)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- = sign not observed / . = observation not performed / + = animal dead

TABLE 6

CLINICAL SIGNS
FEMALES
GROUP 5 (357 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
46	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
47	POSTURE																				
	HUNCHED POSTURE.....	(1)	-	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
48	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
49	BREATHING																				
	QUICK BREATHING.....	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50	POSTURE																				
	HUNCHED POSTURE.....	(1)	-	-	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

GROUP 6 (2000 MG/KG)

Test day			1	1	1	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Time after treatment. Hours:			0	1	3	5	7														
ANIMAL NUMBER	SIGNS	MAX. GRADE																			
56	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
57	BREATHING																				
	QUICK BREATHING.....	(1)	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
58	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
59	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-
60	SECRETION / EXCRETION																				
	FLUID FAECES.....	(1)	1	1	1	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-

- = sign not observed / . = observation not performed / + = animal dead

TABLE 7

BODY WEIGHTS (GRAM)
MALES

	TREATMENT		
DAYS	1	8	15
WEEKS	1	2	3
ANIMAL			
GROUP 1 (0 MG/KG)			
1	189	184	201
2	185	184	197
3	186	179	202
4	192	183	206
5	209	218	229
GROUP 2 (2 MG/KG)			
11	203	200	196
12	173	182	193
13	194	200	217
14	178	180	188
15	198	207	217
GROUP 3 (11 MG/KG)			
21	196	197	213
22	204	204	217
23	190	194	199
24	201	202	218
25	166	169	177
GROUP 4 (64 MG/KG)			
31	170	176	191
32	213	209	212
33	156	154	173
34	200	194	209
35	209	206	226
GROUP 5 (357 MG/KG)			
41	196	199	219
42	197	189	204
43	202	210	220
44	182	160	166
45	188	188	202
GROUP 6 (2000 MG/KG)			
51	201	192	217
52	189	186	205
53	205	201	238
54	207	200	220
55	176	176	198

TABLE 7

BODY WEIGHTS (GRAM)
FEMALES

	TREATMENT		
DAYS	1	8	15
WEEKS	1	2	3
ANIMAL			
GROUP 1 (0 MG/KG)			
6	217	212	227
7	201	198	212
8	191	185	204
9	195	196	216
10	173	179	192
GROUP 2 (2 MG/KG)			
16	197	201	214
17	197	207	225
18	200	197	223
19	209	221	236
20	184	168	160
GROUP 3 (11 MG/KG)			
26	198	200	217
27	199	201	218
28	197	200	221
29	209	215	227
30	197	201	220
GROUP 4 (64 MG/KG)			
36	181	185	196
37	203	207	230
38	210	204	223
39	187	190	211
40	200	192	209
GROUP 5 (357 MG/KG)			
46	196	197	212
47	190	184	211
48	211	203	228
49	186	181	202
50	192	192	217
GROUP 6 (2000 MG/KG)			
56	200	198	209
57	182	186	202
58	201	196	211
59	193	187	209
60	202	191	209

TABLE 8

BODY WEIGHT GAIN (%)
MALES

	TREATMENT	
DAYS	8	15
WEEKS	2	3
ANIMAL		
GROUP 1 (0 MG/KG)		
1	-3	6
2	-1	6
3	-4	9
4	-5	7
5	4	10
GROUP 2 (2 MG/KG)		
11	-1	-3
12	5	12
13	3	12
14	1	6
15	5	10
GROUP 3 (11 MG/KG)		
21	1	9
22	0	6
23	2	5
24	0	8
25	2	7
GROUP 4 (64 MG/KG)		
31	4	12
32	-2	0
33	-1	11
34	-3	5
35	-1	8
GROUP 5 (357 MG/KG)		
41	2	12
42	-4	4
43	4	9
44	-12	-9
45	0	7
GROUP 6 (2000 MG/KG)		
51	-4	8
52	-2	8
53	-2	16
54	-3	6
55	0	13

TABLE 8

BODY WEIGHT GAIN (%)
FEMALES

	TREATMENT	
DAYS	8	15
WEEKS	2	3
ANIMAL		
GROUP 1 (0 MG/KG)		
6	-2	5
7	-1	5
8	-3	7
9	1	11
10	3	11
GROUP 2 (2 MG/KG)		
16	2	9
17	5	14
18	-1	12
19	6	13
20	-9	-13
GROUP 3 (11 MG/KG)		
26	1	10
27	1	10
28	2	12
29	3	9
30	2	12
GROUP 4 (64 MG/KG)		
36	2	8
37	2	13
38	-3	6
39	2	13
40	-4	5
GROUP 5 (357 MG/KG)		
46	1	8
47	-3	11
48	-4	8
49	-3	9
50	0	13
GROUP 6 (2000 MG/KG)		
56	-1	5
57	2	11
58	-2	5
59	-3	8
60	-5	3

TABLE 9

MACROSCOPIC FINDINGS
MALES
GROUP 1 (0 MG/KG)

ANIMAL 1 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 2 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 3 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 4 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 5 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

GROUP 2 (2 MG/KG)

ANIMAL 11 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 12 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 13 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 14 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 15 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

TABLE 9

MACROSCOPIC FINDINGS
MALES
GROUP 3 (11 MG/KG)

ANIMAL 21 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 22 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 23 (SCHEDULED NECROPSY, 17-SEP-98)

HEART.....	ATRIUM: ENLARGED.
LIVER.....	NODULE(S).

ANIMAL 24 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 25 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

GROUP 4 (64 MG/KG)

ANIMAL 31 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 32 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 33 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 34 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 35 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

TABLE 9

MACROSCOPIC FINDINGS
MALES
GROUP 5 (357 MG/KG)

ANIMAL 41 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 42 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 43 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 44 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 45 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

GROUP 6 (2000 MG/KG)

ANIMAL 51 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 52 (SCHEDULED NECROPSY, 17-SEP-98)

TESTES..... DISCOLOURATION, BLACK.

ANIMAL 53 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 54 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 55 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

TABLE 9

MACROSCOPIC FINDINGS
FEMALES
GROUP 1 (0 MG/KG)

ANIMAL 6 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 7 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 8 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 9 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 10 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

GROUP 2 (2 MG/KG)

ANIMAL 16 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 17 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 18 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 19 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 20 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

TABLE 9

MACROSCOPIC FINDINGS
FEMALES
GROUP 3 (11 MG/KG)

ANIMAL 26 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 27 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 28 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 29 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 30 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

GROUP 4 (64 MG/KG)

ANIMAL 36 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 37 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 38 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 39 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 40 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

TABLE 9

MACROSCOPIC FINDINGS
FEMALES
GROUP 5 (357 MG/KG)

ANIMAL 46 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 47 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 48 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 49 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 50 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

GROUP 6 (2000 MG/KG)

ANIMAL 56 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 57 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 58 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 59 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

ANIMAL 60 (SCHEDULED NECROPSY, 17-SEP-98)

NO FINDINGS NOTED

APPENDIX 3

DIET CERTIFICATE OF ANALYSIS

SDS
SPECIAL DIETS SERVICES

Special Quality Control
Certificate of Analysis

PRODUCT: AVIAN LAYER (GRD)

BATCH NO: 4728 PREMIX BATCH NO:

DATE OF MANUFACTURE: 29-APR-98

Nutrient	Found Analysis		Contaminant	Found Analysis		Limit of Detection
Moisture	8.6	%	Fluoride	22	mg/kg	1.0 mg/kg
Crude Fat	7.4	%	Nitrate as NaNO3	24	mg/kg	1.0 mg/kg
Crude Protein	24.5	%	Nitrite as NaNO2	Non Detected	mg/kg	1.0 mg/kg
Crude Fibre	4.6	%	Lead	0.47	mg/kg	0.25 mg/kg
Ash	9.6	%	Arsenic	0.51	mg/kg	0.2 mg/kg
Calcium	2.45	%	Cadmium	0.10	mg/kg	0.05 mg/kg
Phosphorus	0.80	%	Mercury	Non Detected	mg/kg	0.01 mg/kg
Sodium	0.26	%	Selenium	0.20	mg/kg	0.05 mg/kg
Chloride	0.43	%				
Potassium	0.80	%				
Magnesium	0.17	%	Total Aflatoxins	Non Detected	mcg/kg	1 mcg/kg each of B1,B2,G1,G2
Iron	148	mg/kg				
Copper	13	mg/kg	Total P.C.B	Non Detected	mcg/kg	10.0 mcg/kg
Manganese	83	mg/kg	Total D.D.T	Non Detected	mcg/kg	10.0 mcg/kg
Zinc	134	mg/kg	Dieldrin	Non Detected	mcg/kg	10.0 mcg/kg
			Lindane	Non Detected	mcg/kg	10.0 mcg/kg
			Heptachlor	Non Detected	mcg/kg	10.0 mcg/kg
			Malathion	Non Detected	mcg/kg	20.0 mcg/kg
Vitamin A	14.7	iu/g	Total Viable Organisms x 1000	10.38	per grm	1000/g
Vitamin E	107	mg/kg				
Vitamin C		mg/kg	Mesophilic Spores x 100	65.00	per grm	100/g
			Salmonellae Species	Non Detected	per grm	Absent in 20 grm
			Entero Bacteriaceae	Non Detected	per grm	Absent in 20 grm
			Escherichia Coli	Non Detected	per grm	Absent in 20 grm
			Fungal Units	25	per grm	Absent in 20 grm
			Antibiotic Activity	Non Detected		

Signed R S F Quelch

Dated 22/5/98