

Data Requirement

Test Guideline 83-5

STUDY NO. 90-3641

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

Final Report

VOLUME I OF XIV

Author: Ira W. Daly, Ph.D., D.A.B.T.

Performed by: Huntingdon Life Sciences
Mettlers Road
P.O. Box 2360
East Millstone, New Jersey 08873

Sponsor: Cheminova Agro A/S
P.O. Box 9, DK-7620
Lemvig, Denmark

Date: 27 February 1996
Amendment Date: 8 April 1999

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STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA Section 10(d)(1)(A), (B), or (C).

Company: Cheminova Agro A/S

Company Agent: Mr. Jon Weis

Title: Manager of Patents and Registration

Date: February 28, 1996

Signature:

Jon Weis

GLP Statement

This study was conducted in compliance with the United States Environmental Protection Agency's Good Laboratory Practice Standards 40 CFR Part 160.

Study Director: Ira W. Daly
Ira W. Daly, Ph.D., D.A.B.T.

2/27/96
Date

Sponsor/Submitter: Judith W. Hauswirth
Judith W. Hauswirth, Ph.D.
Jellinek, Schwartz & Connolly, Inc.
Authorized Representative of
Cheminova Agro A/S

2/29/96
Date

Flagging Statement

I have applied the criteria of 40 CFR 158.34 for flagging studies for potential adverse effects to the results of the attached study. This study meets or exceeds the criteria numbered (1, 2, 3).

Sponsor/Submitter: Judith W. Hauswirth

Judith W. Hauswirth, Ph.D.
Jellinek, Schwartz & Connolly, Inc.
Authorized Representative of
Cheminova Agro A/SAuthorized representative:

2/29/96

Date

STUDY NO. 90-3641

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OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

ABSTRACT

This study, conducted for Cheminova Agro A/S, was designed to assess the potential toxicologic and oncogenic effects of Malathion following prolonged and repeated exposure when administered orally, via dietary admixture to Fischer 344 rats (55/sex/group) at dose levels of 100/50, 500, 6000 and 12000 ppm for a period of at least 24 months and to (15/sex/group) for a period of 12 months. In addition, 10 animals per sex per group were sacrificed at 3 and 6 months after dietary administration at these dose levels. Following 3 months of study the low-dose level was reduced from 100 ppm to 50 ppm. Control animals (90/sex) received untreated standard laboratory diet.

Physical observations, ophthalmoscopic examinations, body weight, and food consumption were performed on all animals pretest and at selected intervals during the treatment period. Electroretinograms, fundic photographs, hematology, clinical chemistry, urinalyses and cholinesterase evaluations were performed on select animals at scheduled intervals during the treatment period.

After approximately 12 and 24 months of treatment, animals were sacrificed, to assess test substance related pathology. At 12 months and at study termination (24 months), selected organs were weighed and organ/body weight and organ/brain weight ratios were calculated. Complete macroscopic postmortem examinations were conducted on all animals. Histopathological evaluations of tissues were conducted on all animals from the control and high-dose groups. In addition, selected tissues and target organs were evaluated from the lower-dose groups.

Malathion administration adversely affected survival mainly in male rats at the 6000 and 12000 ppm dose levels. Early deaths occurred in males from the 12000 ppm group beginning around day 400 (Month 14) and from the 6000 ppm dose group around day 600 (Month 20). In females, survival was adversely affected only at the high dose (12000 ppm) and toward the end of the study. The most common cause of death and/or moribundity was chronic nephropathy and mononuclear cell leukemia.

The only treatment-related physical observation was yellow ano-genital staining which was seen in females at the 12000 ppm dose level consistently throughout the study period. The yellow ano-genital staining was not observed in males. No other treatment-related physical observations were noted in the treated animals during the study period.

Treatment-related decreases in body weight and body weight gain were noted, throughout most of the study period, in males and females at the 6000 and 12000 ppm dose levels. These decreases were statistically significant when compared with the control animals.

The mean food consumption values of the 6000 and 12000 ppm males were, overall, slightly greater than control during the first (2.2% and 4.2%, respectively) and second year (6.4% and 11.4%, respectively) of study. The mean food consumption values of the 6000 and 12000 ppm females were also greater than control during the second year of study. Differences from control reached a maximum of 13% at 6000 ppm during Week 98 and 26% at 12000 ppm during Week 102. These differences from control were considered a reflection of the lower body weights observed in these animals.

Statistically significant and treatment-related decreases in mean hemoglobin concentration, hematocrit, mean corpuscular volume, and mean corpuscular hemoglobin were noted in males and females at the 6000 and 12000 ppm dose levels at the 6, 12 and 18 month intervals. A statistically significant increase in platelet count was also noted in males and females at 6000 and 12000 ppm at these same time intervals. Most of these changes were not observed in females at the 24 month interval (with the exception of interim sacrifices all 12000 ppm males were unscheduled deaths).

In the males and females mean plasma, erythrocyte and brain cholinesterase levels were statistically significantly reduced, relative to control values, at 6000 and 12000 ppm at 3, 6, 12 and 24 months. In the females, at 3 months, mean erythrocyte cholinesterase values were statistically significantly reduced at the 100, 500, 6000 and 12000 ppm dose levels. Due to the absence of a no effect level for erythrocyte cholinesterase depression in the females at 3 months, the low dose level was reduced (on Test Day 113) from 100 ppm to 50 ppm. Six weeks after this reduction in dose level, erythrocyte cholinesterase was evaluated in 10 animals/sex from the control and low-dose (50 ppm) groups. The erythrocyte cholinesterase values of the 50 ppm animals were comparable to control at this additional interval. Mean erythrocyte cholinesterase levels were unremarkable at the 50 ppm dose level at 6, 12 and 24 months.

At 12 and 24 months erythrocyte cholinesterase activity was statistically significantly reduced at the 500 ppm dose level in the females only. In males, plasma cholinesterase was statistically significantly reduced at the 500 ppm dose level at 24 months.

Based on these cholinesterase data the overall no observed effect level for cholinesterase inhibition was 50 ppm in the males and females.

Differences from control which appeared to be treatment-related were noted in a number of clinical chemistry parameters. These included; alkaline phosphatase activity, statistically significantly reduced in the males and females at 6000 and 12000 ppm at 6 and 12 months and at 12000 ppm at 18 months; and aspartate aminotransferase activity, statistically significantly reduced in the females at 500, 6000 and 12000 ppm at 12 months. Gamma glutamyl transpeptidase activity was statistically significantly increased in the males at 6000 ppm and 12000 ppm at 12, 18, and 24 months and in females at 6, 12 (at 12000 ppm), 18 (at 6000 ppm), and 24 months. Cholesterol concentration was also statistically significantly increased in the males and females at 6000 and 12000 ppm at 6, 12, 18 and 24 months.

No evidence of ocular toxicity was observed during this study as determined from ophthalmoscopic and electroretinographic examinations and fundic observations.

A number of statistically significant increases from control were observed in the mean absolute and relative (organ to body weight; organ to brain weight ratios) organ weights of the treated animals at the 12 month and/or terminal sacrifice. These included the liver and kidney weights of the males and females at 6000 and 12000 ppm and the spleen and thyroid/parathyroid weights of the males at 6000 and 12000 ppm. Increases in organ weights were considered to be treatment related.

Microscopic findings which were considered related to treatment with malathion were seen in the nasoturbinal and nasopharyngeal tissues and in the kidneys and liver.

Degeneration and focal hyperplasia of the olfactory epithelium was seen in numerous males and females from the 6000 and 12000 ppm dose levels. Small cysts were frequently associated with the hyperplasia.

In several rats from the 6000 and 12000 ppm dose levels, foci of olfactory epithelium were replaced by ciliated and non-ciliated columnar epithelium which was hyperplastic. Other findings in the olfactory mucosa included subacute (chronic active)/chronic inflammation and dilated and hyperplastic mucosal glands.

Subacute (chronic active)/chronic inflammation, dilated mucosal glands, and hyperplasia of the respiratory epithelium were seen most frequently in rats from the 6000 and 12000 ppm dose levels. In the nasal lumen, inflammatory cells/cell debris were seen most frequently in males and females from the 6000 and 12000 ppm dose levels.

Hyperplasia of the respiratory type epithelium lining the nasopharynx was seen in a number of rats from the treatment and control groups. Overall, an increased incidence was seen in males and females from the 6000 ppm and females from the 12000 ppm dose levels.

In the kidneys, subacute-chronic inflammation/chronic nephropathy was seen in numerous rats from all groups. Overall, the severities in both males and females from the 6000 ppm and 12000 ppm dose levels were greater than their comparable controls.

Neoplasms which were considered to be related to treatment with malathion were seen in the nasoturbinal tissues and liver. In the nasoturbinal tissues, an adenoma was observed in one male from the 6000 ppm dose level and a carcinoma was observed in one male from the 12000 ppm dose level.

Hepatocellular adenoma and carcinoma were seen in a small number of males and females from the treatment and/or control group. Among the females, the incidence was statistically significantly increased for both neoplasms at the 12000 ppm dose level and for the incidence of hepatocellular adenoma at the 6000 ppm dose level.

Overall, the incidence and/or severities of these findings were greatest in the 6000 and 12000 ppm dose levels. Under the conditions of this study, the NOEL (No Observable Effect Level) with respect to microscopic findings in the nasoturbينات, nasopharynx, kidneys and liver was considered to be at 500 ppm.

In conclusion, significant toxicity was observed during this study at dose levels of 6000 and 12000 ppm as evidenced by decreased body weights, alterations in hematology and clinical chemistry parameters, cholinesterase depression, increased kidney, liver, spleen and thyroid/parathyroid weights, and microscopic alterations in the nasoturbinal and nasopharyngeal tissues and in the kidneys and liver. The occurrence in the males, of a nasal turbinal adenoma at 6000 ppm and a nasal turbinal carcinoma at 12000 ppm was considered treatment-related. In addition, the occurrence in the females of hepatocellular adenoma and carcinoma at 12000 ppm and hepatocellular adenomas at 6000 ppm were considered treatment-related. No evidence of ocular toxicity was observed during this study. The no observed effect level (NOEL) was 50 ppm. The NOEL was determined based upon cholinesterase depression observed at dose levels of 100 ppm and greater. The overall no observed effect level (excluding cholinesterase data) for the study was 500 ppm.

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I. INTRODUCTION:

The purpose of this study, was to assess the potential toxicologic and oncogenic effects of Malathion via dietary admixture, to Fischer 344 rats (CDF[®] (F-344) Cr1 BR) at dose levels of 100/50, 500, 6000 and 12000 ppm for a period of at least 24 months. The low-dose level was reduced from 100 ppm to 50 ppm after 3 months in an attempt to establish a no effect level for erythrocyte cholinesterase depression.

This study met or exceeded the requirements of FIFRA (Federal Insecticide, Fungicide and Rodenticide Act), Pesticide Assessment Guidelines Subdivision F; Hazard Evaluation: Human and Domestic Animals; U.S. Environmental Protection Agency, Guideline Number 83-5, Combined Chronic Toxicity/Oncogenicity Studies and was conducted in compliance with Part 160 of 40 CFR (EPA/FIFRA Good Laboratory Practice Regulations).

The following Animal Welfare Act regulations were complied with during the study conduct: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163 effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505 effective March 18, 1991.

I. INTRODUCTION (cont.):

Species and strain of test animal, method and route of test substance administration and dose levels were determined by the Sponsor. This study was conducted at Huntingdon Life Sciences (formerly Pharmacol LSR, Toxicology Services Worldwide), Mettlers Road, P.O. Box 2360, East Millstone, New Jersey 08875-2360, where all raw data, specimens, the original study protocol, the original final report, and samples of the test substance are archived.

II. MATERIALS AND METHODS:

A. Study Dates:

Study Initiation Date: 21 December 1992
(Date Study Director signed the protocol)

Receipt of Test Animals: 10 December 1992

Initiation of Dosing: 30 December 1992
(Experimental start date)

Termination of Dosing:

Month 3: 5 or 6 April 1993
Month 6: 6 or 7 July 1993
Month 12: 5, 6, or 7 January 1994
Termination: 3, 4, 5, 6, 9, or 10 January 1995.

Necropsy:

Month 3: 5 and 6 April 1993
Month 6: 6 and 7 July 1993
Month 12: 5, 6, and 7 January 1994
Termination: 3, 4, 5, 6, 9, and 10 January 1995

Study Completion Date: Date final report is signed by the Study Director.

II. MATERIALS AND METHODS (cont.):

B. Test Substance: Malathion,
Butanedioic acid,
((dimethoxyphosphinothioyl)
thio) diethyl ester

Supplier: Cheminova Agro A/S
Lemvig, Denmark

Description: Clear yellow liquid

Lot Number	Concentration (percent)	Date(s) Received	Dates Used in Diet	Test Days Used	Expiration Date
11029-01	96.4	24 January 1992	20 December 1992 through 7 December 1993	1 - 343	3 December 1993
30628-01	96.4	2 September 1993	8 December 1993 through 9 January 1995	343 - 741	27 July 1995
01112-00 Analytical Standard	99.5	6 December 1991 1 February 1993	Not used in diet, analytical standard.	-	7 September 1996

Analysis: Documentation of the identity, strength, purity and composition; and synthesis, fabrication, and/or derivation of the test substance was the responsibility of the Sponsor.

Stability: Documentation of the stability of the test substance was the responsibility of the Sponsor. The stability of the test substance was verified by conducting purity analyses during the study period. Analysis for stability in rodent diet was conducted by Huntingdon Life Sciences in a previous study (Pharmaco LSR Study Number 92-3806). The diets were found to be stable for a fourteen day period at room temperature.

II. MATERIALS AND METHODS (cont.):

B. Test Substance (cont.):

Storage:	In steel drums, at room temperature, in a temperature monitored room. Prepared diets were stored in clear polyethelene bags inside of dark plastic buckets with lids at room temperature.
Sampling:	An archival sample of approximately 10 grams from each lot of test substance and 0.02 grams of the analytical standard are stored at room temperature (between 50-80°F) in the Archives of the Testing Facility.
Additional Sampling:	Analysis for purity of the bulk chemical was performed during the first 3 months of study, at 1 year and at study termination. Results are presented in Appendix O.
Disposition:	All remaining test substance will be returned to the Sponsor after completion of the study.

II. MATERIALS AND METHODS (cont.):

C. Test Animals:

Albino Rats (Outbred)

Strain:

Fischer 344
CDF® (F-344) Cr1BR

Justification for
Animal Selection:

The rat is a rodent animal model commonly utilized in toxicity/oncogenicity studies as recommended in the referenced guidelines. In addition, a historical data base is available for comparative evaluation. The use of the Fischer 344 strain was recommended by the EPA in order to compare previous chronic toxicity and oncogenicity data that were generated in this strain of rats with Malathion.

Number of Animals:

Received:

1131 total (566 males,
565 females)

Placed on Test:

900 total (450 males,
450 females)

Females were nulliparous and non-pregnant.

Supplier:

Charles River Laboratories
Kingston, New York 12484

Date Received:

10 December 1992

Age at Receipt:

Approximately 28 days

Age at Initiation of
Treatment:

Approximately 48 days

II. MATERIALS AND METHODS (cont.):

C. Test Animals (cont.):

Weight at Initiation of

		<u>Mean</u>	<u>Range</u>
Treatment (grams):	Males:	140	110 - 165
	Females:	103	77 - 129

Acclimation Period:

Animals were acclimated for 20 days (10 December 1992 to 29 December 1992). All animals were examined by the staff veterinarian during the acclimation period.

D. Selection:

More animals than required for the study were purchased and acclimated. Animals considered unsuitable for the study on the basis of pretest physical examinations, outlying body weight or ophthalmoscopic data were eliminated prior to random selection for group assignment. The disposition of all animals not utilized in the study is recorded in the study file.

E. Group Assignment:

Animals considered suitable for study were distributed into 5 groups of 90 animals per sex by a computerized random sort program so that body weight means for each group were comparable.

II. MATERIALS AND METHODS (cont.):

F. Animal Identification:

Each rat was identified with a metal ear tag bearing its assigned animal number. The assigned animal number, plus the study number comprised the unique animal number for each animal. If the tag was lost, it was replaced. In addition, each cage was provided with a cage card which was color coded for dose level identification and contained the project number, animal number, sex and dose-group information.

G. Experimental Outline:

Detailed outlines are presented on pages 19 through 21.

SUMMARY OUTLINE

Group	Test Substance	Dose Level (ppm)	Initial Number On-Test		Oncogenicity Animals		Satellite Animals	
			M	F	M	F	M	F
I	Control ^a	0	90	90	55	55	35	35
II	Malathion	100/50 ^b	90	90	55	55	35	35
III	Malathion	500	90	90	55	55	35	35
IV	Malathion	6000	90	90	55	55	35	35
V	Malathion	12000	90	90	55	55	35	35

^aControl animals received untreated standard laboratory diet.

^bDoses given represent doses of test substance (Malathion) as supplied. The Group II dose level was reduced on 21 April 1993 (Test Day 113), at the sponsors request, from 100 ppm to 50 ppm.

G. Experimental Outline (cont.):

ONCOGENICITY ANIMALS

Group Dose Level (ppm)	Initial		Hematology ^a				Clinical Chemistry ^a				Cholin- esterase ^b		Urinalysis ^a				ERG Evaluat- ions ^c		Necropsy		Histo- pathology ^d		Unscheduled Deaths	
			Month 18		Month 24		Month 18		Month 24		Month 24		Month 24		Month 24		Month 24							
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F		
I 0	55	55	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	37	38	55	55	17	17
II 100/50	55	55	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	41	41	14	14	14	14
III 500	55	55	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	29	41	23	14	26	14
IV 6000	55	55	10	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	14	34	55	20	41	20
V 12000	55	55	10	10	e	10	10	10	e	10	e	10	10	10	10	e	5	0	20	54	53	54	34	

^aThe same animals were used to the maximum extent possible for the Month 18 and 24 hematology, clinical chemistry and urinalysis evaluations.

^bThese animals may be different from those used for hematology and clinical chemistry evaluations.

Electroretinogram animals were bled via the orbital sinus using the eye that was not used for evaluation of the electroretinogram.

Histopathology was performed on all animals in Groups I and V as well as on any animal which died an unscheduled death during the study.

histopathology was performed on all animals in Groups I and V as well as on any animal which died an unscheduled death during the study. In addition, due to all Group V males being unscheduled deaths (with the exception of those animals which were sacrificed at 3, 6, or 12 months), histopathology was also performed on all Group IV males.

Due to the high mortality rate in the Group V (12000 ppm) male animals, there were no survivors present for evaluation at study termination.

M = Male, F = Female

II. MATERIALS AND METHODS (cont.):

G. Experimental Outline (cont.):

SATELLITE ANIMALS

Group	Dose Level (ppm)	Initial Number On-Test		Clinical Laboratory Studies ^a						Cholinesterase ^b					
				Month 6			Month 12			Month 3			Month 6		
		M	F	M	F	M	M	F	F	M	M	F	M	F	F
I	0	35	35	10	10	10	10	10	10	10	10	10	10	10	10
II	100/50	35	35	10	10	10	10	10	10	10	10	10	10	10	9
III	500	35	35	10	10	10	10	10	10	10	10	10	10	10	10
IV	6000	35	35	10	10	10	10	10	10	10	10	10	10	10	10
V	12000	35	35	10	10	10	10	10	10	10	10	10	10	9	10

^aTen animals/sex/group were evaluated for hematology, clinical chemistry and urinalysis at Months 6 and 12. The same 10 animals were used, when possible, at both bleeding intervals. At Month 12, the same animals were also used in cholinesterase evaluations and sacrificed. If however, a designated animal died prior to a bleeding interval it was replaced by an oncogenicity animal but was not sacrificed at Month 12.

^bCholinesterase evaluations were performed on the animals selected for the 3, 6, and 12 month sacrifices. In addition, erythrocyte cholinesterase evaluations were performed on select animals in Groups I and II six weeks after the dose level reduction.

M = Male, F = Female

II. MATERIALS AND METHODS (cont.):

G. Experimental Outline (cont.):

SATELLITE ANIMALS (cont.)

Group	Electroretinogram Evaluations ^c						Necropsy						Histopathology ^{d,e}					
	Pretest		Month 3		Month 6		Month 12		Month 3		Month 6		Month 12		Month 3		Month 6	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
I	7	7	7	7	7	7	7	7	10	10	10	10	15	15	10	10	15	15
II	7	7	7	7	7	7	7	7	10	10	10	10	15	14	-	-	-	1
III	7	7	7	7	7	7	7	7	10	10	10	10	15	15	-	-	-	-
IV	7	7	7	7	7	7	7	7	10	10	10	10	15	15	-	-	-	1
V	7	7	7	7	7	7	7	7	10	10	10	10	14	15	10	10	15	16

^cERG evaluations were performed on 7 animals/sex/group pretest, 3, 6, and 12 months. The same 7/sex/group were used to the maximum extent possible.

^dEyes, optic nerve, retina and ocular muscle were evaluated microscopically for Groups I and V from the 3 and 6 month interim sacrifices.

^eAll tissues were evaluated for all animals in Groups I and V sacrificed at 12 months and for those animals which died during the first 12 months of study.

M = Male, F = Female

II. MATERIALS AND METHODS (cont.):

H. Husbandry:

Facility Accreditation: Huntingdon Life Sciences, East Millstone, New Jersey, is fully accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

Housing: Animals were doubly housed in elevated stainless steel wire mesh cages for four days and individually housed thereafter. Racks were rotated in the animal room once every two weeks as outlined in the Testing Facility's Standard Operating Procedures. This procedure was initiated on 2 September 1993.

Food: Certified Rodent Chow[®], No. 5002; (Meal) (Purina Mills Inc., St. Louis, MO). Appropriate amounts of test material were mixed in the rodent chow. Test diets were prepared weekly and were offered to the animals *ad libitum*. The animal feeders were clear, 16 ounce, cylindrical glass jars with a metal ringlike lid. The jars are approximately 3½" in height and 3½" in diameter. For weighing intervals a followthrough (circular flat metal disk with six half inch circular holes) was added to the animal feeder to deter the animal from spilling feed so a more accurate weight could be obtained during food consumption measurement intervals.

II. MATERIALS AND METHODS (cont.):

H. Husbandry (cont.):

Analysis of Feed:

Analysis of each feed lot used during this study was performed by Purina Mills, Inc. Results are maintained on file at the Testing Facility.

Water:

ad libitum; by automated watering system (Elizabethtown Water Company).

Analysis of Water:

Monthly analysis of water supplied to this facility was provided by Elizabethtown Water Company, Westfield, New Jersey (Raritan-East Millstone Plant). Results are maintained on file at the Testing Facility.

Biannual chemical and microbiological analysis of water samples collected from representative rooms in this facility were conducted to assure that water met standards specified under the EPA National Primary Drinking Water Regulations (40 CFR Part 141). Results are maintained on file at the Testing Facility.

Contaminants:

There were no known contaminants in the feed or water which were expected to interfere with the results of this study.

II. MATERIALS AND METHODS (cont.):

H. Husbandry (cont.):

Environmental Conditions: 12 hour light/dark cycle via automatic timer. Temperature was monitored and recorded twice daily; humidity was monitored and recorded once daily.

Temperature: Desired: 64 to 78°F
(18 to 26°C)
Actual: 67 to 76°F
(19 to 24°C)

Humidity: Desired: 40 to 70%
Actual: 22 to 84%

I. Test Substance Administration:

Route: Oral, via dietary admixture at a constant concentration.

Justification of Route of Administration: The oral route is one of the potential routes of human exposure to this test substance and is the route specified in the referenced guidelines.

Analyses of Diet: Analyses to determine homogeneity and concentration of the test substance under the conditions of this study were performed. Results of these analyses are presented in Appendix 0.

II. MATERIALS AND METHODS (cont.):

I. Test Substance
Administration (cont.):

Homogeneity:

Prior to initiation of the study, batches of low-concentration and high-concentration diets were prepared. Three samples each from the top, middle and bottom portion of each mixture were analyzed for homogeneity. Homogeneity analysis was performed, in the same manner as stated above, on the 50 ppm batch prior to administration to the test animals.

Confirmation Analysis:

All 5 dietary levels were assayed weekly for the first eight weeks (2 samples per concentration) and once every two weeks for the following eight weeks. Subsequent assays were performed at monthly intervals.

Preparation of
Test Diets:

Appropriate amounts of Certified Purina Rodent Chow (CPRC) were weighed into labeled dose group buckets. Approximately 100 grams of untreated CPRC was placed in a mortar, (from the dose group bucket that was being prepared). The appropriate amount of test substance for the group being prepared was poured into the layer of feed in the mortar and then pestled until homogeneous.

II. MATERIALS AND METHODS (cont.):

I. Test Substance
Administration (cont.):

One kilogram of untreated CPRC (from the dose group bucket being prepared) was placed into the bowl of a Hobart mixer. The mixture from the mortar and pestel was added to the Hobart mixer. The mortar and pestel was then rinsed with several grams of CPRC (from the dose group bucket being prepared) and added to the Hobart mixer. An additional 2.0 kilograms of CPRC, (from the dose group bucket being prepared) was added to the bowl of the Hobart mixer. Using a paddle blade, the Hobart mixer was run on speed 1 for approximately 10 minutes. Half of the remaining CPRC (from the dose group bucket being prepared) was poured into the Twin Shell mixer.

II. MATERIALS AND METHODS (cont.):

I. Test Substance Administration (cont.):

Preparation of Test Diets (cont.):

The mixture from the Hobart mixer was added to the Twin Shell mixer. The Hobart mixer was rinsed with several grams of CPRC (from the dose group bucket being prepared) into the Twin Shell mixer. The remaining CPRC (from the dose group bucket being prepared) was added to the Twin Shell mixer. The mixer was run for approximately 15 minutes. Upon completion of the mixing, the prepared diet was emptied into the appropriately identified dose group bucket lined with a polyethylene bag and the appropriate identification tag was placed on the bucket. Control animals received untreated CPRC. Fresh diets were prepared weekly.

Frequency:

Daily (7 days per week); *ad libitum* through the day of necropsy.

Duration:

Duration of treatment depends upon date of sacrifice.

Satellite Animals:

Month 3:	97 or 98 days
Month 6:	189 or 190 days
Month 12:	371, 372 or 373 days

Oncogenicity Animals:

Month 24 (Termination):	735, 736, 737, 738, 741 or 742 days
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II. MATERIALS AND METHODS (cont.):

I. . Test Substance
Administration (cont.):

Justification
for Frequency
and Duration:

As referenced in FIFRA
(Federal Insecticide,
Fungicide and Rodenticide
Act): Pesticide Assessment
Guidelines Subdivision F;
Hazard Evaluation: Human and
Domestic Animals; Office of
Pesticide Programs, U.S.
Environmental Protection
Agency, Office of Pesticide
and Toxic Substances, Revised
November, 1984: Section 83-5,
Combined Chronic
Toxicity/Oncogenicity Studies.

Dates of Treatment:

Date of treatment depends upon
date of sacrifice.

Satellite Animals:

Month 3:	30 December 1992 through 5 or 6 April 1993
Month 6:	30 December 1992 through 6 or 7 July 1993
Month 12:	30 December 1992 through 4, 5 or 6 January 1994

Oncogenicity Animals:

Month 24 (Termination):	30 December 1992 through 3, 4, 5, 6, 9 or 10 January 1995
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II. MATERIALS AND METHODS (cont.):

J. Observations:

For Mortality and Gross
Signs of Toxicologic or
Pharmacologic Effects:

Twice daily, once in the
morning and once in the
afternoon.

Detailed Physical Examina-
tion for Signs of Local or
Systemic Toxicity, Pharma-
cologic Effects and Pal-
pation for Tissue Masses:

(Methodology and References,
Appendix A)

Pretest and weekly thereafter.

K. Ophthalmoscopic Examination: (Methodology and References, Appendix A)

Satellite Animals:

Number of Animals:

Up to 35/sex/group

Time Intervals

Pretest:
Month 3:
Month 6:
Month 12:

14, 15 December 1992
24 March 1993
24 June 1993
23 December 1993

Oncogenicity Animals:

Number of Animals:

Up to 55/sex/group

Time Intervals

Pretest:
Month 12:
Termination:

14, 15 December 1992
23 December 1993
21, 22 and 28 December 1994

II. MATERIALS AND METHODS (cont.):

L. **Electroretinograms:** (Methodology and References, Appendix A)

Satellite Animals:

Number of Animals: Up to 7/sex/group

Time Intervals

Pretest:	17, 18, 21-24 December 1992
Month 3:	30, 31 March 1993 and 1 April 1993
Month 6:	29, 30 June 1993 and 1 July 1993
Month 12:	29-31 December 1993

Oncogenicity Animals:

Number of Animals: Up to 5/sex/group

Time Intervals

Termination: 27-30 December 1994

II. MATERIALS AND METHODS (cont.):

M. Fundic Photos: (Methodology and References, Appendix A)

Satellite Animals:

Number of animals: Pretest evaluations were performed on all satellite animals. At Months 3, 6, and 12, evaluations were performed on all remaining animals in Groups I and V (up to 35/sex/group).

Time Intervals

Pretest:	28, 29 December 1992
Month 3:	24 March 1993
Month 6:	24 June 1993
Month 12:	23 December 1993

Oncogenicity:

Number of animals: Up to 55/sex/group, Groups I and IV δ , Groups I and V ϕ

Time Intervals

Termination:	21, 22, 28 December 1994
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N. Body Weight: (Methodology and References, Appendix A)

Three times pretest, weekly Week 1 through Week 14, once every two weeks from Week 16 through Week 26 and monthly thereafter and terminally.

O. Food Consumption: (Methodology and References, Appendix A)

Pretest, weekly Week 1 through Week 14, once every two weeks from Week 16 through Week 26 and monthly thereafter.

Test Substance Intake: (Methodology and References, Appendix A)

Calculated from food consumption data and based on nominal concentrations.

II. MATERIALS AND METHODS (cont.):

P. Laboratory Studies:

(Methodology and References,
Appendix A)

1. Hematology and Clinical Chemistry:

Satellite Animals:

Blood was collected from 10 animals/sex/group at Months 6 and 12. The same 10 animals were used, when possible, at both intervals. The Month 12 animals were also used for cholinesterase evaluations and were sacrificed. If a designated animal died prior to the scheduled bleeding interval it was replaced by an animal from the oncogenicity study but was not sacrificed at Month 12.

Oncogenicity:

Blood was collected from 10 animals/sex/group at Month 18 and at the study termination. The same animals were used at both intervals to the maximum extent possible.

Method of Blood Collection:

Blood was collected from all animals via venipuncture of the orbital sinus (retrobulbar venous plexus) under light CO₂/O₂ anesthesia.

Animals were fasted overnight prior to blood collection.

II. MATERIALS AND METHODS (cont.):

P. Laboratory Studies (cont.):

1. Hematology and
Clinical Chemistry (cont.):

Hematology Parameters Evaluated

hemoglobin concentration
hematocrit
erythrocyte count
reticulocyte count
platelet count
mean corpuscular volume
mean corpuscular hemoglobin
mean corpuscular hemoglobin
concentration
total and differential
leukocyte counts
erythrocyte morphology

Time Intervals

Month 6: 2 July 1993
Month 12: 30 December 1993
Month 18: 30 June 1994
1 July 1994
Termination: 30 December 1994

II. MATERIALS AND METHODS (cont.):

P. Laboratory Studies (cont.):

1. Hematology and
Clinical Chemistry (cont.):

Clinical Chemistry Parameters Evaluated

aspartate aminotransferase
(SGOT)
alanine aminotransferase
(SGPT)
alkaline phosphatase
blood urea nitrogen
fasting glucose
cholesterol
total protein
albumin
globulin (calculated)
A/G ratio (calculated)
creatinine
creatinine kinase
total bilirubin
direct bilirubin
sodium
potassium
chloride
calcium
inorganic phosphorus
gamma glutamyl transpeptidase

Time Intervals

Month 6: 2 July 1993,
Month 12: 30 December 1993
Month 18: 30 June 1994
1 July 1994
Termination: 30 December 1994

II. MATERIALS AND METHODS (cont.):

P. Laboratory Studies (cont.):

2. Cholinesterase:

brain
erythrocyte
plasma

The last 10 animals/sex/group were used at each scheduled interval, Month 3, 6 and 12, for the cholinesterase evaluations. Ten animals per sex per group were randomly selected for cholinesterase evaluations at study termination. If an animal died prior to its scheduled bleeding interval it was replaced with an animal from the oncogenicity group. Animals selected for cholinesterase evaluations were not fasted prior to blood collection. Animals were bled via the abdominal aorta for cholinesterase evaluations. Animals designated for cholinesterase evaluations at 3, 6, and 12 months were sacrificed after bleeding and the brain was excized and used for cholinesterase activity determinations.

The following procedures were employed for the preparation of the brain tissue for use in cholinesterase evaluations. The brain was excized as quickly as possible and rinsed in saline to remove excess blood. The blood vessels were exposed on the ventral surface and removed as much as possible since they do not homogenize well and tend to clot. The brain was then blotted dry and sectioned. The right hemisphere of the brain was used to evaluate cholinesterase activity.

II. MATERIALS AND METHODS (cont.):

P. Laboratory Studies (cont.):

2. Cholinesterase (cont.):

A 50 mL plastic tube was tared and the brain sample was added. The weight of the brain sample was then recorded. The appropriate amount (19 times the weight of the sample) of buffer (1% Triton X-100) was added. The brain sample was then homogenized and stored at 4°C (under wet ice) until assay (approximately 4-6 hours after being excized). The homogenate was then centrifuged at 3000 rpm for 5 minutes. The supernatant was then removed for analysis, placed into a pre-labeled cup on the analyzer (Hitachi 717) and assayed at 37°C. Results were then multiplied by the dilution factor when necessary.

The following procedures were employed for plasma and erythrocyte cholinesterase evaluations. Collect EDTA, whole blood samples, placed on ice. The samples were then centrifuged at 3000 rpm (2000 g) for 5 minutes. The plasma was then removed and retained for the plasma cholinesterase analysis. The remaining plasma and buffy coat were then removed and discarded, the remaining packed erythrocytes were retained for erythrocyte cholinesterase evaluation.

II. MATERIALS AND METHODS (cont.):

P. Laboratory Studies (cont.):

2. Cholinesterase (cont.):

Plasma samples were analyzed approximately 1-2 hours after blood collection and erythrocyte samples were analyzed approximately 2-3 hours after blood collection. 100 μ L of packed erythrocytes were pipeted out and added to 900 μ L of Triton X-100 buffer and mixed. The mixture was then centrifuged at 3000 rpm for 5 minutes. The supernatant was then used for erythrocyte cholinesterase analysis.

The neat plasma sample and the supernatant erythrocyte sample were placed into pre-labeled cups and placed on the analyzer (Hitachi 717) for assay at 37°C. Results were multiplied by the dilution factors when necessary.

Time Intervals

Month 3:	5 and 6 April 1993
Week 23:	7 June 1993
	11 June 1993
Month 6:	6 July 1993
	7 July 1993
Month 12:	5 January 1994
	7 January 1994
Termination:	3 January 1995
	4 January 1995

NOTE: Erythrocyte cholinesterase determinations were performed on select 10 animals/sex in Groups I and II at Week 23 (Test Days 160 and 164) due to the dose level change which occurred on Test Day 113. The animals selected were the same animals that were bled for the Month 6 cholinesterase evaluations and sacrifice.

II. MATERIALS AND METHODS (cont.):

P. Laboratory Studies (cont.):

3. Urinalysis:

Urine was collected in collection pans placed beneath each animal's metabolism cage. Urine volume samples were collected over a 16 hour interval from animals that were not deprived of food or water. Freshly voided samples were collected from fasted, water-deprived animals (approximately 2 hours) for assessments of the parameters listed below.

Parameter Evaluated

gross appearance
specific gravity
pH
protein
glucose
ketones
bilirubin
occult blood
microscopic analysis

Time Intervals

Freshly Voided Samples:

Month 6: 28 June 1993
Month 12: 27 December 1993
Month 18: 29 June 1994
Termination: 27 December 1994

16 Hour Urine Volumes:

Month 6: 23-25 June 1993
Month 12: 21-23 December 1994
Month 18: 26-28 June 1994
Termination:
21-23 December 1994

II. MATERIALS AND METHODS (cont.):

Q. Postmortem:

Animals Found Dead, Killed in a
Moribund Condition, or Killed
at the Scheduled Sacrifice
Intervals:

Complete macroscopic
postmortem examinations were
performed on all animals. The
macroscopic postmortem
examination included
examination of the external
surface and all orifices; the
external surfaces of the brain
and spinal cord; the organs
and tissues of the cranial,
thoracic, abdominal and pelvic
cavities and neck; and the
remainder of the carcass.
Animals were not fasted prior
to scheduled sacrifices.

Necropsy Schedule

Satellite Animals:

Month 3:	5, 6 April 1993 (100 animals)
Month 6:	6, 7 July 1993 (100 animals)
Month 12:	5-7 January 1994 (149 animals)

Oncogenicity Animals:

Termination:	3-6, 9, 10 January 1995 (295 animals)
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Sacrifice Method:	Exsanguination following carbon dioxide inhalation. Animals sacrificed for cholinesterase evaluations were sacrificed by CO ₂ /O ₂ anesthesia.
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Sacrifice Order:	An approximately equal number of males and females were designated on each day for necropsy. Animals were sacrificed in the following order: one rat each selected from the control, high-, mid-high, mid-low, and low-dose groups was sacrificed in that order to the extent possible. This sequence was repeated until all the rats were sacrificed.
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II. MATERIALS AND METHODS (cont.):

Q. Postmortem (cont.):

Organs Weighed and
Organ/Body Weight
and Organ/Brain
Weight Ratios Calculated: (Methodology and References,
Appendix A)

The following organs were weighed for all animals at the Month 12 and terminal sacrifice intervals. Prior to weighing, the organs were carefully dissected and properly trimmed to remove adipose and other contiguous tissues in a uniform manner. Organs were weighed as soon as possible after dissection in order to avoid drying. Paired organs were weighed together.

adrenal glands
brain
heart
kidneys
liver
ovaries
testes with epididymides
thyroid/parathyroid glands
(weighed post-fixation)
spleen

II. MATERIALS AND METHODS (cont.):

Q. Postmortem (cont.):

Tissues Preserved\Examined
Histopathologically:

No. ^a	Tissue	Preserved (All Animals)	Microscopic Examination ^c		
			Months 3 and 6	Month 12	Termination
			Groups		
			I, V	I, V	I, IV, V ^g I, IV, V ^g
2	Adrenal glands	X		X	X ^d
1	Aorta (thoracic)	X		X	X
2	Bone (sternum/femur)	X		X	X
2	Bone marrow (sternum/femur) ^b	X		X	X
3	Brain (medulla/pons, cerebrum, cerebellum and hippocampus)	X		X	X
2	Epididymides	X		X	X
1	Esophagus	X		X	X
2	Eye (with optic nerve, retina and ocular muscle)	X	X	X	X ^e
2	Harderian glands	X		X	X
1	Heart	X		X	X
2	Kidneys	X		X	X ^d
2	Lacrimal gland	X		X	X
3	Large intestine (cecum, colon, and rectum)	X		X	X
2	Liver (at least 2 lobes)	X		X	X ^d
2	Lungs (with mainstem bronchi)	X		X	X ^d
1	Lymph node (mesenteric, mediastinal)	X		X	X ^d
1	Mammary gland (female)	X		X	X ^d
1	Muscle (<i>Biceps femoris</i>)	X		X	X
2	Nasal Turbinates	X		X	X ^f
1	Nerve (sciatic)	X		X	X
2	Ovaries	X		X	X
2	Oviducts	X		X	X
1	Pancreas	X		X	X
1	Pituitary gland	X		X	X
1	Prostate	X		X	X
2	Retina	X		X	X
2	Salivary glands (submandibular)	X		X	X
2	Seminal vesicles	X		X	X
1	Skin	X		X	X
3	Small intestine (duodenum, jejunum and ileum)	X		X	X
3	Spinal cord (cervical, thoracic and lumbar)	X		X	X
1	Spleen	X		X	X ^d
1	Stomach	X		X	X ^d
2	Testes	X		X	X
1	Thymus	X		X	X
2	Thyroid gland (with parathyroids)	X		X	X ^d
1	Trachea	X		X	X
1	Urinary bladder	X		X	X
2	Uterus (body/horns) with cervix	X		X	X
1	Vagina	X		X	X
1	Zymbal's Gland	X		X	X
	Gross lesions	X		X	X

^aNumber of organs/sections preserved/examined.^bQualitative examination (not a differential count).^cMicroscopic examinations were performed on animals which died unscheduled deaths during the study.^dExamined for all groups at termination.^eExamined for Groups I and V male and female and Group IV male at termination.^fNasal turbinates were examined for animals in Groups I, III, IV and V male and female.

II. MATERIALS AND METHODS (cont.):

Q. Postmortem (cont.):

Tissues Preserved\Examined
Histopathologically
(cont.):

After decalcification the skull was serially sectioned transversely at approximately 4-7 microns. Two sections were examined, post-fixation, for the presence of morphologic abnormalities. Nasal turbinate section 2 included the area between the incisive papilla and the first palatal ridge. Nasal turbinate section 4 included the area between the first upper molar tooth and nasopharynx.

Preservatives:

Tissues were preserved in 10% neutral buffered formalin. The right eye which was designated for light microscopy evaluations (hematoxylin and eosin) were placed in glutaraldehyde initially and then retained in 10% neutral buffered formalin. The left eyes, designated for electron microscopy were placed in 2.5% glutaraldehyde in a phosphate buffer (Sörensen). After an overnight fixation period the left eyes were removed from the solution and transferred to an 8.6% sucrose solution in phosphate buffer (Sörensen). All specimens in the storage buffer were maintained refrigerated (2-10°C). Lungs and urinary bladder were infused with formalin to insure fixation.

Stains:

Hematoxylin and Eosin
Luxol-fast Blue

II. MATERIALS AND METHODS (cont.):

Q. Postmortem (cont.):

Processing:

After fixation, the tissues and organs were routinely processed, embedded in paraffin, cut at a microtome setting of 4-7 microns, mounted on glass slides, stained with hematoxylin and eosin and examined by light microscopy.

R. Statistical Analysis:

(Methodology and References, Appendix A)

Body weight, body weight change, body weight change from Week 0, food consumption, hematology and clinical chemistry parameters, electroretinogram values, terminal organ and body weights and organ/body weight and organ/brain weight ratios, survivorship and time-to-tumor incidences were analyzed. Mean values of all dose groups were compared to control at each time interval. Statistically significant differences from control are indicated on mean tables of appendices.

The time to tumor analyses were performed using the Thomas, Breslow and Gart analyses which tests for both tumor incidence (chi-square and Fisher tests) and time to tumor (Kaplan-Meier curves, Cox's Tests and the Gehan-Breslow/Kruskal-Wallis Analyses). The chi-square and Fisher Exact Tests consider only simple incidence in a pairwise manner; each treated group is compared to control.

II. MATERIALS AND METHODS (cont.):

R. Statistical Analysis (cont.): Cox's test and the Gehan-Breslow/Kruskal-Wallis Analyses are based on incidence and survival. They separately perform a multiple comparison test, a test for trend, and a series of pairwise tests with each treated group compared to control. The Haseman test is a test that divides the study into time segments, tests each segment for tumor incidence differences, then pools the results for an overall test of differences.

S. Protocol Deviations:

The following protocol deviations occurred during the study but were not considered to have compromised the validity or integrity of the study:

1. Urine volume data recorded at Month 12 for the female animals only was misplaced and is not reported.
2. At study initiation, the individual body weights of four animals (2 males and 2 females) exceeded the mean weight range for their respective sexes by more than 20%.
3. For Month 18, the freshly voided urine sample collection time period exceeded the protocol specified time period by approximately 3 hours.
4. The humidity deviated from the desired range on occasion.

III. RESULTS AND DISCUSSION:

Due to the presence of a statistically significant reduction in erythrocyte cholinesterase in the females at the 100 ppm dose level at the 3 month evaluation interval the lowest dose level was reduced from 100 ppm to 50 ppm for males and females during Test Week 17 (Test Day 113). The 50 ppm dose level was maintained through study termination.

A. Mortality (Appendix B):

After 12, 18 and 24 months of treatment with the test material the percent survivorship in the control and treated groups was as follows:

(%) Percent Survivorship							
Group	Dose Level (ppm)	Month 12		Month 18		Termination (Month 24)	
		Male	Female	Male	Female	Male	Female
I	0	100	100	100	98	67	69
II	100/50	100	98	100	98	75	74
III	500	100	100	95	96	53	75
IV	6000	100	98	98	96	26	62
V	12000	96	98	71	91	0	36

Based on a morphologic examination, chronic nephropathy and mononuclear cell leukemia were the two most common causes for moribundity and/or death in the males and/or females from the 6000 ppm and 12000 ppm dose levels.

III. RESULTS AND DISCUSSION (cont.):

A. Mortality (cont.):

A series of statistical analyses of survivorship data were conducted for the male and female animals. The analyses were performed using the Thomas, Breslow and Gart analyses¹ which tests for both incidence of death (chi-square and Fisher tests) and survivorship (Kaplan-Meier curves, Cox's Tests and the Gehan-Breslow/Kruskal-Wallis Analyses). Median survivorship was estimated from Kaplan-Meier curves and by the Weibull method.

For the male rats, Cox's Test and the Gehan-Breslow/Kruskal-Wallis Analysis indicated a significantly decreasing trend in survivorship with increasing dose at less than the 0.01 level. Pairwise comparisons indicated significantly shorter survivorship in the two highest dose groups relative to the control group beyond the 0.01 level by Cox's Test and the Gehan-Breslow/Kruskal-Wallis test. The incidence of early deaths was greater in the two highest dose groups relative to control by the Fisher Exact test beyond the 0.01 level. In the males the number of early deaths and Kaplan-Meier (K-M) estimated survivorship for the five groups were as follows (page 51):

¹Thomas, D.G., Breslow, N. and Gart, J.J., "Trend and homogeneity analysis of proportions and life table data", Computers and Biomedical Research, 10, 1977, pg. 373-381.

III. RESULTS AND DISCUSSION (cont.):

A. Mortality (cont.):

Kaplan-Meier and Weibull Estimated Median Survival Time
and Number of Early Deaths for Male Rats

Dose (ppm)	0	50	500	6000	12000
Number of Animals	90	90	90	90	90
Number of Early Deaths	18	14	26	39	55
K-M Estimated Median Survivorship (days)	-	-	-	696	575
Weibull Estimated Median Survivorship (days)	807	846	754	684	546

- = Estimate not possible due to greater than 50% survivorship at termination

For the female rats, Cox's Test and the Gehan-Breslow/Kruskal-Wallis Analysis¹ indicated a significantly decreasing trend in survivorship with increasing dose at less than the 0.01 level. Pairwise comparisons indicated significantly shorter survivorship in the highest dose group relative to the control group beyond the 0.01 level by Cox's Test and the Gehan-Breslow/Kruskal Wallis test. The incidence of early deaths was greater in the highest dose group relative to control by the Fisher Exact test beyond the 0.01 level. In the females, the number of early deaths and the Kaplan-Meier estimated survivorship for the five groups were as follows (page 45):

¹Thomas, D.G., Breslow, N. and Gart, J.J., "Trend and homogeneity analysis of proportions and life table data", Computers and Biomedical Research, 10, 1977, pg. 373-381.

III. RESULTS AND DISCUSSION (cont.):

A. Mortality (cont.):

Kaplan-Meier and Weibull Estimated Median Survival Time
and Number of Early Deaths for Female Rats

Dose (ppm)	0	50	500	6000	12000
Number of Animals	90	90	90	90	90
Number of Early Deaths	17	15	14	21	35
K-M Estimated Median Survivorship (days)	-	-	-	-	719
Weibull Estimated Median Survivorship (days)	810	842	842	786	711

- = Estimate not possible due to greater than 50% survivorship at termination

The effect of Malathion on survivorship was seen with a dose related trend with specific differences between the control and 12000 ppm group for males and females, and between the control and 6000 ppm dose groups for males. In the females, the increase in deaths occurred toward the end of the animals' lifespan. In the males, the early deaths were seen beginning around day 400 (Month 14) for the 12000 ppm dose group and around day 600 (Month 20) for the 6000 ppm dose group.

III. RESULTS AND DISCUSSION (cont.):

B. Observations (Appendix C):

The only treatment-related physical observation was yellow ano-genital staining that was seen consistently in females at the 12000 ppm dose level throughout the study. Yellow-anogenital staining was observed sporadically in the control and treated females from the 100/50, 500, and 6000 ppm groups. However, there was no indication that this finding was treatment-related at dose levels up to 6000 ppm. This finding was considered to be treatment related in females at the 12000 ppm dose level because of its high incidence and consistency throughout the study. Yellow ano-genital staining was not observed in the males.

Among the other physical observations, alopecia of extremities and snout, chromodacryorrhea, lacrimation, and corneal irregularities were seen at comparable incidences between the control and treated groups and were not considered to be treatment related.

C. Ophthalmoscopic Examinations (Appendix D):

Ophthalmoscopic examinations were performed pretest (all animals) and at 3 (35/sex/group), 6 (25/sex/group), 12 (All animals), and 24 months (all animals). No treatment related findings were evident at any dose level. There was an increase in the incidence of corneal scarring in the control and all treated males and females at the 12 month and terminal examination. This finding was not considered biologically significant because of its distribution among control and treated groups. In addition, the observed corneal irregularities were those that are expected to be seen in Fischer 344 rats (Section D).

Representative fundic photographs are presented in Appendix F.

III. RESULTS AND DISCUSSION (cont.):

D. Electroretinogram Examinations with Correlation to Histologic Findings (Appendix E):

Electroretinograms were conducted pretest and following 3, 6, 12, and 24 months of treatment. Comparison of the a- and b- wave amplitudes and latencies at 3, 6, 12, and 24 months failed to indicate an electroretinographic effect attributable to the administration of the test material.

The data at 12 and 24 months are discussed in more detail below for both the a- and b- wave amplitude in light of age related changes commonly associated with Fischer 344 rats.

Since the number of retinal neurons decreases with age, there is also an absolute decrease in the number of retinal neurons responding to a flash of light in older animals. Comparison of the b- wave amplitudes to pretest values demonstrates this decrease in response, especially in males. If the test material caused a more rapid dropout of retinal neurons, one would expect the ratio of the 12 month values to the pretest values to decrease in a dose-related fashion. When comparing b-wave amplitudes to pretest values, there is no evidence of a dose-related decreased response (and by inference no dose-related decrease in retinal neurons).

III. RESULTS AND DISCUSSION (cont.):

D. Electroretinogram Examinations with Correlation to Histologic Findings (cont.):

12 month b-wave amplitudes expressed as a percent of pretest values			
Group	Dose Level (ppm)	Male	Female
I	0	62	83
II	100/50	98	93
III	500	71	88
IV	6000	62	111
V	12000	59	93

Using similar reasoning for a-wave amplitudes, there is no evidence of a dose-related response.

12 month a-wave amplitudes expressed as a percent of pretest values			
Group	Dose Level (ppm)	Male	Female
I	0	70	65
II	100/50	93	85
III	500	57	45
IV	6000	61	98
V	12000	61	92

It is not possible to compare the 24 month electroretinographic responses to the pretest values since these were different individuals. However, if one compares the mean b-wave amplitudes of the 24 month groups to the mean b-wave amplitude of all pretest animals, there is no evidence of a dose-related response in b-wave amplitude.

III. RESULTS AND DISCUSSION (cont.):

D. Electroretinogram Examinations with Correlation to Histologic Findings (cont.):

24 month mean b-wave amplitudes expressed as a percent of mean pretest values for the entire pretest population			
Group	Dose Level (ppm)	Male (189.4 μV^*)	Female (135.4 μV^*)
I	0	62	87
II	100/50	49	22
III	500	13	22
IV	6000	52	62
V	12000		51
* pretest mean			

If one compares the a-wave amplitudes of the individual 24 month groups to the mean a-wave amplitude of all pretest animals, the a-wave amplitude is lower in the treated animals than in the untreated ones. The lack of dose response and the high degree of variability of the data make a compound related effect unlikely.

24 month mean a-wave amplitudes expressed as a percent of mean pretest values for the entire pretest population			
Group	Dose Level (ppm)	Male (107.4 μV^*)	Female (87.4 μV^*)
I	0	37	71
II	100/50	51	20
III	500	15	2
IV	6000	35	44
V	12000		29
* pretest mean			

III. RESULTS AND DISCUSSION (cont.):

D. Electroretinogram Examinations with Correlation to Histologic Findings (cont.):

The number of abnormal or non-recordable electroretinograms of treated rats is greater in each treated group when compared to the untreated group at the 24 month interval, but there is no indication of a dose-related suppression of electroretinographic response. When one excludes animals in which unilateral disease indicates the animal is not capable of providing a response to stimulation with light (because of the presence clinically of phthisis bulbi and its sequelae, cataracts, glaucoma, unilateral focal retinopathy, or unilateral retinal degeneration and its sequelae), there remains no evidence of a dose-response relationship.

Abnormal electroretinograms in eyes at risk were observed with the following incidence at 24 months:

Group	Dose Level (ppm)	Total Incidence	Male Incidence	Female Incidence
I	0	1/9	1/4	0/5
II	100/50	4/8	2/4	2/4
III	500	7/9	3/4	4/5
IV	6000	3/8	1/4	2/4
V	12000	2/4	-	2/4

III. RESULTS AND DISCUSSION (cont.):

D. Electoretinogram Examinations with Correlation to Histologic Findings (cont.):

Electoretinographic and retinal abnormalities are not uncommon in older Fischer 344 rats^{2,3,4,5}. Lai et al.^{3,4}, indicate that the numbers of photoreceptor cells in Fischer 344 rats generally decrease as the rats age. The outer nuclear layer is reduced by one third by 18 months. The decrease of photoreceptor cells is more pronounced in rats housed under a light intensity of 32-ft-c (normal laboratory lighting) than in rats housed in very dim light. The spontaneous occurrence of thinning and of various retinal diseases in Fischer 344 rats suffices to explain the high incidence of electoretinographic abnormalities. One would have expected extinction of the electoretinogram in a dose-related fashion had the test compound had a significant effect. There was no indication of any test material related electoretinographic abnormality after 3, 6, 12 or 24 months of treatment.

²DiLorenzo D, del Cerro C, Grover D, Lazar E, del Cerro M: Peripheral, paving stone and cystoid retinal degenerations in the aging Fischer 344 rat. Invest Ophthalmol Vis Sci 34(suppl): 1076, 1993.

³Lai Y-L, Jacoby RO, Yao PC: Age-related and light-associated retinal changes in Fischer rats. Invest Ophthalmol Vis Sci 17: 634-638, 1978.

⁴Lai Y-L, Jacoby RO, Yao PC: Animal model: peripheral retinal degeneration in rats. Am J Pathol 97:449-452, 1979.

⁵Lee EW, Render JA, Garner CD, Brady AN, Li LC: Unilateral degeneration of retina and optic nerve in Fischer-344 rats. Vet Pathol 27:439-444, 1990.

III. RESULTS AND DISCUSSION (cont.):

D. Electroretinogram Examinations with Correlation to Histologic Findings (cont.):

The peripheral retinal degeneration involving the photoreceptor layers and the outer nuclear layer has been described by Lai et al^{3,4} and by DiLoreto et al². In male rats, they found the superior peripheral retina underwent a precipitous and complete degeneration between 12 and 18 months, the inferior periphery showing less severe degeneration. Females were less severely affected. This type of degeneration, they claim, is typical of the Fischer 344 rat and is not seen in age-matched animals of the Sprague-Dawley strain.

Unilateral retinal degeneration (and optic nerve) lesions develop spontaneously in Fischer 344 rats, in some instances ranging in incidence from 16 to 25% at 26 weeks, depending on diet received (Lee et al⁵, 1990). While it is the inner portion of retina that is involved, degeneration which includes Müller cells would affect (suppress) the electroretinogram.

³Lai Y-L, Jacoby RO, Yao PC: Age-related and light-associated retinal changes in Fischer rats. Invest Ophthalmol Vis Sci 17: 634-638, 1978.

⁴Lai Y-L, Jacoby RO, Yao PC: Animal model: peripheral retinal degeneration in rats. Am J Pathol 97:449-452, 1979.

²DiLoreto D, del Cerro C, Grover D, Lazar E, del Cerro M: Peripheral, paving stone and cystoid retinal degenerations in the aging Fischer 344 rat. Invest Ophthalmol Vis Sci 34(suppl): 1076, 1993.

⁵Lee EW, Render JA, Garner CD, Brady AN, Li LC: Unilateral degeneration of retina and optic nerve in Fischer-344 rats. Vet Pathol 27:439-444, 1990.

III. RESULTS AND DISCUSSION (cont.):

D. Electroretinogram Examinations with Correlation to Histologic Findings (cont.):

There was no significant difference in the histologic appearance of the retina between untreated (Group I) animals and high-dose (Group V females and Group IV males) at termination (24 months). The histology of the fellow eyes (i.e., the left eye rather than the ERG-tested right eye) was compared in high-dose and control animals. Most (4/5) Group I males had a peripheral retinal degeneration of a slight to moderate degree. Four of five Group IV males had peripheral retinal degeneration and one rat had generalized retinal degeneration. In the histologic sections of all 24 month Group I male rats, two rats had generalized retinal degeneration. Overall, there is no indication of a compound-related retinal degeneration in male rats.

In the untested eyes of female rats subjected to electroretinography, all Group I animals (5/5) had peripheral retinal degeneration histologically. In four of five Group V female rats the preparation of the retinas was good; in the fifth rat there were sufficient fracture artifacts of the tissue to make interpretation difficult. Two of the four Group V female rats had peripheral retinal degeneration; the other two had no significant retinal degeneration. From a morphologic viewpoint, there appears to be no retinal effect of the administration of the test compound at the 24 month interval. In the histologic sections of all 24 month Group V females, four rats had generalized retinal degeneration. In the histologic sections of all 24 month Group I rats, six rats had generalized retinal degeneration. Overall, there is no indication of a compound-related retinal degeneration in female rats.

III. RESULTS AND DISCUSSION (cont.):

E. Body Weights and Body Weight Change (Figure 1 and Appendix G):

The mean body weights and body weight gains of the male and female animals at the 6000 and 12000 ppm dose levels were reduced compared to the controls throughout most of the study. Differences from control were statistically significant in the males and females at 12000 ppm throughout the treatment period. At 6000 ppm, differences from control were statistically significant in the males from Week 13 through termination and in the females from Week 3 through Week 50.

The mean percent differences from control body weight at select intervals during the treatment period were as follows:

Mean Percent Difference From Control Body Weight											
Group	Dose Level (ppm)	Month 3 (Week 14)		Month 6 (Week 30)		Month 12 (Week 50)		Month 18 (Week 78)		Termination (Month 24) (Week 102)	
		M	F	M	F	M	F	M	F	M	F
II	100/50	0.1	0.7	0.2	1.0	-1.0	0.9	0.0	1.3	-0.2	0.4
III	500	0.8	0.0	0.9	1.3	-0.7	0.8	-0.5	1.7	-4.6	2.8
IV	6000	-3.4	-4.2	-3.1	-3.6	-5.0	-4.0	-6.4	-2.2	-11.1	-5.1
V	12000	-6.3	-6.6	-7.4	-7.6	-9.4	-10.9	-16.8	-8.5	a	-16.8

M = Male, F = Female

^aValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

The effect on body weight and body weight gains observed in the males and females at 6000 and 12000 ppm were considered to be treatment related.

III. RESULTS AND DISCUSSION (cont.):

F. Food Consumption (Figure 2 and Appendix G):

The mean food consumption values of the 6000 and 12000 ppm males were, overall, slightly greater than control during the first (2.2% and 4.2%, respectively) and second year (6.4% and 11.4%, respectively) of study. The maximum difference from control noted in the high-dose males reached +19% during Weeks 74 and 78. The mean food consumption values of the 6000 and 12000 ppm females were also greater than control during the second year of study. Differences from control reached a maximum of 13% at 6000 ppm during Week 98 and 26% at 12000 ppm during Week 102. These differences from control were considered a reflection of the lower body weights observed in these animals. The mean percent differences from control at select intervals during the treatment period were as follows:

Mean Percent Difference From Control Food Consumption											
Group	Dose Level (ppm)	Month 3 (Week 14)		Month 6 (Week 30)		Month 12 (Week 50)		Month 18 (Week 78)		Termination (Month 24) (Week 102)	
		M	F	M	F	M	F	M	F	M	F
II	100/50	1.4	0.7	1.8	1.4	4.9	4.3	3.8	3.8	-3.9	-4.8
III	500	0.2	2.1	3.3	4.4	3.6	2.1	5.2	4.9	-1.0	-3.1
IV	6000	4.4	-4.0	2.0	-2.2	4.7	2.9	8.6	8.8	9.7	6.6
V	12000	6.5	2.3	7.4	3.8	10.2	3.4	19.6	25.0	a	26.4

M = Male, F = Female

^aValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

III. RESULTS AND DISCUSSION (cont.):

F. Food Consumption (cont.):

The mean food consumption values of the males and females in the remaining treated groups exhibited the degree of variability normally seen in studies of this type and were considered unremarkable.

G. Test Substance Intake (Appendix G):

Mean test substance intake values were calculated over the duration of the study based on individual body weights and food consumption data and nominal dose levels as follows:

Mean Test Substance Intake Values (mg/kg/day)				
Group	Dose Level (ppm)	Weeks	Male	Female
I	0	1-102	0	0
II	100	1-16	7	8
	50	18-102	2	3
	100/50	1-102	4	5
III	500	1-102	29	35
IV	6000	1-102	359	415
V	12000	1-102	739	868

H. Clinical Laboratory Studies:

1. Hematology (Appendices H and I):

Alterations in several hematology parameters were noted consistently in the 6000 ppm and/or 12000 ppm males and/or females as noted in the following tables (pages 65 and 66)

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

1. Hematology (cont.):

Group		Dose Level (ppm)	Hemoglobin Concentration (g/dL)				Hematocrit (%)				Erythrocyte Count (mil/ μ L)				Platelet Count (thous/ μ L)			
MONTH			6	12	18	T	6	12	18	T	6	12	18	T	6	12	18	T
MALES																		
I		0	15.5	15.6	15.1	14.5	43.4	44.2	44.4	40.2	9.07	9.15	8.39	7.84	590	584	553	621
II		100/50 ^a	15.5	15.6	15.2	14.5	43.5	44.6	44.3	40.2	9.21	9.30	8.62	7.87	612	578	579	526
III		500	15.5	15.8	15.4	14.0	43.4	45.2	45.1	38.9	9.11	9.28	8.71	7.51	595	538	610	556
IV		6000	**	**	**	*	*	*	*								*	
			14.7	14.6	14.2	12.3	41.7	42.3	42.0	34.5	9.06	8.92	8.36	6.78	679	637	688	764
V		12000	**	**	**	b	*	**	**	b	9.05	8.52	7.48	b	**	**	**	b
			14.6	13.8	12.7		41.4	40.2	37.8						721	694	830	
FEMALES																		
I		0	14.9	15.6	15.2	14.0	40.9	44.3	43.6	39.6	8.00	8.48	8.24	7.28	627	560	478	509
II		100/50 ^a	14.7	15.4	14.8	13.5	40.5	43.7	42.7	38.3	7.91	8.38	8.09	7.13	635	529	533	460
III		500	14.9	15.6	15.6	13.6	40.9	44.1	44.7	37.8	8.00	8.48	8.43	6.97	624	569	489	455
IV		6000	*	**	**	12.1	*	*	*								**	
			14.3	15.0	14.9		39.4	42.7	42.6	34.5	7.83	8.38	8.21	6.41	630	555	573	512
V		12000	**	**	**	13.4	*	*	*								**	*
			14.3	15.2	15.2		39.5	43.3	43.3	38.6	7.97	8.63	8.43	7.51	640	615	596	631

^aReduced from 100 ppm to 50 ppm on Test Day 112.

^bValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

* = Statistically Significant $p \leq 0.05$, ** = Statistically Significant $p \leq 0.01$, T = Terminal Sacrifice.

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

1. Hematology (cont.):

Group	Dose Level (ppm)	Mean Corpuscular Volume (fL)				Mean Corpuscular Hemoglobin (pg)				Mean Corpuscular Hemoglobin Concentration (g/dL)				Total Leukocyte Count (thous/ μ L)			
		6	12	18	T	6	12	18	T	6	12	18	T	6	12	18	T
MONTH																	
MALES																	
I	0	47.8	48.2	53.0	51.4	17.1	17.0	18.1	18.5	35.7	35.3	34.1	36.0	11.37	8.02	8.03	7.60
II	100/50 ^a	47.2	48.0	51.4	51.9	*	16.8	17.6	18.7	35.6	34.9	34.3	36.1	11.93	8.60	7.17	12.51
III	500	47.7	48.8	51.9	53.2	17.0	17.1	17.7	19.1	35.7	35.0	34.1	36.0	11.05	8.31	6.40	13.59
IV	6000	**	46.0	47.4	50.3	**	**	**	18.5	*	*						
V	12000	**	45.7	47.1	50.8	b	**	**	b	35.2	34.4	33.5	b	11.80	10.11	8.31	b
FEMALES																	
I	0	51.1	52.2	53.0	54.7	18.6	18.4	18.4	19.3	36.3	35.3	34.7	35.4	8.95	5.49	6.53	8.51
II	100/50 ^a	51.3	52.1	52.7	57.4	18.6	18.3	18.1	19.8	36.4	35.2	34.3	34.9	8.41	5.72	5.90	7.15
III	500	51.1	52.0	53.1	57.3	18.6	18.4	18.6	20.3	36.3	35.4	35.0	35.7	8.13	6.05	5.10	13.42
IV	6000	**	50.3	51.0	55.9	**	**	**	19.1	36.4	35.2	35.0	34.5	9.55	6.34	6.05	17.40
V	12000	**	49.5	50.2	51.4	**	**	**	**	36.2	35.2	35.0	34.8	8.77	6.61	5.20	7.42

^aReduced from 100 ppm to 50 ppm on Test Day 112.

^bValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

* = Statistically significant $p \leq 0.05$, ** = Statistically significant $p \leq 0.01$, T = Terminal Sacrifice.

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

1. Hematology (cont.):

Although the changes in hematology parameters in treated animals were generally small, they were statistically significantly different when compared with the control group and were generally observed at more than one bleeding interval in both males and females.

Therefore, the statistically significant decreases noted in mean hemoglobin concentration, hematocrit, mean corpuscular volume, and mean corpuscular hemoglobin and increases in platelet count at the 6000 and 12000 ppm dose levels in the males and females were considered to be treatment-related.

There were no alterations noted in the mean hematology data of the treated animals at the 100/50 or 500 ppm dose level that were considered to be treatment related.

2. Cholinesterase Evaluations (Appendix J):

Plasma, erythrocyte and brain cholinesterase determinations were performed on 10 animals/sex/group at the 3, 6, 12 and 24 months on unfasted animals. Cholinesterase determinations were not conducted in the males at 12000 ppm at 24 months due to the lack of male survivors at this dose level. An erythrocyte cholinesterase determination was performed during Week 23 on 10 animals/sex in Groups I and II only (6 weeks after decreasing the dose level from 100ppm to 50 ppm).

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

2. Cholinesterase Evaluations (cont.):

In the males and females mean plasma, erythrocyte and brain cholinesterase activities were statistically significantly depressed, relative to control values, at 6000 and 12000 ppm at the 3, 6, 12 and 24 months (The 12000 ppm males were not evaluated at 24 months). In the females, at 3 months, mean erythrocyte cholinesterase values were statistically significantly depressed at the 100, 500, 6000 and 12000 ppm dose levels. Because of the absence of a no effect level for erythrocyte cholinesterase depression in the females at 3 months, the low dose level was reduced (on Test Day 113) from 100 ppm to 50 ppm. Six weeks after this reduction in dose level erythrocyte cholinesterase activity was evaluated in 10 animals/sex from the control and low-dose (50 ppm) group. The erythrocyte cholinesterase values of the 50 ppm animals were comparable to control at this additional interval in both males and females. Mean erythrocyte cholinesterase levels at the 50 ppm dose level were comparable to the control values at the 6, 12 and 24 month intervals.

At 12 and 24 months erythrocyte cholinesterase activity was statistically significantly decreased at the 500 ppm dose level in the females only. In males, plasma cholinesterase activity was statistically significantly decreased at the 500 ppm dose level at 24 months. Mean cholinesterase levels at each study interval were as follows (page 69):

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

2. Cholinesterase Evaluations (cont.):

Mean Cholinesterase Values															
Group	Dose Level (ppm)	Plasma (IU/mL)					Erythrocyte (IU/mL)					Brain (IU/g)			
		3	6	12	T		3	6A	6B	12	T	3	6	12	
MALES															
I	0	0.623	0.533	0.737	1.869		0.90	0.75	1.03	1.43	1.16	10.77	10.02	9.93	10.76
II	50 ^a	0.609	0.621	0.698	1.615		**	0.72	1.16	1.43	1.11	10.82	9.85	9.83	10.59
III	500	0.631	0.591	0.736	1.327	**	1.01	-	0.97	1.33	0.96	10.71	9.80	9.69	10.44
IV	6000	**	**	*	**	**	**	-	**	**	**	**	**	**	**
		0.456	0.481	0.615	0.675	0.47	0.47	-	0.59	0.78	0.66	9.43	8.85	8.85	7.41
V	12000	**	**	**	c	**	**	-	**	**	c	**	**	**	c
		0.292	0.299	0.419		0.47	0.47	-	0.44	0.60		9.10	8.16	8.45	
FEMALES															
I	0	2.928	3.330	3.319	3.495		1.46	0.99	1.37	1.50	1.35	10.75	9.99	9.89	10.73
II	50 ^a	2.868	3.327	3.581	3.475		**	0.85	1.38	1.52	1.34	10.78	9.68	10.09	10.69
III	500	2.760	3.305	3.408	2.879		**	-	1.37	1.29	0.99	10.41	9.62	9.75	10.58
IV	6000	**	**	**	**	**	**	-	**	**	**	**	**	*	**
		1.449	1.777	2.053	1.374	0.62	0.62	-	0.77	0.83	0.76	9.12	8.27	8.70	8.78
V	12000	**	**	**	**	**	**	-	**	**	**	**	**	**	**
		0.566	0.654	1.004	0.389	0.49	0.49	-	0.62	0.74	0.65	6.72	5.05	7.17	3.52

^aThe low-dose level was reduced from 100 to 50 ppm following the Month 3 cholinesterase evaluation interval.

^bMonth 6A represents erythrocyte cholinesterase determinations performed on 6/7/93 and 6/11/93 (Week 23) 6 weeks after the reduction in dose level from 100 to 50 ppm. Month 6B represents the scheduled 6 month cholinesterase evaluations/sacrifice.

^cValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

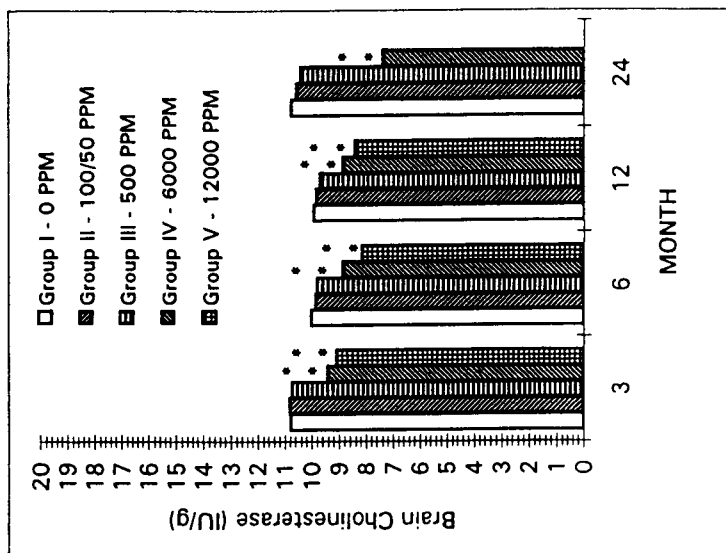
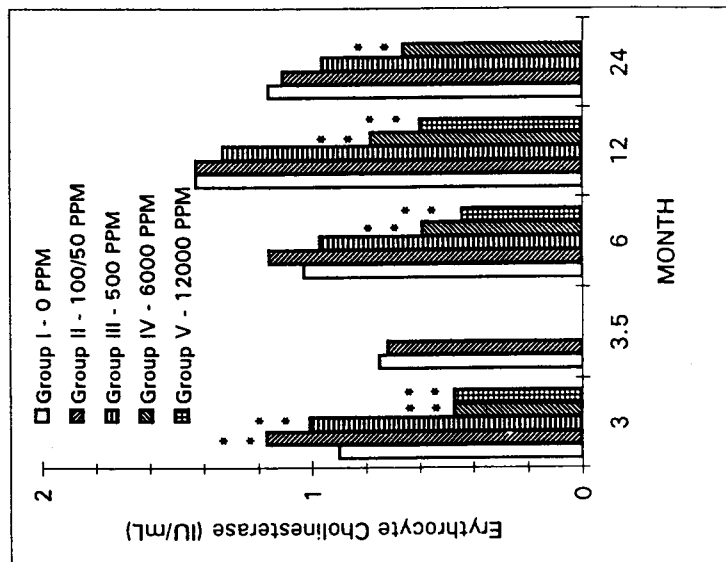
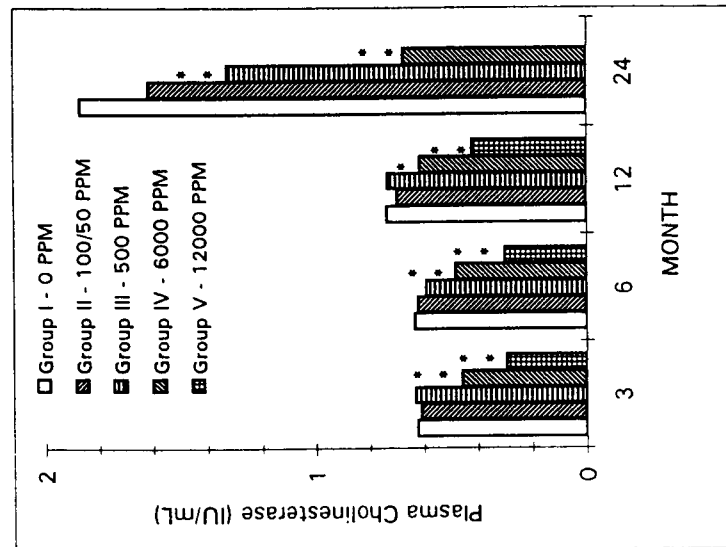
T = Termination, * = Statistically Significant p≤0.05, ** = Statistically Significant p≤0.01

III. RESULTS AND DISCUSSION:

H. Clinical Laboratory Studies (cont.):

2. Cholinesterase Evaluations (cont.):

Cholinesterase Evaluations - Males



* = Statistically significant at $p \leq 0.05$.

*

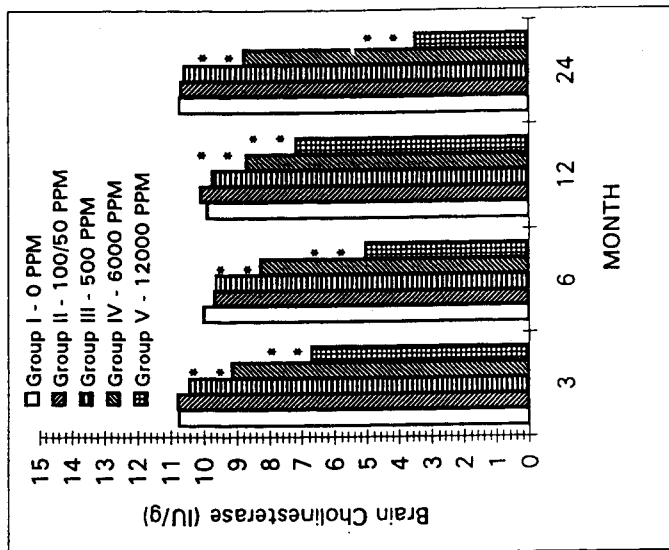
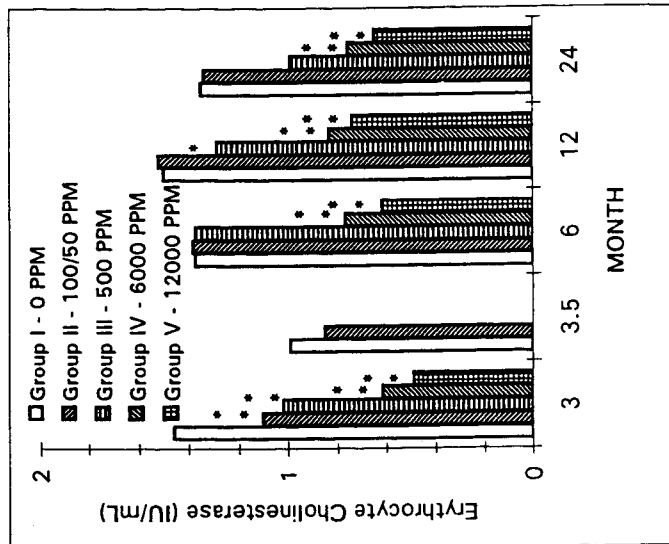
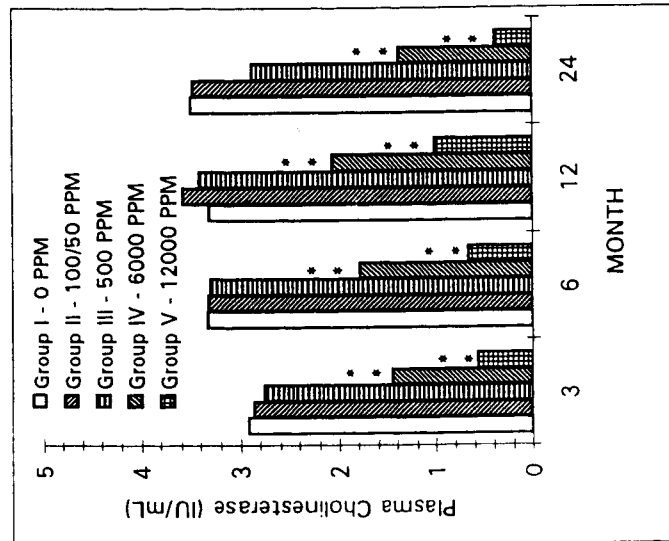
* = Statistically significant at $p \leq 0.05$.

III. RESULTS AND DISCUSSION (CONT.):

H. Clinical Laboratory Studies (cont.):

2. Cholinesterase Evaluations (cont.):

Cholinesterase Evaluations - Females



* = Statistically significant at $p \leq 0.05$.

*

* = Statistically significant at $p \leq 0.01$.

III. RESULTS AND DISCUSSION (cont.):**H. Clinical Laboratory Studies (cont.):****2. Cholinesterase Evaluations (cont.):**

The overall no observed effect level for cholinesterase inhibition was determined to be 50 ppm in the males and females.

**3. Clinical Chemistry Determinations
(Appendices J and P):**

Differences from control which appeared to be treatment-related were noted in a number of clinical chemistry parameters. These included:

1	Alkaline Phosphatase	Statistically significantly reduced in the males and females at 6000 and 12000 ppm at 6 and 12 months and at 12000 ppm at 18 months.
2	Aspartate Aminotransferase	Statistically significantly reduced in the females at 500, 6000 and 12000 ppm at 12 months and at 12000 ppm at 18 months.
3	Gamma Glutamyl Transpeptidase	Statistically significantly increased in females at 6000 ppm and 12000 ppm at the 6, 12 (12000 ppm only), and at 24 month intervals. Statistically significantly increased in the males at 6000 ppm and 12000 ppm at the 12, 18, and 24 month (12000 ppm only) intervals.
4	Cholesterol	Statistically significantly increased in the males and females at 6000 and 12000 ppm at 6, 12, 18 and 24 months.

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

3. Clinical Chemistry Determinations (cont.):

The significance of the decreases observed in alkaline phosphatase and aspartate aminotransferase activities is unclear. The observed activities were generally within the range of historical control data (Appendix P). However, the apparent dose response suggests that the observed decreases were treatment-related. Alanine aminotransferase activity was statistically significantly reduced in the females at 500, 6000, and 12000 ppm at 12 months. These statistically significant differences from control were attributed to a slightly greater mean value in the controls rather than to a treatment-related effect. The alanine aminotransferase activity levels of the treated animals were within the range of the historical control data (Appendix P). The blood urea nitrogen concentration was statistically significantly reduced at 6 months in the males at the 6000 and 12000 ppm dose levels and in the females at the 6000 ppm dose level. The blood urea nitrogen level was also statistically significantly reduced at 12 months in the males at the 6000 ppm dose levels and in the females at all dose levels. These values were within the range of the historical control data (Appendix P). At 18 months the blood urea nitrogen level of the 12000 ppm males was statistically significantly elevated and deviated from the range of the historical control data (Appendix P).

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

3. Clinical Chemistry Determinations (cont.):

The significance of these changes is unclear. The statistically increased cholesterol concentration observed in the males and females at 6000 and 12000 ppm throughout the study and the statistically increased gamma glutamyl transpeptidase activity of the 6000 and 12000 ppm males and females observed at most study intervals were considered treatment related. The increases generally exhibited a dose response and were outside the range of historical control data (Appendix P).

Mean values are summarized in the following pages
(Pages 75 and 76)

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

3. Clinical Chemistry Determinations (cont.):

Group	Dose Level (ppm)	Aspartate Aminotransferase (IU/L)				Alanine Aminotransferase (IU/L)				Alkaline Phosphatase (IU/L)			
		6	12	18	T	6	12	18	T	6	12	18	T
MONTH													
MALES													
I	0	99	87	61	70	63	62	40	50	76	78	63	79
II	100/50 ^a	109	98	71	63	75	73	47	42	79	82	67	63
III	500	90	101	66	88	59	70	45	54	72	77	65	82
IV	6000	78	85	70	50	53	57	53	49	**	**	57	50
V	12000	90	82	74	b	67	55	80	b	**	**	**	b
FEMALES													
I	0	80	132	76	73	57	86	52	57	51	48	46	44
II	100/50 ^a	66	93	57	73	46	67	44	44	47	44	67	103
III	500	63	78	67	76	44	**	51	54	46	44	48	53
IV	6000	61	79	55	210	40	**	54	120	**	**	39	101
V	12000	60	**	**	44	46	**	42	67	**	**	*	39

^aThe low-dose level was reduced from 100 to 50 ppm following the Month 3 cholinesterase evaluation interval.

^bValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

T = Termination, * = Statistically Significant $p \leq 0.05$, ** = Statistically Significant $p \leq 0.01$.

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

3. Clinical Chemistry Determinations (cont.):

Group	Dose Level (ppm)	Blood Urea Nitrogen (mg/dL)				Cholesterol (mg/dL)				Gamma-Glutamyl Transferase (IU/L)			
MONTH		6	12	18	T	6	12	18	T	6	12	18	T
MALES													
I	0	18.2	17.1	16.6	18.7	78	94	153	218	0	0	1	3
II	100/50 ^a	17.4	16.4	16.7	22.0	80	90	144	222	0	0	1	2
III	500	17.8	16.7	15.5	22.7	81	93	137	263	0	0	1	6
IV	6000	**	**	**	24.0	**	*	**	**	2	*	**	**
V	12000	**	15.4	16.9	24.0	129	134	224	522	2	1	5	15
		**	16.1	16.2	31.7	b	**	**	b	7	**	**	b
FEMALES													
I	0	15.5	17.5	16.7	13.9	99	130	126	263	1	1	1	0
II	100/50 ^a	15.7	*	15.4	18.0	99	123	142	162	0	1	1	1
III	500	14.5	**	14.7	16.3	102	127	157	284	1	1	1	0
IV	6000	**	**	14.9	30.9	**	*	**	**	**	2	*	*
V	12000	14.7	*	15.6	19.0	**	**	**	**	**	**	4	**

^aThe low-dose level was reduced from 100 to 50 ppm following the Month 3 cholinesterase evaluation interval.
^bValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

T = Termination, * = Statistically Significant $p \leq 0.05$, ** = Statistically Significant $p \leq 0.01$.

III. RESULTS AND DISCUSSION (cont.):

H. Clinical Laboratory Studies (cont.):

3. Clinical Chemistry Determinations (cont.):

Statistically significant differences from control values occurred sporadically in other clinical chemistry parameters. However, these were not consistent over time, dose, nor sex and therefore were not considered treatment related.

4. Urinalysis (Appendix K):

There were no treatment related findings evident in the urinalysis data of the treated animals at any evaluation interval during the study.

I. Organ Weights (Appendix L):

A number of statistically significant differences from control values were observed in the mean absolute and relative (organ to body weight; organ to brain weight ratios) organ weights of the treated animals at the 12 month interim and terminal sacrifices.

Numerous tissues and organs from the decedents were congested. These animals were either not exsanguinated (found dead or accidental death) or were incompletely exsanguinated (sacrificed in extremis) prior to postmortem examination. In the decedents from the treatment groups, this finding was not considered to be related to the dietary administration of malathion. The statistically significant increases noted in the absolute and relative organ weight data of the following organs were considered to be treatment related at 12 and/or 24 months:

III. RESULTS AND DISCUSSION (cont.):**I. Organ Weights (cont.):**

ORGAN	OBSERVED	AFFECTED DOSE GROUP	INTERVAL (MONTHS)
Kidney	Males and Females	6000 and 12000 ^a ppm	12 and 24
Liver	Males and Females	6000 and 12000 ^a ppm	12 and 24
Spleen	Males	6000 and 12000 ^a ppm	12
Thyroid/Parathyroid	Males	6000 and 12000 ^a ppm	12 and 24

^aOrgan weights were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

The apparent dose response and consistency in both sexes of these organ weight changes and the fact that the changes were, in all cases, increases observed in animals that exhibited reduced terminal body weights, suggests that these organ weight changes were treatment-related. The changes noted in the kidney weights were supported by macroscopic and microscopic findings. The organ weight changes observed in the remaining organs were not clearly associated with microscopic findings.

Absolute and relative organ weights of select organs were as follows (pages 79 through 82).

III. RESULTS AND DISCUSSION (cont.):

I. Organ Weights (cont.):

12 MONTH INTERIM SACRIFICE - ORGAN WEIGHTS									
Group	Dose Level (ppm)	Males				Females			
		TBW (Grams)	WT (Grams)	O/BW	O/BR	TBW (Grams)	WT (Grams)	O/BW	O/BR
KIDNEYS									
I	0	363	2.539	6.99	1.34	211	1.653	7.86	.95
II	50	360	2.587	7.19	1.38	215	1.661	7.77	.97
III	500	358	2.565	7.17	1.38	206	1.675	8.15	.97
IV	6000	345	** 2.884	** 8.35	** 1.52	204	** 1.795	** 8.79	** 1.04
V	12000	** 323	** 3.282	** 10.14	1.75	** 191	** 1.864	** 9.78	** 1.09
LIVER									
I	0	363	11.798	3.25	6.22	211	7.096	3.37	4.07
II	50	360	11.422	3.17	6.09	215	7.096	3.29	4.13
III	500	358	11.613	3.23	6.23	206	6.810	3.30	3.92
IV	6000	345	** 14.440	** 4.18	** 7.63	204	7.644	** 3.74	4.41
V	12000	** 323	** 16.056	** 4.96	** 8.54	** 191	** 8.225	** 4.32	** 4.80

TBW = Terminal Body Weight, WT = Absolute Organ Weight, O/BW = Organ to Body Weight Ratio, O/BR = Organ to Brain Weight Ratio.
 * = Statistically Significant p<0.05, ** = Statistically Significant p<0.01

III. RESULTS AND DISCUSSION:

I. Organ Weights (cont.):

12 MONTH INTERIM SACRIFICE - ORGAN WEIGHTS									
Group	Dose Level (ppm)	Males			Females				
		TBW (Grams)	WT (Grams)	O/BW	TBW (Grams)	WT (Grams)	O/BW	O/BR	
SPLEEN									
I	0	363	.711	1.96	3.75	211	.568	2.71	3.26
II	50	360	.709	1.97	3.78	215	.507	2.37	2.95
III	500	358	.711	1.99	3.82	206	.536	2.61	3.09
IV	6000	345	.773	* 2.24	4.08	204	.538	2.64	3.11
V	12000	** 323	* .877	** 2.70	** 4.65	** 191	.549	2.89	3.20
THYROID/PARATHYROID									
I	0	363	.0211	5.82	1.11	211	.0178	8.49	1.03
II	50	360	.0227	6.31	1.21	215	.0174	8.16	1.01
III	500	358	.0226	6.34	1.21	206	.0179	8.74	1.04
IV	6000	345	* .0242	** 7.00	* 1.28	204	.0198	* 9.68	1.14
V	12000	** 323	** .0264	** 8.16	** 1.41	** 191	.0181	9.51	1.06

TBW = Terminal Body Weight, WT = Absolute Organ Weight, O/BW = Organ to Body Weight Ratio, O/BR = Organ to Brain Weight Ratio.
 * = Statistically Significant p<0.05, ** = Statistically Significant p<0.01

III. RESULTS AND DISCUSSION:

I. Organ Weights (cont.):

TERMINAL SACRIFICE - ORGAN WEIGHTS									
Group	Dose Level (ppm)	Males			Females			O/BW	O/BR
		TBW (Grams)	WT (Grams)	O/BW	O/BR	TBW (Grams)	WT (Grams)		
KIDNEYS									
I	0	345	3.767	1.10	1.92	243	2.262	.94	1.25
II	50	337	3.245	.98	1.64	252	2.286	.91	1.27
III	500	339	3.570	1.05*	1.79	250	2.409	.98	1.33
IV	6000	** 315	** 4.193	1.34	** 2.20	233	** 2.760	** 1.20	** 1.54
V	12000	a	a	a	a	** 194	** 3.090	** 1.62	** 1.76
LIVER									
I	0	345	15.297	4.44	7.79	243	10.168	4.23	5.62
II	50	337	14.530	4.33	7.34	252	10.296	4.08	5.73
III	500	339	16.569	4.89	8.33	250	10.921	4.42	6.02
IV	6000	** 315	** 20.428	** 6.52	** 10.74	233	** 13.187	** 5.69	** 7.34
V	12000	a	a	a	a	** 194	** 13.315	** 6.82	** 7.56

TBW = Terminal Body Weight, WT = Absolute Organ Weight, O/BW = Organ to Body Weight Ratio, O/BR = Organ to Brain Weight Ratio.
 * = Statistically Significant p<0.05, ** = Statistically Significant p<0.01

III. RESULTS AND DISCUSSION:

I. Organ Weights (cont.):

TERMINAL SACRIFICE - ORGAN WEIGHTS									
Group	Dose Level (ppm)	Males			Females				
		TBW (Grams)	WT (Grams)	O/BW	TBW (Grams)	WT (Grams)	O/BW		
SPLEEN									
I	0	345	2.077	6.06	243	.974	4.07	5.37	
II	50	337	2.520	7.55	252	1.001	4.12	5.58	
III	500	339	2.575	7.62	250	1.413	5.95	7.80	
IV	6000	** 315	1.456	4.57	233	.890	3.83	4.95	
V	12000	a	a	a	** 194	.903	4.73	5.06	
THYROID/PARATHYROID									
I	0	345	.0354	1.04	243	.0381	1.61	2.11	
II	50	337	.0401	1.25	252	.0278	1.11	1.55	
III	500	339	.0640	1.89	250	.0302	1.21	1.66	
IV	6000	** 315	** .0420	** 1.34	233	** .0349	** 1.51	** 1.95	
V	12000	a	a	a	** 194	.0281	** 1.48	1.60	

TBW = Terminal Body Weight, WT = Absolute Organ Weight, O/BW = Organ to Body Weight Ratio, O/BR = Organ to Brain Weight Ratio.
 * = Statistically Significant $p \leq 0.05$, ** = Statistically Significant $p \leq 0.01$

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (Appendix M):

1. Macroscopic Findings:

Emaciation and irregular kidney surfaces were the major macroscopic findings and were mainly observed in animals which died prior to study termination. Several males and females from the 12000 ppm dose level and males from the 6000 ppm dose level had kidneys with irregular surfaces. The incidence of this finding in males and females from the 100/50, and 500 ppm and in females from the 6000 ppm dose levels was low and was comparable to the control animals. Several animals from the 12000 ppm dose level were noted to be emaciated prior to their unscheduled deaths. The incidence of emaciation in the 100/50, 500, and 6000 ppm dose levels in both sexes was low and was comparable to the control animals.

Other macroscopic findings occurred with similar incidence and severities in the treatment and control groups or they occurred sporadically. These findings have been seen in rats of similar strain and age used in comparable studies conducted in this laboratory. They were considered to be incidental and not related to the dietary administration of malathion.

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (Appendix M):

2. Microscopic Findings:

Findings which were considered to be related to treatment with malathion were seen in the nasoturbinal and nasopharyngeal tissues and in the kidneys and liver. Overall, the incidence and/or severities of these findings were greatest in the 6000 and 12000 ppm dose levels. Similar types of findings occurred at lower incidence and severities in rats from the 100/50, and 500 ppm dose levels and were comparable to the control group incidence. Under the conditions of this study, the NOEL (No Observable Effect Level) with respect to microscopic findings in the nasoturbinates, nasopharynx, kidneys and liver was considered to be 500 ppm.

Non Neoplastic:

NASOTURBINAL TISSUES:

Degeneration of the olfactory epithelium was seen in several males and females from the 6000 and 12000 ppm dose levels. The degenerative changes were characterized by epithelial disorganization, cytoplasmic disruption, fragmentation and/or exfoliation. In the affected areas the basement membrane appeared to remain intact. The degenerative changes, while most pronounced in the dorsal meatus, also affected the olfactory epithelium covering the nasal septum and the nasoturbinal scrolls. Focal degeneration of olfactory epithelium, characterized only by disorganization, was seen in a very small and comparable number of rats from the control, 100/50 and 500 ppm dose levels and was frequently associated with the presence of food particles in the nasal cavity and/or focal subacute (chronic active)/chronic inflammation.

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Non Neoplastic:

NASOTURBINAL TISSUES:

Focal hyperplasia of olfactory epithelium was seen in many rats from the 6000 and 12000 ppm dose levels only. This was characterized by focal thickening of the epithelium and focal proliferation of basal cells forming clusters in the underlying lamina propria. Small cysts were frequently associated with the hyperplasia.

Other findings in the olfactory mucosa included subacute (chronic active)/chronic inflammation and dilated and hyperplastic mucosal glands. These were seen most frequently in rats from the 6000 and 12000 ppm dose levels. In numerous rats from the 6000 and 12000 ppm dose levels, foci of olfactory epithelium were replaced by ciliated and non-ciliated columnar epithelium which was hyperplastic in a number of the affected rats. Small foci of similar columnar epithelium replaced olfactory epithelium in a very small and comparable number of rats from the control, 100/50 and 500 ppm dose levels; in these rats, this finding was usually associated with the presence of food particles in the nasal cavity and/or focal subacute (chronic active)/chronic inflammation.

Regarding the respiratory mucosa, subacute (chronic active)/chronic inflammation, dilated mucosal glands, and hyperplasia of the respiratory epithelium were seen in a number of rats from the treatment and controls groups. These findings were also most frequent in rats from the 6000 and 12000 ppm dose levels.

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Non Neoplastic (cont.):

NASOTURBINAL TISSUES (cont.):

In the nasal lumen, inflammatory cells/cell debris, frequently admixed with amorphous metachromatic-basophilic material (inspissated secretory product), were seen in numerous rats from the treatment and control groups. This occurred most frequently in males and females from the 6000 and 12000 ppm dose levels.

CONSOLIDATED NASOTURBINAL TISSUE FINDINGS										
Sex	Males					Females				
Group	I	II	III	IV	V	I	II	III	IV	V
OVERALL NUMBER OF ANIMALS EXAMINED	90	90	90	90	90	90	90	90	90	90
Nose/turbinates Number Examined	69	14	70	70	70	67	14	69	69	69
Twelve Month Sacrifice	15	0	15	15	14	14	0	15	15	14
Terminal Sacrifice	37	0	29	14	0	36	0	40	34	20
Unscheduled Deaths	17	14	26	41	56	17	14	14	20	35
NASAL MUCOSA (OLFACTORY): GLANDS DILATED										
Minimal	1	0	0	4	2	2	0	0	4	4
Slight	1	0	0	18	19	0	1	0	25	22
Moderate	0	1	0	9	6	0	0	0	9	7
Total	2	1	0	31	27	2	1	0	38	33
NASAL MUCOSA (OLFACTORY): SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION										
Minimal	2	0	0	0	2	0	0	1	1	0
Slight	3	0	5	19	21	0	1	1	21	16
Moderate	1	1	2	31	12	0	2	0	20	4
Moderately Severe	0	0	0	2	0	0	0	0	0	0
Total	6	1	7	52	35	0	3	2	42	20
NASAL MUCOSA (OLFACTORY): EPITHELIUM-DEGENERATION										
Minimal	2	0	1	1	0	0	0	0	0	2
Slight	1	1	4	4	6	0	2	1	4	8
Moderate	0	1	0	31	24	2	0	0	46	42
Moderately Severe	1	0	0	30	39	0	0	0	19	14
Total	4	2	5	66	69	2	2	1	69	66
NASAL MUCOSA (OLFACTORY): EPITHELIUM-CYSTS										
Minimal	0	0	0	34	25	0	0	0	10	17
Slight	0	0	0	9	30	0	0	0	41	32
Moderate	0	0	0	0	0	0	0	0	7	13
Total	0	0	0	43	55	0	0	0	58	62

III. RESULTS AND DISCUSSION:

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Non Neoplastic (cont.):

NASOTURBINAL TISSUES (cont.):

CONSOLIDATED NASOTURBINAL TISSUE FINDINGS										
Sex	Males					Females				
Group	I	II	III	IV	V	I	II	III	IV	V
OVERALL NUMBER OF ANIMALS EXAMINED	90	90	90	90	90	90	90	90	90	90
Nose/turbinates Number Examined	69	14	70	70	70	67	14	69	69	69
Twelve Month Sacrifice	15	0	15	15	14	14	0	15	15	14
Terminal Sacrifice	37	0	29	14	0	36	0	40	34	20
Unscheduled Deaths	17	14	26	41	56	17	14	14	20	35
NASAL MUCOSA (OLFACTORY): GLANDULAR HYPERPLASIA										
Minimal	0	0	0	2	2	0	0	0	2	1
Slight	0	0	0	11	12	0	0	0	19	11
Moderate	0	0	0	4	4	0	0	0	3	2
Total	0	0	0	17	18	0	0	0	24	14
NASAL MUCOSA (OLFACTORY): EPITHELIUM-HYPERPLASIA										
Minimal	0	0	0	20	12	0	0	0	10	4
Slight	0	0	0	21	29	0	0	0	37	24
Moderate	0	0	0	1	10	0	0	0	10	26
Moderately Severe	0	0	0	0	0	0	0	1	0	0
Total	0	0	0	42	51	0	0	1	57	54
NASAL MUCOSA (OLFACTORY): OLFACTORY EPITHELIUM REPLACED BY CILATED AND NONCILATED COLUMNAR EPITHELIAL CELLS										
Minimal	3	0	4	6	1	0	1	0	8	2
Slight	2	0	2	8	15	0	0	1	15	12
Moderate	0	1	1	18	20	2	1	0	22	8
Moderately Severe	1	0	0	11	7	0	0	0	5	3
Total	6	1	7	43	43	2	2	1	50	25
NASAL MUCOSA (OLFACTORY): HYPERPLASIA OF THE CILIATED AND NONCILATED COLUMNAR EPITHELIAL CELLS WHICH REPLACED THE OLFACTORY EPITHELIUM										
Minimal	1	0	1	1	1	0	0	0	7	0
Slight	2	0	2	7	13	0	0	0	17	7
Moderate	0	1	1	9	8	2	1	0	7	4
Moderately Severe	0	0	0	1	0	0	0	0	2	0
Total	3	1	4	18	22	2	1	0	33	11
NASAL MUCOSA (RESPIRATORY): SUBACUTE (CHRONIC ACTIVE)/CHRONIC INFLAMMATION										
Minimal	1	0	0	0	0	0	0	2	2	0
Slight	2	1	3	9	13	3	1	2	17	6
Moderate	6	1	9	32	8	3	3	1	15	4
Moderately Severe	1	0	0	0	0	1	0	0	0	0
Total	10	2	12	41	21	7	4	5	34	10

III. RESULTS AND DISCUSSION:

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Non Neoplastic (cont.):

NASOTURBINAL TISSUES (cont.):

CONSOLIDATED NASOTURBINAL TISSUE FINDINGS										
Sex	Males					Females				
Group	I	II	III	IV	V	I	II	III	IV	V
OVERALL NUMBER OF ANIMALS EXAMINED	90	90	90	90	90	90	90	90	90	90
Nose/turbinates Number Examined	69	14	70	70	70	67	14	69	69	69
Twelve Month Sacrifice	15	0	15	15	14	14	0	15	15	14
Terminal Sacrifice	37	0	29	14	0	36	0	40	34	20
Unscheduled Deaths	17	14	26	41	56	17	14	14	20	35
NASAL MUCOSA (RESPIRATORY): GLANDS DILATED										
Minimal	8	0	5	5	14	4	1	5	7	7
Slight	7	0	8	21	8	4	3	1	7	12
Moderate	3	0	0	2	2	0	0	0	0	1
Total	18	0	13	28	24	8	4	6	14	20
NASAL MUCOSA (RESPIRATORY): HYPERPLASIA										
Minimal	6	1	0	1	9	3	0	0	5	3
Slight	1	0	1	15	19	1	0	7	20	22
Moderate	5	1	11	27	12	3	3	0	18	7
Moderately Severe	1	0	0	1	1	0	0	0	1	1
Total	13	2	12	44	41	7	3	7	44	33
NASAL LUMEN: INFLAMMATORY CELLS/CELL DEBRIS/METACHROMATIC-BASOPHILIC AMORPHOUS MATERIAL										
Minimal	4	0	5	4	6	3	1	4	1	3
Slight	6	2	5	13	22	1	1	4	17	16
Moderate	3	2	9	46	34	4	4	0	42	37
Moderately Severe	2	1	3	5	1	2	1	1	4	2
Severe	0	0	0	1	0	0	0	0	0	0
Total	15	5	22	69	63	10	7	9	64	58

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Non Neoplastic (cont.):

NASOPHARYNX:

Hyperplasia of the respiratory type epithelium lining the nasopharynx was seen in a number of rats from the treatment and control groups. Overall, an increased incidence was seen in males and females from the 6000 ppm and females from the 12000 ppm dose levels.

PHARYNX FINDINGS										
Sex	Males					Females				
Group	I	II	III	IV	V	I	II	III	IV	V
OVERALL NUMBER OF ANIMALS EXAMINED	90	90	90	90	90	90	90	90	90	90
Pharynx Number Examined	61	14	69	68	66	66	13	68	67	63
MUCOSA: EPITHELIAL HYPERPLASIA										
Minimal	7	0	8	11	7	7	0	13	14	8
Slight	3	0	5	8	7	4	1	1	10	12
Moderate	0	0	2	2	0	3	0	0	2	1
Moderately Severe	0	0	0	1	0	0	0	0	0	0
Total	10	0	15	22	14	14	1	14	26	21

KIDNEYS:

Subacute-chronic inflammation/chronic nephropathy was seen in numerous rats from all groups, including the controls. This was first noted in rats which were sacrificed at the twelve month interim. At twelve months, the incidence and severity in males from the 12000 ppm dose level were slightly greater than in the comparable controls; in the females this was seen only in the 12000 ppm dose level. In the decedents and in those terminally sacrificed, almost all of the rats were affected. In these rats, overall, the severities in both males and females from the 6000 ppm and 12000 ppm dose

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Non Neoplastic (cont.):

KIDNEYS (cont.):

levels were greater than their comparable controls; the severities in the 0, 100/50, and 500 ppm dose levels were considered to be similar. Subacute-chronic inflammation/chronic nephropathy is commonly seen in aging/aged rats. In this study, treatment with malathion appeared to have exacerbated the severity. This finding correlated with the surface irregularities of the kidneys which were noted macroscopically and with the increased kidney weights observed at necropsy.

KIDNEY FINDINGS										
Sex	Males					Females				
Group	I	II	III	IV	V	I	II	III	IV	V
OVERALL NUMBER OF ANIMALS EXAMINED	90	90	90	90	90	90	90	90	90	90
Kidneys Number Examined	70	55	55	55	70	70	55	55	55	70
Twelve Month Sacrifice	15	0	0	0	14	15	0	0	0	15
Terminal Sacrifice	37	41	29	14	0	38	41	41	34	20
Unscheduled Deaths	18	14	26	41	56	17	14	14	21	35
U/ INTERSTITIUM: SUBACUTE-CHRONIC INFLAMMATION/CHRONIC NEPHROPATHY										
Slight	0	0	0	0	1	0	0	0	0	0
Moderate	0	0	0	0	1	0	0	0	0	0
Total	0	0	0	0	2	0	0	0	0	0
B/ INTERSTITIUM: SUBACUTE-CHRONIC INFLAMMATION/CHRONIC NEPHROPATHY										
Minimal	2	0	0	0	0	4	2	1	0	5
Slight	16	6	8	3	1	21	27	11	3	5
Moderate	30	39	33	8	20	19	22	38	32	18
Moderately Severe	15	6	11	37	44	5	1	2	18	30
Severe	2	3	2	7	3	0	1	0	1	1
Total	65	54	54	55	68	49	53	52	54	59

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

OTHER FINDINGS:

When examined by light microscopy, squamous cell hyperplasia and hyperkeratosis of the epithelium covering the forestomach (non-glandular portion) were seen in numerous decedents from the 6000 ppm and 12000 ppm dose levels and in a small number of those from the 0, 100/50, and 500 ppm dose levels. Congestion, edema, erosions/ulcers and acute to chronic inflammation were also seen in one or more of the affected animals. Similar findings were seen in only a very small number of the terminally sacrificed rats.

Animals which are moribund prior to death usually have a decreased appetite leading to a decrease or cessation of food intake. Even though moribund, it can be assumed that the squamous epithelium covering the forestomach continues to proliferate. In the absence of food intake, the proliferating squamous epithelium covering the forestomach may become quite prominent with cornification of the superficial layers (squamous cell hyperplasia/hyperkeratosis). This is a possible explanation for the increased incidence of this lesion among the treatment groups.⁶

⁶Brown, R. H. and Hardisty, J. F.: Oral Cavity, Esophagus and Stomach. Pathology of the Fischer Rat; Boorman, G. A., et. al. (editors); Academic Press, Inc., New York, New York; 1990; (9-30).

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Non Neoplastic (cont.):

OTHER FINDINGS (cont.):

In addition, erosions and/or ulcers of the stomach were seen in a relatively small number of the affected rats. This effect can be attributed to stress related to moribundity and eventual death of the affected animals. Gastric erosions and ulcers are well known to be induced by stress.⁷ Also considered to be stress associated was the lymphoid cell depletion/atrophy in the thymus and spleen and the mediastinal and mesenteric lymph nodes in a number of the animals which were killed in extremis or were found dead.

Numerous tissues and organs from the decedents were congested. These animals were either not exsanguinated (found dead or accidental death) or were incompletely exsanguinated (sacrificed in extremis) prior to postmortem examination. In the decedents from the treatment groups, this finding was not considered to be related to the dietary administration of malathion.

⁷Daniel E. Hernandez and Gary B. Glavin, eds., Neurobiology of Stress Ulcers, Annals of the New York Academy of Sciences, Vol. 597, 1990.

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Other non-neoplastic findings, including those seen in the nasoturbinal tissues and kidneys, were considered to be incidental and not related to the dietary administration of malathion. They occurred with comparable incidence and severities in rats from the treatment and control groups or they occurred sporadically. These have been seen in rats of this strain and age used in comparable studies conducted in this laboratory (Appendix P).

Neoplastic Findings:

Neoplasms which were considered to be related to treatment with malathion were seen in the nasoturbinal tissues and liver. In the nasoturbinal tissues, an adenoma was observed in one male (Animal Number 4033) from the 6000 ppm dose level and a carcinoma was observed in one male (Animal Number 5040) from the 12000 ppm dose level. Spontaneous neoplasms of the nasoturbinal tissues are rare in F344 rats. In untreated dietary and cornoil control animals from eight recent NTP studies only six were identified from nearly 4000 control males and none occurred in a similar number of control females.⁸ None have been observed in this laboratory in six previous studies (238 control males and 241 control females, Appendix P).

⁸Boorman, Gary A. and Morgan, Kevin T.: Nose, Larynx and Trachea. Pathology of the Fischer Rat, Boorman, Gary A., *et. al.*, Montgomery, Charles A. Jr. and Mackenzie, William F. (editors). Academic Press, Inc. New York, New York, 1990, (pp 315-337).

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Neoplastic Findings:

Hepatocellular adenomas and carcinomas were seen in a small number of males and females from the treatment and/or control group. Among the females, the incidence was statistically significantly increased for both neoplasms at the 12000 ppm dose level and for the incidence of hepatocellular adenoma at the 6000 ppm dose level. At these dose levels, the increased incidences of both neoplasms were considered to be attributed to the dietary administration of malathion. In the NTP historical control data, the incidence of hepatocellular adenoma in 1979 comparable, untreated F344 females was 2.3% with a range of 0-10%; the incidence of hepatocellular carcinoma was 0.2% with a range of 0-2%.⁹ In this laboratory, in six previous studies (254 control females, Appendix P), the incidence of hepatocellular adenoma was 1.6% with a range of 0-5.4%; the incidence of hepatocellular carcinoma was 1.1% with a range of 0-2.4% (Appendix P).

⁹Haseman, J.K., Arnold, A. and Eustis, S.L.: Tumor Incidences in Fischer 344 Rats: NTP Historical Data. Pathology of the Fischer Rat; Boorman, G. A., et. al. (editors); Academic Press, Inc., New York, New York; 1990; (pp 555-564).

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Neoplastic Findings (cont.):

Liver Tumor Incidence

Dose Levels (ppm)	0	100/50	500	6000	12000
MALES					
Hepatocellular Adenoma	2/70 (2.9%)	2/55 (3.6%)	3/55 (5.5%)	2/55 (3.6%)	1/70 (1.4%)
Hepatocellular Carcinoma	1/70 (1.4%)	2/55 (3.6%)	1/55 (1.8%)	1/55 (1.8%)	0/70 (0%)
FEMALES					
Hepatocellular Adenoma	0/70 (0%)	1/55 (1.8%)	1/55 (1.8%)	3/55 ^{a,c} (5.5%)	3/70 ^b (4.3%)
Hepatocellular Carcinoma	0/70 (0%)	1/55 (1.8%)	1/55 (1.8%)	0/55 (0%)	3/70 ^b (4.3%)

^ap≤0.05 (Fisher Exact Test, Haseman Test, and Cox's Test).

^bp≤0.05 (Haseman Test, Cox's Test and Gehan-Breslow).

^cp≤0.01 (Gehan-Breslow).

Historical Control Data (Hepatocellular Tumors in Female F344 Rats)

Type of Tumor	NTP		HLS	
	Mean	Range	Mean	Range
Hepatocellular Adenoma	2.3%	0-10% (N = 1900)	1.6%	0-5.4% (n = 254)
Hepatocellular Carcinoma	0.2%	0-2% (n = 1900)	1.1%	0-2.4% (n = 254)

Interstitial cell tumors in the testes were seen in numerous rats from all groups. Statistically, the dietary administration of malathion was considered to be associated with increased incidence of this tumor. However, interstitial tumor is very common in the F344 rat and nearly all will develop this tumor if allowed to complete their natural life span. In this laboratory, in six

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Neoplastic Findings (cont.):

previous studies in which rats were sacrificed at the end of 18 and/or 24 months of treatment (234 control males), the incidence of interstitial cell tumor was 90% with a range of 82-94% (Appendix P). In the NTP historical control data, the incidence of interstitial cell tumor in 1910 comparable, untreated F344 males was 88% with a range of 64-98%.⁸ In this study, the incidence of interstitial cell tumor of males from the treatment and control groups were within the expected range and, therefore, they were not considered to be related to the dietary administration of malathion (Appendix P).

Testes Neoplasms					
Sex	Males				
Group	I	II	III	IV	V
OVERALL NUMBER OF ANIMALS	90	90	90	90	90
TESTES NUMBER EXAMINED	70	55	55	55	70
B-U/ INTERSTITIAL CELL TUMOR	5	2	1	12	10
B-B/ INTERSTITIAL CELL TUMOR	49	50	52	42	48
INTERSTITIAL CELL TUMOR /COMBINED	54	52 ^a	53 ^a	54 ^{a,b}	58 ^c

^ap≤0.01 (Fishers Exact Test)

^bp≤0.01 (Cox's and Gehan-Breslow)

^cp≤0.01 (Cox's, Gehan-Breslow and Haseman)

⁸Boorman, Gary A, and Morgan, Kevin T.: Nose, Larynx and Trachea. Pathology of the Fischer Rat, Boorman, Gary A., et. al., Montgomery, Charles A. Jr. and Mackenzie, William F. (editors). Academic Press, Inc. New York, New York, 1990, (pp 315-337).

III. RESULTS AND DISCUSSION (cont.):

J. Pathology (cont.):

2. Microscopic Findings (cont.):

Neoplastic Findings (cont.):

Neoplasms in other tissues and organs occurred with comparable incidence in the treatment and control groups or they occurred sporadically. The incidences of several neoplasms, although somewhat greater in one or more dose levels than in others did not show evidence of a dose response. These neoplasms have been seen in rats of this strain and age used in comparable studies conducted in this laboratory (Appendix P). Under the conditions of this study, these other neoplasm were not considered to be related to the dietary administration of malathion for up to 24 months.

K. Test Material Analysis (Appendix N):

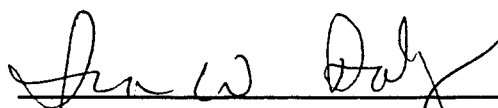
Treated diets and test material purity analysis confirmed that the animals were presented diets which were homogeneously prepared and were at the appropriate concentration level. In addition, analysis of the test material confirmed that it was of appropriate purity throughout the study.

IV. CONCLUSION:

In conclusion, significant toxicity was observed during this study at dose levels of 6000 and 12000 ppm as evidenced by decreased body weights, alterations in hematology and clinical chemistry parameters, cholinesterase depression, increased kidney, liver, spleen and thyroid/parathyroid weights, and microscopic alterations in the nasoturbinal and nasopharyngeal tissues and in the kidneys and liver. The occurrence in the males, of a nasal turbinal adenoma at 6000 ppm and a nasal turbinal carcinoma at 12000 ppm was considered treatment-related. In addition, the occurrence in the females of hepatocellular adenoma and carcinoma at 12000 ppm and hepatocellular adenomas at 6000 ppm were considered treatment-related. No evidence of ocular toxicity was observed during this study. The no observed effect level


IV. CONCLUSION (cont.):

(NOEL) was 50 ppm. The NOEL was determined based upon cholinesterase depression observed at dose levels of 100 ppm and greater. The overall no observed effect level (excluding cholinesterase data) for the study was 500 ppm.



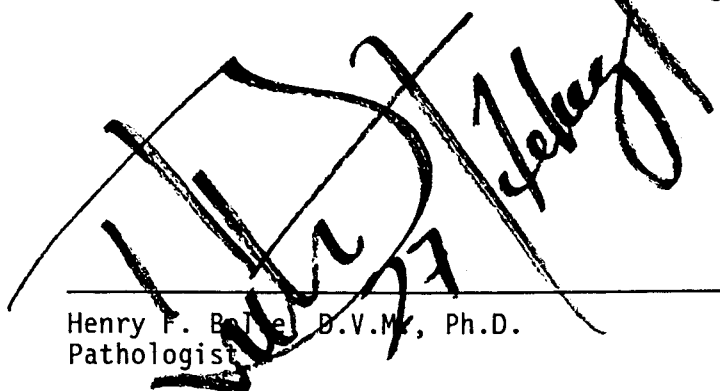
Ira W. Daly, Ph.D., D.A.B.T.
Study Director

2/27/96
Date





Carol S. Auletta, B.A., D.A.B.T.
Director of Toxicology

2/27/96
Date



Henry F. Bolter, D.V.M., Ph.D.
Pathologist

Date

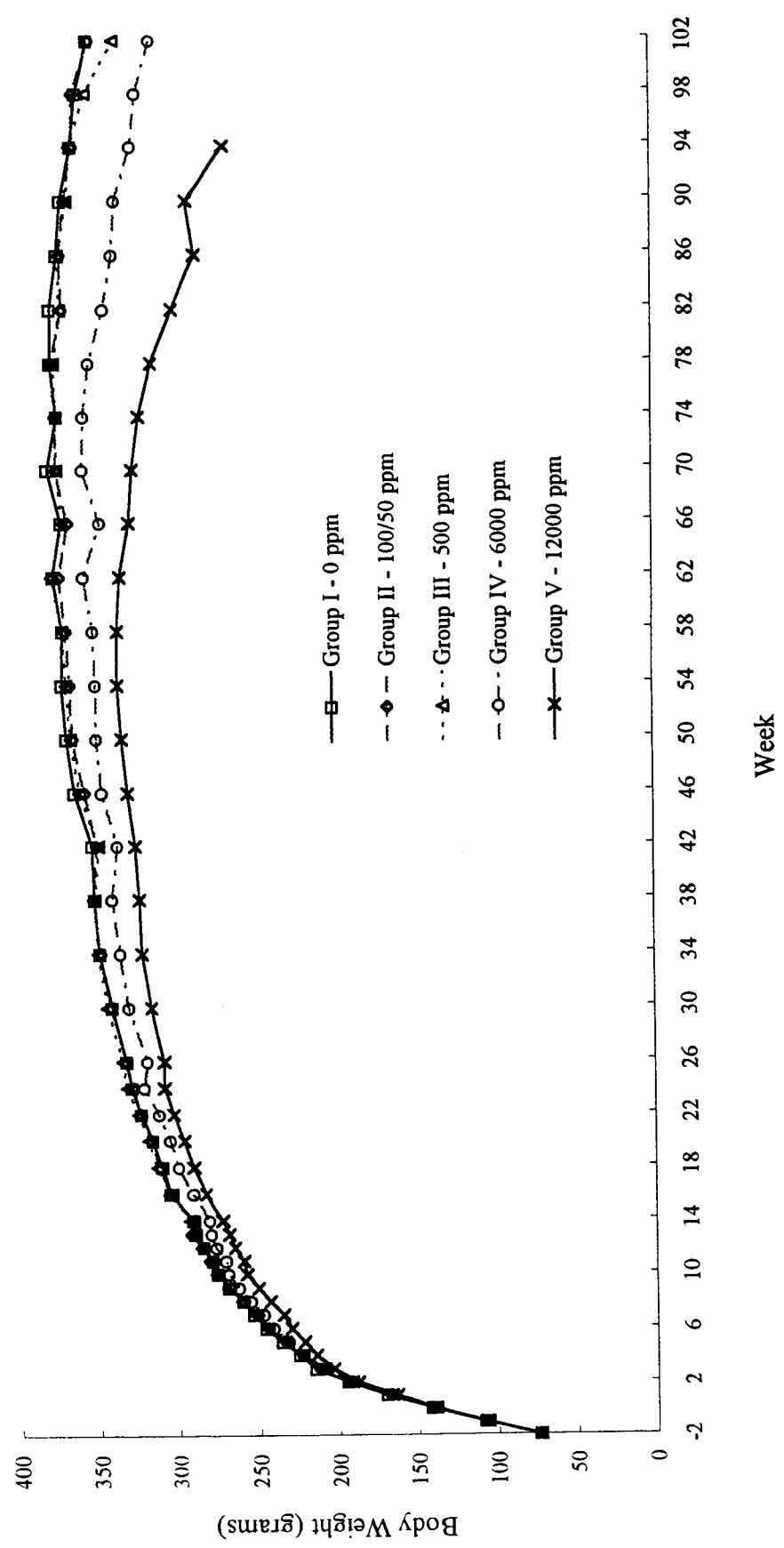



Ward R. Richter, D.V.M., M.S., A.C.V.P.
Vice President and Director of Science
and Technology

2/27/96
Date

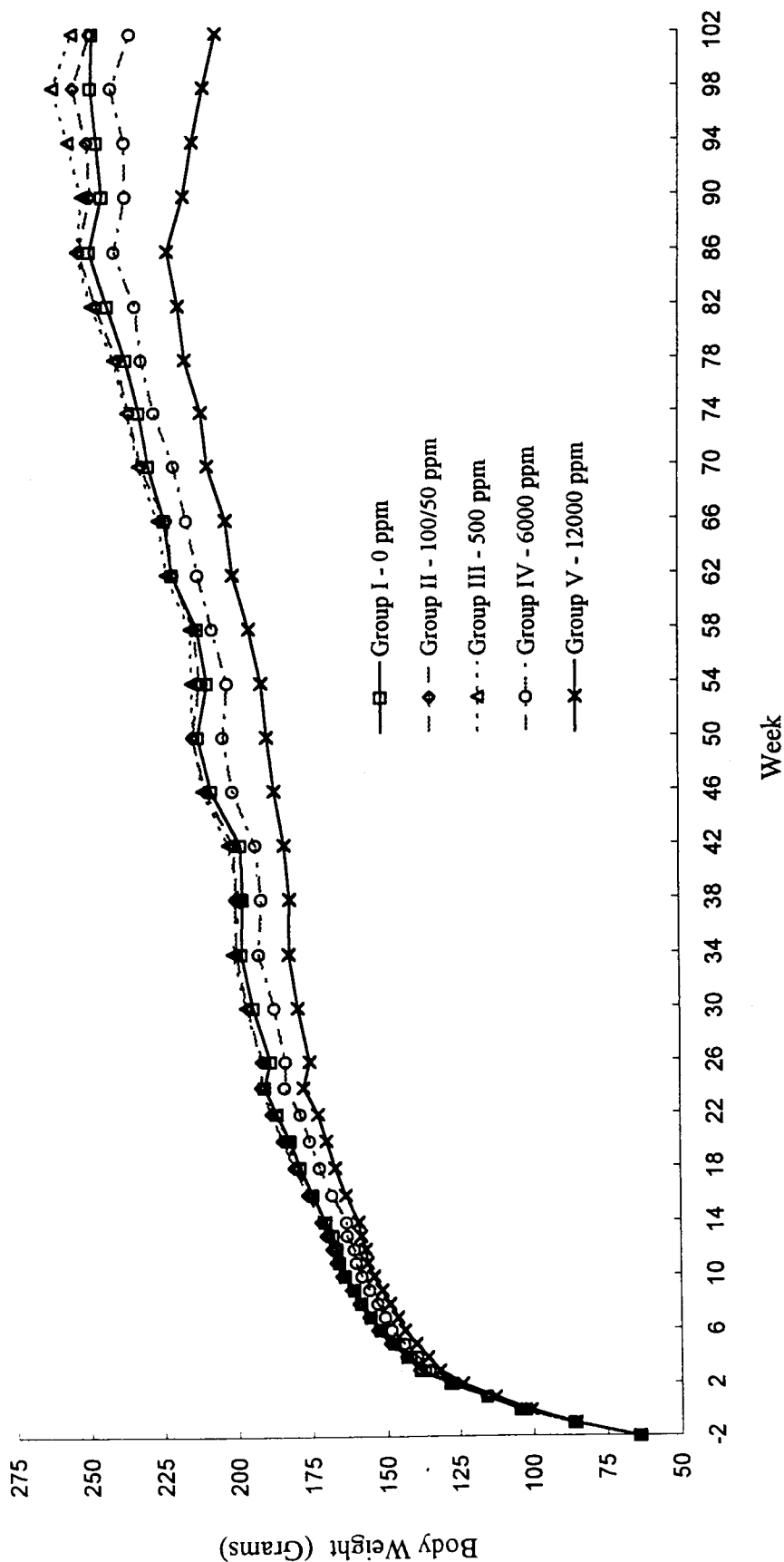
Figure 1
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Group Mean Body Weights - Males



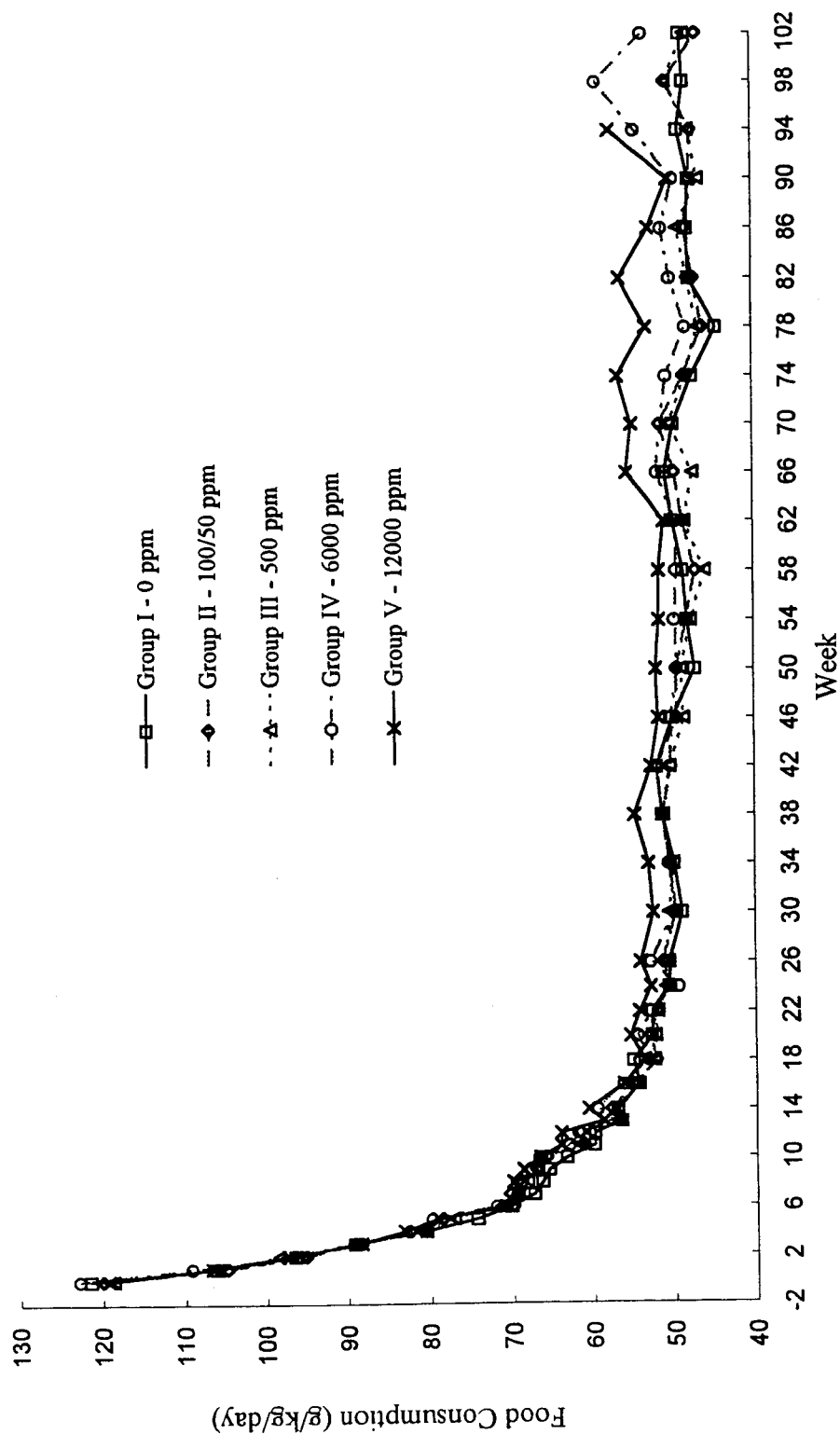
F 1-2
Figure 1 (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Group Mean Body Weights - Females



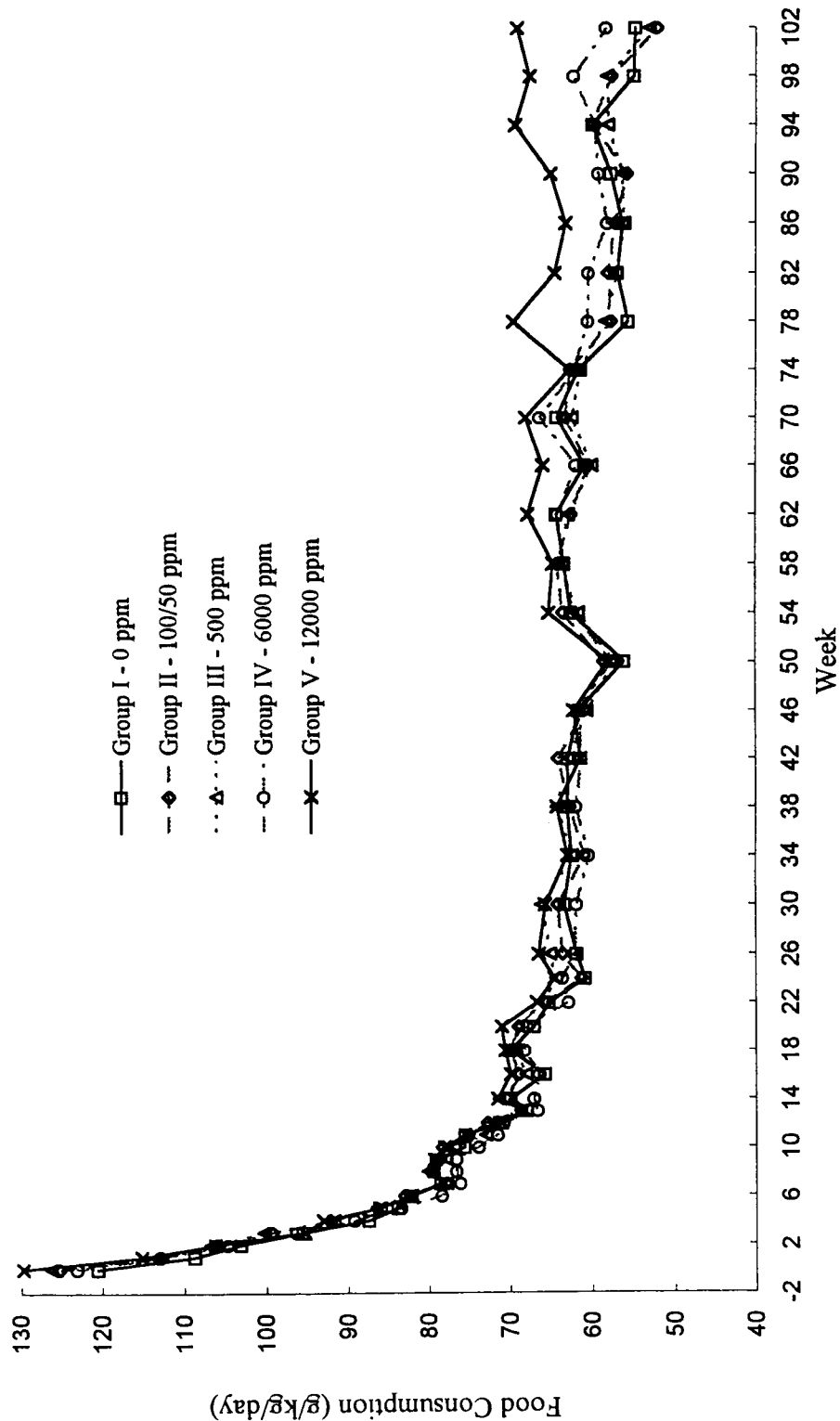
F 2-1
Figure 2
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Group Mean Food Consumption - Males



F 2-2
Figure 2 (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Group Mean Food Consumption - Females



A-1
Appendix A
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - General

Parameter	Reference or Description
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Physical Examination

Behavior:	aggressiveness, increased or decreased activity.
Respiration:	nasal discharge and rales.
Ocular:	chromodacryorrhea, excessive lacrimation and percent opacity.
Appearance:	alopecia, ano-genital staining and general condition.
Gastrointestinal:	abdominal shape and fecal consistency. Palpation for tissue masses.
Other:	includes any unusual observation not included above.

Ophthalmoscopic Examination: Lids, lacrimal apparatus and conjunctiva examined grossly, cornea, anterior chamber, lens, iris, vitreous humor, retina and optic disc examined by indirect ophthalmoscopy. Optycil 1% was used to induce mydriasis.

Fundic Photographs: Optycil 1%, Mydryafair 1%, and Tropicamide 1% were used to induce mydriasis.

Appendix A (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - General (cont.)

Parameter	Reference or Description
Electroretinography	LKC Technologies, Epic II, Photic Stimulator, Model PS22. Photographs were taken on anesthetized animals.
Body Weight	Sartorius Universal Electronic Toploading Balance, Model U3600.
Food Consumption	<p>Sartorius Universal Electronic Toploading Balance, Model U3600. Feed was available <i>ad libitum</i> 7 days/week. Animals were presented with full feeders weighing 570 grams (includes weight of feed, jar and lid). After 6 days feeders were reweighed and resulting weight was subtracted from the full feeder weight. Resulting value = g/6 days (g/interval).</p> <p>When body weights were taken weekly:</p> $\text{g/kg/day} = \frac{\text{g/interval}}{\text{average body weight (kg)}} \div 6 \text{ Days}$ $\text{Average BW} = \frac{\text{Previous BW} + \text{Current BW}}{2}$ <p>When body weights were taken biweekly/monthly:</p> $\text{g/kg/day} = \frac{\text{g/interval}}{\text{current body weight (kg)}} \div 6 \text{ Days}$
Test Material Intake	$\text{mg/kg/day} = \text{g/kg/day} \times \text{nominal dose level} \div 1000.$
Terminal Body Weight (TBW)	Ohaus B 5000. Represents a body weight measured just prior to necropsy.

A-3
Appendix A (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - General (cont.)

Parameter	Reference or Description
Organ Weights	Mettler AK-160
Histological Methods	
Preservative:	
Stain - Luxol fast blue (myelin sheath)	Sheehan, D.C., and Hrapchak, B.B., <i>Theory and Practice of Histotechnology</i> . 2 nd Edition. Columbus: Battelle Press, 1987, pp. 263-264.

A-4
Appendix A (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Hematology

Abbr	Parameter	Specimen	Reporting Units	Reference or Description
HGB	Hemoglobin Concentration	Whole Blood	g/dL	Technicon® H-1™ Hematology System, Miles, Inc.
HCT	Hematocrit	Whole Blood	%	Technicon® H-1™ Hematology System, Miles, Inc.
RBC	Erythrocyte Count	Whole Blood	10 ⁶ /micro-liter (mil/μL)	Technicon® H-1™ Hematology System, Miles, Inc.
RETIC	Reticulocyte Count	Whole Blood	% RBC	Henry, John Bernard, M.D. <i>Clinical Diagnosis and Management by Laboratory Methods</i> . 18 th Edition. W.B. Saunders Co., 1991. pp. 581.
PLT	Platelet Count	Whole Blood	10 ³ /micro-liter (thous/μL)	Technicon® H-1™ Hematology System, Miles Inc.
MCV	Mean Corpuscular Volume	Whole Blood	fL	Technicon® H-1™ Hematology System, Miles Inc.
MCH	Mean Corpuscular Hemoglobin	Whole Blood	pg	Technicon® H-1™ Hematology System, Miles Inc.

Appendix A (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Hematology (cont.)

Abbr	Parameter	Specimen	Reporting Units	Reference or Description
MCHC	Mean Corpuscular Hemoglobin Concentration	Whole Blood	g/dL	Technicon® H-1™ Hematology System, Miles Inc.
WBC	Total Leukocyte Count	Whole Blood	10 ³ /micro-liter (thous/μL)	Technicon® H-1™ Hematology System, Miles Inc.
	Differential Leukocytes and Erythrocyte Morphology	Whole Blood	% WBC	Henry, John Bernard, M.D. <i>Clinical Diagnosis and Management by Laboratory Methods</i> . 18 th Edition. W.B. Saunders Co., 1991. pp. 590-597.
	Absolute Lymphocytes	Whole Blood	10 ³ /micro-liter (thous/μL)	Calculated value. Technicon H-1 Hematology System, Miles Inc.
	Absolute Segmented Neutrophils	Whole Blood	10 ³ /micro-liter (thous/μL)	Calculated value. Technicon H-1 Hematology System, Miles Inc.
				Manual calculation for verification when questionable values occur. $WBC \times [Neut. \text{ or } Lymph] \div 100 = \text{Absolute value.}$

A-6
Appendix A (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Clinical Chemistry

Abbr	Parameter	Specimen	Reporting Units	Reference or Description
AST	Aspartate Aminotransferase (SGOT)	Serum	IU/L	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; (Kinetic) Modified IFCC Technique.
ALT	Alanine Aminotransferase (SGPT)	Serum	IU/L	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; (Kinetic) Modified IFCC Technique.
ALKP	Alkaline Phosphatase	Serum	IU/L	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; (AMP Buffer) Modified Bessey-Lowry-Brock Technique.
BUN	Blood Urea Nitrogen	Serum	mg/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Modified Urease Technique.
CREAT	Creatinine	Serum	mg/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Jaffe Reaction - (Kinetic) Alkaline Picrate.
GLU	Glucose	Serum	mg/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Hexokinase Method.

A-7
Appendix A (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Clinical Chemistry (cont.)

Abbr	Parameter	Specimen	Reporting Units	Reference or Description
CK	Creatine Kinase	Serum	IU/L	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Szasz-NAC Activated Method.
CHOL	Cholesterol (Enzymatic)	Serum	mg/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Cholesterol esterase-cholesterol oxidase Method.
T PROT	Total Protein	Serum	g/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Biuret Technique.
ALB	Albumin	Serum	g/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Bromocresol Green Method.
GLOB	Globulin	Serum	g/dL	Calculated value. Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer.
A/G	Albumin/ Globulin Ratio	-	-	Calculated value. Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer.

A-8
Appendix A (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Clinical Chemistry (cont.)

Abbr	Parameter	Specimen	Reporting Units	Reference or Description
T BILI	Total Bilirubin	Serum	mg/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Modified Jendrassik and Grof Method.
D BILI	Direct Bilirubin	Serum	mg/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Modified Jendrassik and Grof Method.
Na ⁺	Sodium	Serum	mEq/L	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Ion Selective Electrode.
K ⁺	Potassium	Serum	mEq/L	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Ion Selective Electrode.
Cl ⁻	Chloride	Serum	mEq/L	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Ion Selective Electrode.
Ca ⁺⁺	Calcium	Serum	mg/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Cresolphthalein Complexone Method.

Appendix A (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Clinical Chemistry (cont.)

Abbr	Parameter	Specimen	Reporting Units	Reference or Description
PHOS	Inorganic Phosphorus	Serum	mg/dL	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Phosphomolybdate-UV Method.
GGT	Gamma-Glutamyl Transferase	Serum	IU/L	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; (Kinetic) Szasz, G.
CHOLINESTERASE				
PCHE	Cholinesterase	Plasma	$\mu\text{M/ml/min}$ (IU/mL)	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Modified Ellman Method (Kinetic).
RCHE	Cholinesterase	Erythrocyte (RBC)	$\mu\text{M/ml/min}$ (IU/mL)	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Modified Ellman Method (Kinetic).
BCHE	Cholinesterase	Brain	$\mu\text{M/g/min}$ (IU/g)	Hitachi 717, Boehringer Mannheim Diagnostics Automatic Analyzer; Modified Ellman Method (Kinetic).

A-10
Appendix A (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Urinalysis

Abbr	Parameter	Specimen	Reporting Units	Reference or Description
	Urinalysis	Urine		Clinitek 200 Urine Chemistry Analyzer (Miles Inc., Diagnostics Division) Reflectance Spectro-photometer. Clinical Refractometer (Atago, Uricon-N) for specific gravity. Three percent sulfo-salicylic acid test for protein verification. Ictotest reagent tablets (Miles Inc., Diagnostics Division) for bilirubin verification. Henry, John Bernard, M.D., <i>Clinical Diagnosis and Management by Laboratory Methods</i> . 18 th Edition. W.B. Saunders Co., 1991.
	Microscopic Analysis	Urine		Centrifugation of urine - manual microscopy. Henry, John Bernard, M.D., <i>Clinical Diagnosis and Management by Laboratory Methods</i> . 18 th Edition. W.B. Saunders Co., 1991, p. 431.
	Volume	Urine	mL	16 hour overnight collection period.

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Statistical Analysis

Reference or Description

Parameters analyzed statistically: Body weight, body weight change, body weight change from Week 0, food consumption, change in food consumed, hematology, clinical chemistry, terminal organ and body weights, organ to body and organ to brain weight ratios, and electroretinogram values.

Statistical evaluation not performed when the standard deviation for the control group or more than one group is zero, due to lack of variance. If a standard deviation for one treated group is zero, or when N (number of animals) is less than or equal to two animals for any treated group, the variances of the two groups remaining were tested for equality using the F-test (see Two Group Analysis, page A-14) and/or the variances of the remaining groups were tested using the same procedures outlined on the following page. If the N (number of animals) for the control group is less than or equal to two animals, no statistics are presented due to lack of variance.

MULTIPLE GROUP ANALYSIS
STAT SYMBOL

STATISTICAL STATEMENT

No Sig p≤0.05 p≤0.01

Parametric

A-

No statistical differences among the means (parametric ANOVA).

A

A+

The means differ significantly (parametric ANOVA).

L-

The response is not linearly related to the dose levels.

L

L+

The response is linearly related to the dose levels.

Q

Q+

The response shows a lack of fit.

*

**

Significantly different from control (Dunnett's).

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Statistical Analysis (cont.)

Reference or Description

MULTIPLE GROUP ANALYSIS STAT SYMBOL			STATISTICAL STATEMENT
<u>No Sig</u>	<u>p≤0.05</u>	<u>p≤0.01</u>	
<u>Nonparametric</u>			
K-			No statistical differences among the means (Kruskal-Wallis, nonparametric).
	K	K+	The means differ significantly (Kruskal-Wallis nonparametric).
J-			There is not an ordered response to dosage.
	J	J+	There is an ordered response to dosage.
	*	**	Significantly different from control (Dunn's Rank Sum).
NT			Not tested due to lack of variance.

Statistical evaluation of equality of means was made by the appropriate one way analysis of variance technique, followed by a multiple comparison procedure if needed. First, Bartlett's test was performed to determine if groups had equal variance. If the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. The parametric procedures were the standard one way ANOVA using the F distribution to assess significance. If significant differences among the means were indicated, Dunnett's test was used to determine which means were significantly different from the control. If a nonparametric procedure for testing equality of means was needed, the Kruskal-Wallis test was used, and if differences were indicated a summed rank test (Dunn) was used to determine which treatments differed from control.

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Appendix A (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Statistical Analysis (cont.)

Reference or Description

A statistical test for trend in the dose levels was also performed. In the parametric case (i.e., equal variance) standard regression techniques with a test for trend and lack of fit were used. In the nonparametric case Jonckheere's test for monotonic trend was used.

The test for equal variance (Bartlett's) was conducted at the 1%, two-sided risk level. All other statistical tests were conducted at the 5% and 1%, two-sided risk level.

References for these techniques are Snedecor, G.W., and Cochran, W.G., *Statistical Methods*. 6th edition, Iowa State University Press (1967); Hollander, M. and Wolfe, D.A., *Nonparametric Statistical Methods*. John Wiley and Sons, New York (1973); Dunnett, C.W., *J. Am. Sta. Assn.* Vol. 50 (1955) and *Biometrics*. Vol. 20 (1964).

Bartlett's Test	pp. 296-298	S&C
ANOVA	pp. 277-279	S&C
Dunnett's	pp. 1096-1121	D
	pp. 482-491	Bio
Kruskal-Wallis	pp. 114-116	H&W
Summed Rank Test (Dunn)	p. 131	H&W
Regression Analysis		
Trend	pp. 135-153	S&C
Lack of Fit	pp. 456-459	S&C
Jonckheere's Statistic	pp. 120-123	H&W

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Appendix A (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Statistical Analysis (cont.)

Reference or Description

TWO GROUP ANALYSIS STAT SYMBOL			STATISTICAL STATEMENT
<u>No Sig</u>	<u>p≤0.05</u>	<u>p≤0.01</u>	
F-			Variances are equal.
		F+	Variances are unequal.
	*	**	Significantly different from control (t-tests).
NT			Not tested due to lack of variance.

The variances of the two groups were tested for equality using the F test. If the variances were equal, a standard independent two sample t-test was used to determine equality of means. If the variances differed at the 1% level of significance, Welch's t-test was used to determine equality of means. t-tests were conducted at the 5% and 1%, two-sided risk level.

References for these techniques are:

- F-test: Gill, J.L., *Design and Analysis of Experiments in the Animal and Medical Sciences*. Iowa State University Press, Ames, Iowa (1978). Vol. I, pp. 63-65.
- t-test: Ibid., pp. 67-68.
- Welch's t-test: Ibid., p. 71.

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Appendix A
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Methodology and References - Statistical Analysis
Survivorship and Tumor Data

Survival data were analyzed for each sex separately by the series of programs included in the National Cancer Institute (N.C.I.) package for time to death. An assessment of mortality was made by the Kaplan-Meier method.

In addition, if survivorship did differ among groups, tumor analysis was performed and adjusted according to N.C.I. procedures or IARC Monographs Supplement #2, 1980.

Reference for the N.C.I. package is Thomas, D.G., Breslow, N., and Gart, J.J. "Trend and Homogeneity Analyses of Proportions and Life Table Data", *Computers and Biomedical Research* 10, pp. 373-381 (1977).

Reference Haseman, Joseph K., "Statistical Issues in the design, analysis and interpretation of animal carcinogenicity studies", *Environmental Health Perspectives*, 58, pp. 385-392 (1984).

Appendix B
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Mortality Summary^a
Males

Number of Animals Initial Potential ^b On-test Survivors	MONTH																								Total Dead	Total Survivors	Percent Survivorship		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24				25	
Group I - 0 ppm																													
90	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2	4	5	5	0	18	37	37/55 = 67%	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	4	8	13	18	18				
				[10]			[10]					[15]													[37]				
Group II - 100/50 ppm																													
90	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	2	3	2	4	0	14	41	41/55 = 75%	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	3	5	8	10	14	14				
				[10]			[10]					[15]													[41]				
Group III - 500 ppm																													
90	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	4	1	0	3	11	3	26	29	29/55 = 53%	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	2	3	4	8	9	9	12	23	26				
				[10]			[10]					[15]													[29]				
Group IV - 6000 ppm																													
90	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3	3	4	8	9	11	0	39	14	14/53 = 26%
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	4	7	11	19	28	39	39			
				[10]			[10]					[15]													(2) [14]				
Group V - 12000 ppm																													
90	0	0	0	0	1	0	0	0	0	0	0	1 ^c	1	1	1	4	5	12	16	29	41	49	52	55	55	0	55	0	55/55 = 100%
	0	0	0	0	1	0	0	0	0	0	0	1 ^c	1	1	1	4	5	12	16	29	41	49	52	55	55				
				[10]		[10]						[14]													[0]				

^aThe numbers above the line represent mortality occurring monthly and the numbers below the line represent cumulative mortality. Accidental deaths/human sacrifices are presented in parentheses at the time of occurrence but are excluded from cumulative and total values.

^b10 animals/group were predesignated to be sacrificed at the 3 and 6 Month interim sacrifice and 15/animals/group were predesignated to be sacrificed at the 12 Month interim sacrifice; thus, decreasing the number of potential survivors to 55 animals/group. The interim sacrifice animals are presented in brackets and are excluded from cumulative and total values. If a predesignated animal died prior to its sacrifice interval, it was not replaced and its death was also excluded from the cumulative and total values. Animals sacrificed at study termination (Month 25) are also presented in brackets.

^cRepresents predesignated animal which died prior to its interim sacrifice.

Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Mortality Summary^a
Females

Number of Animals Initial Potential On-test Survivors ^b	MONTH																								Total Dead	Total Survivors	Percent Survivorship		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24				25	
Group I - 0 ppm																													
90	0	0	0	[10]	0	0	0	0	0	0	0	[15]	0	0	1	0	0	0	3	2	6	1	1	3	0	[38]	17	38	38/55 = 69%
Group II - 100/50 ppm																													
90	0	0	0	[10]	0	0	0	0	1 ^c	0	0	[14]	0	0	0	0	0	1	1	0	1	2	0	7	2	[41]	14	41	41/55 = 75%
Group III - 500 ppm																													
90	0	0	0	[10]	0	0	0	0	0	0	0	[15]	0	0	1	0	0	1	0	3	1	1	4	0	2	[41]	14	41	41/55 = 75%
Group IV - 6000 ppm																													
90	0	0	0	[10]	0	0	0	0	0	1	0	[15]	0	0	0	0	0	1	0	0	0	3	6	3	6	[34]	21	34	34/55 = 62%
Group V - 12000 ppm																													
90	0	0	0	[10]	0	0	0	0	0	0	1	[15]	0	0	1	1	1	2	2	2	5	11	14	20	21	[20]	35	20	20/55 = 36%

^aThe numbers above the line represent mortality occurring monthly and the numbers below the line represent cumulative mortality. Accidental deaths/human sacrifices are presented in parentheses at the time of occurrence but are excluded from cumulative and total values.

^b10 animals/group were predesignated to be sacrificed at the 3 and 6 Month interim sacrifice and 15/animals/group were predesignated to be sacrificed at the 12 Month interim sacrifice; thus, decreasing the number of potential survivors to 55 animals/group. The interim sacrifice animals are presented in brackets and are excluded from cumulative and total values. If a predesignated animal died prior to its sacrifice interval, it was not replaced and its death was also excluded from the cumulative and total values. Animals sacrificed at study termination (Month 25) are also presented in brackets.

^cRepresents predesignated animal which died prior to its interim sacrifice.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group I - 0 ppm							
1001	5 Jan 95	T	737	1027	6 Jan 95	T	738
1002	5 Jan 95	T	737	1028	4 Jan 95	T	736
1003	5 Jan 95	T	737	1029	9 Jan 95	T	741
1004	3 Jan 95	T	735	1030	9 Jan 95	T	741
1005	3 Jan 95	T	735	1031	16 Dec 94	F	717
1006	5 Jan 95	T	737	1032	9 Jan 95	T	741
1007	5 Jan 95	T	737	1033	30 Nov 94	F	701
1008	5 Jan 95	T	737	1034	9 Jan 95	T	741
1009	12 Oct 94	F	652	1035	9 Jan 95	T	741
1010	5 Jan 95	T	737	1036	4 Jan 95	T	736
1011	16 Sep 94	F	626	1037	9 Jan 95	T	741
1012	3 Jan 95	T	735	1038	9 Jan 95	T	741
1013	6 Jan 95	T	738	1039	6 Aug 94	F	585
1014	3 Jan 95	T	735	1040	3 Nov 94	F	674
1015	6 Jan 95	T	738	1041	4 Jan 95	T	736
1016	6 Jan 95	T	738	1042	13 Nov 94	F	684
1017	12 Oct 94	F	652	1043	10 Jan 95	T	742
1018	6 Jan 95	T	738	1044	10 Jan 95	T	742
1019	5 Dec 94	F	706	1045	10 Jan 95	T	742
1020	11 Sep 94	F	621	1046	10 Jan 95	T	742
1021	3 Jan 95	T	735	1047	4 Jul 94	F	552
1022	8 Oct 94	F	648	1048	19 Nov 94	F	690
1023	6 Jan 95	T	738	1049	16 Dec 94	F	717
1024	6 Jan 95	T	738	1050	19 Dec 94	M	720
1025	4 Jan 95	T	736	1051	4 Jan 95	T	736
1026	7 Nov 94	F	678	1052	10 Jan 95	T	742

^dF = Found Dead, M = Moribund Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

Appendix B (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group I - 0 ppm							
1053	10 Jan 95	T	742	1079	7 Jul 93	I(6)	190
1054	14 Nov 94	F	685	1080	7 Jul 94	I(6)	190
1055	23 Oct 94	F	663	1081	5 Apr 93	I(3)	97
1056 ^f				1082	5 Apr 93	I(3)	97
1057	6 Jan 94	I(12)	373	1083	5 Apr 93	I(3)	97
1058	6 Jan 94	I(12)	373	1084	5 Apr 93	I(3)	97
1059	6 Jan 94	I(12)	373	1085	5 Apr 93	I(3)	97
1060 ^f				1086	6 Apr 93	I(3)	98
1061	7 Jan 94	I(12)	374	1087	6 Apr 93	I(3)	98
1062	5 Jan 94	I(12)	372	1088	6 Apr 93	I(3)	98
1063	5 Jan 94	I(12)	372	1089	6 Apr 93	I(3)	98
1064	5 Jan 94	I(12)	372	1090	6 Apr 93	I(3)	98
1065	5 Jan 94	I(12)	372	1091 ^g	6 Jan 94	I(12)	373
1066	5 Jan 94	I(12)	372	1092 ^g	6 Jan 94	I(12)	373
1067	5 Jan 94	I(12)	372				
1068	7 Jan 94	I(12)	374				
1069	7 Jan 94	I(12)	374				
1070	7 Jan 94	I(12)	374				
1071	6 Jul 93	I(6)	189				
1072	6 Jul 93	I(6)	189				
1073	6 Jul 93	I(6)	189				
1074	6 Jul 93	I(6)	189				
1075	6 Jul 93	I(6)	189				
1076	7 Jul 93	I(6)	190				
1077	7 Jul 93	I(6)	190				
1078	7 Jul 93	I(6)	190				

^dF = Found Dead, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 Month Interim Sacrifice, M = Moribund Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^fAnimal replaced prior to test substance administration due to eye damage sustained during pretest electroretinogram evaluations. Animal number 1056 was replaced by Animal Number 1092 and Animal Number 1060 was replaced by Animal Number 1091.

^gReplacement animal.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group II - 100/50 ppm ^h							
2001	5 Jan 95	T	737	2027	9 Jan 95	T	741
2002	3 Jan 95	T	735	2028	9 Jan 95	T	741
2003	5 Jan 95	T	737	2029	29 Oct 94	F	669
2004	5 Jan 95	T	737	2030	9 Jan 95	T	741
2005	21 Jul 94	F	569	2031	21 Oct 94	F	661
2006	5 Jan 95	T	737	2032	26 Jul 94	F	574
2007	19 Aug 94	F	598	2033	9 Jan 95	T	741
2008	5 Jan 95	T	737	2034	9 Jan 95	T	741
2009	5 Jan 95	T	737	2035	9 Jan 95	T	741
2010	3 Jan 95	T	735	2036	10 Dec 94	F	711
2011	5 Jan 95	T	737	2037	9 Jan 95	T	741
2012	30 Nov 94	F	701	2038	3 Jan 95	T	735
2013	6 Jan 95	T	738	2039	9 Jan 95	T	741
2014	7 Oct 94	F	647	2040	10 Jan 95	T	742
2015	8 Nov 94	F	679	2041	10 Jan 95	T	742
2016	7 Sep 94	F	617	2042	10 Jan 95	T	742
2017	14 Sep 94	F	624	2043	10 Jan 95	T	742
2018	6 Jan 95	T	738	2044	10 Jan 95	T	742
2019	6 Jan 95	T	738	2045	4 Jan 95	T	736
2020	6 Jan 95	T	738	2046	25 Dec 94	M	726
2021	6 Jan 95	T	738	2047	4 Jan 95	T	736
2022	6 Jan 95	T	738	2048	4 Jan 95	T	736
2023	6 Jan 95	T	738	2049	10 Jan 95	T	742
2024	3 Jan 95	T	735	2050	14 Nov 94	F	685
2025	9 Jan 95	T	741	2051	4 Jan 95	T	736
2026	3 Jan 95	T	735	2052	11 Dec 94	F	712

^dF = Found Dead, M = Moribund Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^hThe Group II dose level was reduced on 21 April 1993 (Test Day 113), at the sponsors request, from 100 ppm to 50 ppm.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group II - 100/50 ppm ^h							
2053	4 Jan 95	T	736	2079	7 Jul 93	I(6)	190
2054	10 Jan 95	T	742	2080	7 Jul 93	I(6)	190
2055	10 Jan 95	T	742	2081	5 Apr 93	I(3)	97
2056	6 Jan 94	I(12)	373	2082	5 Apr 93	I(3)	97
2057 ⁱ				2083	5 Apr 93	I(3)	97
2058	6 Jan 94	I(12)	373	2084	5 Apr 93	I(3)	97
2059	6 Jan 94	I(12)	373	2085	5 Apr 93	I(3)	97
2060	6 Jan 94	I(12)	373	2086	6 Apr 93	I(3)	98
2061	7 Jan 94	I(12)	374	2087	6 Apr 93	I(3)	98
2062	5 Jan 94	I(12)	372	2088	6 Apr 93	I(3)	98
2063	5 Jan 94	I(12)	372	2089	6 Apr 93	I(3)	98
2064	5 Jan 94	I(12)	372	2090	6 Apr 93	I(3)	98
2065	5 Jan 94	I(12)	372	2091 ^f			
2066	5 Jan 94	I(12)	372	2092 ^g	6 Jan 94	I(12)	373
2067	5 Jan 94	I(12)	372				
2068	7 Jan 94	I(12)	374				
2069	7 Jan 94	I(12)	374				
2070	7 Jan 94	I(12)	374				
2071	6 Jul 93	I(6)	189				
2072	6 Jul 93	I(6)	189				
2073	6 Jul 93	I(6)	189				
2074	6 Jul 93	I(6)	189				
2075	6 Jul 93	I(6)	189				
2076	7 Jul 93	I(6)	190				
2077	7 Jul 93	I(6)	190				
2078	7 Jul 93	I(6)	190				

^dF = Found Dead, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 month Interim Sacrifice, M = Moribund Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^fAnimal replaced prior to test substance administration due to eye damage sustained during pretest electroretinogram evaluations. Animal Number 2091 was replaced by Animal Number 2092.

^gReplacement animal.

^hThe Group II dose level was reduced on 21 April 1993 (Test Day 113), at the sponsors request, from 100 ppm to 50 ppm.

ⁱAnimal died prior to test substance administration due to fatal reaction to halothane anesthesia. Animal Number 2057 was replaced by Animal Number 2091.

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Appendix B (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group III - 500 ppm							
3001	7 Dec 94	F	708	3027	4 Dec 94	F	705
3002	16 Dec 94	M	717	3028	6 Jan 95	T	738
3003	13 Aug 94	F	592	3029	4 Jan 95	T	736
3004	22 Mar 94	F	448	3030	6 Jan 95	T	738
3005	30 Jul 94	F	578	3031	9 Jan 95	T	741
3006	5 Jan 95	T	737	3032	9 Jan 95	T	741
3007	8 Dec 94	F	709	3033	14 Dec 94	M	715
3008	22 Dec 94	F	723	3034	9 Jan 95	T	741
3009	9 Jun 94	F	527	3035	9 Jan 95	T	741
3010	3 Jan 95	T	735	3036	9 Jan 95	T	741
3011	3 Jan 95	T	735	3037	9 Jan 95	T	741
3012	5 Jan 95	T	737	3038	13 Dec 94	F	714
3013	4 Jan 95	T	736	3039	10 Jan 95	T	742
3014	28 Aug 94	F	607	3040	10 Jan 95	T	742
3015	13 May 94	F	500	3041	10 Jan 95	T	742
3016	5 Jan 95	T	737	3042	10 Dec 94	F	711
3017	10 Nov 94	F	681	3043	4 Jan 95	T	736
3018	3 Jan 95	T	735	3044	7 Nov 94	F	678
3019	5 Jan 95	T	737	3045	17 Jul 94	F	565
3020	6 Jan 95	T	738	3046	30 Dec 94	M	731
3021	2 Jan 95	F	734	3047	4 Jan 95	F	736
3022	6 Jan 95	T	738	3048	18 Dec 94	F	719
3023	3 Jan 95	T	735	3049	16 Aug 94	F	595
3024	3 Jan 95	T	735	3050	10 Jan 95	T	742
3025	4 Jan 95	T	736	3051	14 Nov 94	F	685
3026	19 Sep 94	F	629	3052	10 Jan 95	T	742

^dF = Found Dead, M = Moribund Sacrifice, T = Terminal Sacrifice.^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

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Appendix B (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group III - 500 ppm							
3053	21 Dec 94	F	722	3079	7 Jul 93	I(6)	190
3054	4 Jan 95	T	736	3080	7 Jul 93	I(6)	190
3055	20 Dec 94	F	721	3081	5 Apr 93	I(3)	97
3056	6 Jan 94	I(12)	373	3082	5 Apr 93	I(3)	97
3057	6 Jan 94	I(12)	373	3083	5 Apr 93	I(3)	97
3058	6 Jan 94	I(12)	373	3084	5 Apr 93	I(3)	97
3059	6 Jan 94	I(12)	373	3085	5 Apr 93	I(3)	97
3060	6 Jan 94	I(12)	373	3086	6 Apr 93	I(3)	98
3061	7 Jan 94	I(12)	374	3087	6 Apr 93	I(3)	98
3062	5 Jan 94	I(12)	372	3088	6 Apr 93	I(3)	98
3063	5 Jan 94	I(12)	372	3089	6 Apr 93	I(3)	98
3064	5 Jan 94	I(12)	372	3090	6 Apr 93	I(3)	98
3065	5 Jan 94	I(12)	372				
3066	5 Jan 94	I(12)	372				
3067	5 Jan 94	I(12)	372				
3068	7 Jan 94	I(12)	374				
3069	7 Jan 94	I(12)	374				
3070	7 Jan 94	I(12)	374				
3071	6 Jul 93	I(6)	189				
3072	6 Jul 93	I(6)	189				
3073	6 Jul 93	I(6)	189				
3074	6 Jul 93	I(6)	189				
3075	6 Jul 93	I(6)	189				
3076	7 Jul 93	I(6)	190				
3077	7 Jul 93	I(6)	190				
3078	7 Jul 93	I(6)	190				

^dF = Found Dead, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 Month Interim Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

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Appendix B (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group IV - 6000 ppm							
4001	11 Nov 94	F	682	4027	15 Oct 94	F	655
4002	3 Jan 95	T	735	4028	11 Oct 94	F	651
4003	18 Dec 94	F	719	4029	6 Jan 95	T	738
4004	13 Sep 94	F	623	4030	3 Dec 94	F	704
4005	5 Jan 95	T	737	4031	2 Dec 94	F	703
4006	9 Dec 94	F	710	4032	14 Dec 94	F	715
4007	28 Nov 94	F	699	4033	4 Nov 94	F	675
4008	3 Jan 95	T	735	4034	20 Oct 94	F	660
4009	30 Jul 94	F	578	4035	30 Dec 94	AT	731
4010	11 Dec 94	F	712	4036	4 Jan 95	T	736
4011	11 Nov 94	F	682	4037	4 Jan 95	T	736
4012	3 Jan 95	T	735	4038	14 Dec 94	F	715
4013	3 Jan 95	T	735	4039	4 Jan 95	T	736
4014	23 Nov 94	F	694	4040	2 Dec 94	M	703
4015	1 Sep 94	F	611	4041	8 Oct 94	F	648
4016	2 Nov 94	F	673	4042	23 Oct 94	F	663
4017	29 Jul 94	F	577	4043	23 Oct 94	M	663
4018	13 Dec 94	F	714	4044	6 Jan 95	T	738
4019	6 Oct 94	F	646	4045	30 Oct 94	F	670
4020	4 Jan 95	T	736	4046	6 Jul 94	F	554
4021	13 Jul 94	F	561	4047	18 Sep 94	F	628
4022	5 Jan 95	T	737	4048	30 Dec 94	AT	731
4023	13 Oct 94	F	653	4049	22 Dec 94	F	723
4024	3 Jan 95	T	735	4050	4 Jan 95	T	736
4025	13 Dec 94	F	714	4051	31 May 94	F	518
4026	14 Sep 94	F	624	4052	29 Aug 94	F	608

^dAT = Accidental Traumatic, F = Found Dead, M = Moribund Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group IV - 6000 ppm							
4053	22 Aug 94	F	601	4079	7 Jul 93	I(6)	190
4054	10 Nov 94	F	681	4080	7 Jul 93	I(6)	190
4055	9 Nov 94	F	680	4081	5 Apr 93	I(3)	97
4056	6 Jan 94	I(12)	373	4082	5 Apr 93	I(3)	97
4057	6 Jan 94	I(12)	373	4083	5 Apr 93	I(3)	97
4058	6 Jan 94	I(12)	373	4084	5 Apr 93	I(3)	97
4059	6 Jan 94	I(12)	373	4085	5 Apr 93	I(3)	97
4060	6 Jan 94	I(12)	373	4086	6 Apr 93	I(3)	98
4061	5 Jan 94	I(12)	372	4087	6 Apr 93	I(3)	98
4062	7 Jan 94	I(12)	374	4088	6 Apr 93	I(3)	98
4063	5 Jan 94	I(12)	372	4089	6 Apr 93	I(3)	98
4064	5 Jan 94	I(12)	372	4090	6 Apr 93	I(3)	98
4065	5 Jan 94	I(12)	372				
4066	5 Jan 94	I(12)	372				
4067	5 Jan 94	I(12)	372				
4068	7 Jan 94	I(12)	374				
4069	7 Jan 94	I(12)	374				
4070	7 Jan 94	I(12)	374				
4071	6 Jul 93	I(6)	189				
4072	6 Jul 93	I(6)	189				
4073	6 Jul 93	I(6)	189				
4074	6 Jul 93	I(6)	189				
4075	6 Jul 93	I(6)	189				
4076	7 Jul 93	I(6)	190				
4077	7 Jul 93	I(6)	190				
4078	7 Jul 93	I(6)	190				

^dF = Found Dead, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 Month Interim Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group V - 12000 ppm							
5001	9 Aug 94	F	588	5027	16 Jul 94	F	564
5002	6 Nov 94	F	677	5028	15 Aug 94	F	594
5003	21 Mar 94	M	447	5029	31 Oct 94	F	671
5004	7 Sep 94	F	617	5030	15 Jun 94	F	533
5005	19 Jun 94	F	537	5031	17 Jul 94	F	565
5006	21 Jul 94	F	575	5032	31 Oct 94	F	671
5007	17 Jul 94	F	565	5033	9 May 94	F	496
5008	11 Aug 94	F	590	5034	1 Jul 94	F	549
5009	8 Aug 94	F	587	5035	4 Aug 94	F	583
5010	6 Mar 94	F	432	5036	24 Sep 94	F	634
5011	1 Aug 94	F	580	5037	24 May 94	F	511
5012	28 Jul 94	F	576	5038	28 Aug 94	F	607
5013	21 Oct 94	F	661	5039	7 May 94	F	494
5014	1 May 94	F	488	5040	31 Jul 94	F	579
5015	21 Oct 94	F	661	5041	19 Sep 94	F	629
5016	24 Aug 94	F	603	5042	1 Sep 94	F	611
5017	28 Jul 94	F	576	5043	20 May 94	F	507
5018	18 May 94	F	505	5044	29 Oct 94	F	669
5019	25 Jul 94	F	573	5045	2 Jul 94	F	550
5020	26 Aug 94	F	605	5046	9 Sep 94	F	619
5021	15 Jul 94	F	563	5047	12 May 94	F	499
5022	5 Aug 94	F	584	5048	9 Aug 94	M	588
5023	6 Sep 94	F	616	5049	5 Jul 94	F	553
5024	28 Jul 94	F	576	5050	13 Mar 94	F	439
5025	13 May 93	M	135	5051	4 Jul 94	F	552
5026	28 Apr 94	F	485	5052	26 Sep 94	M	636

^dF = Found Dead, M = Moribund Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Males (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group IV - 12000 ppm							
5053	17 Jun 94	F	535	5079	7 Jul 93	I(6)	190
5054	10 Jun 94	F	528	5080	7 Jul 93	I(6)	190
5055	30 Aug 94	F	609	5081	5 Apr 93	I(3)	97
5056	6 Jan 94	I(12)	373	5082	5 Apr 93	I(3)	97
5057	6 Jan 94	I(12)	373	5083	5 Apr 93	I(3)	97
5058	6 Jan 94	I(12)	373	5084	5 Apr 93	I(3)	97
5059	6 Jan 94	I(12)	373	5085	5 Apr 93	I(3)	97
5060	6 Jan 94	I(12)	373	5086	6 Apr 93	I(3)	98
5061	5 Jan 94	I(12)	372	5087	6 Apr 93	I(3)	98
5062 ^f				5088	6 Apr 93	I(3)	98
5063	5 Jan 94	I(12)	372	5089	6 Apr 93	I(3)	98
5064	5 Jan 94	I(12)	372	5090	6 Apr 93	I(3)	98
5065	5 Jan 94	I(12)	372	5091 ^g	5 Jan 94	I(12)	372
5066	5 Jan 94	I(12)	372				
5067	7 Jan 94	I(12)	374				
5068	7 Jan 94	I(12)	374				
5069	7 Jan 94	I(12)	374				
5070	24 Dec 93	F	360				
5071	6 Jul 94	I(6)	189				
5072	6 Jul 93	I(6)	189				
5073	6 Jul 93	I(6)	189				
5074	6 Jul 93	I(6)	189				
5075	6 Jul 93	I(6)	189				
5076	7 Jul 93	I(6)	190				
5077	7 Jul 93	I(6)	190				
5078	7 Jul 93	I(6)	190				

^dF = Found Dead, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 Month Interim Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^fAnimal replaced prior to test substance administration due to eye damage sustained during pretest electroretinogram evaluations. Animal Number 5062 was replaced by Animal Number 5091.

^gReplacement animal.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group I - 0 ppm							
1501	5 Jan 95	T	737	1527	23 Nov 94	F	694
1502	3 Jan 95	T	735	1528	11 Jul 94	F	559
1503	5 Jan 95	T	737	1529	4 Jan 95	T	736
1504	3 Jan 95	T	735	1530	9 Jan 95	T	741
1505	3 Jan 95	T	735	1531	9 Jan 95	T	741
1506	5 Jan 95	T	737	1532	9 Jan 95	T	741
1507	1 Aug 94	F	580	1533	6 Sep 94	F	616
1508	5 Jan 95	T	737	1534	9 Jan 95	T	741
1509	5 Jan 95	T	737	1535	9 Jan 95	T	741
1510	5 Jan 95	T	737	1536	6 Jul 94	F	554
1511	17 Dec 94	F	718	1537	9 Jan 95	T	741
1512	5 Jan 95	T	737	1538	10 Jan 95	T	742
1513	6 Jan 95	T	738	1539	4 Jan 95	T	736
1514	6 Jan 95	T	738	1540	19 Sep 94	F	629
1515	6 Jan 95	T	738	1541	5 Sep 94	F	615
1516	6 Jan 95	T	738	1542	4 Jan 95	T	736
1517	6 Jan 95	T	738	1543	1 Dec 94	F	702
1518	19 Sep 94	F	629	1544	4 Jan 95	T	736
1519	1 Aug 94	F	580	1545	12 Sep 94	F	622
1520	6 Jan 95	T	738	1546	10 Jan 95	T	742
1521	6 Jan 95	T	738	1547	4 Jan 95	T	736
1522	21 Oct 94	F	661	1548	19 Sep 94	F	629
1523	29 Mar 94	H	455	1549	10 Jan 95	T	742
1524	9 Jan 95	T	741	1550	12 Jul 94	F	560
1525	3 Jan 95	T	735	1551	10 Jan 95	T	742
1526	3 Jan 95	T	735	1552	10 Jan 95	T	742

^dF = Found Dead, H = Humane Sacrifice, M = Moribund Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^b
Group I - 0 ppm							
1553	26 Dec 94	F	727	1579	7 Jul 93	I(6)	190
1554	10 Jan 95	T	742	1580	7 Jul 93	I(6)	190
1555	10 Jan 95	T	742	1581	5 Apr 93	I(3)	97
1556	6 Jan 94	I(12)	373	1582	5 Apr 93	I(3)	97
1557	6 Jan 94	I(12)	373	1583	5 Apr 93	I(3)	97
1558	6 Jan 94	I(12)	373	1584	5 Apr 93	I(3)	97
1559	6 Jan 94	I(12)	373	1585	5 Apr 93	I(3)	97
1560	6 Jan 94	I(12)	373	1586	6 Apr 93	I(3)	98
1561	5 Jan 94	I(12)	372	1587	6 Apr 93	I(3)	98
1562	5 Jan 94	I(12)	372	1588	6 Apr 93	I(3)	98
1563	5 Jan 94	I(12)	372	1589	6 Apr 93	I(3)	98
1564	5 Jan 94	I(12)	372	1590	6 Apr 93	I(3)	98
1565	5 Jan 94	I(12)	372				
1566	5 Jan 94	I(12)	372				
1567	7 Jan 94	I(12)	374				
1568	7 Jan 94	I(12)	374				
1569	7 Jan 94	I(12)	374				
1570	7 Jan 94	I(12)	374				
1571	6 Jul 93	I(6)	189				
1572	6 Jul 93	I(6)	189				
1573	6 Jul 93	I(6)	189				
1574	6 Jul 93	I(6)	189				
1575	6 Jul 93	I(6)	189				
1576	7 Jul 93	I(6)	190				
1577	7 Jul 93	I(6)	190				
1578	7 Jul 93	I(6)	190				

^dF = Found Dead, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 Month Interim Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group II - 100/50 ppm ^h							
2501	5 Jan 95	T	737	2527	9 Jan 95	T	741
2502	5 Jan 95	T	737	2528	4 Jan 95	T	736
2503	28 Oct 94	F	668	2529	4 Jan 95	T	736
2504	5 Jan 95	T	737	2530	9 Jan 95	T	741
2505	5 Jan 95	T	737	2531	9 Jan 95	T	741
2506	5 Jan 95	T	737	2532	2 Jan 95	M	734
2507	5 Jan 95	T	737	2533	30 Dec 94	F	731
2508	5 Jan 95	T	737	2534	27 Jun 94	F	545
2509	3 Jan 95	T	735	2535	28 Dec 94	F	729
2510	3 Jan 95	T	735	2536	9 Jan 95	T	741
2511	5 Jan 95	T	737	2537	1 Dec 94	M	702
2512	3 Jan 95	T	735	2538	9 Jan 95	T	741
2513	6 Jan 95	T	738	2539	10 Jan 95	T	742
2514	6 Jan 95	T	738	2540	10 Jan 95	T	742
2515	6 Jan 95	T	738	2541	5 Dec 94	F	706
2516	6 Jan 95	T	738	2542	14 Dec 94	M	715
2517	6 Jan 95	T	738	2543	10 Jan 95	T	742
2518	3 Jan 95	T	735	2544	10 Jan 95	T	742
2519	3 Jan 95	T	735	2545	28 Sep 94	F	638
2520	6 Jan 95	T	738	2546	15 Dec 94	F	716
2521	6 Jan 95	T	738	2547	10 Jan 95	T	742
2522	4 Jan 95	T	736	2548	10 Jan 95	T	742
2523	4 Jan 95	T	736	2549	10 Jan 95	T	742
2524	6 Jan 95	T	738	2550	19 Jul 94	F	567
2525	29 Oct 94	F	669	2551	4 Jan 95	T	736
2526	9 Jan 95	T	741	2552	18 Dec 94	F	719

^dF = Found Dead, M = Moribund Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^hThe Group II dose level was reduced on 21 April 1993 (Test Day 113), at the sponsors request, from 100 ppm to 50 ppm.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group II - 100/50 ppm ^h							
2553	10 Jan 95	T	742	2579	7 Jul 93	I(6)	190
2554	14 Dec 94	F	715	2580	7 Jul 93	I(6)	190
2555	10 Jan 95	T	742	2581	5 Apr 93	I(3)	97
2556	6 Jan 94	I(12)	373	2582	5 Apr 93	I(3)	97
2557	6 Jan 94	I(12)	373	2583	5 Apr 93	I(3)	97
2558	6 Jan 94	I(12)	373	2584	5 Apr 93	I(3)	97
2559	6 Jan 94	I(12)	373	2585	5 Apr 93	I(3)	97
2560	6 Jan 94	I(12)	373	2586	6 Apr 93	I(3)	98
2561	7 Jan 94	I(12)	374	2587	6 Apr 93	I(3)	98
2562	5 Jan 94	I(12)	372	2588	6 Apr 93	I(3)	98
2563	5 Jan 94	I(12)	372	2589	6 Apr 93	I(3)	98
2564	5 Jan 94	I(12)	372	2590	6 Apr 93	I(3)	98
2565	5 Jan 94	I(12)	372				
2566	24 Sep 94	H	269				
2567	5 Jan 94	I(12)	372				
2568	7 Jan 94	I(12)	374				
2569	7 Jan 94	I(12)	374				
2570	7 Jan 94	I(12)	374				
2571	6 Jul 93	I(6)	189				
2572	6 Jul 93	I(6)	189				
2573	6 Jul 93	I(6)	189				
2574	6 Jul 93	I(6)	189				
2575	6 Jul 93	I(6)	189				
2576	7 Jul 93	I(6)	190				
2577	7 Jul 93	I(6)	190				
2578	7 Jul 93	I(6)	190				

^dF = Found Dead, H = Humane Sacrifice, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 Month Interim Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^hThe Group II dose level was reduced on 21 April 1993 (Test Day 113), at the sponsors request, from 100 ppm to 50 ppm.

Appendix B (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group III - 500 ppm							
3501	5 Jan 95	T	737	3527	6 Jan 95	T	738
3502	5 Jan 95	T	737	3528	6 Jan 95	T	738
3503	5 Jan 95	T	737	3529	6 Jan 95	T	738
3504	3 Jan 95	T	735	3530	9 Jan 95	T	741
3505	3 Jan 95	T	735	3531	4 Jan 95	T	736
3506	23 Oct 94	M	663	3532	9 Jan 95	T	741
3507	10 Jul 94	F	558	3533	4 Jan 95	T	736
3508	3 Jan 95	T	735	3534	4 Jan 95	T	736
3509	5 Jan 95	T	737	3535	3 Sep 94	F	613
3510	12 Aug 94	F	591	3536	9 Jan 95	T	741
3511	2 Jan 95	F	734	3537	9 Jan 95	T	741
3512	5 Jan 95	T	737	3538	15 Oct 94	F	655
3513	3 Jan 95	T	735	3539	9 Jan 95	T	741
3514	16 May 94	F	503	3540	9 Jan 95	T	741
3515	6 Jul 94	F	554	3541	9 Jan 95	T	741
3516	5 Jan 95	T	737	3542	9 Jan 95	T	741
3517	20 Jan 94	M	387	3543	7 Oct 94	F	647
3518	6 Jan 95	T	738	3544	24 Dec 94	F	725
3519	6 Jan 95	T	738	3545	10 Jan 95	T	742
3520	4 Jul 94	F	552	3546	10 Jan 95	T	742
3521	3 Jan 95	T	735	3547	11 Dec 94	F	712
3522	6 Jan 95	T	738	3548	10 Jan 95	T	742
3523	6 Jan 95	T	738	3549	10 Jan 95	T	742
3524	4 Jan 95	T	736	3550	10 Jan 95	T	742
3525	6 Jan 95	T	738	3551	10 Jan 95	T	742
3526	17 Oct 94	F	657	3552	10 Jan 95	T	742

^dF = Found Dead, M = Moribund Sacrifice, T = Terminal Sacrifice.^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group III - 500 ppm							
3553	10 Jan 95	T	742	3577	7 Jul 93	I(6)	190
3554	4 Jan 94	T	736	3578	7 Jul 93	I(6)	190
3555	10 Jan 95	T	742	3579	7 Jul 93	I(6)	190
3556 ^f				3580	7 Jul 93	I(6)	190
3557	6 Jan 94	I(12)	373	3581	5 Apr 93	I(3)	97
3558	6 Jan 94	I(12)	373	3582	5 Apr 93	I(3)	97
3559	6 Jan 94	I(12)	373	3583	5 Apr 93	I(3)	97
3560	6 Jan 94	I(12)	373	3584	5 Apr 93	I(3)	97
3561 ⁱ				3585	5 Apr 93	I(3)	97
3562	5 Jan 94	I(12)	372	3586	6 Apr 93	I(3)	98
3563	5 Jan 94	I(12)	372	3587	6 Apr 93	I(3)	98
3564	5 Jan 94	I(12)	372	3588 ^j			
3565	5 Jan 94	I(12)	372	3589	6 Apr 93	I(3)	98
3566	5 Jan 94	I(12)	372	3590	6 Apr 93	I(3)	98
3567	7 Jan 94	I(12)	374	3591 ^g	5 Jan 94	I(12)	372
3568	7 Jan 94	I(12)	374	3592 ^g	6 Apr 93	I(3)	98
3569	7 Jan 94	I(12)	374	3593 ^g	6 Jan 94	I(12)	373
3570	7 Jan 94	I(12)	374				
3571	6 Jul 93	I(6)	189				
3572	6 Jul 93	I(6)	189				
3573	6 Jul 93	I(6)	189				
3574	6 Jul 93	I(6)	189				
3575	6 Jul 93	I(6)	189				
3576	7 Jul 93	I(6)	190				

^dI = Interim Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^fAnimal replaced prior to test substance administration due to eye damage sustained during pretest electroretinogram evaluations. Animal Number 3556 was replaced by Animal Number 3593.

^gReplacement animal.

ⁱAnimal replaced prior to test substance administration due to fatal reaction to halothane anesthesia sustained during pretest electroretinogram evaluations. Animal Number 3561 was replaced by Animal Number 3591.

^jAnimal Number 3588 was found dead prior to study initiation (12/22/92) and was replaced by Animal Number 3592.

B-19
Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group IV - 6000 ppm							
4501	5 Jan 95	T	737	4527	21 Oct 93	F	296
4502	3 Jan 95	T	735	4528	9 Jan 95	T	741
4503	29 Nov 94	F	700	4529	9 Jan 95	T	741
4504	5 Jan 95	T	737	4530	28 Dec 94	F	729
4505	5 Jan 95	T	737	4531	9 Jan 95	T	741
4506	25 Dec 94	F	726	4532	8 Sep 94	F	618
4507	5 Jan 95	T	737	4533	26 Nov 94	F	697
4508	3 Jan 95	T	735	4534	4 Jan 95	T	736
4509	3 Jan 95	T	735	4535	9 Jan 95	T	741
4510	16 Oct 94	F	656	4536	11 Oct 94	F	651
4511	18 Dec 94	F	719	4537	4 May 94	F	491
4512	3 Jan 95	T	735	4538	25 Oct 94	F	665
4513	5 Jan 95	T	737	4539	9 Jan 95	T	741
4514	3 Jan 95	T	735	4540	9 Jan 95	T	741
4515	23 Oct 94	F	663	4541	6 Sep 94	F	616
4516	5 Jan 95	T	737	4542	9 Jan 95	T	741
4517	6 Jan 95	T	738	4543	4 Jan 95	T	736
4518	6 Jan 95	T	738	4544	10 Jan 95	T	742
4519	6 Jan 95	T	738	4545	10 Jan 95	T	742
4520	6 Jan 95	T	738	4546	10 Jan 95	T	742
4521	4 Jan 95	T	736	4547	10 Jan 95	T	742
4522	6 Jan 95	T	738	4548	10 Jan 95	T	742
4523	4 Dec 94	F	705	4549	4 Jan 95	T	736
4524	5 Oct 94	F	645	4550	11 Dec 94	F	712
4525	4 Jan 95	T	736	4551	13 Nov 94	F	684
4526	30 Dec 94	M	731	4552	18 Sep 94	F	628

^dF = Found dead, M = Moribund sacrifice, T = Terminal sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

B-20
Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group IV - 6000 ppm							
4553	29 Oct 94	F	669	4579	7 Jul 93	I(6)	190
4554	10 Jan 95	T	742	4580	7 Jul 93	I(6)	190
4555	25 Dec 94	F	726	4581	5 Apr 93	I(3)	97
4556	6 Jan 94	I(12)	373	4582	5 Apr 93	I(3)	97
4557	6 Jan 94	I(12)	373	4583	5 Apr 93	I(3)	97
4558	6 Jan 94	I(12)	373	4584	5 Apr 93	I(3)	97
4559	6 Jan 94	I(12)	373	4585	5 Apr 93	I(3)	97
4560	6 Jan 94	I(12)	373	4586	6 Apr 93	I(3)	98
4561	7 Jan 94	I(12)	374	4587	6 Apr 93	I(3)	98
4562 ^f				4588	6 Apr 93	I(3)	98
4563	5 Jan 94	I(12)	372	4589	6 Apr 93	I(3)	98
4564	5 Jan 94	I(12)	372	4590	6 Apr 93	I(3)	98
4565	5 Jan 94	I(12)	372	4591 ^g	7 Jan 94	I(3)	374
4566	5 Jan 94	I(12)	372				
4567	5 Jan 94	I(12)	372				
4568	5 Jan 94	I(12)	372				
4569	7 Jan 94	I(12)	374				
4570	7 Jan 94	I(12)	374				
4571	6 Jul 93	I(6)	189				
4572	6 Jul 93	I(6)	189				
4573	6 Jul 93	I(6)	189				
4574	6 Jul 93	I(6)	189				
4575	6 Jul 93	I(6)	189				
4576	7 Jul 93	I(6)	190				
4577	7 Jul 93	I(6)	190				
4578	7 Jul 93	I(6)	190				

^dF = Found dead, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 Month Interim Sacrifice, T = Terminal sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^fAnimal replaced prior to test substance administration due to eye damage sustained during pretest electroretinogram evaluations. Animal Number 4562 was replaced by Animal Number 4591.

^gReplacement animal.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group V - 12000 ppm							
5501	24 Dec 94	F	725	5527	3 Jan 95	T	735
5502	11 Dec 94	F	712	5528	4 Jan 95	T	736
5503	3 Jan 95	T	735	5529	10 Dec 94	F	711
5504	3 Jan 95	T	735	5530	15 May 94	F	502
5505	19 Dec 94	F	720	5531	1 Jan 95	F	733
5506	4 Dec 94	M	705	5532	17 Nov 93	F	323
5507	3 Dec 94	F	704	5533 ^j			
5508	22 Dec 94	F	723	5534	9 Jan 95	T	741
5509	4 Dec 94	F	705	5535	13 Nov 94	F	684
5510	1 Apr 94	F	458	5536	9 Jan 95	T	741
5511	5 Jan 95	T	737	5537	20 Dec 94	F	721
5512	3 Jan 95	T	735	5538	4 Jan 95	T	736
5513	17 Dec 94	F	718	5539	25 Dec 94	F	726
5514	5 Jan 95	T	737	5540	4 Jan 95	T	736
5515	10 Dec 94	F	711	5541	29 Nov 94	F	700
5516	4 Jan 95	T	736	5542	18 Nov 94	F	689
5517	6 Jan 95	T	738	5543	10 Jan 95	T	742
5518	16 Oct 94	F	656	5544	10 Jan 95	T	742
5519	12 Dec 94	F	713	5545	23 Nov 94	F	694
5520	3 Jan 95	T	735	5546	1 Dec 94	F	702
5521	22 Dec 94	F	723	5547	26 Jul 94	F	574
5522	19 Oct 94	F	659	5548	10 Jan 95	T	742
5523	3 Oct 94	F	643	5549	10 Dec 94	F	711
5524	6 Jan 95	T	738	5550	10 Nov 94	F	681
5525	6 Jan 95	T	738	5551	15 Nov 94	F	686
5526	25 Sep 94	F	635	5552	4 Jan 95	T	736

^dF = Found dead, M = Moribund sacrifice, T = Terminal sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^jAnimal Number 5533 was found dead prior to study initiation (12/22/92) and was replaced by Animal Number 5591.

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Appendix B (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Animal Termination History - Females (cont.)

Animal Number	Date of Death	Type of Death ^d	Days on Test ^e	Animal Number	Date of Death	Type of Death ^d	Days on Test ^e
Group IV - 12000 ppm							
5553	27 Apr 94	F	484	5579	7 Jul 93	I(6)	190
5554	9 Nov 94	F	680	5580	7 Jul 93	I(5)	190
5555	23 Dec 94	F	724	5581	5 Apr 93	I(3)	97
5556	6 Jan 94	I(12)	373	5582	5 Apr 93	I(3)	97
5557	6 Jan 94	I(12)	373	5583	5 Apr 93	I(3)	97
5558	6 Jan 94	I(12)	373	5584	5 Apr 93	I(3)	97
5559	6 Jan 94	I(12)	373	5585	5 Apr 93	I(3)	97
5560	6 Jan 94	I(12)	373	5586	6 Apr 93	I(3)	98
5561 ^f				5587	6 Apr 93	I(3)	98
5562	7 Jan 94	I(12)	374	5588	6 Apr 93	I(3)	98
5563	5 Jan 94	I(12)	372	5589	6 Apr 93	I(3)	98
5564	5 Jan 94	I(12)	372	5590	6 Apr 93	I(3)	98
5565	5 Jan 94	I(12)	372	5591 ^g	2 Jun 94	F	520
5566	5 Jan 94	I(12)	372	5592 ^g	7 Jan 94	I(12)	374
5567	5 Jan 94	I(12)	372				
5568	5 Jan 94	I(12)	372				
5569	7 Jan 94	I(12)	374				
5570	7 Jan 94	I(12)	374				
5571	6 Jul 93	I(6)	189				
5572	6 Jul 93	I(6)	189				
5573	6 Jul 93	I(6)	189				
5574	6 Jul 93	I(6)	189				
5575	6 Jul 93	I(6)	189				
5576	7 Jul 93	I(6)	190				
5577	7 Jul 93	I(6)	190				
5578	7 Jul 93	I(6)	190				

^dF = Found dead, I(12) = 12 Month Interim Sacrifice, I(6) = 6 Month Interim Sacrifice, I(3) = 3 Month Interim Sacrifice, M = Moribund Sacrifice, T = Terminal Sacrifice.

^eDays on Test includes days on which test substance was not administered due to fasting for clinical laboratory studies.

^fAnimal replaced prior to test substance administration due to eye damage sustained during pretest electroretinogram evaluations. Animal Number 5561 was replaced by Animal Number 5592.

^gReplacement animal.

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Physical Observations
Preface

Number of animals examined represents the total number of animals observed and/or animals which were found dead, died accidentally, were killed in a moribund condition, sacrificed for humane purposes or killed at a scheduled sacrifice for a given interval. If more than one degree was noted in data for different locations, the most extreme degree was presented (i.e., slight lacrimation, right eye and moderate lacrimation, left eye were recorded, moderate lacrimation was presented in the report).

For summarization purposes, descriptive comments [i.e., location of alopecia, scab(s) and sore(s), etc.] are not presented in this appendix. These data are contained in the study raw data if needed.

Corresponding dose levels for each group were as follows:

Group I	-	0 ppm
Group II	-	100/50 ppm ^a
Group III	-	500 ppm
Group IV	-	6000 ppm
Group V	-	12000 ppm

^aThe Group II dose level was reduced on 21 April 1993 (Test Day 113) at the sponsor request, from 100 ppm to 50 ppm.

[illegible]

C-3
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
# OF ANIMALS EXAMINED	I	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	II	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	III	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	IV	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	V	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
<u>DERMAL-GENERAL</u>																						
YELLOW ANO-GENITAL STAINING	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ALOPECIA-GENERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	II	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SCABS	I	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	II	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	III	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ULCERATION-CERVICAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ALOPECIA EXTREMITIES/SNOUT	I	0	0	0	0	0	0	0	0	0	0	1	1	1	1	2	2	2	1	1	1	1
	II	0	0	0	0	0	0	0	0	0	1	1	1	2	2	1	1	1	1	0	0	1
	III	0	0	0	0	0	0	0	0	1	2	1	0	1	0	1	0	0	1	1	1	2
	IV	0	0	0	0	0	0	0	0	3	2	1	1	1	3	2	2	2	2	2	2	5
	V	0	0	0	0	0	0	0	0	1	1	2	1	1	1	2	0	0	0	0	0	0
<u>OCULAR</u>																						
CHROMODACRYORRHEA - UNILATERAL	I	0	1	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	0	1	1	2
	II	0	1	0	0	0	0	0	0	0	0	0	0	1	1	2	5	3	1	2	4	3
	III	0	0	1	0	0	0	0	0	0	0	0	1	3	3	3	7	3	1	1	2	4
	IV	0	0	0	0	0	0	0	0	0	1	1	1	3	2	1	0	0	1	0	1	1
	V	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	2	0	1	1	1	0

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
# OF ANIMALS EXAMINED	I 90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	II 90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	III 90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	IV 90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	V 90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
EYE(S) APPEAR DAMAGED	I 0	0	1	1	1	1	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	II 0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OPACITY - UNILATERAL	I 0	1	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXOPHTHALMOS - UNILATERAL	I 0	1	1	1	1	1	1	1	1	1	1	2	2	2	3	3	3	3	3	3	3	3
	II 0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	III 0	0	0	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
	IV 0	0	1	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1
	V 0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1
CORNEAL IRREGULARITY - UNILATERAL	I 0	0	2	2	3	5	6	8	12	13	14	14	17	17	17	16	18	17	17	18	19	19
	II 0	0	3	3	4	8	7	7	8	8	8	9	13	13	14	15	18	15	15	15	15	15
	III 0	0	6	5	5	7	6	6	6	6	6	6	11	12	13	14	15	14	14	15	15	15
	IV 0	0	2	2	2	2	2	3	3	4	4	4	5	6	6	7	8	8	8	9	9	9
	V 0	0	3	3	3	3	3	3	4	4	4	4	4	4	4	4	5	5	5	5	5	5
EYE(S) VASCULARIZED	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
LACRIMATION-UNILATERAL	I 0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	2	2	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	3	1	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	3	3	0	1	2	0
	IV 0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	1	0	0	0	0	0	0

WEEK: -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

[illegible]

INCISORS MALOCCLUDED

[illegible][illegible][illegible]

C-6
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
# OF ANIMALS EXAMINED	I 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	II 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	III 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	IV 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	V 80	79	79	79	79	79	79	79	74	69	69	69	69	69	69	69	69	69	69	69	69
<u>NORMAL</u>																					
WITHIN NORMAL LIMITS	I 56	57	58	61	57	59	57	61	51	53	46	51	50	50	50	49	51	49	51	50	52
	II 60	59	61	62	61	59	60	65	53	58	52	52	49	50	52	52	53	50	52	54	51
	III 60	60	62	61	58	60	62	60	50	51	47	48	50	50	49	49	49	50	53	52	52
	IV 62	63	64	64	62	62	62	65	57	59	59	59	56	59	59	58	55	52	51	50	52
	V 70	69	70	68	68	67	68	69	52	56	54	59	56	56	58	57	56	55	54	54	56
<u>DEAD</u>																					
INTERIM SACRIFICE	I 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
MORIBUND-SACRIFICED	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>GENL APPEARANCE</u>																					
EMACIATION	I 0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>DERMAL-GENERAL</u>																					
ALOPECIA-GENERAL	I 1	1	1	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	0	0	0
	II 0	0	0	0	0	0	1	1	0	0	0	0	1	1	1	1	1	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	1	2	1	1	0	0	1	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	1	0

[illegible]

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
# OF ANIMALS EXAMINED	I 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	II 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	III 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	IV 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	V 80	79	79	79	79	79	79	79	74	69	69	69	69	69	69	69	69	69	69	69	69
<u>ORAL/BUCCAL</u>																					
INCISORS MALOCCLUDED	I 1	1	1	1	1	1	1	0	0	0	0	0	1	1	1	1	1	1	1	1	1
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INCISORS BROKEN/MISSING	I 1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>MISCELLANEOUS</u>																					
LIMB(S) APPEAR IMPAIRED	I 0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
TAIL BUMPS	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
<u>MASS(ES)</u>																					
	I 0	0	0	0	0	1	1	1	1	1	1	3	1	1	1	1	1	0	0	0	0
	II 0	1	1	1	1	1	2	0	1	0	0	1	3	4	2	2	1	0	0	0	1
	III 0	0	0	0	0	0	0	0	0	2	2	2	2	3	4	5	4	4	2	2	1
	IV 2	3	2	2	2	3	3	3	0	0	0	0	0	0	0	1	1	2	4	4	2
	V 0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	1	1	1	0	0	0

C-11
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
# OF ANIMALS EXAMINED	I	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	II	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	III	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	IV	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	V	69	69	69	69	69	69	69	69	69	69	69	68	68	54	54	54	54	54	54
<u>DERMAL-GENERAL</u>																				
YELLOW ANO-GENITAL STAINING	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	1	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0
ALOPECIA-GENERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	1	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SCABS	I	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0
	IV	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	1	1	1	1	1	1	2	1	2	2	2	2	2	2	2
ALOPECIA EXTREMITIES/SNOUT	I	1	1	5	3	2	0	0	0	0	0	0	1	1	0	0	0	0	0	0
	II	4	3	3	3	2	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	III	2	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	4	1	1	4	4	2	0	0	1	1	0	0	0	0	0	0	0	0	0
	V	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>OCULAR</u>																				
CHROMODACRYORRHEA - UNILATERAL	I	2	1	2	3	4	4	4	3	3	2	10	7	7	7	4	4	8	6	6
	II	2	3	3	3	2	3	4	3	2	1	9	10	7	8	4	4	10	7	8
	III	2	3	3	3	1	2	4	2	1	3	5	6	3	5	1	0	6	3	4
	IV	2	2	1	1	2	3	4	2	3	2	1	3	5	3	3	4	3	4	4
	V	3	3	3	2	2	3	4	3	3	1	2	3	5	4	4	2	5	6	5
EYE(S) APPEAR DAMAGED	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

	WEEK:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
# OF ANIMALS EXAMINED	I	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70
	II	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70
	III	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70
	IV	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70	70
	V	69	69	69	69	69	69	69	69	69	69	69	69	69	68	68	54	54	54	54	54
LACRIMATION - BILATERAL	I	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	III	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1
	IV	0	0	0	1	1	1	0	0	1	1	1	1	1	1	1	2	1	1	1	1
	V	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0
EYE ATROPHIED - UNILATERAL	I	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
	II	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
	V	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
ENOPHTHALMOS - UNILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL IRREGULARITY - BILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	2	4	4	4	4	3	2	2	0	0	0	0	0	0	0
	IV	0	0	0	0	0	2	2	1	1	1	1	1	1	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>ORAL/BUCCAL</u>																					
INCISORS MALOCCLUDED	I	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INCISORS BROKEN/MISSING	I	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1	1	1	1	1	1
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

WEEK:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
I	70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
II	70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
III	70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
IV	70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
V	69	69	69	69	69	69	69	69	69	69	69	69	68	68	54	54	54	54	54	54

I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
V	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0

I	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
V	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0

I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
V	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0

[illegible]

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	II	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55
	III	55	55	55	55	54	54	54	54	54	54	54	53	53	53	53	52	52	52	52
	IV	55	55	55	55	55	55	55	55	55	55	55	55	55	54	54	54	54	54	54
	V	54	54	53	52	51	51	51	51	51	49	47	46	43	43	43	42	39	39	35

NORMAL

WITHIN NORMAL LIMITS	I	39	40	40	40	38	39	38	37	37	34	36	36	35	34	34	37	37	36	36	35
	II	41	43	43	42	41	41	43	44	41	41	42	43	42	41	41	43	41	42	41	37
	III	42	42	44	41	41	40	42	44	42	41	41	41	38	37	37	38	37	37	37	36
	IV	41	41	40	40	37	39	37	37	33	36	38	38	38	38	38	38	37	38	36	35
	V	37	38	36	38	36	37	34	34	35	35	34	31	26	25	24	27	26	24	21	17

DEAD

MORIBUND - SACRIFICED	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

FOUND DEAD	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1
	V	0	1	1	0	0	0	0	0	2	2	1	3	0	0	1	3	0	4	0

GENL APPEARANCE

ABDOMINAL DISTENSION	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

EMACIATION	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
	V	0	1	2	1	0	0	0	0	1	1	0	2	0	0	0	0	0	2	0

[illegible]

WEEK: 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80

[illegible]

C-18
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

	WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	II	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55
	III	55	55	55	55	54	54	54	54	54	54	54	54	53	53	53	53	52	52	52	52
	IV	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54	54	54	54	54	54
	V	54	54	53	52	51	51	51	51	51	51	49	47	46	43	43	43	42	39	39	35
CORNEAL IRREGULARITY - UNILATERAL	I	5	5	5	5	6	6	6	6	7	7	7	7	7	7	7	6	6	6	6	5
	II	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	III	6	6	6	6	4	4	4	4	5	4	4	4	4	4	4	4	4	4	4	4
	IV	5	5	4	3	3	3	4	4	4	3	1	1	1	1	1	1	1	1	1	0
	V	3	3	3	2	2	2	3	3	2	2	3	2	2	2	2	2	2	2	3	3
EYE(S) VASCULARIZED	I	2	2	2	2	2	2	2	2	2	2	3	3	3	3	4	4	4	4	4	4
	II	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	4	4	4	4	6
	III	4	4	4	4	4	4	4	4	5	5	5	5	5	6	6	6	6	6	6	7
	IV	3	4	4	4	5	4	4	5	5	6	6	6	6	6	6	6	6	6	6	6
	V	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	4	4	4	4	4
LACRIMATION-UNILATERAL	I	5	7	8	8	9	8	8	10	9	11	9	9	10	11	11	9	9	9	9	10
	II	6	7	7	5	5	8	6	6	8	4	5	5	6	7	7	5	7	6	6	10
	III	6	5	3	4	6	5	3	4	5	5	5	4	5	5	6	6	3	3	4	5
	IV	3	3	4	5	6	6	7	6	8	6	9	8	8	8	8	8	8	7	7	7
	V	7	5	5	7	6	4	5	6	7	4	4	4	5	3	3	3	5	5	5	5
CHROMODACRYORRHEA - BILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	II	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1
	III	1	1	1	2	0	1	1	0	0	1	1	2	2	2	2	1	2	2	2	1
	IV	1	1	1	1	1	1	1	2	2	2	1	2	2	2	2	2	3	3	3	3
	V	0	0	2	1	0	0	0	0	0	2	1	0	1	0	1	1	0	0	2	1
LACRIMATION - BILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	II	1	0	0	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1
	III	1	1	1	2	0	1	1	0	0	1	1	2	2	2	2	1	2	2	2	1
	IV	1	1	1	1	1	1	1	2	2	2	1	2	2	2	2	2	3	3	3	3
	V	0	0	0	0	0	0	0	0	0	2	2	0	1	0	1	1	0	0	2	1
ENOPHTHALMOS - UNILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	2	2	2
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	2	1	2	2	2
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	2	2	2	3
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I 55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	II 55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55
	III 55	55	55	55	54	54	54	54	54	54	54	54	53	53	53	53	52	52	52	52
	IV 55	55	55	55	55	55	55	55	55	55	55	55	55	55	54	54	54	54	54	54
	V 54	54	53	52	51	51	51	51	51	51	49	47	46	43	43	43	42	39	39	35
<u>ORAL/BUCCAL</u>																				
INCISORS MALOCCLUDED	I 1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INCISORS BROKEN/MISSING	I 1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXCESSIVE SALIVATION	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
<u>BEHAV/ACTIVITY</u>																				
LETHARGY	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0
PROSTRATION	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HUNCHED APPEARANCE	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I 55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	II 55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55
	III 55	55	55	55	54	54	54	54	54	54	54	54	53	53	53	53	52	52	52	52
	IV 55	55	55	55	55	55	55	55	55	55	55	55	55	55	54	54	54	54	54	54
	V 54	54	53	52	51	51	51	51	51	51	49	47	46	43	43	43	42	39	39	35
<u>RESPIRATORY</u>																				
LABORED BREATHING	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0
RALES - MOIST	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>MISCELLANEOUS</u>																				
DECREASED FECAL VOLUME	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0
	V 0	1	2	1	0	0	0	0	0	1	0	2	2	0	0	1	1	0	2	1
NO STOOL	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
HYPOTHERMIA	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0

C-21
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	II	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55
	III	55	55	55	55	54	54	54	54	54	54	54	53	53	53	53	52	52	52	52
	IV	55	55	55	55	55	55	55	55	55	55	55	55	55	54	54	54	54	54	54
	V	54	54	53	52	51	51	51	51	51	49	47	46	43	43	43	42	39	39	35
MASS(ES)	I	0	0	0	0	0	0	0	0	0	1	1	2	2	2	2	2	3	3	3
	II	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	III	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	IV	0	0	1	1	1	1	1	2	2	1	1	1	1	1	1	1	1	1	1
	V	0	0	0	0	0	0	0	0	0	0	0	2	1	2	2	1	1	1	0

WEEK: 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

NORMAL

DEAD

GENL APPEARANCE

[illegible]

[illegible]

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

[illegible]

90-3641

WEEK: 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

EYE(S) APPEAR DAMAGED	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0
II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
III	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IV	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	1	1	1	1	1
V	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	-	-	-	-

90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

	WEEK:	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
# OF ANIMALS EXAMINED	I	54	54	54	54	53	53	53	53	53	52	51	51	51	50	48	47	47	45	43	42
	II	55	55	53	53	53	53	52	52	52	51	50	50	50	49	49	48	47	46	45	45
	III	52	51	51	50	50	48	48	47	47	47	46	46	46	46	46	46	46	45	43	43
	IV	53	52	52	50	50	50	49	48	47	46	44	44	44	41	39	36	35	33	29	29
	V	35	31	29	24	19	17	17	13	11	9	8	6	6	6	6	4	1	0	0	0
OPACITY - UNILATERAL	I	4	5	5	6	7	7	7	7	7	7	7	7	7	7	7	8	8	8	7	8
	II	7	7	7	6	7	7	7	7	7	8	8	8	8	8	8	9	11	11	11	11
	III	7	7	7	7	7	7	7	7	7	7	6	6	6	6	6	6	5	5	5	8
	IV	6	6	6	7	7	7	7	6	6	6	6	6	6	6	5	5	5	5	5	5
	V	4	4	3	3	3	2	3	3	3	3	3	1	1	1	1	1	0	-	-	-
EXOPHTHALMOS - UNILATERAL	I	3	3	3	3	5	5	5	3	3	3	3	3	3	3	3	3	3	2	2	2
	II	2	2	2	2	4	4	4	4	4	4	4	4	4	4	4	3	3	3	3	2
	III	0	0	0	0	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	V	2	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	-	-	-
CORNEAL IRREGULARITY - UNILATERAL	I	5	4	4	4	4	4	4	4	4	4	4	4	4	4	4	3	3	3	3	3
	II	2	2	2	2	3	3	3	3	3	3	3	3	3	3	4	3	5	5	5	5
	III	4	4	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0
	V	2	2	1	1	1	2	2	1	1	1	1	1	1	1	1	0	0	-	-	-
EYE(S) VASCULARIZED	I	4	5	5	6	7	7	7	7	7	7	7	7	7	8	8	8	8	8	7	7
	II	6	6	6	6	6	6	7	7	7	8	8	8	8	9	9	9	9	9	9	9
	III	7	7	7	7	7	7	7	7	7	7	6	6	6	6	6	6	6	6	6	6
	IV	6	6	6	6	6	6	6	5	5	6	6	6	6	6	5	5	5	5	5	5
	V	4	4	4	3	2	1	1	1	1	2	3	1	1	1	1	0	0	-	-	-
LACRIMATION-UNILATERAL	I	8	7	5	4	8	8	8	9	8	6	8	7	10	7	8	9	9	6	7	6
	II	9	8	2	3	4	5	3	4	5	8	9	7	8	8	8	10	14	14	15	12
	III	3	4	2	3	5	5	5	5	7	8	9	9	9	9	6	7	10	11	8	10
	IV	7	9	2	5	5	8	7	8	8	8	7	5	5	2	4	4	5	4	3	3
	V	3	2	3	2	1	2	2	1	2	3	2	2	2	3	3	1	0	-	-	-
CHROMODACRYORRHEA - BILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	II	1	1	1	1	1	1	1	1	1	1	2	1	1	1	2	1	2	1	1	1
	III	2	2	1	2	2	1	1	2	2	3	1	1	1	1	1	1	1	1	1	1
	IV	3	3	2	4	4	4	4	4	4	4	3	3	3	4	3	3	4	3	3	2
	V	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	-

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[illegible]

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK:	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
# OF ANIMALS EXAMINED	I 54	54	54	54	53	53	53	53	53	52	51	51	51	50	48	47	47	45	43	42
	II 55	55	53	53	53	53	52	52	52	51	50	50	50	49	49	48	47	46	45	45
	III 52	51	51	50	50	48	48	47	47	47	46	46	46	46	46	46	46	45	43	43
	IV 53	52	52	50	50	50	49	48	47	46	44	44	44	41	39	36	35	33	29	29
	V 35	31	29	24	19	17	17	13	11	9	8	6	6	6	6	4	1	0	0	0
RESPIRATORY																				
LABORED BREATHING	I 0	0	1	1	0	0	0	0	0	0	0	0	0	0	2	1	1	1	0	1
	II 0	1	0	0	0	0	0	1	0	0	0	0	1	1	1	1	0	0	1	1
	III 0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	4	0	0	0	0	1	1	1	1	1	1	1	0	0	0	0	0	0
	V 0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	-	-	-
RALES - MOIST	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
	II 0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	3	3	3	2
	IV 0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	-
RALES - DRY	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	-
MISCELLANEOUS																				
LIMB(S) APPEAR IMPAIRED	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	-
TAIL BUMPS	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	2	2	2	2
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	-
DECREASED FECAL VOLUME	I 0	0	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
	II 0	1	0	0	0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0
	III 0	0	1	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1
	IV 0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	0	4	0	0	0
	V 0	0	1	1	0	1	0	0	0	0	0	0	1	0	0	0	1	-	-	-

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

[illegible]

C-30
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK: 101 102 103 104 105 106

OF ANIMALS EXAMINED

I	42	40	40	37	37	32
II	45	44	42	42	41	36
III	43	42	38	34	32	25
IV	27	24	20	17	16	9
V	0	0	0	0	0	0

NORMAL

WITHIN NORMAL LIMITS

I	22	23	22	20	14	10
II	19	19	17	17	15	10
III	18	16	15	11	9	6
IV	10	9	6	5	3	2
V	-	-	-	-	-	-

DEAD

MORIBUND - SACRIFICED

I	0	0	1	0	0	0
II	0	0	0	1	0	0
III	0	0	2	0	1	0
IV	1	0	0	0	0	0
V	-	-	-	-	-	-

FOUND DEAD

I	2	0	2	0	0	0
II	1	2	0	0	0	0
III	1	4	2	2	1	1
IV	2	4	3	1	0	0
V	-	-	-	-	-	-

ACCIDENTAL - TRAUMATIC

I	0	0	0	0	0	0
II	0	0	0	0	0	0
III	0	0	0	0	0	0
IV	0	0	0	0	2	0
V	-	-	-	-	-	-

TERMINAL SACRIFICE

I	0	0	0	0	5	32
II	0	0	0	0	5	36
III	0	0	0	0	5	24
IV	0	0	0	0	5	9
V	-	-	-	-	-	-

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK: 101 102 103 104 105 106

# OF ANIMALS EXAMINED	I	42	40	40	37	37	32
	II	45	44	42	42	41	36
	III	43	42	38	34	32	25
	IV	27	24	20	17	16	9
	V	0	0	0	0	0	0

GENL APPEARANCE

SWOLLEN PAW(S)	I	0	1	1	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

ABDOMINAL DISTENSION	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	1	1	1	1	1	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

EMACIATION	I	0	0	0	0	0	0
	II	1	1	0	0	0	1
	III	0	0	1	0	1	0
	IV	1	0	0	0	0	0
	V	-	-	-	-	-	-

PALE	I	1	0	2	0	0	0
	II	1	1	1	1	0	2
	III	2	2	4	1	1	0
	IV	3	2	2	1	1	0
	V	-	-	-	-	-	-

YELLOWISH APPEARANCE	I	0	0	0	0	0	0
	II	0	0	1	1	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

PARAPHIMOSIS	I	0	0	0	0	0	0
	II	0	0	0	0	1	0
	III	0	0	0	0	0	0
	IV	0	1	1	0	0	0
	V	-	-	-	-	-	-

C-32
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

	WEEK: 101 102 103 104 105 106						
# OF ANIMALS EXAMINED	I	42	40	40	37	37	32
	II	45	44	42	42	41	36
	III	43	42	38	34	32	25
	IV	27	24	20	17	16	9
	V	0	0	0	0	0	0
POOR CONDITION	I	0	0	1	0	0	0
	II	0	0	0	0	0	0
	III	0	0	2	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
<u>DERMAL-GENERAL</u>							
YELLOW ANO-GENITAL STAINING	I	2	2	4	2	2	0
	II	1	1	1	2	1	1
	III	5	4	5	1	3	0
	IV	6	4	2	1	2	0
	V	-	-	-	-	-	-
ALOPECIA-GENERAL	I	2	1	1	1	2	1
	II	0	0	0	0	1	1
	III	0	0	0	0	0	0
	IV	2	2	1	1	2	0
	V	-	-	-	-	-	-
SCABS	I	1	1	1	1	3	0
	II	4	4	4	4	3	4
	III	0	0	1	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
ALOPECIA EXTREMITIES/SNOUT	I	1	1	1	1	1	1
	II	2	2	1	1	1	1
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
NECROTIC TIP OF TAIL	I	0	0	0	0	0	0
	II	1	1	1	1	1	0
	III	0	0	2	3	3	1
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

	WEEK: 101 102 103 104 105 106						
# OF ANIMALS EXAMINED	I	42	40	40	37	37	32
	II	45	44	42	42	41	36
	III	43	42	38	34	32	25
	IV	27	24	20	17	16	9
	V	0	0	0	0	0	0
BLACK/BROWN STAINS SNOUT/FOREPAWS	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	1	0
	IV	1	1	0	0	0	0
	V	-	-	-	-	-	-
CAGE SORES/SCABS - PAWS	I	0	0	0	0	0	0
	II	0	0	0	0	1	1
	III	0	0	0	0	0	0
	IV	1	1	0	0	0	0
	V	-	-	-	-	-	-
YELLOW STAINS VENTRAL SURFACE	I	0	0	0	0	0	0
	II	0	0	0	0	1	1
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
<u>OCULAR</u>							
CHROMODACRYORRHEA - UNILATERAL	I	5	7	5	6	9	4
	II	12	12	12	14	13	6
	III	11	11	9	7	7	3
	IV	4	2	3	3	4	0
	V	-	-	-	-	-	-
EYE(S) APPEAR DAMAGED	I	0	0	0	0	0	0
	II	1	1	0	0	0	0
	III	0	0	0	0	0	0
	IV	1	1	1	1	1	0
	V	-	-	-	-	-	-
OPACITY - UNILATERAL	I	7	7	7	6	7	5
	II	11	11	11	11	11	7
	III	8	6	6	5	5	4
	IV	5	4	3	3	4	0
	V	-	-	-	-	-	-

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

	WEEK: 101 102 103 104 105 106						
# OF ANIMALS EXAMINED	I	42	40	40	37	37	32
	II	45	44	42	42	41	36
	III	43	42	38	34	32	25
	IV	27	24	20	17	16	9
	V	0	0	0	0	0	0
EXOPHTHALMOS - UNILATERAL	I	2	2	2	1	1	1
	II	2	2	2	2	2	2
	III	1	1	1	1	1	2
	IV	1	1	1	1	1	0
	V	-	-	-	-	-	-
CORNEAL IRREGULARITY - UNILATERAL	I	2	2	2	2	2	2
	II	5	5	5	5	5	2
	III	5	4	3	3	3	2
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
EYE(S) VASCULARIZED	I	6	6	7	6	6	4
	II	9	9	9	9	9	4
	III	6	5	5	5	5	4
	IV	5	4	3	3	3	0
	V	-	-	-	-	-	-
LACRIMATION-UNILATERAL	I	6	4	3	5	9	5
	II	11	11	12	14	12	6
	III	10	11	9	8	8	2
	IV	4	2	3	3	4	0
	V	-	-	-	-	-	-
CHROMODACRYORRHEA - BILATERAL	I	1	0	0	0	0	0
	II	1	0	0	0	0	0
	III	1	2	1	2	3	0
	IV	2	1	1	1	1	0
	V	-	-	-	-	-	-
LACRIMATION - BILATERAL	I	0	0	0	0	0	0
	II	1	0	0	0	0	0
	III	1	2	1	2	2	0
	IV	2	1	1	1	1	0
	V	-	-	-	-	-	-

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

	WEEK:	101	102	103	104	105	106
# OF ANIMALS EXAMINED	I	42	40	40	37	37	32
	II	45	44	42	42	41	36
	III	43	42	38	34	32	25
	IV	27	24	20	17	16	9
	V	0	0	0	0	0	0
ENOPHTHALMOS - UNILATERAL	I	2	2	2	1	1	1
	II	2	2	2	2	2	1
	III	2	2	2	2	2	2
	IV	2	2	2	2	2	0
	V	-	-	-	-	-	-
OPACITY - BILATERAL	I	0	0	0	0	0	0
	II	1	1	1	1	1	0
	III	1	1	1	1	1	1
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
<u>ORAL/BUCCAL</u>							
INCISORS MALOCCLUDED	I	0	1	1	1	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
INCISORS BROKEN/MISSING	I	1	0	0	0	1	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
EXCESSIVE SALIVATION	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	2	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-
NASAL DISCHARGE - CLEAR	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	1	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

C-36
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK: 101 102 103 104 105 106

# OF ANIMALS EXAMINED	I	42	40	40	37	37	32
	II	45	44	42	42	41	36
	III	43	42	38	34	32	25
	IV	27	24	20	17	16	9
	V	0	0	0	0	0	0

BEHAV/ACTIVITY

LETHARGY	I	1	1	2	0	0	0
	II	1	1	0	0	0	2
	III	0	2	1	1	2	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

BODY LEANS TO LEFT	I	0	0	1	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

RESPIRATORY

LABORED BREATHING	I	0	0	2	0	1	0
	II	1	1	1	1	0	0
	III	0	0	3	1	1	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

RALES - MOIST	I	0	0	0	0	1	0
	II	0	0	1	0	0	0
	III	3	3	1	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

RALES - DRY	I	0	0	1	1	1	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

C-37
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - MALES

WEEK: 101 102 103 104 105 106

# OF ANIMALS EXAMINED	I	42	40	40	37	37	32
	II	45	44	42	42	41	36
	III	43	42	38	34	32	25
	IV	27	24	20	17	16	9
	V	0	0	0	0	0	0

MISCELLANEOUS

LIMB(S) APPEAR IMPAIRED	I	1	1	1	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

TAIL BUMPS	I	0	0	0	0	0	0
	II	2	2	2	2	2	2
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

DECREASED FECAL VOLUME	I	0	0	2	1	1	0
	II	0	0	0	0	0	0
	III	1	2	3	1	1	0
	IV	2	0	1	0	1	0
	V	-	-	-	-	-	-

HYPOTHERMIA	I	0	0	1	0	0	0
	II	0	0	0	0	0	0
	III	0	0	1	0	1	0
	IV	0	0	0	0	0	0
	V	-	-	-	-	-	-

MASS(ES)	I	2	2	2	2	3	2
	II	3	3	3	3	3	1
	III	2	1	0	1	1	0
	IV	1	2	2	2	3	0
	V	-	-	-	-	-	-

C-38
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

	WEEK:	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
# OF ANIMALS EXAMINED	I	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	II	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	III	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	IV	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	V	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
<u>NORMAL</u>																							
WITHIN NORMAL LIMITS	I	90	90	90	89	86	84	84	86	87	81	80	78	74	78	81	75	69	58	55	51	53	49
	II	90	89	88	88	87	85	79	79	79	75	74	68	68	70	76	73	66	59	58	57	52	50
	III	90	90	90	89	89	89	86	82	81	83	79	80	72	76	80	72	70	63	56	60	59	56
	IV	90	90	90	89	86	87	86	84	82	81	81	80	77	80	76	77	69	62	57	60	58	52
	V	90	90	89	84	84	88	83	86	84	83	83	82	76	77	78	76	76	60	60	66	67	57
<u>DEAD</u>																							
INTERIM SACRIFICE	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0
<u>GENL APPEARANCE</u>																							
EMACIATION	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TISSUE AROUND EYE(S) SWOLLEN	I	0	0	0	0	0	0	0	0	0	0	0	0	1	2	1	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	III	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	2	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
# OF ANIMALS EXAMINED	I	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80	
	II	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80	
	III	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80	
	IV	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80	
	V	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80	
<u>DERMAL-GENERAL</u>																							
ALOPECIA	I	0	0	0	0	3	2	2	1	0	2	3	4	8	6	1	6	9	12	16	23	20	24
EXTREMITIES/SNOUT	II	0	0	0	0	0	0	0	0	0	2	2	4	7	5	0	2	4	4	6	5	9	9
	III	0	0	0	1	1	1	2	1	2	2	3	4	9	4	0	2	5	6	10	14	12	12
	IV	0	0	0	0	1	2	2	2	2	2	3	4	4	3	4	4	5	8	12	10	11	
	V	0	0	0	0	0	2	0	0	3	2	3	4	3	0	4	6	4	4	4	3	7	
YELLOW ANO-GENITAL STAINING	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	
	II	0	1	1	1	2	1	1	2	2	2	2	2	2	1	1	1	1	2	2	1	3	
	III	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	
	IV	0	0	0	0	1	0	1	3	4	2	2	2	2	2	0	0	1	1	1	1	1	
	V	0	0	1	6	6	0	1	0	1	3	2	5	5	4	3	4	8	8	8	6	8	
BLACK/BROWN STAINS ORAL/BUCCAL AREA	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	II	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	III	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
YELLOW STAINS VENTRAL SURFACE	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	V	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
SCABS	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
<u>OCULAR</u>																							
CHROMODACRYORRHEA - UNILATERAL	I	0	0	0	0	1	0	1	0	0	1	1	3	3	0	3	6	6	8	10	4	2	6
	II	0	0	0	0	0	0	1	0	0	1	1	2	1	0	0	2	5	3	2	4	1	
	III	0	0	0	0	0	0	3	1	2	6	6	3	2	3	6	4	8	13	9	10	9	
	IV	0	0	0	0	1	0	0	0	1	1	1	1	1	0	4	3	4	8	12	5	7	7
	V	0	0	0	0	0	1	2	2	2	1	1	1	1	1	4	4	4	9	8	1	3	2

	WEEK:	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
# OF ANIMALS EXAMINED	I	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	II	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	III	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	IV	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
	V	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	80	80	80	80	80
OPACITY - UNILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
	III	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE(S) APPEAR DAMAGED	I	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LACRIMATION-UNILATERAL	I	0	0	0	0	0	2	0	0	0	0	0	2	3	0	0	2	5	4	2	1	1	
	II	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	1	6	3	1	4	5	7
	III	0	0	0	0	0	0	0	2	5	1	3	3	6	4	8	8	5	5	7	5	10	
	IV	0	0	0	0	0	0	0	1	0	0	0	0	3	0	0	6	1	2	3	2	8	6
	V	0	0	0	0	0	0	0	0	1	1	1	1	4	3	2	2	6	1	2	1	2	6
CORNEAL IRREGULARITY - UNILATERAL	I	0	0	0	0	0	1	3	3	3	6	6	6	6	6	4	5	5	5	5	5	5	5
	II	0	0	0	0	0	4	6	7	7	10	11	12	12	12	12	12	11	11	11	11	11	
	III	0	0	0	0	0	0	2	2	2	1	1	1	1	1	1	1	1	0	0	0	0	
	IV	0	0	0	0	0	1	1	1	1	5	5	5	5	5	5	5	6	6	6	6	6	
	V	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	1	1	1	1	1
CORNEAL IRREGULARITY - BILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	III	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHROMODACRYORRHEA - BILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	1	3	2	
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	1	0
	III	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	2	2	1	3	1	3	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	0	0	2	1
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

WEEK: -2 -1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

[illegible]

[illegible]

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
# OF ANIMALS EXAMINED	I 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	II 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	69
	III 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	IV 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	V 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
<u>NORMAL</u>																					
WITHIN NORMAL LIMITS	I 47	51	49	44	48	52	44	52	51	49	49	44	39	42	41	34	35	45	45	38	36
	II 49	43	44	38	45	47	38	38	31	35	38	36	37	38	39	37	31	36	29	34	32
	III 56	46	45	45	48	50	38	40	42	38	47	45	41	41	40	45	41	44	39	46	45
	IV 54	44	44	43	48	52	42	38	34	33	36	37	41	40	39	38	35	34	32	42	36
	V 59	44	46	46	47	56	46	40	36	26	31	34	35	32	29	31	28	36	30	28	25
<u>DEAD</u>																					
INTERIM SACRIFICE	I 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	5	5	0	0	0	0	0	0	0	0	0	0	0	0
HUMANE SACRIFICE	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>GENL APPEARANCE</u>																					
EMACIATION	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TISSUE AROUND EYE(S) SWOLLEN	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

	WEEK:	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
# OF ANIMALS EXAMINED	I	80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	II	80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	69
	III	80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	IV	80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	V	80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
RED EXUDATE FROM ANO-GENITAL AREA	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
<u>DERMAL-GENERAL</u>																						
ALOPECIA EXTREMITIES/SNOUT	I	28	18	19	13	18	17	21	14	12	12	11	15	21	21	22	21	29	13	12	15	14
	II	12	10	12	10	14	15	22	21	19	15	15	15	16	16	17	18	21	20	24	11	11
	III	17	15	19	17	18	16	28	26	20	22	19	20	17	24	22	23	26	21	18	20	12
	IV	16	11	11	9	16	15	25	28	26	26	21	23	20	19	20	20	22	20	18	18	7
	V	9	4	6	4	9	9	16	17	15	21	19	21	22	24	22	19	18	19	20	17	13
YELLOW ANO-GENITAL STAINING	I	2	6	2	5	3	1	4	1	1	1	0	3	1	2	2	4	2	0	0	0	0
	II	4	12	6	10	7	4	6	7	10	7	3	5	4	7	4	3	3	3	1	0	0
	III	0	1	0	0	0	0	0	0	1	1	0	1	0	1	0	0	1	2	2	0	0
	IV	2	12	9	10	7	4	5	5	5	8	5	6	4	2	2	3	4	3	4	1	2
	V	6	18	14	15	13	2	8	11	13	25	19	17	12	14	18	21	21	13	17	23	24
SCABS	I	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	1	1	1	1	1	1	1	1	2	2	1	1	1	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ALOPECIA-GENERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	III	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	1	6	3	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	1	1
<u>OCULAR</u>																						
CHROMODACRYORRHEA - UNILATERAL	I	10	11	12	17	13	11	13	13	7	9	10	12	8	6	9	10	9	8	5	10	16
	II	6	10	15	13	3	4	4	8	13	7	9	12	4	4	7	6	7	8	5	3	15
	III	14	22	24	23	4	10	9	13	11	11	3	6	9	10	7	5	6	10	6	4	6
	IV	12	13	13	14	5	8	12	14	11	10	9	9	6	11	7	9	16	15	5	6	20
	V	4	11	13	13	10	13	13	16	13	12	6	7	5	9	6	4	8	7	8	1	12

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
# OF ANIMALS EXAMINED	I 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	II 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	69
	III 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	IV 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
	V 80	80	80	80	80	80	80	80	75	70	70	70	70	70	70	70	70	70	70	70	70
OPACITY - UNILATERAL	I 0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	II 2	2	2	3	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	III 1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	1	1	1	1	2
EYE(S) APPEAR DAMAGED	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
LACRIMATION-UNILATERAL	I 4	4	6	14	4	6	6	5	6	6	3	14	17	7	8	15	12	11	14	9	17
	II 5	8	7	18	3	4	12	12	16	12	6	11	8	3	4	6	10	9	11	14	16
	III 10	20	9	15	11	15	19	18	14	15	6	8	7	4	8	7	5	9	16	1	13
	IV 2	8	8	9	3	7	12	11	10	10	8	6	6	6	6	12	10	14	14	4	5
	V 1	9	2	10	7	5	6	7	7	6	3	7	2	3	4	3	2	9	11	5	8
CORNEAL IRREGULARITY - UNILATERAL	I 5	5	5	5	4	4	5	4	3	3	3	3	3	3	3	3	4	4	4	4	4
	II 11	11	11	11	9	9	9	9	6	5	5	5	5	6	6	6	7	7	7	8	8
	III 0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	2	1	1	1	1
	IV 6	6	6	6	5	4	4	4	4	4	4	4	5	5	5	5	5	5	5	4	5
	V 1	1	1	1	1	1	1	1	1	1	1	1	1	3	3	3	2	2	2	2	3
CORNEAL IRREGULARITY - BILATERAL	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHROMODACRYORRHEA - BILATERAL	I 3	2	2	2	1	1	1	0	0	0	0	0	1	2	1	1	2	0	0	0	1
	II 1	0	1	1	0	0	1	1	0	0	0	0	0	0	0	0	0	2	1	0	0
	III 2	3	4	6	2	3	2	7	3	1	1	1	1	1	1	1	1	1	1	1	2
	IV 2	1	3	4	2	4	5	7	3	2	2	3	1	0	3	3	2	2	3	2	5
	V 0	0	1	1	0	2	2	5	1	1	1	0	0	0	1	1	1	2	2	0	0

WEEK: 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40

[illegible]

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WEEK: 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40

[illegible]

INCISORS BROKEN/MISSING

ORAL SORE

EXCESSIVE SALIVATION

[illegible]

DECREASED FECAL VOLUME

[illegible]

[illegible]

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

	WEEK:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
# OF ANIMALS EXAMINED	I	70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	II	69	69	69	69	69	69	69	69	69	69	69	69	69	69	55	55	55	55	55	55
	III	70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	54	54	54	54
	IV	70	70	70	69	69	69	69	69	69	69	69	69	69	69	54	54	54	54	54	54
	V	70	70	70	70	70	70	70	69	69	69	69	69	69	69	54	54	54	54	54	54
<u>NORMAL</u>																					
WITHIN NORMAL LIMITS	I	35	26	36	33	34	26	28	37	42	40	44	37	36	27	24	29	30	26	25	28
	II	30	25	31	34	33	19	19	29	30	28	25	27	24	20	18	18	16	18	17	21
	III	42	41	49	42	36	21	39	48	48	44	50	39	32	28	29	28	30	33	30	30
	IV	37	29	33	37	32	23	25	43	42	39	38	32	29	23	24	27	29	29	25	27
	V	29	22	28	31	23	10	15	24	34	35	46	39	31	32	31	36	34	31	26	29
<u>DEAD</u>																					
FOUND DEAD	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERIM SACRIFICE	I	0	0	0	0	0	0	0	0	0	0	0	0	0	15	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	14	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	15	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	15	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	15	0	0	0	0	0	0
MORIBUND - SACRIFICED	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>GENL APPEARANCE</u>																					
EMACIATION	I	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	IV	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1

	WEEK:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
# OF ANIMALS EXAMINED	I	70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	II	69	69	69	69	69	69	69	69	69	69	69	69	69	69	55	55	55	55	55	55
	III	70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	54	54	54	54
	IV	70	70	70	69	69	69	69	69	69	69	69	69	69	69	54	54	54	54	54	54
	V	70	70	70	70	70	70	70	69	69	69	69	69	69	69	54	54	54	54	54	54
TISSUE AROUND EYE(S) SWOLLEN	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1
	II	1	1	1	1	1	1	1	1	1	2	2	1	1	1	3	3	3	2	5	4
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	1
RED EXUDATE FROM ANO-GENITAL AREA	I	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	II	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABDOMINAL DISTENSION	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>DERMAL-GENERAL</u>																					
ALOPECIA EXTREMITIES/SNOUT	I	22	32	17	20	22	4	2	1	3	4	4	2	3	3	4	4	5	5	3	3
	II	16	25	17	20	21	9	9	3	3	3	4	2	2	2	2	2	4	3	4	4
	III	10	18	12	15	18	3	0	0	1	2	3	1	1	0	0	1	3	2	2	2
	IV	11	16	9	12	17	4	2	1	1	1	2	2	2	1	2	2	1	3	2	2
	V	13	21	8	17	23	11	9	4	4	4	2	1	1	0	1	1	1	1	2	3
YELLOW ANO-GENITAL STAINING	I	0	3	2	1	1	0	0	0	1	0	1	0	1	0	1	1	2	2	2	2
	II	1	4	1	1	1	1	0	0	2	0	1	2	1	1	4	4	5	4	3	3
	III	0	0	0	0	1	1	0	0	1	2	1	1	3	0	3	3	5	2	1	1
	IV	2	5	6	3	2	3	1	0	2	2	0	2	5	4	2	2	4	3	3	3
	V	17	27	21	12	20	23	23	22	17	17	6	8	3	1	1	2	5	5	8	7
BLACK/BROWN STAINS ORAL/BUCCAL AREA	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
# OF ANIMALS EXAMINED	I 70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	II 69	69	69	69	69	69	69	69	69	69	69	69	69	69	55	55	55	55	55	55
	III 70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	54	54	54	54
	IV 70	70	70	69	69	69	69	69	69	69	69	69	69	69	54	54	54	54	54	54
	V 70	70	70	70	70	70	70	69	69	69	69	69	69	69	54	54	54	54	54	54
SCABS	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ALOPECIA-GENERAL	I 0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 1	2	1	1	1	2	2	1	1	2	2	2	2	2	2	2	2	2	2	2
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BLACK/BROWN STAINS ANO-GENITAL AREA	I 0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>OCULAR</u>																				
CHROMODACRYORRHEA - UNILATERAL	I 15	18	14	11	10	17	17	15	8	9	5	17	15	11	12	10	5	11	15	12
	II 15	18	13	10	10	21	19	11	10	13	9	23	20	22	20	17	18	17	22	15
	III 9	11	10	12	12	21	13	9	9	9	5	22	18	13	9	9	10	11	14	13
	IV 19	19	13	11	15	13	15	3	3	6	3	19	15	17	11	12	7	10	12	14
	V 6	12	7	10	14	20	19	5	6	6	4	14	15	13	9	6	6	8	14	10
OPACITY - UNILATERAL	I 1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	II 4	4	4	4	5	6	6	6	6	6	6	6	7	3	3	3	3	3	3	5
	III 1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV 0	0	0	1	1	3	3	3	3	3	3	3	4	1	1	1	1	1	1	1
	V 2	2	2	2	2	2	3	3	3	3	3	3	4	3	3	3	3	4	4	4
EYE(S) APPEAR DAMAGED	I 0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	II 0	0	0	0	1	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
# OF ANIMALS EXAMINED	I 70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	II 69	69	69	69	69	69	69	69	69	69	69	69	69	69	55	55	55	55	55	55
	III 70	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	54	54	54	54
	IV 70	70	70	69	69	69	69	69	69	69	69	69	69	69	54	54	54	54	54	54
	V 70	70	70	70	70	70	70	69	69	69	69	69	69	69	54	54	54	54	54	54
LACRIMATION-UNILATERAL	I 15	18	10	8	9	26	23	16	14	14	11	16	18	14	16	13	13	11	16	16
	II 15	18	10	6	8	31	33	18	18	21	24	23	23	23	24	18	24	18	18	18
	III 20	18	4	6	11	31	20	13	14	16	12	17	22	17	15	18	12	11	14	16
	IV 11	14	13	7	11	18	18	4	8	11	13	16	18	18	13	12	9	9	12	14
	V 9	9	7	8	7	29	27	16	11	13	8	15	20	14	14	9	9	10	14	10
CORNEAL IRREGULARITY - UNILATERAL	I 4	4	5	4	4	8	8	8	6	6	6	4	4	2	2	2	2	2	3	1
	II 8	8	9	9	7	16	19	18	16	16	15	13	13	11	11	11	11	10	10	8
	III 1	1	1	1	1	6	7	7	5	5	3	3	3	3	3	3	3	3	3	2
	IV 5	5	5	5	6	9	10	13	11	11	10	10	9	9	9	9	9	7	7	6
	V 3	3	3	3	3	3	3	7	6	5	7	7	6	4	4	4	4	4	4	4
CORNEAL IRREGULARITY - BILATERAL	I 0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	II 2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHROMODACRYORRHEA - BILATERAL	I 2	5	8	7	5	9	11	9	3	3	3	9	8	8	5	4	2	8	9	6
	II 0	0	0	0	0	1	1	0	1	2	1	2	7	5	4	4	3	3	4	3
	III 2	4	1	1	1	7	5	2	2	2	1	4	8	7	7	5	5	6	7	5
	IV 2	6	5	5	5	13	14	4	2	2	1	5	4	3	3	2	1	2	5	4
	V 3	7	4	1	1	8	8	4	3	2	0	0	2	0	2	0	2	2	2	3
EYE(S) VASCULARIZED	I 1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	II 4	4	4	4	5	5	5	5	5	5	5	5	6	2	2	2	3	3	3	4
	III 1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV 0	0	0	1	1	3	3	3	3	3	3	3	4	1	1	1	1	1	1	1
	V 2	2	2	2	2	2	2	3	3	3	3	4	4	3	3	3	3	4	4	4
LACRIMATION-BILATERAL	I 1	1	2	3	3	11	12	10	6	9	7	9	7	7	7	5	5	6	6	5
	II 0	0	0	0	0	4	4	1	3	4	5	2	6	4	5	6	5	6	5	3
	III 2	2	2	1	1	9	6	2	2	2	2	2	6	6	7	5	5	6	6	6
	IV 1	2	2	1	2	8	10	4	2	2	5	2	4	3	5	2	2	2	5	4
	V 2	1	3	1	2	8	7	5	4	3	0	0	5	1	2	0	2	2	1	3

[illegible]

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
# OF ANIMALS EXAMINED	I	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	55	55	55	55
	II	69	69	69	69	69	69	69	69	69	69	69	69	69	55	55	55	55	55	55
	III	70	70	70	70	70	70	70	70	70	70	70	70	70	55	55	54	54	54	54
	IV	70	70	70	69	69	69	69	69	69	69	69	69	69	54	54	54	54	54	54
	V	70	70	70	70	70	70	69	69	69	69	69	69	69	54	54	54	54	54	54
MASS	I	0	0	0	0	0	0	0	1	1	2	2	2	2	2	2	2	2	2	2
	II	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	1	2
	III	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0
	IV	0	0	0	1	1	1	1	2	2	2	1	1	1	2	2	2	2	2	2
	V	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0

A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I 55	55	55	55	55	54	54	54	54	54	54	54	54	54	54	54	54	54	54	54
	II 55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	III 54	54	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	52
	IV 54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	53	53	53
	V 54	54	54	54	54	54	53	53	53	53	52	52	51	51	51	50	50	50	50	50
TISSUE AROUND EYE(S) SWOLLEN	I 0	0	0	0	0	0	1	3	3	2	2	0	0	0	0	0	0	0	0	0
	II 1	1	1	1	1	1	1	3	0	0	0	2	2	1	1	1	1	1	1	1
	III 0	0	0	0	0	0	0	2	1	1	1	3	3	3	3	2	1	1	1	1
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	1	1	1	1	1	2	2	1	1	1	1	1	1	1	1	1	1	1	1
RED EXUDATE FROM ANO-GENITAL AREA	I 0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0
	II 0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABDOMINAL DISTENSION	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PALE	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	III 0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>DERMAL-GENERAL</u>																				
ALOPECIA	I 2	2	2	2	6	5	4	4	2	3	2	3	4	6	6	7	7	7	7	7
EXTREMITIES/SNOUT	II 2	2	3	3	5	5	5	4	2	2	2	2	2	2	2	2	2	1	2	2
	III 0	0	0	0	1	1	2	2	1	1	1	3	5	5	5	5	5	6	6	6
	IV 2	2	2	3	3	3	3	4	2	2	2	2	2	2	2	2	2	3	3	4
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1
YELLOW ANO-GENITAL STAINING	I 3	3	3	3	5	3	4	4	3	3	2	2	2	2	2	2	2	2	1	2
	II 5	6	9	6	6	5	6	5	5	3	2	3	3	4	4	3	4	5	3	2
	III 2	2	4	4	4	5	5	6	4	5	5	3	1	3	3	4	4	2	3	2
	IV 6	6	9	8	6	6	7	13	9	8	6	10	8	5	5	5	6	6	6	7
	V 7	8	9	8	8	10	12	14	16	13	8	9	9	6	8	8	9	8	7	7

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	WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I	55	55	55	55	55	54	54	54	54	54	54	54	54	54	54	54	54	54	54	54
	II	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	III	54	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	53	52
	IV	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	53	53	53
	V	54	54	54	54	54	54	53	53	53	53	52	52	51	51	51	50	50	50	50	50
SCABS	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	1	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
	III	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ALOPECIA-GENERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	II	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	2	2
	III	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	IV	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RED STAINS A-G AREA	I	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
NECROTIC TIP OF TAIL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>OCULAR</u>																					
CHROMODACRYORRHEA - UNILATERAL	I	15	20	16	22	21	22	16	20	20	22	21	20	19	18	16	13	14	16	16	13
	II	25	25	25	21	26	27	28	29	25	23	22	21	20	21	18	20	20	20	20	16
	III	14	20	21	17	18	21	24	21	20	21	25	27	23	23	22	19	19	21	20	18
	IV	11	18	15	18	23	24	23	24	20	19	19	21	21	21	23	22	22	20	17	14
	V	12	15	22	17	15	21	20	22	16	17	18	17	18	12	13	9	9	9	11	7
OPACITY - UNILATERAL	I	1	1	1	1	1	1	1	2	2	2	2	2	2	2	3	3	3	3	3	3
	II	5	5	5	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV	1	1	1	1	2	2	2	2	2	2	2	4	4	4	4	4	4	4	4	4
	V	4	4	4	4	4	4	4	3	3	3	3	3	3	3	3	3	3	3	4	4

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

	WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I	55	55	55	55	55	54	54	54	54	54	54	54	54	54	54	54	54	54	54	54
	II	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54	54
	III	54	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	53	52
	IV	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	53	53	53
	V	54	54	54	54	54	54	53	53	53	53	52	52	51	51	51	50	50	50	50	50
EYE(S) APPEAR DAMAGED	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LACRIMATION-UNILATERAL	I	13	19	17	22	24	23	17	21	18	22	25	18	21	20	18	15	16	16	16	13
	II	18	24	25	23	25	27	29	29	22	25	24	21	23	22	22	20	21	20	20	16
	III	12	22	21	18	22	24	26	26	20	22	26	27	25	23	22	19	18	21	20	18
	IV	9	17	12	20	25	25	24	23	16	18	18	21	22	19	22	24	24	22	17	14
	V	10	13	21	17	18	25	21	22	18	18	18	17	18	13	13	11	11	10	12	8
CORNEAL IRREGULARITY - UNILATERAL	I	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
	II	8	8	8	8	6	6	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV	4	4	4	4	3	3	3	3	3	3	3	4	4	4	4	4	4	4	4	4
	V	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
CORNEAL IRREGULARITY - BILATERAL	I	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CHROMODACRYORRHEA - BILATERAL	I	7	8	12	6	7	7	9	7	4	4	4	7	7	9	9	10	10	10	9	8
	II	2	3	7	6	5	4	4	3	4	4	3	1	1	2	2	1	1	3	1	2
	III	6	7	9	10	9	9	8	4	7	5	5	3	6	5	7	3	2	3	4	4
	IV	8	7	13	10	10	11	12	9	10	8	6	8	8	4	4	4	4	4	4	5
	V	4	6	5	5	5	4	3	3	3	2	2	3	3	3	2	2	3	3	2	2
EYE(S) VASCULARIZED	I	1	1	1	1	1	1	1	2	2	2	2	2	2	2	3	3	3	3	3	3
	II	4	4	4	4	4	4	4	4	4	4	5	5	5	5	5	5	5	5	5	5
	III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV	1	1	1	1	2	2	2	2	2	2	2	3	4	4	4	5	5	5	5	5
	V	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	5	5	5

	WEEK:	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
# OF ANIMALS EXAMINED	I	55	55	55	55	55	54	54	54	54	54	54	54	54	54	54	54	54	54	54	54
	II	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	III	54	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	53	52
	IV	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	53	53	53
	V	54	54	54	54	54	54	53	53	53	53	52	52	51	51	51	50	50	50	50	50
LACRIMATION-BILATERAL	I	5	7	12	6	7	7	9	7	4	4	4	6	6	7	7	10	10	11	10	9
	II	2	3	7	6	8	6	6	4	5	4	3	3	3	3	2	1	1	3	1	2
	III	7	6	8	8	6	8	8	4	6	4	4	3	6	5	7	3	2	3	4	4
	IV	6	7	13	9	9	11	12	10	10	8	6	8	8	4	4	4	4	4	4	5
	V	4	6	5	5	6	3	3	3	3	2	2	2	2	2	2	2	3	3	2	2
EXOPHTHALMOS - UNILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
OPACITY - BILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1
ENOPHTHALMOS - UNILATERAL	I	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1
	II	1	1	1	1	1	1	1	1	1	1	2	1	1	2	2	2	2	2	2	3
	III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV	0	0	0	0	0	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1
	V	1	1	1	1	1	1	2	0	0	0	0	1	1	1	2	4	4	4	4	4
<u>ORAL/BUCCAL</u>																					
INCISORS BROKEN/MISSING	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INCISORS MALOCCLUDED	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

WEEK: 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80

# OF ANIMALS EXAMINED	I	55	55	55	55	55	54	54	54	54	54	54	54	54	54	54	54	54	54
	II	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	55	54
	III	54	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	52
	IV	54	54	54	54	54	54	54	54	54	54	54	53	53	53	53	53	53	53
	V	54	54	54	54	54	54	53	53	53	53	52	52	51	51	51	50	50	50

BEHAV/ACTIVITY

[illegible]

RESPIRATORY

[illegible][illegible]

MISCELLANEOUS

[illegible][illegible]

90-3641

WEEK: 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80

# OF ANIMALS EXAMINED	I II III IV V	55 55 54 54 54	55 55 54 54 54	55 55 54 54 54	55 55 54 54 54	55 55 54 54 54	54 55 54 54 53	54 55 54 54 53	54 55 54 54 53	54 55 54 54 53	54 55 54 54 52	54 55 54 54 52	54 55 53 53 51	54 55 53 53 51	54 55 53 53 51	54 55 53 53 50	54 55 53 53 50	54 55 53 53 50	54 54 53 53 50	54 54 52 53 50
TAIL BUMPS	I II III IV V	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	1 0 0 0 0	1 0 0 0 0	1 0 0 0 0	1 0 0 0 0
HYPOTHERMIA	I II III IV V	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 1 0 0
-																				
MASS	I II III IV V	2 1 0 2 0	2 1 0 2 0	2 1 0 2 0	2 2 0 2 0	1 1 0 2 0	1 1 0 3 0	1 0 0 2 0	2 0 0 2 0	2 1 1 2 0	2 0 1 2 0	2 0 1 2 0	2 0 1 3 0	2 0 1 3 0	2 0 1 3 0	2 0 1 3 0	2 0 1 3 0	3 0 1 3 0	3 0 1 3 0	3 0 3 3 0

C-62
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
# OF ANIMALS EXAMINED	I	51	51	51	49	49	49	49	47	46	43	43	43	43	43	42	42	42	42	42
	II	54	53	53	53	53	53	53	53	53	53	53	52	52	52	52	50	50	50	50
	III	50	50	50	50	50	49	49	49	48	48	48	48	47	45	44	44	44	44	44
	IV	53	53	53	53	53	53	53	52	51	50	50	50	48	47	45	44	44	43	43
	V	50	50	49	49	49	49	49	49	49	49	48	47	47	46	45	45	45	41	40
<u>NORMAL</u>																				
WITHIN NORMAL LIMITS	I	19	27	21	18	22	13	13	22	23	20	19	19	20	21	16	18	19	17	16
	II	24	25	21	19	25	20	15	19	27	21	20	20	21	20	23	18	19	20	19
	III	25	27	27	23	28	24	20	26	27	22	21	21	26	25	26	23	21	26	26
	IV	25	25	21	21	26	22	23	21	30	25	25	21	23	22	23	19	15	18	19
	V	24	29	23	23	29	25	22	21	27	18	19	20	22	22	26	24	21	22	19
<u>DEAD</u>																				
FOUND DEAD	I	0	0	2	0	0	0	0	2	1	3	0	0	0	0	0	0	0	0	1
	II	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
	III	0	0	0	0	1	0	0	1	0	0	0	0	0	2	0	0	0	0	0
	IV	0	0	0	0	0	0	0	1	1	1	0	0	2	1	2	1	0	1	0
	V	0	1	0	0	0	0	0	0	0	0	1	1	0	1	1	0	0	4	1
<u>MORIBUND - SACRIFICED</u>																				
	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>FOUND DEAD/DIED DURING PHYSICAL OBSERVATIONS</u>																				
	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>GENL APPEARANCE</u>																				
EMACIATION	I	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	1	1
	II	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	2
	III	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	IV	1	1	1	1	1	1	2	1	2	1	1	1	1	2	2	1	1	2	3
	V	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	2	2	3	1

WEEK: 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

[illegible]

C-64
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
# OF ANIMALS EXAMINED	I 51	51	51	49	49	49	49	49	47	46	43	43	43	43	43	42	42	42	42	42
	II 54	53	53	53	53	53	53	53	53	53	53	53	52	52	52	52	50	50	50	50
	III 50	50	50	50	50	49	49	49	48	48	48	48	48	47	45	44	44	44	44	44
	IV 53	53	53	53	53	53	53	52	51	50	50	50	50	48	47	45	44	44	43	43
	V 50	50	49	49	49	49	49	49	49	49	49	48	47	47	46	45	45	45	41	40
ENTIRE BODY SWOLLEN	I 0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>DERMAL-GENERAL</u>																				
ALOPECIA	I 4	2	0	0	1	1	1	1	1	0	0	0	0	0	1	0	0	0	1	2
EXTREMITIES/SNOUT	II 2	2	2	2	2	2	2	3	2	2	2	3	4	3	3	3	2	3	4	3
	III 5	4	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0
	IV 4	4	4	4	4	4	4	4	1	1	1	1	1	1	1	1	1	1	1	1
	V 1	1	1	1	1	1	1	1	0	0	0	2	2	3	3	3	3	3	3	3
YELLOW ANO-GENITAL STAINING	I 4	1	4	3	1	3	3	6	1	2	2	2	1	2	3	0	1	1	2	0
	II 3	1	2	2	2	3	3	6	1	2	2	1	1	1	2	3	3	2	2	2
	III 2	2	3	3	1	2	3	4	2	3	3	3	3	4	1	0	1	1	0	1
	IV 8	7	8	8	2	3	4	6	3	4	4	4	1	3	5	5	7	7	5	3
	V 10	8	12	12	9	14	15	12	9	18	18	17	12	11	2	9	13	12	11	11
BLACK/BROWN STAINS ORAL/BUCCAL AREA	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
YELLOW STAINS VENTRAL SURFACE	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
SCABS	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 1	1	1	1	0	1	1	1	1	2	2	3	3	4	3	2	3	2	2	3
	III 0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	1	1	1	1
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	V 0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1

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APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

205
90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK:	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
# OF ANIMALS EXAMINED	I 51	51	51	49	49	49	49	49	47	46	43	43	43	43	43	42	42	42	42	42
	II 54	53	53	53	53	53	53	53	53	53	53	53	52	52	52	52	50	50	50	50
	III 50	50	50	50	50	49	49	49	48	48	48	48	48	47	45	44	44	44	44	44
	IV 53	53	53	53	53	53	53	53	52	51	50	50	50	48	47	45	44	44	43	43
	V 50	50	49	49	49	49	49	49	49	49	48	47	47	46	45	45	45	41	40	
ALOPECIA-GENERAL	I 1	1	1	1	1	1	1	1	0	1	1	1	2	2	1	1	1	1	1	1
	II 2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	1
	III 1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1	1	0	0
	IV 1	2	3	2	2	2	2	2	0	0	0	0	0	1	1	0	0	1	1	1
	V 0	0	0	0	0	0	1	1	2	2	3	4	3	5	5	6	8	7	4	3
CAGE SORES/SCABS - PAWS	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV 0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>OCULAR</u>																				
CHROMODACRYORRHEA - UNILATERAL	I 18	13	16	20	15	21	21	16	16	17	14	13	8	11	11	11	10	10	10	11
	II 14	13	16	16	12	19	21	16	11	16	18	18	14	17	8	12	11	14	11	13
	III 17	16	17	19	15	19	22	13	15	20	18	20	15	15	13	15	14	8	11	13
	IV 14	14	17	17	14	16	18	13	8	13	13	18	15	12	7	9	11	11	8	10
	V 13	10	11	11	6	6	7	7	5	11	11	12	10	9	4	7	9	7	9	12
OPACITY - UNILATERAL	I 3	3	3	3	2	2	2	2	2	2	2	2	3	3	3	3	3	3	3	3
	II 6	6	6	6	6	6	6	7	7	8	8	8	8	8	8	8	8	8	9	9
	III 1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV 4	4	5	5	5	5	5	5	4	4	4	4	5	4	5	5	6	5	5	5
	V 4	4	4	4	5	5	5	5	5	5	5	5	5	5	5	5	5	4	4	4
EYE(S) APPEAR DAMAGED	I 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III 0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
	IV 2	2	2	2	2	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0
	V 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LACRIMATION-UNILATERAL	I 19	12	15	18	14	20	23	14	14	14	12	11	9	11	11	10	8	11	10	8
	II 14	13	14	15	11	17	21	13	8	16	17	16	14	16	8	13	12	14	10	12
	III 17	15	16	17	12	19	22	11	14	19	17	19	15	15	13	15	14	10	11	12
	IV 14	14	19	19	14	16	19	12	8	14	14	19	16	12	8	9	11	12	12	10
	V 15	12	12	12	8	7	8	8	7	11	11	12	10	11	4	7	12	9	10	14

**A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION**

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

	WEEK:	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
# OF ANIMALS EXAMINED	I	51	51	51	49	49	49	49	49	47	46	43	43	43	43	43	42	42	42	42	42
	II	54	53	53	53	53	53	53	53	53	53	53	53	52	52	52	52	50	50	50	50
	III	50	50	50	50	50	49	49	49	48	48	48	48	48	47	45	44	44	44	44	44
	IV	53	53	53	53	53	53	53	53	52	51	50	50	50	48	47	45	44	44	43	43
	V	50	50	49	49	49	49	49	49	49	49	49	49	48	47	47	46	45	45	45	41
CORNEAL IRREGULARITY - UNILATERAL	I	1	1	1	1	2	2	2	2	2	2	2	2	2	2	1	2	2	3	3	3
	II	5	5	5	5	5	5	6	6	6	6	6	6	6	6	6	5	5	5	6	6
	III	1	1	2	2	1	1	2	2	1	2	2	2	2	2	2	2	2	3	3	3
	IV	4	4	4	4	4	4	3	3	3	4	4	4	3	3	3	2	2	2	2	2
	V	2	2	2	2	1	1	2	3	3	2	2	2	2	2	1	2	2	2	2	2
CORNEAL IRREGULARITY - BILATERAL	I	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	0	0
CHROMODACRYORRHEA - BILATERAL	I	7	7	6	6	6	11	11	5	3	5	5	6	7	5	5	6	5	7	7	6
	II	3	3	4	5	3	3	5	3	2	3	4	3	3	3	1	2	3	2	3	2
	III	6	6	3	6	4	4	5	3	1	2	5	5	2	4	1	0	1	1	1	1
	IV	4	4	4	4	2	6	6	7	4	4	3	4	2	3	3	5	3	3	2	6
	V	2	2	2	2	2	4	4	3	3	2	3	4	3	3	5	3	2	3	1	2
EYE(S) VASCULARIZED	I	3	3	3	3	3	3	3	3	3	3	3	3	4	4	4	4	4	4	4	4
	II	5	5	5	5	5	5	7	7	7	7	7	7	7	7	7	7	7	7	8	8
	III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	IV	5	5	5	5	5	5	5	5	4	4	4	6	6	6	6	5	5	5	5	5
	V	5	5	5	5	6	6	6	6	6	6	6	6	6	6	6	5	5	5	4	4
LACRIMATION-BILATERAL	I	7	7	6	6	6	10	10	5	3	5	5	6	6	4	4	6	5	5	5	4
	II	3	3	4	5	3	3	4	3	2	3	4	4	4	2	1	2	2	2	3	1
	III	6	6	3	5	3	3	4	4	2	1	3	5	1	3	1	0	1	1	0	1
	IV	4	4	4	4	2	5	4	5	4	4	3	4	3	3	3	5	3	3	3	4
	V	2	2	2	2	2	2	2	1	1	1	2	3	3	3	3	2	1	3	1	1
EXOPHTHALMOS - UNILATERAL	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0
	II	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	1	1
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	V	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0

WEEK: 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

I	51	51	51	49	49	49	49	49	47	46	43	43	43	43	42	42	42	42	42
II	54	53	53	53	53	53	53	53	53	53	53	52	52	52	52	50	50	50	50
III	50	50	50	50	50	49	49	49	48	48	48	48	47	45	44	44	44	44	44
IV	53	53	53	53	53	53	53	53	52	51	50	50	50	48	47	45	44	44	43
V	50	50	49	49	49	49	49	49	49	49	48	47	47	46	45	45	45	41	40

LETHARGY

I	0	0	1	0	0	0	0	0	1	0	0	0	0	0	1	1	0	0
II	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	1
III	0	0	0	0	0	1	1	1	0	0	0	1	1	1	0	0	0	0
IV	0	0	0	0	1	1	1	1	0	1	0	0	0	0	0	0	0	1
V	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0

I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IV	0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0	0	0
V	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0

[illegible][illegible]

LABORED BREATHING

I	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
II	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IV	0	0	0	0	1	1	1	1	0	1	0	0	0	0	0	1	0	1	0	1
V	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0

[illegible]

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

	WEEK:	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100
# OF ANIMALS EXAMINED	I	51	51	51	49	49	49	49	49	47	46	43	43	43	43	43	42	42	42	42	42
	II	54	53	53	53	53	53	53	53	53	53	53	53	52	52	52	52	50	50	50	50
	III	50	50	50	50	50	49	49	49	48	48	48	48	48	47	45	44	44	44	44	44
	IV	53	53	53	53	53	53	53	53	52	51	50	50	50	48	47	45	44	44	43	43
	V	50	50	49	49	49	49	49	49	49	49	49	48	47	47	46	45	45	45	41	40

MISCELLANEOUS

DECREASED FECAL VOLUME	I	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	1	1	0	0
	II	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	1	2	2	1
	III	0	0	0	0	0	1	1	1	0	0	0	0	1	1	0	0	0	0	0
	IV	0	1	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	1	0
	V	0	0	0	0	0	0	0	1	1	0	1	0	1	2	0	1	0	2	1

NO STOOL	I	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	V	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0

[illegible][illegible][illegible]

C-70
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

210

90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK: 101 102 103 104 105 106

# OF ANIMALS EXAMINED	I	41	40	40	39	38	33
	II	50	48	48	44	44	36
	III	44	44	43	43	42	36
	IV	41	40	39	38	36	29
	V	38	34	29	26	21	15

NORMAL

WITHIN NORMAL LIMITS	I	9	11	17	15	18	9
	II	11	9	18	17	18	5
	III	13	12	18	16	18	7
	IV	13	13	17	17	19	6
	V	11	12	13	10	8	1

DEAD

FOUND DEAD	I	1	0	1	1	0	0
	II	1	0	3	0	2	0
	III	0	1	0	1	1	0
	IV	1	1	1	2	1	0
	V	3	5	3	5	1	0

MORIBUND - SACRIFICED	I	0	0	0	0	0	0
	II	1	0	1	0	1	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	1	0
	V	1	0	0	0	0	0

TERMINAL SACRIFICE	I	0	0	0	0	5	33
	II	0	0	0	0	5	36
	III	0	0	0	0	5	36
	IV	0	0	0	0	5	29
	V	0	0	0	0	5	15

GENL APPEARANCE

EMACIATION	I	0	0	0	1	0	0
	II	1	0	1	0	0	0
	III	0	1	0	0	0	0
	IV	2	1	0	1	0	0
	V	3	1	2	2	0	0

C-71
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

211
90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

		101	102	103	104	105	106
# OF ANIMALS EXAMINED	I	41	40	40	39	38	33
	II	50	48	48	44	44	36
	III	44	44	43	43	42	36
	IV	41	40	39	38	36	29
	V	38	34	29	26	21	15
TISSUE AROUND EYE(S) SWOLLEN	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	1	1	1	1	1	1
RED EXUDATE FROM ANO-GENITAL AREA	I	0	0	0	0	0	0
	II	1	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	1	0	0
	V	0	0	0	0	0	0
PALE	I	0	0	0	0	0	0
	II	0	1	1	0	0	1
	III	0	0	1	1	3	0
	IV	2	2	2	1	0	0
	V	0	0	1	0	1	0
<u>DERMAL-GENERAL</u>							
ALOPECIA	I	2	2	2	2	2	0
EXTREMITIES/SNOUT	II	4	3	3	3	3	0
	III	0	0	0	0	0	0
	IV	1	1	1	1	1	0
	V	3	3	1	0	0	0
YELLOW ANO-GENITAL STAINING	I	1	1	2	2	1	0
	II	2	2	1	0	1	1
	III	1	1	1	2	3	0
	IV	6	5	5	4	2	1
	V	16	11	10	8	10	1
BLACK/BROWN STAINS ORAL/BUCCAL AREA	I	0	0	0	1	0	0
	II	1	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	1	1	1	0	0	0
	V	2	2	0	0	0	0

C-72
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

212
90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

		WEEK: 101	102	103	104	105	106
# OF ANIMALS EXAMINED	I	41	40	40	39	38	33
	II	50	48	48	44	44	36
	III	44	44	43	43	42	36
	IV	41	40	39	38	36	29
	V	38	34	29	26	21	15
SCABS	I	0	0	0	0	0	0
	II	3	3	3	3	3	1
	III	1	1	1	1	2	1
	IV	1	0	0	0	0	0
	V	1	1	1	0	0	0
ALOPECIA-GENERAL	I	1	1	1	1	1	1
	II	1	1	1	1	1	0
	III	0	0	0	0	0	0
	IV	1	1	2	4	3	2
	V	6	6	3	1	1	0
BLACK/BROWN STAINS ANO-GENITAL AREA	I	0	0	0	0	0	0
	II	0	2	0	0	0	0
	III	0	1	0	1	0	0
	IV	0	0	0	1	0	0
	V	0	3	0	0	0	0
RED STAINS A-G AREA	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	1	0
	V	0	0	0	0	0	0
NECROTIC TIP OF TAIL	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	1	0	0
	V	0	0	0	0	0	0
CAGE SORES/SCABS - PAWS	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	2	2	2	2	1	0
	V	0	0	0	0	0	0

C-73
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

213
90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK: 101 102 103 104 105 106

# OF ANIMALS EXAMINED	I	41	40	40	39	38	33
	II	50	48	48	44	44	36
	III	44	44	43	43	42	36
	IV	41	40	39	38	36	29
	V	38	34	29	26	21	15

OCULAR

CHROMODACRYORRHEA - UNILATERAL	I	17	15	8	9	9	0
	II	26	22	10	12	10	5
	III	21	21	14	15	12	4
	IV	14	13	9	9	6	5
	V	13	13	8	8	8	2

OPACITY - UNILATERAL	I	3	3	3	3	3	2
	II	8	8	8	8	10	3
	III	1	1	1	1	1	0
	IV	5	5	5	5	6	3
	V	4	4	2	1	1	1

EYE(S) APPEAR DAMAGED	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	2
	IV	0	0	0	0	0	0
	V	0	0	0	0	0	0

LACRIMATION-UNILATERAL	I	10	8	6	7	6	2
	II	19	16	8	11	9	4
	III	16	16	13	14	11	4
	IV	15	14	9	9	5	5
	V	13	13	7	7	7	2

CORNEAL IRREGULARITY - UNILATERAL	I	3	3	3	3	3	0
	II	7	7	7	6	6	1
	III	4	4	4	4	4	4
	IV	2	2	2	2	2	1
	V	3	3	1	1	1	0

CORNEAL IRREGULARITY - BILATERAL	I	1	1	1	1	1	0
	II	0	0	0	0	0	0
	III	1	1	1	1	1	0
	IV	0	0	0	0	0	0
	V	0	0	0	0	0	0

C-74
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

214
90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

	WEEK:	101	102	103	104	105	106
# OF ANIMALS EXAMINED	I	41	40	40	39	38	33
	II	50	48	48	44	44	36
	III	44	44	43	43	42	36
	IV	41	40	39	38	36	29
	V	38	34	29	26	21	15
CHROMODACRYORRHEA - BILATERAL	I	7	8	6	6	3	0
	II	4	4	3	2	1	0
	III	1	1	0	0	0	0
	IV	4	4	3	3	2	0
	V	2	2	1	0	0	0
EYE(S) VASCULARIZED	I	4	4	4	4	4	2
	II	8	8	8	8	8	3
	III	1	1	1	1	1	0
	IV	5	5	5	5	5	3
	V	4	3	2	1	1	1
LACRIMATION-BILATERAL	I	6	8	6	6	3	0
	II	1	1	1	0	0	0
	III	1	1	0	1	0	0
	IV	2	2	2	2	2	0
	V	1	1	1	0	0	0
EXOPHTHALMOS - UNILATERAL	I	0	0	0	0	0	0
	II	1	1	1	2	2	1
	III	0	0	0	0	0	1
	IV	0	0	0	0	0	0
	V	0	0	0	0	0	0
OPACITY - BILATERAL	I	1	1	1	1	1	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	0	0	0	0	0	0
ENOPHTHALMOS - UNILATERAL	I	2	2	2	2	2	0
	II	2	2	2	2	2	0
	III	1	1	1	1	1	0
	IV	1	1	1	1	1	1
	V	3	2	1	1	1	1

C-75
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

215
90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK: 101 102 103 104 105 106

# OF ANIMALS EXAMINED	I	41	40	40	39	38	33
	II	50	48	48	44	44	36
	III	44	44	43	43	42	36
	IV	41	40	39	38	36	29
	V	38	34	29	26	21	15

EYE ATROPHIED - UNILATERAL	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	1	1	1	1	0	0
	V	0	0	0	0	0	0

ORAL/BUCCAL

INCISORS MALOCCLUDED	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	1	1	1	1	1	0
	IV	0	0	0	0	0	0
	V	0	0	0	0	0	0

BEHAV/ACTIVITY

LETHARGY	I	0	1	0	0	1	0
	II	0	2	1	0	0	0
	III	0	1	0	1	1	0
	IV	1	0	1	1	0	1
	V	2	2	2	2	0	0

PROSTRATION	I	0	0	1	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	0	0	0	0	0	0

IRREGULAR GAIT	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	0	1	0	0	0	0

C-76
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

216
90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

WEEK: 101 102 103 104 105 106

# OF ANIMALS EXAMINED	I	41	40	40	39	38	33
	II	50	48	48	44	44	36
	III	44	44	43	43	42	36
	IV	41	40	39	38	36	29
	V	38	34	29	26	21	15

RESPIRATORY

LABORED BREATHING	I	0	0	1	0	0	0
	II	0	1	1	0	0	0
	III	0	0	0	0	1	0
	IV	0	1	1	0	0	0
	V	0	1	1	0	0	0

MISCELLANEOUS

DECREASED FECAL VOLUME	I	0	1	1	1	0	0
	II	2	2	1	0	0	0
	III	0	0	1	1	1	0
	IV	1	1	0	3	1	0
	V	1	0	1	1	1	0

NO STOOL	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	1	0	0	0	0
	IV	1	0	0	1	0	0
	V	1	3	0	0	0	0

TAIL BUMPS	I	0	0	0	0	0	0
	II	2	2	2	1	1	0
	III	0	0	0	0	0	0
	IV	0	0	0	0	0	0
	V	0	0	0	0	0	0

HYPOTHERMIA	I	0	0	1	0	0	0
	II	0	0	0	0	0	0
	III	0	1	0	0	0	0
	IV	0	0	0	0	0	0
	V	0	0	0	0	0	0

WATERY STOOL	I	0	0	0	0	0	0
	II	0	0	0	0	0	0
	III	0	0	0	0	0	0
	IV	0	0	1	1	0	0
	V	0	0	0	0	1	0

C-77
APPENDIX C (CONT.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

217
90-3641

SUMMARY OF IN-LIFE PHYSICAL OBSERVATIONS - FEMALES

	WEEK:	101	102	103	104	105	106
# OF ANIMALS EXAMINED	I	41	40	40	39	38	33
	II	50	48	48	44	44	36
	III	44	44	43	43	42	36
	IV	41	40	39	38	36	29
	V	38	34	29	26	21	15

MASS	I	3	3	4	4	4	1
	II	7	7	6	6	6	2
	III	8	8	7	7	7	2
	IV	2	1	1	1	1	1
	V	1	1	1	1	1	1

D-1
Appendix D

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LIONEL F. RUBIN, V.M.D.
1116 SAINT ANDREWS ROAD
BRYN MAWR, PENNSYLVANIA 19010

TELEPHONE (215) 520-9430

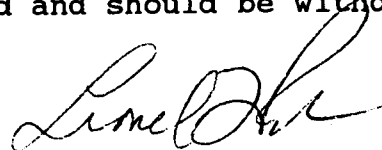
Pretest

December 15, 1992

Bio/dynamics
Mettlers Road, Box 2360
East Millstone NJ 08875-2360

Re: project J-11 90-3641

Pretest ophthalmoscopic examination of project J-11 90-3641 rats was performed December 14 (males) and 15 (females), 1992. Rats with ocular abnormalities were identified and should be withdrawn from inclusion in the study if possible.



Lionel F. Rubin, V.M.D.

LIONEL F. RUBIN, V.M.D.
1116 SAINT ANDREWS ROAD
BRYN MAWR, PENNSYLVANIA 19010

TELEPHONE (215) 520-9430

Month 3

March 25, 1993

Pharmaco LSR, Inc.
Mettlers Road, Box 2360
East Millstone NJ 08875-2360

Re: project J-11 90-3641

Ophthalmoscopic examination of project J-11 90-3641 rats was performed March 24, 1993. I have reviewed the findings of the type and incidence of ocular abnormalities. There is no indication of dose or compound related ocular disease. In my opinion, none of the ocular abnormalities is attributable to the administration of the test compound. Retinal photographs were taken.



Lionel F. Rubin, V.M.D.

LIONEL F. RUBIN, V.M.D.
1116 SAINT ANDREWS ROAD
BRYN MAWR, PENNSYLVANIA 19010
TELEPHONE (215) 520-9430

Month 6

June 29, 1993

Pharmaco LSR
Mettlers Road, Box 2360
East Millstone NJ 08875-2360

Re: project J-11 90-3641

Ophthalmoscopic examination of project J-11 90-3641 rats was performed June 24, 1993. I have reviewed the findings of the type and incidence of ocular abnormalities. There is no indication of dose or compound related ocular disease. In my opinion, none of the ocular abnormalities is attributable to the administration of the test compound.



Lionel F. Rubin, V.M.D.

Appendix D (cont.)

LIONEL F. RUBIN, V.M.D.

1116 SAINT ANDREWS ROAD
BRYN MAWR, PENNSYLVANIA 19010

TELEPHONE (215) 520-9430

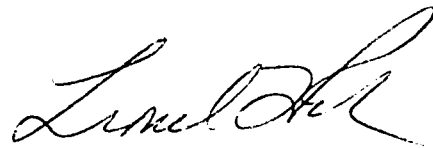
Month 12

December 26, 1993

Pharmaco LSR
Mettlers Road, Box 2360
East Millstone NJ 08875-2360

Re: project J-11 90-3641

Ophthalmoscopic examination of project J-11 90-3641 rats was performed December 23, 1993. I have reviewed the findings of the type and incidence of ocular abnormalities. There is no indication of dose or compound related ocular disease. In my opinion, none of the ocular abnormalities is attributable to the administration of the test compound.



Lionel F. Rubin, V.M.D.

D-5
Appendix D (cont.)
LIONEL F. RUBIN, V.M.D.
1116 SAINT ANDREWS ROAD
BRYN MAWR, PENNSYLVANIA 19010
—
TELEPHONE (610) 520-9430

222

Termination

December 30, 1994

Pharmaco LSR
Mettlers Road, Box 2360
East Millstone NJ 08875-2360

Re: project J-11 90-3641

Ophthalmoscopic examination of project J-11 90-3641 rats was performed December 21 and 22, 1994. I have reviewed the findings of the type and incidence of ocular abnormalities. There is a slight increase in the prevalence of corneal scarring in treated male rats, but this is probably not of biologic significance. There is no other indication of dose or compound related ocular disease. In my opinion, none of the ocular abnormalities is attributable to the administration of the test compound.



Lionel F. Rubin, V.M.D.

TELEPHONE (215) 520-9430

Additional Ophthalmoscopic Examinations

February 10, 1993

Pharmaco::LSR
Mettlers Road, Box 2360
East Millstone NJ 08875-2360

Attention: Dr. Ira Daly

Re: project J-11 90-3641

I observed the "corneal irregularities" reported by the technicians performing the observations. Their findings are those expected in Fischer rats, and will not have any impact on the study or its interpretation. The rats had mineralized streaks in the superficial corneal epithelial layer and possibly the anterior corneal stroma. The position and morphologic appearance was typical of Fischer rat corneal dystrophy. This dystrophy is easily recognizable, quite common (its incidence approaches 100%), and should be considered normal for the strain. The condition becomes more apparent with age. The most recent literature is summarized below:

1. Stitzel KA, Bruner RH, Newmann EA, Reer PJ, Petersen DW, Alden CL, Hysell DK: Spontaneous corneal dystrophy in F344 rats. VII Internat Symp Soc Toxicologic Pathologists, June 5-8, 1988 (abstract)

Linear opacities were observed in 94% of 5 month old Fischer rats. The lesions ranged from multifocal superficial ulceration to well-defined opacities. The abnormalities initially stained with fluorescein. The intensity of the change was greater in males. Rats were affected as early as 31 days. Histologically there were mineral deposits in the corneal epithelial basement membrane.

2. Losco PE, Troup CM: Corneal dystrophy in F344 rats. Lab Anim Sci 38: 703-710 (1988)

A calcific band shaped dystrophy was present in up to 15% of F344 rats from a closed breeding colony. The abnormalities were present in the interpalpebral fissure unilaterally or bilaterally as punctate or linear opacities. Occasionally there was pitting or roughening of the corneal surface. There was mineralization of the epithelial basement membrane.


Lionel F. Rubin, V.M.D.

D-7
Appendix D (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Ophthalmology
Preface

Ophthalmoscopic examinations were performed as follows: Pretest - Week -2, Month 3 - Week 13, Month 6 - Week 26, Month 12 - Week 52 and Termination - Week 104. Only animals which were within normal limits at the pretest examination were placed on test.

Key to codes used for individual animal data:

P = Present
1 = Right
2 = Left
3 = Both

Corresponding dose levels for each group were as follows:

Group I	-	0 ppm
Group II	-	100/50 ppm ^a
Group III	-	500 ppm
Group IV	-	6000 ppm
Group V	-	12000 ppm

Ophthalmoscopic Examination Schedule:

Satellite Animals:

Number of Animals: Up to 35/sex/group

Time Intervals

Pretest:	14, 15 December 1992
Month 3:	24 March 1993
Month 6:	24 June 1993
Month 12:	23 December 1993

Oncogenicity Animals:

Number of Animals: Up to 55/sex/group

Time Intervals

Pretest:	14, 15 December 1992
Month 12:	23 December 1993
Termination:	21, 22 and 28 December 1994

^aThe Group II dose level was reduced on 21 April 1993 (Test Day 113) at the sponsor request, from 100 ppm to 50 ppm.

D-8
APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

225
90-3641

SUMMARY INCIDENCE OF OPHTHALMOSCOPIC EXAMINATIONS - MALES

	WEEK:	-2	13	26	52	104
# OF ANIMALS EXAMINED	I	90	35	25	70	37
	II	90	35	25	70	42
	III	90	35	25	70	33
	IV	90	35	25	70	17
	V	90	34	25	69	0

NORMAL

WITHIN NORMAL LIMITS	I	90	30	19	45	15
	II	90	30	20	43	13
	III	90	30	21	45	12
	IV	90	33	23	53	3
	V	90	33	23	53	-

OCULAR

FOCAL RETINOPATHY	I	0	1	1	2	0
	II	0	1	1	2	0
	III	0	1	1	3	0
	IV	0	0	0	3	0
	V	0	0	0	2	-

POSTERIOR SUBCAPSULAR CATARACT	I	0	0	0	1	5
	II	0	0	0	1	3
	III	0	0	0	1	3
	IV	0	0	0	0	1
	V	0	0	0	0	-

COMPLETE CATARACT	I	0	0	0	2	5
	II	0	0	0	1	12
	III	0	0	0	4	6
	IV	0	0	0	3	5
	V	0	0	0	2	-

ANTERIOR SYNECHIA	I	0	1	1	1	1
	II	0	0	0	1	2
	III	0	0	0	0	0
	IV	0	0	0	0	0
	V	0	0	0	0	-

IRITIS OR UVEITIS	I	0	0	0	0	2
	II	0	0	0	1	3
	III	0	0	0	0	4
	IV	0	0	0	0	3
	V	0	0	0	1	-

D-9
APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

SUMMARY INCIDENCE OF OPHTHALMOSCOPIC EXAMINATIONS - MALES

	WEEK:	-2	13	26	52	104
# OF ANIMALS EXAMINED	I	90	35	25	70	37
	II	90	35	25	70	42
	III	90	35	25	70	33
	IV	90	35	25	70	17
	V	90	34	25	69	0
CORNEAL SCAR	I	0	3	4	14	13
	II	0	4	3	13	22
	III	0	1	4	10	16
	IV	0	2	2	7	10
	V	0	0	0	6	-
RETINAL DEGENERATION	I	0	3	3	6	4
	II	0	1	0	8	1
	III	0	0	0	7	1
	IV	0	0	0	5	0
	V	0	1	1	7	-
PHTHISIS BULBI	I	0	0	0	1	2
	II	0	0	0	2	4
	III	0	0	0	3	3
	IV	0	0	0	1	2
	V	0	0	0	1	-
CONJUNCTIVITIS	I	0	0	1	9	8
	II	0	0	1	11	12
	III	0	3	0	8	8
	IV	0	0	0	4	4
	V	0	0	1	5	-
GLAUCOMA	I	0	0	0	1	1
	II	0	0	0	1	1
	III	0	0	0	0	0
	IV	0	0	0	1	1
	V	0	0	0	2	-
PROPTOSIS AND CORNEAL NECROSIS	I	0	0	0	0	0
	II	0	0	1	0	0
	III	0	0	0	0	0
	IV	0	0	0	0	0
	V	0	0	0	0	-

D-10
APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY INCIDENCE OF OPHTHALMOSCOPIC EXAMINATIONS - MALES

	WEEK:	-2	13	26	52	104
# OF ANIMALS EXAMINED	I	90	35	25	70	37
	II	90	35	25	70	42
	III	90	35	25	70	33
	IV	90	35	25	70	17
	V	90	34	25	69	0
HYPHEMA	I	0	0	0	0	1
	II	0	0	0	0	0
	III	0	0	0	0	1
	IV	0	0	0	0	1
	V	0	0	0	0	-

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

SUMMARY INCIDENCE OF OPHTHALMOSCOPIC EXAMINATIONS - FEMALES

	WEEK:	-2	13	26	52	104
# OF ANIMALS EXAMINED	I	90	35	25	70	39
	II	90	35	25	69	44
	III	90	35	25	70	43
	IV	90	35	25	69	38
	V	90	35	25	69	24

NORMAL

WITHIN NORMAL LIMITS	I	90	31	18	25	8
	II	90	29	16	20	9
	III	90	30	19	22	10
	IV	90	30	15	25	10
	V	90	30	18	23	3

OCULAR

FOCAL RETINOPATHY	I	0	0	0	2	0
	II	0	0	1	1	1
	III	0	0	0	1	1
	IV	0	2	2	1	0
	V	0	0	0	2	1
POSTERIOR SUBCAPSULAR CATARACT	I	0	0	0	0	1
	II	0	0	0	2	3
	III	0	0	0	0	1
	IV	0	0	0	1	2
	V	0	0	0	1	1
COMPLETE CATARACT	I	0	0	0	1	4
	II	0	0	3	5	10
	III	0	0	0	1	1
	IV	0	0	0	3	5
	V	0	0	1	3	1
ANTERIOR SYNECHIA	I	0	0	1	0	0
	II	0	0	0	1	1
	III	0	1	0	0	0
	IV	0	0	0	0	0
	V	0	0	0	0	0
POSTERIOR SYNECHIA	I	0	0	0	0	0
	II	0	1	0	0	0
	III	0	0	0	0	0
	IV	0	0	0	0	0
	V	0	0	0	0	0

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY INCIDENCE OF OPHTHALMOSCOPIC EXAMINATIONS - FEMALES

	WEEK:	-2	13	26	52	104
# OF ANIMALS EXAMINED	I	90	35	25	70	39
	II	90	35	25	69	44
	III	90	35	25	70	43
	IV	90	35	25	69	38
	V	90	35	25	69	24
IRITIS OR UVEITIS	I	0	0	0	0	0
	II	0	0	0	1	2
	III	0	0	0	0	0
	IV	0	0	0	0	0
	V	0	0	0	0	1
CORNEAL SCAR	I	0	1	2	18	26
	II	0	1	3	19	28
	III	0	0	0	25	31
	IV	0	0	1	11	18
	V	0	1	0	20	19
RETINAL DEGENERATION	I	0	0	2	2	0
	II	0	3	2	7	0
	III	0	0	1	2	0
	IV	0	1	2	9	0
	V	0	2	2	6	0
PHTHISIS BULBI	I	0	0	1	1	3
	II	0	0	1	6	6
	III	0	0	0	1	1
	IV	0	0	0	2	4
	V	0	0	1	2	1
CONJUNCTIVITIS	I	0	3	5	39	22
	II	0	1	1	40	23
	III	0	4	6	47	21
	IV	0	2	6	38	19
	V	0	2	4	33	10
GLAUCOMA	I	0	0	0	0	0
	II	0	0	0	0	0
	III	0	0	0	0	0
	IV	0	0	0	1	0
	V	0	0	0	0	0

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

SUMMARY INCIDENCE OF OPHTHALMOSCOPIC EXAMINATIONS - FEMALES

	WEEK:	-2	13	26	52	104
# OF ANIMALS EXAMINED	I	90	35	25	70	39
	II	90	35	25	69	44
	III	90	35	25	70	43
	IV	90	35	25	69	38
	V	90	35	25	69	24
OPTIC NERVE ATROPHY	I	0	0	1	1	0
	II	0	0	0	0	0
	III	0	0	1	0	0
	IV	0	0	0	0	0
	V	0	0	0	0	0
TUMOR LOWER LID	I	0	0	0	0	0
	II	0	0	0	0	0
	III	0	0	0	0	1
	IV	0	0	0	0	0
	V	0	0	0	0	0
RETINAL HEMORRHAGE	I	0	0	0	0	0
	II	0	0	0	0	0
	III	0	0	0	0	0
	IV	0	0	0	0	1
	V	0	0	0	0	0

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
ANIMAL #: 1001 GROUP I WITHIN NORMAL LIMITS CORNEAL SCAR		P	P			3
ANIMAL #: 1002 GROUP I WITHIN NORMAL LIMITS RETINAL DEGENERATION		P	P			1
ANIMAL #: 1003 GROUP I WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1004 GROUP I WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1005 GROUP I WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1006 GROUP I WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1007 GROUP I WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P	P			3 2
ANIMAL #: 1008 GROUP I WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1009 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1010 GROUP I WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1011 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1012 GROUP I WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1013 GROUP I WITHIN NORMAL LIMITS		P	P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
POSTERIOR SUBCAPSULAR CATARACT						1
IRITIS OR UVEITIS						1
RETINAL DEGENERATION						1
ANIMAL #: 1014 GROUP I						
WITHIN NORMAL LIMITS		P				
POSTERIOR SUBCAPSULAR CATARACT						2
CORNEAL SCAR						2 2
RETINAL DEGENERATION						2 2
ANIMAL #: 1015 GROUP I						
WITHIN NORMAL LIMITS		P	P			
POSTERIOR SUBCAPSULAR CATARACT						1
CORNEAL SCAR						1
ANIMAL #: 1016 GROUP I						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1017 GROUP I						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						3
CONJUNCTIVITIS						2
ANIMAL #: 1018 GROUP I						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 1019 GROUP I						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1020 GROUP I						
WITHIN NORMAL LIMITS		P				
CONJUNCTIVITIS						1
ANIMAL #: 1021 GROUP I						
WITHIN NORMAL LIMITS		P				
CONJUNCTIVITIS						1 1
ANIMAL #: 1022 GROUP I						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						2
CONJUNCTIVITIS						2
ANIMAL #: 1023 GROUP I						
WITHIN NORMAL LIMITS		P	P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
CONJUNCTIVITIS						2
ANIMAL #: 1024 GROUP I WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 1025 GROUP I WITHIN NORMAL LIMITS CONJUNCTIVITIS		P		P		2
ANIMAL #: 1026 GROUP I WITHIN NORMAL LIMITS CONJUNCTIVITIS		P				1
ANIMAL #: 1027 GROUP I WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 1028 GROUP I WITHIN NORMAL LIMITS COMPLETE CATARACT		P		P		1
ANIMAL #: 1029 GROUP I WITHIN NORMAL LIMITS POSTERIOR SUBCAPSULAR CATARACT COMPLETE CATARACT CORNEAL SCAR RETINAL DEGENERATION PHTHISIS BULBI		P				1 1 1 1 1
ANIMAL #: 1030 GROUP I WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 1031 GROUP I WITHIN NORMAL LIMITS CORNEAL SCAR RETINAL DEGENERATION		P				1 1
ANIMAL #: 1032 GROUP I WITHIN NORMAL LIMITS COMPLETE CATARACT RETINAL DEGENERATION GLAUCOMA		P				2 2 2
ANIMAL #: 1033 GROUP I WITHIN NORMAL LIMITS		P				

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0				
		2	3	6	2	4
CORNEAL SCAR						3
CONJUNCTIVITIS						2
ANIMAL #: 1034 GROUP I						
WITHIN NORMAL LIMITS			P			
POSTERIOR SUBCAPSULAR CATARACT						2
COMPLETE CATARACT					1	1
PHTHISIS BULBI						1
ANIMAL #: 1035 GROUP I						
WITHIN NORMAL LIMITS			P			
CORNEAL SCAR					2	2
CONJUNCTIVITIS						2
ANIMAL #: 1036 GROUP I						
WITHIN NORMAL LIMITS			P		P	P
ANIMAL #: 1037 GROUP I						
WITHIN NORMAL LIMITS			P			
COMPLETE CATARACT						1
IRITIS OR UVEITIS						1
CORNEAL SCAR					1	1
RETINAL DEGENERATION					1	
HYPERHEMA						1
ANIMAL #: 1038 GROUP I						
WITHIN NORMAL LIMITS			P		P	P
ANIMAL #: 1039 GROUP I						
WITHIN NORMAL LIMITS			P		P	
ANIMAL #: 1040 GROUP I						
WITHIN NORMAL LIMITS			P		P	
ANIMAL #: 1041 GROUP I						
WITHIN NORMAL LIMITS			P		P	
CORNEAL SCAR						2
ANIMAL #: 1042 GROUP I						
WITHIN NORMAL LIMITS			P			
CORNEAL SCAR						1
ANIMAL #: 1043 GROUP I						
WITHIN NORMAL LIMITS			P		P	P

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY					
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 1044 GROUP I						1
WITHIN NORMAL LIMITS						
POSTERIOR SUBCAPSULAR CATARACT	P					2
ANTERIOR SYNECHIA						2
CORNEAL SCAR						1
RETINAL DEGENERATION						2
CONJUNCTIVITIS						1
ANIMAL #: 1045 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					1
ANIMAL #: 1046 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					P
						3
ANIMAL #: 1047 GROUP I						
WITHIN NORMAL LIMITS						
	P					P
ANIMAL #: 1048 GROUP I						
WITHIN NORMAL LIMITS						
	P					P
ANIMAL #: 1049 GROUP I						
WITHIN NORMAL LIMITS						
	P					P
ANIMAL #: 1050 GROUP I						
WITHIN NORMAL LIMITS						
	P					P
ANIMAL #: 1051 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					
CONJUNCTIVITIS						2
						3
ANIMAL #: 1052 GROUP I						
WITHIN NORMAL LIMITS						
CONJUNCTIVITIS	P					
						2
ANIMAL #: 1053 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					P
CONJUNCTIVITIS						3
						2
ANIMAL #: 1054 GROUP I						
WITHIN NORMAL LIMITS						
	P					

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
RETINAL DEGENERATION						1
ANIMAL #: 1055 GROUP I WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 1091 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 1057 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 1058 GROUP I WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT					2	
CORNEAL SCAR			2	2		
RETINAL DEGENERATION			2	2		
ANIMAL #: 1059 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	
CORNEAL SCAR						1
CONJUNCTIVITIS						1
ANIMAL #: 1092 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 1061 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	
FOCAL RETINOPATHY						1
ANIMAL #: 1062 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 1063 GROUP I WITHIN NORMAL LIMITS		P				
CORNEAL SCAR			2	2	2	
GLAUCOMA						2
ANIMAL #: 1064 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	
PHTHISIS BULBI						1
ANIMAL #: 1065 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
CONJUNCTIVITIS						
ANIMAL #: 1066 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	P
ANIMAL #: 1067 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	P
ANIMAL #: 1068 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	P
ANIMAL #: 1069 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	P
ANIMAL #: 1070 GROUP I WITHIN NORMAL LIMITS FOCAL RETINOPATHY CORNEAL SCAR			P			
				1	1	1
				1	1	1
ANIMAL #: 1071 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	
ANIMAL #: 1072 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	
ANIMAL #: 1073 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	
ANIMAL #: 1074 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	
ANIMAL #: 1075 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	
ANIMAL #: 1076 GROUP I WITHIN NORMAL LIMITS						
			P	P	P	
ANIMAL #: 1077 GROUP I WITHIN NORMAL LIMITS ANTERIOR SYNECHIA RETINAL DEGENERATION			P			
				2	2	
				2	2	
ANIMAL #: 1078 GROUP I WITHIN NORMAL LIMITS						
			P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
CORNEAL SCAR			2			
RETINAL DEGENERATION			2	2		
ANIMAL #: 1079 GROUP I WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 1080 GROUP I WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 1081 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1082 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1083 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1084 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1085 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1086 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1087 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1088 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1089 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 1090 GROUP I WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 2001 GROUP II WITHIN NORMAL LIMITS			P		P	P
ANIMAL #: 2002 GROUP II WITHIN NORMAL LIMITS			P		P	P

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
<hr/>						
ANIMAL #: 2003 GROUP II						
WITHIN NORMAL LIMITS	P					
POSTERIOR SUBCAPSULAR CATARACT				2		
COMPLETE CATARACT				1		
CORNEAL SCAR				2		
RETINAL DEGENERATION			1			
PHTHISIS BULBI			1			
CONJUNCTIVITIS			2	2		
ANIMAL #: 2004 GROUP II						
WITHIN NORMAL LIMITS	P	P				
CORNEAL SCAR			1			
CONJUNCTIVITIS			1			
ANIMAL #: 2005 GROUP II						
WITHIN NORMAL LIMITS	P	P				
ANIMAL #: 2006 GROUP II						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR				3		
CONJUNCTIVITIS			2	2		
ANIMAL #: 2007 GROUP II						
WITHIN NORMAL LIMITS	P	P				
ANIMAL #: 2008 GROUP II						
WITHIN NORMAL LIMITS	P					
COMPLETE CATARACT				1		
RETINAL DEGENERATION			1			
PHTHISIS BULBI			1			
ANIMAL #: 2009 GROUP II						
WITHIN NORMAL LIMITS	P					
COMPLETE CATARACT				1		
IRITIS OR UVEITIS				1		
CORNEAL SCAR				1		
RETINAL DEGENERATION				1		
PHTHISIS BULBI				1		
ANIMAL #: 2010 GROUP II						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR				1		
CONJUNCTIVITIS				1	1	

		1
	WEEK OF	- 1 2 5 0
OBSERVATIONS	STUDY	2 3 6 2 4

ANIMAL #:	2011	GROUP II		
WITHIN NORMAL LIMITS			P	P P
ANIMAL #:	2012	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				2
CONJUNCTIVITIS				2
ANIMAL #:	2013	GROUP II		
WITHIN NORMAL LIMITS			P	
POSTERIOR SUBCAPSULAR CATARACT				2
CORNEAL SCAR				2 2
ANIMAL #:	2014	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2015	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2016	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2017	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2018	GROUP II		
WITHIN NORMAL LIMITS			P	P P
ANIMAL #:	2019	GROUP II		
WITHIN NORMAL LIMITS			P	
FOCAL RETINOPATHY				1
COMPLETE CATARACT				1
ANIMAL #:	2020	GROUP II		
WITHIN NORMAL LIMITS			P	
COMPLETE CATARACT				2
ANTERIOR SYNECHIA				2 2
ANIMAL #:	2021	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1 1
CONJUNCTIVITIS				1 1

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
ANIMAL #: 2022 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR		P	P			3
ANIMAL #: 2023 GROUP II WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 2024 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR		P	P			1
ANIMAL #: 2025 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR		P	P			2
ANIMAL #: 2026 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR		P	P			2
ANIMAL #: 2027 GROUP II WITHIN NORMAL LIMITS COMPLETE CATARACT RETINAL DEGENERATION		P			2 2	
ANIMAL #: 2028 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P			2 1	
ANIMAL #: 2029 GROUP II WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 2030 GROUP II WITHIN NORMAL LIMITS COMPLETE CATARACT CORNEAL SCAR CONJUNCTIVITIS		P			2 2 3 2	
ANIMAL #: 2031 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR RETINAL DEGENERATION		P			1 1	

		1
	WEEK OF	- 1 2 5 0
OBSERVATIONS	STUDY	2 3 6 2 4

ANIMAL #:	2032	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2033	GROUP II		
WITHIN NORMAL LIMITS			P	
POSTERIOR SUBCAPSULAR CATARACT				2
COMPLETE CATARACT				2
IRITIS OR UVEITIS				2
CORNEAL SCAR				1 1
RETINAL DEGENERATION				2
PHTHISIS BULBI				2
CONJUNCTIVITIS				1 1
ANIMAL #:	2034	GROUP II		
WITHIN NORMAL LIMITS			P	P P
ANIMAL #:	2035	GROUP II		
WITHIN NORMAL LIMITS			P	P
POSTERIOR SUBCAPSULAR CATARACT				1
IRITIS OR UVEITIS				1
CORNEAL SCAR				3
RETINAL DEGENERATION				1
ANIMAL #:	2036	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				3
CONJUNCTIVITIS				3
ANIMAL #:	2037	GROUP II		
WITHIN NORMAL LIMITS			P	P P
ANIMAL #:	2038	GROUP II		
WITHIN NORMAL LIMITS			P	
COMPLETE CATARACT				1
CORNEAL SCAR				1 1
CONJUNCTIVITIS				1 1
GLAUCOMA				1 1
ANIMAL #:	2039	GROUP II		
WITHIN NORMAL LIMITS			P	P
COMPLETE CATARACT				2
IRITIS OR UVEITIS				2

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 2040 GROUP II						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR				1		
CONJUNCTIVITIS				1		
ANIMAL #: 2041 GROUP II						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 2042 GROUP II						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 2043 GROUP II						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 2044 GROUP II						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR			2	2		
ANIMAL #: 2045 GROUP II						
WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT				2		
RETINAL DEGENERATION				2		
ANIMAL #: 2046 GROUP II						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 2047 GROUP II						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR				2		
CONJUNCTIVITIS				2		
ANIMAL #: 2048 GROUP II						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 2049 GROUP II						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR				3		
CONJUNCTIVITIS				2		
ANIMAL #: 2050 GROUP II						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 2051 GROUP II						
WITHIN NORMAL LIMITS		P	P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANTERIOR SYNECHIA						2
CORNEAL SCAR						2
CONJUNCTIVITIS						2
ANIMAL #: 2052 GROUP II WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 2053 GROUP II WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 2054 GROUP II WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT						2
CORNEAL SCAR						1
RETINAL DEGENERATION						2
ANIMAL #: 2055 GROUP II WITHIN NORMAL LIMITS		P		P		
CORNEAL SCAR						3
ANIMAL #: 2056 GROUP II WITHIN NORMAL LIMITS		P				
FOCAL RETINOPATHY				2	2	2
CORNEAL SCAR				2	2	2
ANIMAL #: 2092 GROUP II WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 2058 GROUP II WITHIN NORMAL LIMITS		P	P	P		
CONJUNCTIVITIS						2
ANIMAL #: 2059 GROUP II WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 2060 GROUP II WITHIN NORMAL LIMITS		P	P	P		
CONJUNCTIVITIS						2
ANIMAL #: 2061 GROUP II WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 2062 GROUP II WITHIN NORMAL LIMITS		P	P	P	P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	- 1 2 5 0 2 3 6 2 4
ANIMAL #: 2063 GROUP II WITHIN NORMAL LIMITS PHTHISIS BULBI		1 P P P 1
ANIMAL #: 2064 GROUP II WITHIN NORMAL LIMITS		P P P P
ANIMAL #: 2065 GROUP II WITHIN NORMAL LIMITS COMPLETE CATARACT PHTHISIS BULBI CONJUNCTIVITIS		P P 1 1 1
ANIMAL #: 2066 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR		P P P 1
ANIMAL #: 2067 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR		P 2 2 2
ANIMAL #: 2068 GROUP II WITHIN NORMAL LIMITS		P P P P
ANIMAL #: 2069 GROUP II WITHIN NORMAL LIMITS		P P P P
ANIMAL #: 2070 GROUP II WITHIN NORMAL LIMITS		P P P P
ANIMAL #: 2071 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR		P P 1
ANIMAL #: 2072 GROUP II WITHIN NORMAL LIMITS		P P P
ANIMAL #: 2073 GROUP II WITHIN NORMAL LIMITS		P P P
ANIMAL #: 2074 GROUP II WITHIN NORMAL LIMITS		P P P

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4

ANIMAL #:	2075	GROUP II	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	2076	GROUP II	
WITHIN NORMAL LIMITS			P P
PROPTOSIS AND CORNEAL NECROSIS			1
ANIMAL #:	2077	GROUP II	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	2078	GROUP II	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	2079	GROUP II	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	2080	GROUP II	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	2081	GROUP II	
WITHIN NORMAL LIMITS			P
RETINAL DEGENERATION			1
ANIMAL #:	2082	GROUP II	
WITHIN NORMAL LIMITS			P
CORNEAL SCAR			1
ANIMAL #:	2083	GROUP II	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	2084	GROUP II	
WITHIN NORMAL LIMITS			P
CORNEAL SCAR			1
ANIMAL #:	2085	GROUP II	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	2086	GROUP II	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	2087	GROUP II	
WITHIN NORMAL LIMITS			P P

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY					
		1	2	3	4	5
ANIMAL #: 2088 GROUP II WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 2089 GROUP II WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 2090 GROUP II WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 3001 GROUP III WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 3002 GROUP III WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 3003 GROUP III WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 3004 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR RETINAL DEGENERATION		P			1	1
ANIMAL #: 3005 GROUP III WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 3006 GROUP III WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 3007 GROUP III WITHIN NORMAL LIMITS RETINAL DEGENERATION		P			2	
ANIMAL #: 3008 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P		P	3	3
ANIMAL #: 3009 GROUP III WITHIN NORMAL LIMITS COMPLETE CATARACT PHTHISIS BULBI CONJUNCTIVITIS		P			2	2
					1	

		1
OBSERVATIONS	WEEK OF STUDY	- 1 2 5 0 2 3 6 2 4

P P
 1
 2
 2

P P P

P

1 1

1

P

1
2 3

P P

P 1 1

P P_2

P 1

P P P

P
1 2

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4
ANIMAL #: 3020 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR RETINAL DEGENERATION	P	2 2 2
ANIMAL #: 3021 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS	P	3 1
ANIMAL #: 3022 GROUP III WITHIN NORMAL LIMITS	P	P P
ANIMAL #: 3023 GROUP III WITHIN NORMAL LIMITS	P	P P
ANIMAL #: 3024 GROUP III WITHIN NORMAL LIMITS POSTERIOR SUBCAPSULAR CATARACT CORNEAL SCAR RETINAL DEGENERATION	P	1 1 1 1 1
ANIMAL #: 3025 GROUP III WITHIN NORMAL LIMITS	P	P P
ANIMAL #: 3026 GROUP III WITHIN NORMAL LIMITS POSTERIOR SUBCAPSULAR CATARACT RETINAL DEGENERATION	P	1 1
ANIMAL #: 3027 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS	P	3 1
ANIMAL #: 3028 GROUP III WITHIN NORMAL LIMITS POSTERIOR SUBCAPSULAR CATARACT CORNEAL SCAR	P	P 1 1
ANIMAL #: 3029 GROUP III WITHIN NORMAL LIMITS	P	P

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
CORNEAL SCAR						1
ANIMAL #: 3030 GROUP III						
WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT					2	2
IRITIS OR UVEITIS					2	
CORNEAL SCAR					2	
PHTHISIS BULBI					2	
ANIMAL #: 3031 GROUP III						
WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT					1	
IRITIS OR UVEITIS					1	
RETINAL DEGENERATION					1	
HYPHEMA					1	
ANIMAL #: 3032 GROUP III						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR					1	
ANIMAL #: 3033 GROUP III						
WITHIN NORMAL LIMITS		P			1	
CONJUNCTIVITIS						
ANIMAL #: 3034 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 3035 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 3036 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 3037 GROUP III						
WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT					3	
IRITIS OR UVEITIS					1	
RETINAL DEGENERATION					3	
PHTHISIS BULBI					1	
ANIMAL #: 3038 GROUP III						
WITHIN NORMAL LIMITS		P				
FOCAL RETINOPATHY					1	

		1
	WEEK OF	- 1 2 5 0
OBSERVATIONS	STUDY	2 3 6 2 4

ANIMAL #:	3039	GROUP III		
WITHIN NORMAL LIMITS			P	P P
ANIMAL #:	3040	GROUP III		
WITHIN NORMAL LIMITS			P	
COMPLETE CATARACT				1
IRITIS OR UVEITIS				1
PHTHISIS BULBI				1
CONJUNCTIVITIS				1 1
ANIMAL #:	3041	GROUP III		
WITHIN NORMAL LIMITS			P	P P
ANIMAL #:	3042	GROUP III		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				2
ANIMAL #:	3043	GROUP III		
WITHIN NORMAL LIMITS			P	P
CORNEAL SCAR				2
CONJUNCTIVITIS				2
ANIMAL #:	3044	GROUP III		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	3045	GROUP III		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	3046	GROUP III		
WITHIN NORMAL LIMITS			P	P
CORNEAL SCAR				2
CONJUNCTIVITIS				2
ANIMAL #:	3047	GROUP III		
WITHIN NORMAL LIMITS			P	P
CORNEAL SCAR				3
CONJUNCTIVITIS				1
ANIMAL #:	3048	GROUP III		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	3049	GROUP III		
WITHIN NORMAL LIMITS			P	P

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 3050 GROUP III						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR						3
ANIMAL #: 3051 GROUP III						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 3052 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 3053 GROUP III						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 3054 GROUP III						
WITHIN NORMAL LIMITS		P	P			
COMPLETE CATARACT						2
CORNEAL SCAR						1
ANIMAL #: 3055 GROUP III						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 3056 GROUP III						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR						1 3
ANIMAL #: 3057 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		
CORNEAL SCAR						1
ANIMAL #: 3058 GROUP III						
WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 3059 GROUP III						
WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 3060 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		
CONJUNCTIVITIS						2
ANIMAL #: 3061 GROUP III						
WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 3062 GROUP III						
WITHIN NORMAL LIMITS		P	P	P	P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
ANIMAL #: 3063 GROUP III WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 3064 GROUP III WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 3065 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P	P	P	2
ANIMAL #: 3066 GROUP III WITHIN NORMAL LIMITS FOCAL RETINOPATHY CORNEAL SCAR			P	1	1	1
ANIMAL #: 3067 GROUP III WITHIN NORMAL LIMITS COMPLETE CATARACT PHTHISIS BULBI			P	P	P	1
ANIMAL #: 3068 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR			P		P	2
ANIMAL #: 3069 GROUP III WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 3070 GROUP III WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 3071 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3072 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3073 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR			P	P		1
ANIMAL #: 3074 GROUP III WITHIN NORMAL LIMITS			P	P	P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 3075 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3076 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3077 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3078 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3079 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3080 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3081 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3082 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3083 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P		2	
ANIMAL #: 3084 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3085 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P		1	
ANIMAL #: 3086 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3087 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3088 GROUP III WITHIN NORMAL LIMITS			P	P		

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
ANIMAL #: 3089 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3090 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 4001 GROUP IV WITHIN NORMAL LIMITS			P		P	
ANIMAL #: 4002 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR			P		P	3
ANIMAL #: 4003 GROUP IV WITHIN NORMAL LIMITS			P		P	
ANIMAL #: 4004 GROUP IV WITHIN NORMAL LIMITS			P		P	
ANIMAL #: 4005 GROUP IV WITHIN NORMAL LIMITS FOCAL RETINOPATHY POSTERIOR SUBCAPSULAR CATARACT CORNEAL SCAR			P		2	2 2
ANIMAL #: 4006 GROUP IV WITHIN NORMAL LIMITS			P		P	
ANIMAL #: 4007 GROUP IV WITHIN NORMAL LIMITS			P		P	
ANIMAL #: 4008 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS			P		2	2
ANIMAL #: 4009 GROUP IV WITHIN NORMAL LIMITS			P		P	
ANIMAL #: 4010 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR RETINAL DEGENERATION			P		1	1

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
ANIMAL #: 4011 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4012 GROUP IV WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT					1	
IRITIS OR UVEITIS					1	
CORNEAL SCAR					1	
GLAUCOMA					1 1	
HYPERHEMA					1	
ANIMAL #: 4013 GROUP IV WITHIN NORMAL LIMITS		P				
FOCAL RETINOPATHY					1	
COMPLETE CATARACT					1	
CORNEAL SCAR					3	
ANIMAL #: 4014 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4015 GROUP IV WITHIN NORMAL LIMITS		P				
RETINAL DEGENERATION					2	
ANIMAL #: 4016 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4017 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4018 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4019 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4020 GROUP IV WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT					1	
CORNEAL SCAR					2	
CONJUNCTIVITIS					1	
ANIMAL #: 4021 GROUP IV WITHIN NORMAL LIMITS		P	P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
ANIMAL #: 4022 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR					3	
ANIMAL #: 4023 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4024 GROUP IV						
WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT					2	2
CORNEAL SCAR					1	3
PHTHISIS BULBI					2	
ANIMAL #: 4025 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4026 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4027 GROUP IV						
WITHIN NORMAL LIMITS		P				
RETINAL DEGENERATION					1	
ANIMAL #: 4028 GROUP IV						
WITHIN NORMAL LIMITS		P				
CONJUNCTIVITIS					1	
ANIMAL #: 4029 GROUP IV						
WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 4030 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4031 GROUP IV						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR					1	
RETINAL DEGENERATION					3	
ANIMAL #: 4032 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4033 GROUP IV						
WITHIN NORMAL LIMITS		P	P			

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 4034 GROUP IV WITHIN NORMAL LIMITS	P	P				
ANIMAL #: 4035 GROUP IV WITHIN NORMAL LIMITS	P	P	P			
ANIMAL #: 4036 GROUP IV WITHIN NORMAL LIMITS	P					
FOCAL RETINOPATHY			1			
COMPLETE CATARACT				1		
IRITIS OR UVEITIS				1		
CORNEAL SCAR			1	1		
ANIMAL #: 4037 GROUP IV WITHIN NORMAL LIMITS	P	P				
CORNEAL SCAR				3		
CONJUNCTIVITIS				2		
ANIMAL #: 4038 GROUP IV WITHIN NORMAL LIMITS	P	P				
ANIMAL #: 4039 GROUP IV WITHIN NORMAL LIMITS	P					
COMPLETE CATARACT				2		
IRITIS OR UVEITIS				2		
RETINAL DEGENERATION			2			
PHTHISIS BULBI				2		
ANIMAL #: 4040 GROUP IV WITHIN NORMAL LIMITS	P					
CORNEAL SCAR				3		
CONJUNCTIVITIS				3		
ANIMAL #: 4041 GROUP IV WITHIN NORMAL LIMITS	P	P				
ANIMAL #: 4042 GROUP IV WITHIN NORMAL LIMITS	P	P				
ANIMAL #: 4043 GROUP IV WITHIN NORMAL LIMITS	P	P				
ANIMAL #: 4044 GROUP IV WITHIN NORMAL LIMITS	P	P				

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
CORNEAL SCAR						2
ANIMAL #: 4045 GROUP IV WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 4046 GROUP IV WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 4047 GROUP IV WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 4048 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS		P		P		1
ANIMAL #: 4049 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P		P		3 2
ANIMAL #: 4050 GROUP IV WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 4051 GROUP IV WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 4052 GROUP IV WITHIN NORMAL LIMITS COMPLETE CATARACT		P				2
ANIMAL #: 4053 GROUP IV WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 4054 GROUP IV WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 4055 GROUP IV WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 4056 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR		P				1 1 1
ANIMAL #: 4057 GROUP IV WITHIN NORMAL LIMITS		P	P	P	P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 4058 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4059 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4060 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4061 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4062 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4063 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4064 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4065 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4066 GROUP IV WITHIN NORMAL LIMITS PHTHISIS BULBI			P	P	P	1
ANIMAL #: 4067 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4068 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4069 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4070 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 4071 GROUP IV WITHIN NORMAL LIMITS			P	P	P	P

D-44
APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4
ANIMAL #: 4072 GROUP IV WITHIN NORMAL LIMITS		P P P
ANIMAL #: 4073 GROUP IV WITHIN NORMAL LIMITS		P P P
ANIMAL #: 4074 GROUP IV WITHIN NORMAL LIMITS		P P P
ANIMAL #: 4075 GROUP IV WITHIN NORMAL LIMITS		P P P
ANIMAL #: 4076 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR		P 2 2
ANIMAL #: 4077 GROUP IV WITHIN NORMAL LIMITS		P P P
ANIMAL #: 4078 GROUP IV WITHIN NORMAL LIMITS		P P P
ANIMAL #: 4079 GROUP IV WITHIN NORMAL LIMITS		P P P
ANIMAL #: 4080 GROUP IV WITHIN NORMAL LIMITS		P P P
ANIMAL #: 4081 GROUP IV WITHIN NORMAL LIMITS		P P
ANIMAL #: 4082 GROUP IV WITHIN NORMAL LIMITS		P P
ANIMAL #: 4083 GROUP IV WITHIN NORMAL LIMITS		P P
ANIMAL #: 4084 GROUP IV WITHIN NORMAL LIMITS		P P
ANIMAL #: 4085 GROUP IV WITHIN NORMAL LIMITS		P P

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 4086 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4087 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4088 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4089 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4090 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 5001 GROUP V WITHIN NORMAL LIMITS RETINAL DEGENERATION		P				3
ANIMAL #: 5002 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5003 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5004 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5005 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5006 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5007 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5008 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5009 GROUP V WITHIN NORMAL LIMITS		P		P		

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

263
90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
ANIMAL #: 5010 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5011 GROUP V WITHIN NORMAL LIMITS		P				
CORNEAL SCAR					1	
RETINAL DEGENERATION					1	
ANIMAL #: 5012 GROUP V WITHIN NORMAL LIMITS		P				
RETINAL DEGENERATION					1	
ANIMAL #: 5013 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5014 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5015 GROUP V WITHIN NORMAL LIMITS		P				
RETINAL DEGENERATION					1	
ANIMAL #: 5016 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5017 GROUP V WITHIN NORMAL LIMITS		P				
FOCAL RETINOPATHY					1	
CORNEAL SCAR					1	
ANIMAL #: 5018 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5019 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5020 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5021 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5022 GROUP V WITHIN NORMAL LIMITS		P			P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

264
90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 5023 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5024 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5025 GROUP V WITHIN NORMAL LIMITS		P				
ANIMAL #: 5026 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5027 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5028 GROUP V WITHIN NORMAL LIMITS COMPLETE CATARACT IRITIS OR UVEITIS		P			1 1	
ANIMAL #: 5029 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5030 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5031 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P			1 1	
ANIMAL #: 5032 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5033 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5034 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5035 GROUP V WITHIN NORMAL LIMITS		P		P		

OBSERVATIONS	WEEK OF STUDY					
	1					
	1	2	3	4	5	6
	2	3	6	2	4	

P 2
2
2

P P

P P

P 2

P 1

P P

P P

P P

P P

P P

P P

P 1

P

D-49
APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
FOCAL RETINOPATHY						1
ANIMAL #: 5049 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5050 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5051 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5052 GROUP V WITHIN NORMAL LIMITS RETINAL DEGENERATION GLAUCOMA		P			1 1	
ANIMAL #: 5053 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5054 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5055 GROUP V WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5056 GROUP V WITHIN NORMAL LIMITS COMPLETE CATARACT CORNEAL SCAR RETINAL DEGENERATION		P			1 1 1 1	
ANIMAL #: 5057 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 5058 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 5059 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 5060 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 5061 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 5091 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 5063 GROUP V WITHIN NORMAL LIMITS PHTHISIS BULBI CONJUNCTIVITIS		P	P			1 1 1
ANIMAL #: 5064 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 5065 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 5066 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 5067 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR RETINAL DEGENERATION		P	P	P	P	1 1
ANIMAL #: 5068 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 5069 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 5070 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 5071 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 5072 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 5073 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 5074 GROUP V WITHIN NORMAL LIMITS		P	P	P	P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
ANIMAL #: 5075 GROUP V WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5076 GROUP V WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5077 GROUP V WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5078 GROUP V WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5079 GROUP V WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5080 GROUP V WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5081 GROUP V WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 5082 GROUP V WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 5083 GROUP V WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 5084 GROUP V WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 5085 GROUP V WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 5086 GROUP V WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 5087 GROUP V WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 5088 GROUP V WITHIN NORMAL LIMITS			P			
ANIMAL #: 5089 GROUP V WITHIN NORMAL LIMITS			P	P		

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - MALES

OBSERVATIONS	WEEK OF STUDY					
		1	2	3	4	5
		-	1	2	5	0
		2	3	6	2	4

ANIMAL #: 5090 GROUP V
WITHIN NORMAL LIMITS

P P

90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 2 3 4 5				
		0	1	2	3	4
ANIMAL #: 1501 GROUP I						1
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					2
CONJUNCTIVITIS						3 3
ANIMAL #: 1502 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					2
CONJUNCTIVITIS						2
ANIMAL #: 1503 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					1
CONJUNCTIVITIS						1
ANIMAL #: 1504 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					P
CONJUNCTIVITIS						2
ANIMAL #: 1505 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					3
CONJUNCTIVITIS						3 3
ANIMAL #: 1506 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					1
CONJUNCTIVITIS						1 1
ANIMAL #: 1507 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					P
CONJUNCTIVITIS						
ANIMAL #: 1508 GROUP I						
WITHIN NORMAL LIMITS						
COMPLETE CATARACT	P					2 2
CORNEAL SCAR						1
PHTHISIS BULBI						2 2
CONJUNCTIVITIS						1
ANIMAL #: 1509 GROUP I						
WITHIN NORMAL LIMITS						
CORNEAL SCAR	P					P
CONJUNCTIVITIS						1

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4

ANIMAL #:	1510	GROUP I		
WITHIN NORMAL LIMITS			P	P
CONJUNCTIVITIS				3
ANIMAL #:	1511	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				2
CONJUNCTIVITIS				2
ANIMAL #:	1512	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				3
CONJUNCTIVITIS				3 3
ANIMAL #:	1513	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
CONJUNCTIVITIS				1 1
ANIMAL #:	1514	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1 1
CONJUNCTIVITIS				1
ANIMAL #:	1515	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				3
CONJUNCTIVITIS				2 2
ANIMAL #:	1516	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				2
CONJUNCTIVITIS				2 2
ANIMAL #:	1517	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				2 3
CONJUNCTIVITIS				3 3
ANIMAL #:	1518	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 1519 GROUP I WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 1520 GROUP I WITHIN NORMAL LIMITS		P				
CORNEAL SCAR				3	3	
CONJUNCTIVITIS				3	2	
ANIMAL #: 1521 GROUP I WITHIN NORMAL LIMITS		P				
CORNEAL SCAR				2	2	
CONJUNCTIVITIS				2	2	
ANIMAL #: 1522 GROUP I WITHIN NORMAL LIMITS		P				
CONJUNCTIVITIS				2		
ANIMAL #: 1523 GROUP I WITHIN NORMAL LIMITS		P				
CORNEAL SCAR				1		
CONJUNCTIVITIS				1		
ANIMAL #: 1524 GROUP I WITHIN NORMAL LIMITS		P		P		
CORNEAL SCAR					1	
ANIMAL #: 1525 GROUP I WITHIN NORMAL LIMITS		P				
POSTERIOR SUBCAPSULAR CATARACT					1	
CORNEAL SCAR				3	3	
CONJUNCTIVITIS				3	2	
ANIMAL #: 1526 GROUP I WITHIN NORMAL LIMITS		P		P		
CORNEAL SCAR					3	
CONJUNCTIVITIS					3	
ANIMAL #: 1527 GROUP I WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 1528 GROUP I WITHIN NORMAL LIMITS		P				

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
CONJUNCTIVITIS						3
ANIMAL #: 1529 GROUP I WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						2
CONJUNCTIVITIS						2
ANIMAL #: 1530 GROUP I WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 1531 GROUP I WITHIN NORMAL LIMITS		P		P		
CONJUNCTIVITIS						2
ANIMAL #: 1532 GROUP I WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 1533 GROUP I WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 1534 GROUP I WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						1
CONJUNCTIVITIS						3 3
ANIMAL #: 1535 GROUP I WITHIN NORMAL LIMITS		P		P		
COMPLETE CATARACT						2
CORNEAL SCAR						3
ANIMAL #: 1536 GROUP I WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						2
ANIMAL #: 1537 GROUP I WITHIN NORMAL LIMITS		P		P		
CORNEAL SCAR						1
CONJUNCTIVITIS						2
ANIMAL #: 1538 GROUP I WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT						1
CORNEAL SCAR						2
RETINAL DEGENERATION						1
PHTHISIS BULBI						1
CONJUNCTIVITIS						2

[illegible]

ANIMAL #:	1539	GROUP I		
WITHIN NORMAL LIMITS			P	
CONJUNCTIVITIS				3 3
ANIMAL #:	1540	GROUP I		
WITHIN NORMAL LIMITS			P	
CONJUNCTIVITIS				2
ANIMAL #:	1541	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
ANIMAL #:	1542	GROUP I		
WITHIN NORMAL LIMITS			P	
				P P
ANIMAL #:	1543	GROUP I		
WITHIN NORMAL LIMITS			P	
				P
ANIMAL #:	1544	GROUP I		
WITHIN NORMAL LIMITS			P	
COMPLETE CATARACT				3
CORNEAL SCAR				2 2
RETINAL DEGENERATION				3
PHTHISIS BULBI				2
CONJUNCTIVITIS				1
ANIMAL #:	1545	GROUP I		
WITHIN NORMAL LIMITS			P	
CONJUNCTIVITIS				3
ANIMAL #:	1546	GROUP I		
WITHIN NORMAL LIMITS			P	
CONJUNCTIVITIS				2 2
ANIMAL #:	1547	GROUP I		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1 1
CONJUNCTIVITIS				1 1
ANIMAL #:	1548	GROUP I		
WITHIN NORMAL LIMITS			P	
FOCAL RETINOPATHY				1

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 1549 GROUP I WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 1550 GROUP I WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 1551 GROUP I WITHIN NORMAL LIMITS CONJUNCTIVITIS		P			2	2
ANIMAL #: 1552 GROUP I WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 1553 GROUP I WITHIN NORMAL LIMITS CORNEAL SCAR		P		P		3
ANIMAL #: 1554 GROUP I WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 1555 GROUP I WITHIN NORMAL LIMITS CONJUNCTIVITIS		P		P		1
ANIMAL #: 1556 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 1557 GROUP I WITHIN NORMAL LIMITS CONJUNCTIVITIS		P	P			1 1
ANIMAL #: 1558 GROUP I WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS OPTIC NERVE ATROPHY		P	P			1 3 1 1
ANIMAL #: 1559 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	P
ANIMAL #: 1560 GROUP I WITHIN NORMAL LIMITS		P	P	P	P	P

		1
	WEEK OF	- 1 2 5 0
OBSERVATIONS	STUDY	2 3 6 2 4

ANIMAL #:	1561	GROUP I		
WITHIN NORMAL LIMITS			P P P	1
CORNEAL SCAR				
ANIMAL #:	1562	GROUP I		
WITHIN NORMAL LIMITS			P P P P	
ANIMAL #:	1563	GROUP I		
WITHIN NORMAL LIMITS			P P	1 2
CONJUNCTIVITIS				
ANIMAL #:	1564	GROUP I		
WITHIN NORMAL LIMITS			P P P	1
CORNEAL SCAR				1
CONJUNCTIVITIS				
ANIMAL #:	1565	GROUP I		
WITHIN NORMAL LIMITS			P P P	1
CORNEAL SCAR				1
CONJUNCTIVITIS				
ANIMAL #:	1566	GROUP I		
WITHIN NORMAL LIMITS			P P P	1
CORNEAL SCAR				1
CONJUNCTIVITIS				
ANIMAL #:	1567	GROUP I		
WITHIN NORMAL LIMITS			P P P	2
FOCAL RETINOPATHY				2
CORNEAL SCAR				1
CONJUNCTIVITIS				
ANIMAL #:	1568	GROUP I		
WITHIN NORMAL LIMITS			P P P P	
ANIMAL #:	1569	GROUP I		
WITHIN NORMAL LIMITS			P P P	1
CONJUNCTIVITIS				
ANIMAL #:	1570	GROUP I		
WITHIN NORMAL LIMITS			P P	2 2
CONJUNCTIVITIS				

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4

ANIMAL #:	1571	GROUP I	
WITHIN NORMAL LIMITS			P
ANTERIOR SYNECHIA			2
CORNEAL SCAR			2
RETINAL DEGENERATION			2
CONJUNCTIVITIS			1
ANIMAL #:	1572	GROUP I	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	1573	GROUP I	
WITHIN NORMAL LIMITS			P P
PHTHISIS BULBI			1
ANIMAL #:	1574	GROUP I	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	1575	GROUP I	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	1576	GROUP I	
WITHIN NORMAL LIMITS			P
CORNEAL SCAR			1
RETINAL DEGENERATION			1
CONJUNCTIVITIS			2 2
ANIMAL #:	1577	GROUP I	
WITHIN NORMAL LIMITS			P
CONJUNCTIVITIS			2
ANIMAL #:	1578	GROUP I	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	1579	GROUP I	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	1580	GROUP I	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	1581	GROUP I	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	1582	GROUP I	
WITHIN NORMAL LIMITS			P P

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 1583 GROUP I WITHIN NORMAL LIMITS CONJUNCTIVITIS		P				2
ANIMAL #: 1584 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1585 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1586 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1587 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1588 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1589 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 1590 GROUP I WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 2501 GROUP II WITHIN NORMAL LIMITS POSTERIOR SUBCAPSULAR CATARACT CORNEAL SCAR CONJUNCTIVITIS		P				2 2 1 1
ANIMAL #: 2502 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P	P			3 2
ANIMAL #: 2503 GROUP II WITHIN NORMAL LIMITS CONJUNCTIVITIS		P				2
ANIMAL #: 2504 GROUP II WITHIN NORMAL LIMITS		P	P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
CORNEAL SCAR					3	
CONJUNCTIVITIS					2	
ANIMAL #: 2505 GROUP II						
WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 2506 GROUP II						
WITHIN NORMAL LIMITS		P				
FOCAL RETINOPATHY				1	1	
POSTERIOR SUBCAPSULAR CATARACT					1	
CORNEAL SCAR				1	1	
CONJUNCTIVITIS				1	1	
ANIMAL #: 2507 GROUP II						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR				2	3	
CONJUNCTIVITIS				2		
ANIMAL #: 2508 GROUP II						
WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT					2	
CONJUNCTIVITIS				2		
ANIMAL #: 2509 GROUP II						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR				1	3	
CONJUNCTIVITIS				1	2	
ANIMAL #: 2510 GROUP II						
WITHIN NORMAL LIMITS		P				
ANTERIOR SYNECHIA					2	
CORNEAL SCAR				2	3	
CONJUNCTIVITIS				2	2	
ANIMAL #: 2511 GROUP II						
WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 2512 GROUP II						
WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 2513 GROUP II						
WITHIN NORMAL LIMITS		P		P		
COMPLETE CATARACT					1	
IRITIS OR UVEITIS					1	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
<hr/>						
ANIMAL #: 2514 GROUP II						
WITHIN NORMAL LIMITS	P					
COMPLETE CATARACT					1	
RETINAL DEGENERATION					1	
CONJUNCTIVITIS					2	
ANIMAL #: 2515 GROUP II						
WITHIN NORMAL LIMITS	P					
CONJUNCTIVITIS					1	1
ANIMAL #: 2516 GROUP II						
WITHIN NORMAL LIMITS	P					
POSTERIOR SUBCAPSULAR CATARACT					2	
COMPLETE CATARACT					2	
RETINAL DEGENERATION					2	
PHTHISIS BULBI					2	
ANIMAL #: 2517 GROUP II						
WITHIN NORMAL LIMITS	P					
POSTERIOR SUBCAPSULAR CATARACT					2	
COMPLETE CATARACT					2	
IRITIS OR UVEITIS					2	
CORNEAL SCAR					1	
RETINAL DEGENERATION					2	
PHTHISIS BULBI					2	
ANIMAL #: 2518 GROUP II						
WITHIN NORMAL LIMITS	P					
COMPLETE CATARACT					2	2
IRITIS OR UVEITIS					2	
PHTHISIS BULBI					2	
ANIMAL #: 2519 GROUP II						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR					3	
CONJUNCTIVITIS					1	1
ANIMAL #: 2520 GROUP II						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR					2	
CONJUNCTIVITIS					2	2
ANIMAL #: 2521 GROUP II						
WITHIN NORMAL LIMITS	P				P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
CORNEAL SCAR						2
ANIMAL #: 2522 GROUP II						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						2
CONJUNCTIVITIS						2 2
ANIMAL #: 2523 GROUP II						
WITHIN NORMAL LIMITS		P				
CONJUNCTIVITIS						2 2
ANIMAL #: 2524 GROUP II						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR						3
CONJUNCTIVITIS						1
ANIMAL #: 2525 GROUP II						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 2526 GROUP II						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						1 3
CONJUNCTIVITIS						3 3
ANIMAL #: 2527 GROUP II						
WITHIN NORMAL LIMITS		P	P			
CONJUNCTIVITIS						1
ANIMAL #: 2528 GROUP II						
WITHIN NORMAL LIMITS		P	P P			
ANIMAL #: 2529 GROUP II						
WITHIN NORMAL LIMITS		P	P P			
ANIMAL #: 2530 GROUP II						
WITHIN NORMAL LIMITS		P	P			
CONJUNCTIVITIS						3
ANIMAL #: 2531 GROUP II						
WITHIN NORMAL LIMITS		P				
POSTERIOR SUBCAPSULAR CATARACT						1
CORNEAL SCAR						2
CONJUNCTIVITIS						3 2

		1
	WEEK OF	- 1 2 5 0
OBSERVATIONS	STUDY	2 3 6 2 4

ANIMAL #:	2532	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				2 3
ANIMAL #:	2533	GROUP II		
WITHIN NORMAL LIMITS			P	
COMPLETE CATARACT				1 1
CORNEAL SCAR				2 3
PHTHISIS BULBI				1 1
CONJUNCTIVITIS				2 2
ANIMAL #:	2534	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2535	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
CONJUNCTIVITIS				1 1
ANIMAL #:	2536	GROUP II		
WITHIN NORMAL LIMITS			P	P
CORNEAL SCAR				2
ANIMAL #:	2537	GROUP II		
WITHIN NORMAL LIMITS			P	
ANTERIOR SYNECHIA				2
ANIMAL #:	2538	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1 1
CONJUNCTIVITIS				2 3
ANIMAL #:	2539	GROUP II		
WITHIN NORMAL LIMITS			P	
COMPLETE CATARACT				1
CORNEAL SCAR				3 3
CONJUNCTIVITIS				2 2
ANIMAL #:	2540	GROUP II		
WITHIN NORMAL LIMITS			P	
COMPLETE CATARACT				1
CORNEAL SCAR				1 1
RETINAL DEGENERATION				1
PHTHISIS BULBI				1
CONJUNCTIVITIS				3

OBSERVATIONS	WEEK OF STUDY				
	1	2	5	0	
	2	3	6	2	4

ANIMAL #:	2541	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2542	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
CONJUNCTIVITIS				1
ANIMAL #:	2543	GROUP II		
WITHIN NORMAL LIMITS			P	P
CORNEAL SCAR				3
CONJUNCTIVITIS				2
ANIMAL #:	2544	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
CONJUNCTIVITIS				1 1
ANIMAL #:	2545	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2546	GROUP II		
WITHIN NORMAL LIMITS			P	
CONJUNCTIVITIS				2
ANIMAL #:	2547	GROUP II		
WITHIN NORMAL LIMITS			P	P P
ANIMAL #:	2548	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				3
CONJUNCTIVITIS				2 3
ANIMAL #:	2549	GROUP II		
WITHIN NORMAL LIMITS			P	P P
ANIMAL #:	2550	GROUP II		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	2551	GROUP II		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
CONJUNCTIVITIS				1

OBSERVATIONS	WEEK OF STUDY				
	1	2	3	4	5
	1	2	3	4	5

P 33

P

2

2 2

2

2

2 2

P 1

P 1 1
2

P

2 2

2

2

2

P P P 1

P P 3
2 2

P

1 1

1

1

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
ANIMAL #: 2560 GROUP II WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 2561 GROUP II WITHIN NORMAL LIMITS PHTHISIS BULBI CONJUNCTIVITIS		P	P	P	1 3	
ANIMAL #: 2562 GROUP II WITHIN NORMAL LIMITS COMPLETE CATARACT PHTHISIS BULBI CONJUNCTIVITIS		P	P	1 1 3 3		
ANIMAL #: 2563 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P	P	P 1 1		
ANIMAL #: 2564 GROUP II WITHIN NORMAL LIMITS RETINAL DEGENERATION PHTHISIS BULBI CONJUNCTIVITIS		P	P	2 3 3		
ANIMAL #: 2565 GROUP II WITHIN NORMAL LIMITS CORNEAL SCAR RETINAL DEGENERATION		P	2 2	2 2		
ANIMAL #: 2566 GROUP II WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 2567 GROUP II WITHIN NORMAL LIMITS CONJUNCTIVITIS		P	P	P 3		
ANIMAL #: 2568 GROUP II WITHIN NORMAL LIMITS CONJUNCTIVITIS		P	P	P 3		
ANIMAL #: 2569 GROUP II WITHIN NORMAL LIMITS		P	P	P		

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
CONJUNCTIVITIS						3
ANIMAL #: 2570 GROUP II						
WITHIN NORMAL LIMITS			P	P		
CORNEAL SCAR				2	2	
RETINAL DEGENERATION					2	
CONJUNCTIVITIS					2	
ANIMAL #: 2571 GROUP II						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 2572 GROUP II						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 2573 GROUP II						
WITHIN NORMAL LIMITS			P	P		
FOCAL RETINOPATHY					1	
CORNEAL SCAR					1	
ANIMAL #: 2574 GROUP II						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 2575 GROUP II						
WITHIN NORMAL LIMITS			P	P		
CONJUNCTIVITIS					1	
ANIMAL #: 2576 GROUP II						
WITHIN NORMAL LIMITS			P			
CORNEAL SCAR				2	2	
PHTHISIS BULBI					1	
ANIMAL #: 2577 GROUP II						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 2578 GROUP II						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 2579 GROUP II						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 2580 GROUP II						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 2581 GROUP II						
WITHIN NORMAL LIMITS			P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
POSTEROIR SYNECHIA		1				
ANIMAL #: 2582 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 2583 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 2584 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 2585 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 2586 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 2587 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 2588 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 2589 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 2590 GROUP II WITHIN NORMAL LIMITS		P P				
ANIMAL #: 3501 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS		P			P	1
ANIMAL #: 3502 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P			1 1 1 1	
ANIMAL #: 3503 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR		P			1 3	
ANIMAL #: 3504 GROUP III WITHIN NORMAL LIMITS		P			P P	

OBSERVATIONS	WEEK OF STUDY				
	1	2	3	4	5
	1	2	3	4	5

P

1 1
3

P 23

P P

P P P

P 1 P

P P

P

1 3

P

1	3
1	1

P

1	1
3	1

P

P

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
CONJUNCTIVITIS						1
ANIMAL #: 3516 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR						3
CONJUNCTIVITIS						2
ANIMAL #: 3517 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR						2
CONJUNCTIVITIS						2
ANIMAL #: 3518 GROUP III						
WITHIN NORMAL LIMITS	P					P
CONJUNCTIVITIS						1
ANIMAL #: 3519 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR						3 3
CONJUNCTIVITIS						3
ANIMAL #: 3520 GROUP III						
WITHIN NORMAL LIMITS	P					P
ANIMAL #: 3521 GROUP III						
WITHIN NORMAL LIMITS	P					P
CORNEAL SCAR						3
ANIMAL #: 3522 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR						1
CONJUNCTIVITIS						3
TUMOR LOWER LID						1
ANIMAL #: 3523 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR						2 3
CONJUNCTIVITIS						2 2
ANIMAL #: 3524 GROUP III						
WITHIN NORMAL LIMITS	P					
POSTERIOR SUBCAPSULAR CATARACT						1
CORNEAL SCAR						2
CONJUNCTIVITIS						2 2

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
ANIMAL #: 3525 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR				2		
CONJUNCTIVITIS				3		
ANIMAL #: 3526 GROUP III						
WITHIN NORMAL LIMITS	P					
CONJUNCTIVITIS				1		
ANIMAL #: 3527 GROUP III						
WITHIN NORMAL LIMITS	P					
COMPLETE CATARACT				2	2	
CORNEAL SCAR				1	1	
PHTHISIS BULBI				2	2	
CONJUNCTIVITIS				1		
ANIMAL #: 3528 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR				1	3	
CONJUNCTIVITIS				2	1	
ANIMAL #: 3529 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR				1	1	
CONJUNCTIVITIS				1	3	
ANIMAL #: 3530 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR				2	2	
CONJUNCTIVITIS				2	2	
ANIMAL #: 3531 GROUP III						
WITHIN NORMAL LIMITS	P	P	P			
ANIMAL #: 3532 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR				2		
CONJUNCTIVITIS				2	2	
ANIMAL #: 3533 GROUP III						
WITHIN NORMAL LIMITS	P	P				
CORNEAL SCAR				2		

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4
<hr/>		
ANIMAL #: 3534 GROUP III		
WITHIN NORMAL LIMITS	P	
CORNEAL SCAR		3 3
CONJUNCTIVITIS		3 3
ANIMAL #: 3535 GROUP III		
WITHIN NORMAL LIMITS	P	
CORNEAL SCAR		1
RETINAL DEGENERATION		1
CONJUNCTIVITIS		2
ANIMAL #: 3536 GROUP III		
WITHIN NORMAL LIMITS	P	
CORNEAL SCAR		2 2
CONJUNCTIVITIS		2 2
ANIMAL #: 3537 GROUP III		
WITHIN NORMAL LIMITS	P	
CORNEAL SCAR		1 3
CONJUNCTIVITIS		3 2
ANIMAL #: 3538 GROUP III		
WITHIN NORMAL LIMITS	P	
CORNEAL SCAR		1
CONJUNCTIVITIS		1
ANIMAL #: 3539 GROUP III		
WITHIN NORMAL LIMITS	P	
CORNEAL SCAR		2 3
CONJUNCTIVITIS		2 2
ANIMAL #: 3540 GROUP III		
WITHIN NORMAL LIMITS	P	P
CORNEAL SCAR		3
CONJUNCTIVITIS		3
ANIMAL #: 3541 GROUP III		
WITHIN NORMAL LIMITS	P	
CONJUNCTIVITIS		2 1
ANIMAL #: 3542 GROUP III		
WITHIN NORMAL LIMITS	P	

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
FOCAL RETINOPATHY					2	2
CORNEAL SCAR					3	
CONJUNCTIVITIS					1	1
ANIMAL #: 3543 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR					1	
CONJUNCTIVITIS					1	
ANIMAL #: 3544 GROUP III						
WITHIN NORMAL LIMITS	P		P			
CORNEAL SCAR					3	
CONJUNCTIVITIS					3	
ANIMAL #: 3545 GROUP III						
WITHIN NORMAL LIMITS	P		P			
CONJUNCTIVITIS					3	
ANIMAL #: 3546 GROUP III						
WITHIN NORMAL LIMITS	P		P			
CONJUNCTIVITIS					2	
ANIMAL #: 3547 GROUP III						
WITHIN NORMAL LIMITS	P		P			
ANIMAL #: 3548 GROUP III						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR					3	3
CONJUNCTIVITIS					3	2
ANIMAL #: 3549 GROUP III						
WITHIN NORMAL LIMITS	P		P			
CORNEAL SCAR					3	
ANIMAL #: 3550 GROUP III						
WITHIN NORMAL LIMITS	P		P			
CORNEAL SCAR					2	
ANIMAL #: 3551 GROUP III						
WITHIN NORMAL LIMITS	P		P	P		
ANIMAL #: 3552 GROUP III						
WITHIN NORMAL LIMITS	P		P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
CONJUNCTIVITIS						3
ANIMAL #: 3553 GROUP III						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR				1	1	
CONJUNCTIVITIS				1	1	
ANIMAL #: 3554 GROUP III						
WITHIN NORMAL LIMITS		P		P	P	
ANIMAL #: 3555 GROUP III						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR				3	3	
CONJUNCTIVITIS				3		
ANIMAL #: 3593 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		
CORNEAL SCAR				1		
CONJUNCTIVITIS				1		
ANIMAL #: 3557 GROUP III						
WITHIN NORMAL LIMITS		P		P		
CONJUNCTIVITIS			3	3		
ANIMAL #: 3558 GROUP III						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR				1		
CONJUNCTIVITIS				1	1	
ANIMAL #: 3559 GROUP III						
WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 3560 GROUP III						
WITHIN NORMAL LIMITS		P	P	P	P	
ANIMAL #: 3591 GROUP III						
WITHIN NORMAL LIMITS		P	P		P	
CONJUNCTIVITIS				2		
ANIMAL #: 3562 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		
CONJUNCTIVITIS				3		
ANIMAL #: 3563 GROUP III						
WITHIN NORMAL LIMITS		P	P	P		

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		-	1	2	5	0
		2	3	6	2	4
CONJUNCTIVITIS						3
ANIMAL #: 3564 GROUP III WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 3565 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P	P	P	1
ANIMAL #: 3566 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P	P	P	2
ANIMAL #: 3567 GROUP III WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS			P	P	P	1 1
ANIMAL #: 3568 GROUP III WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 3569 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P	P		1 3
ANIMAL #: 3570 GROUP III WITHIN NORMAL LIMITS			P	P	P	P
ANIMAL #: 3571 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3572 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3573 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3574 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3575 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS OPTIC NERVE ATROPHY			P			2 2 2

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 3576 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P	P		3
ANIMAL #: 3577 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3578 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3579 GROUP III WITHIN NORMAL LIMITS RETINAL DEGENERATION CONJUNCTIVITIS			P	P		2 1
ANIMAL #: 3580 GROUP III WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 3581 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3582 GROUP III WITHIN NORMAL LIMITS ANTERIOR SYNECHIA			P			2
ANIMAL #: 3583 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P			1
ANIMAL #: 3584 GROUP III WITHIN NORMAL LIMITS CONJUNCTIVITIS			P			2
ANIMAL #: 3585 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3586 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3587 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3592 GROUP III WITHIN NORMAL LIMITS			P	P		

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 3589 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 3590 GROUP III WITHIN NORMAL LIMITS			P	P		
ANIMAL #: 4501 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS			P	P	2	2
ANIMAL #: 4502 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS			P	P	2	
ANIMAL #: 4503 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS			P		1	
ANIMAL #: 4504 GROUP IV WITHIN NORMAL LIMITS POSTERIOR SUBCAPSULAR CATARACT CONJUNCTIVITIS			P		1	3
ANIMAL #: 4505 GROUP IV WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 4506 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS			P		2	2
ANIMAL #: 4507 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS			P	P	3	
ANIMAL #: 4508 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS			P		2	2
ANIMAL #: 4509 GROUP IV WITHIN NORMAL LIMITS			P	P	P	

					1
		WEEK OF	-	1 2 5 0	
OBSERVATIONS		STUDY	2 3 6 2 4		

P 1

P 1
1

P

2

2

2

1

P

1 1

1 1

P P P

P 1 1

P P 33

P

2

2

2

P

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
CORNEAL SCAR						3 1
CONJUNCTIVITIS						3 1
ANIMAL #: 4519 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS	P					2 3
ANIMAL #: 4520 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR	P	P				1
ANIMAL #: 4521 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS	P		P			1
ANIMAL #: 4522 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS	P	P				2 2
ANIMAL #: 4523 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR	P					3
ANIMAL #: 4524 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS	P					2
ANIMAL #: 4525 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS	P		P			3
ANIMAL #: 4526 GROUP IV WITHIN NORMAL LIMITS PHTHISIS BULBI CONJUNCTIVITIS RETINAL HEMORRHAGE	P	P				1 1 2
ANIMAL #: 4527 GROUP IV WITHIN NORMAL LIMITS	P					
ANIMAL #: 4528 GROUP IV WITHIN NORMAL LIMITS	P	P				

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0				
		2	3	6	2	4
CONJUNCTIVITIS						2
ANIMAL #: 4529 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS		P	P			3
ANIMAL #: 4530 GROUP IV WITHIN NORMAL LIMITS		P	P	P		
ANIMAL #: 4531 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P	P			1 1
ANIMAL #: 4532 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS		P				2
ANIMAL #: 4533 GROUP IV WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4534 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P				3 1 3
ANIMAL #: 4535 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR RETINAL DEGENERATION CONJUNCTIVITIS		P			2 1 1 3 3	
ANIMAL #: 4536 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS		P				3
ANIMAL #: 4537 GROUP IV WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P				1 1
ANIMAL #: 4538 GROUP IV WITHIN NORMAL LIMITS		P				

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0				
		2	3	6	2	4
RETINAL DEGENERATION						1
CONJUNCTIVITIS						3
ANIMAL #: 4539 GROUP IV						
WITHIN NORMAL LIMITS		P				1
COMPLETE CATARACT						1 1
CORNEAL SCAR						1
RETINAL DEGENERATION						2 1
CONJUNCTIVITIS						
ANIMAL #: 4540 GROUP IV						
WITHIN NORMAL LIMITS		P	P			2
CORNEAL SCAR						2
CONJUNCTIVITIS						
ANIMAL #: 4541 GROUP IV						
WITHIN NORMAL LIMITS		P				1
FOCAL RETINOPATHY						2
RETINAL DEGENERATION						
ANIMAL #: 4542 GROUP IV						
WITHIN NORMAL LIMITS		P				1
CORNEAL SCAR						1 1
CONJUNCTIVITIS						
ANIMAL #: 4543 GROUP IV						
WITHIN NORMAL LIMITS		P	P			2
POSTERIOR SUBCAPSULAR CATARACT						
ANIMAL #: 4544 GROUP IV						
WITHIN NORMAL LIMITS		P				1
COMPLETE CATARACT						3
CONJUNCTIVITIS						
ANIMAL #: 4545 GROUP IV						
WITHIN NORMAL LIMITS		P				2 3
CORNEAL SCAR						2 2
CONJUNCTIVITIS						
ANIMAL #: 4546 GROUP IV						
WITHIN NORMAL LIMITS		P	P			2
CORNEAL SCAR						
ANIMAL #: 4547 GROUP IV						
WITHIN NORMAL LIMITS		P	P	P		

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
<hr/>						
ANIMAL #: 4548 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
CORNEAL SCAR				1		
ANIMAL #: 4549 GROUP IV						
WITHIN NORMAL LIMITS		P		P		
CORNEAL SCAR				1		
CONJUNCTIVITIS				1		
ANIMAL #: 4550 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4551 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4552 GROUP IV						
WITHIN NORMAL LIMITS		P				
CONJUNCTIVITIS				2		
ANIMAL #: 4553 GROUP IV						
WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 4554 GROUP IV						
WITHIN NORMAL LIMITS		P				
COMPLETE CATARACT				2		
CORNEAL SCAR				2	1	
RETINAL DEGENERATION				2		
PHTHISIS BULBI					2	
CONJUNCTIVITIS				2	2	
ANIMAL #: 4555 GROUP IV						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR					3	
CONJUNCTIVITIS				2	3	
ANIMAL #: 4556 GROUP IV						
WITHIN NORMAL LIMITS		P				
FOCAL RETINOPATHY			2	2		
POSTERIOR SUBCAPSULAR CATARACT					2	
RETINAL DEGENERATION					2	
CONJUNCTIVITIS					3	
ANIMAL #: 4557 GROUP IV						
WITHIN NORMAL LIMITS		P				

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
FOCAL RETINOPATHY				1		
COMPLETE CATARACT					1	
RETINAL DEGENERATION				3	1	
CONJUNCTIVITIS					2	
ANIMAL #: 4558 GROUP IV						
WITHIN NORMAL LIMITS				P	P	P
CONJUNCTIVITIS						1
ANIMAL #: 4559 GROUP IV						
WITHIN NORMAL LIMITS				P	P	P
ANIMAL #: 4560 GROUP IV						
WITHIN NORMAL LIMITS				P		
COMPLETE CATARACT						2
RETINAL DEGENERATION				2	2	
ANIMAL #: 4561 GROUP IV						
WITHIN NORMAL LIMITS				P	P	P
ANIMAL #: 4591 GROUP IV						
WITHIN NORMAL LIMITS				P	P	P
PHTHISIS BULBI						1
ANIMAL #: 4563 GROUP IV						
WITHIN NORMAL LIMITS				P	P	
CONJUNCTIVITIS					2	3
ANIMAL #: 4564 GROUP IV						
WITHIN NORMAL LIMITS				P	P	
CONJUNCTIVITIS					1	3
ANIMAL #: 4565 GROUP IV						
WITHIN NORMAL LIMITS				P	P	P
CONJUNCTIVITIS						3
ANIMAL #: 4566 GROUP IV						
WITHIN NORMAL LIMITS				P	P	P
ANIMAL #: 4567 GROUP IV						
WITHIN NORMAL LIMITS				P	P	P
PHTHISIS BULBI						1
CONJUNCTIVITIS						3

		1
	WEEK OF	- 1 2 5 0
OBSERVATIONS	STUDY	2 3 6 2 4

ANIMAL #:	4568	GROUP IV	
WITHIN NORMAL LIMITS			P P
CORNEAL SCAR			1
CONJUNCTIVITIS			1 1
ANIMAL #:	4569	GROUP IV	
WITHIN NORMAL LIMITS			P P
CORNEAL SCAR			3
CONJUNCTIVITIS			3 3
ANIMAL #:	4570	GROUP IV	
WITHIN NORMAL LIMITS			P P P P
ANIMAL #:	4571	GROUP IV	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	4572	GROUP IV	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	4573	GROUP IV	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	4574	GROUP IV	
WITHIN NORMAL LIMITS			P
CONJUNCTIVITIS			2 2
ANIMAL #:	4575	GROUP IV	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	4576	GROUP IV	
WITHIN NORMAL LIMITS			P P
FOCAL RETINOPATHY			1
CORNEAL SCAR			1
ANIMAL #:	4577	GROUP IV	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	4578	GROUP IV	
WITHIN NORMAL LIMITS			P P
CONJUNCTIVITIS			2
ANIMAL #:	4579	GROUP IV	
WITHIN NORMAL LIMITS			P P P

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1			
		- 1	2	5	0
		2	3	6	2
<hr/>					
ANIMAL #: 4580 GROUP IV WITHIN NORMAL LIMITS			P	P	P
ANIMAL #: 4581 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 4582 GROUP IV WITHIN NORMAL LIMITS CONJUNCTIVITIS			P		2
ANIMAL #: 4583 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 4584 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 4585 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 4586 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 4587 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 4588 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 4589 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 4590 GROUP IV WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 5501 GROUP V WITHIN NORMAL LIMITS CONJUNCTIVITIS			P	P	2
ANIMAL #: 5502 GROUP V WITHIN NORMAL LIMITS			P	P	
ANIMAL #: 5503 GROUP V WITHIN NORMAL LIMITS			P	P	
<hr/>					

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
CORNEAL SCAR						1
ANIMAL #: 5504 GROUP V						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR					1	3
CONJUNCTIVITIS					3	3
ANIMAL #: 5505 GROUP V						
WITHIN NORMAL LIMITS	P		P			
ANIMAL #: 5506 GROUP V						
WITHIN NORMAL LIMITS	P					
COMPLETE CATARACT					1	
PHTHISIS BULBI					1	
ANIMAL #: 5507 GROUP V						
WITHIN NORMAL LIMITS	P					
CONJUNCTIVITIS					1	
ANIMAL #: 5508 GROUP V						
WITHIN NORMAL LIMITS	P					
CONJUNCTIVITIS					2	
ANIMAL #: 5509 GROUP V						
WITHIN NORMAL LIMITS	P		P			
ANIMAL #: 5510 GROUP V						
WITHIN NORMAL LIMITS	P					
CONJUNCTIVITIS					1	
ANIMAL #: 5511 GROUP V						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR					2	2
ANIMAL #: 5512 GROUP V						
WITHIN NORMAL LIMITS	P		P			
CORNEAL SCAR						3
ANIMAL #: 5513 GROUP V						
WITHIN NORMAL LIMITS	P					
CORNEAL SCAR					1	
ANIMAL #: 5514 GROUP V						
WITHIN NORMAL LIMITS	P		P	P		

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
ANIMAL #: 5515 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5516 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR		P				1 3
ANIMAL #: 5517 GROUP V WITHIN NORMAL LIMITS		P			P P	
ANIMAL #: 5518 GROUP V WITHIN NORMAL LIMITS		P			P	
ANIMAL #: 5519 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P				1 1
ANIMAL #: 5520 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR		P			P	3
ANIMAL #: 5521 GROUP V WITHIN NORMAL LIMITS RETINAL DEGENERATION		P				1
ANIMAL #: 5522 GROUP V WITHIN NORMAL LIMITS POSTERIOR SUBCAPSULAR CATARACT RETINAL DEGENERATION		P				3 3
ANIMAL #: 5523 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P				2 2
ANIMAL #: 5524 GROUP V WITHIN NORMAL LIMITS		P			P P	
ANIMAL #: 5525 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P				2 2

		1
	WEEK OF	- 1 2 5 0
OBSERVATIONS	STUDY	2 3 6 2 4

ANIMAL #:	5526	GROUP V		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	5527	GROUP V		
WITHIN NORMAL LIMITS			P	P
CORNEAL SCAR				3
CONJUNCTIVITIS				1
ANIMAL #:	5528	GROUP V		
WITHIN NORMAL LIMITS			P	
FOCAL RETINOPATHY				1
POSTERIOR SUBCAPSULAR CATARACT				1
IRITIS OR UVEITIS				1
ANIMAL #:	5529	GROUP V		
WITHIN NORMAL LIMITS			P	
RETINAL DEGENERATION				1
ANIMAL #:	5530	GROUP V		
WITHIN NORMAL LIMITS			P	P
ANIMAL #:	5531	GROUP V		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
CONJUNCTIVITIS				3
ANIMAL #:	5532	GROUP V		
WITHIN NORMAL LIMITS			P	
ANIMAL #:	5591	GROUP V		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
CONJUNCTIVITIS				1
ANIMAL #:	5534	GROUP V		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				1
CONJUNCTIVITIS				2
ANIMAL #:	5535	GROUP V		
WITHIN NORMAL LIMITS			P	
CORNEAL SCAR				3
CONJUNCTIVITIS				3

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
ANIMAL #: 5536 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P		2 3 2 2		
ANIMAL #: 5537 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR		P		1		
ANIMAL #: 5538 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR		P		2 3		
ANIMAL #: 5539 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P		3 1		
ANIMAL #: 5540 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P	P	3 2		
ANIMAL #: 5541 GROUP V WITHIN NORMAL LIMITS		P	P			
ANIMAL #: 5542 GROUP V WITHIN NORMAL LIMITS CONJUNCTIVITIS		P		3		
ANIMAL #: 5543 GROUP V WITHIN NORMAL LIMITS COMPLETE CATARACT CORNEAL SCAR PHTHISIS BULBI CONJUNCTIVITIS		P		3 3 3 2 1 1		
ANIMAL #: 5544 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS		P		1 1 3		
ANIMAL #: 5545 GROUP V WITHIN NORMAL LIMITS		P				

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1 - 1 2 5 0 2 3 6 2 4				
CONJUNCTIVITIS						1
ANIMAL #: 5546 GROUP V						
WITHIN NORMAL LIMITS		P				
FOCAL RETINOPATHY						1
CONJUNCTIVITIS						3
ANIMAL #: 5547 GROUP V						
WITHIN NORMAL LIMITS		P				
CONJUNCTIVITIS						1
ANIMAL #: 5548 GROUP V						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						1
CONJUNCTIVITIS						1 1
ANIMAL #: 5549 GROUP V						
WITHIN NORMAL LIMITS		P				
CONJUNCTIVITIS						1
ANIMAL #: 5550 GROUP V						
WITHIN NORMAL LIMITS		P				
CORNEAL SCAR						1
CONJUNCTIVITIS						1
ANIMAL #: 5551 GROUP V						
WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5552 GROUP V						
WITHIN NORMAL LIMITS		P		P		
CORNEAL SCAR						1
ANIMAL #: 5553 GROUP V						
WITHIN NORMAL LIMITS		P		P		
ANIMAL #: 5554 GROUP V						
WITHIN NORMAL LIMITS		P				
RETINAL DEGENERATION						1
CONJUNCTIVITIS						1
ANIMAL #: 5555 GROUP V						
WITHIN NORMAL LIMITS		P		P		
CORNEAL SCAR						3
CONJUNCTIVITIS						3

OBSERVATIONS	WEEK OF STUDY	1				
		- 1 2 5 0	2 3 6 2 4			
ANIMAL #: 5556 GROUP V WITHIN NORMAL LIMITS			P P P P			
ANIMAL #: 5557 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS			P P 2 1 2			
ANIMAL #: 5558 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS			P P P 2 2			
ANIMAL #: 5559 GROUP V WITHIN NORMAL LIMITS RETINAL DEGENERATION			P P 2 2			
ANIMAL #: 5560 GROUP V WITHIN NORMAL LIMITS			P P P P			
ANIMAL #: 5592 GROUP V WITHIN NORMAL LIMITS CORNEAL SCAR CONJUNCTIVITIS			P P 1 1 1			
ANIMAL #: 5562 GROUP V WITHIN NORMAL LIMITS PHTHISIS BULBI			P P P 1			
ANIMAL #: 5563 GROUP V WITHIN NORMAL LIMITS CONJUNCTIVITIS			P P P 2			
ANIMAL #: 5564 GROUP V WITHIN NORMAL LIMITS RETINAL DEGENERATION CONJUNCTIVITIS			P P P 1 2			
ANIMAL #: 5565 GROUP V WITHIN NORMAL LIMITS CONJUNCTIVITIS			P P P 2			
ANIMAL #: 5566 GROUP V WITHIN NORMAL LIMITS			P P			

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APPENDIX D (cont.)
A 24-MONTH ORAL TOXICITY/ONCOGENICITY STUDY
OF MALATHION IN THE RAT VIA DIETARY ADMINISTRATION

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90-3641

INDIVIDUAL OPHTHALMOSCOPIC FINDINGS - FEMALES

OBSERVATIONS	WEEK OF STUDY	1				
		- 1	2	5	0	
		2	3	6	2	4
CORNEAL SCAR						3
CONJUNCTIVITIS						3 2
ANIMAL #: 5567 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
CONJUNCTIVITIS						2
ANIMAL #: 5568 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
CONJUNCTIVITIS						2
ANIMAL #: 5569 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
CORNEAL SCAR						1
CONJUNCTIVITIS						2
ANIMAL #: 5570 GROUP V						
WITHIN NORMAL LIMITS			P			
COMPLETE CATARACT						1
RETINAL DEGENERATION			1	1		
ANIMAL #: 5571 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5572 GROUP V						
WITHIN NORMAL LIMITS			P	P		
CONJUNCTIVITIS						1
ANIMAL #: 5573 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5574 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5575 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5576 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5577 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	
ANIMAL #: 5578 GROUP V						
WITHIN NORMAL LIMITS			P	P	P	

OBSERVATIONS	WEEK OF STUDY				
	1	2	3	4	5
	1	2	3	4	5

ANIMAL #:	5579	GROUP V	
WITHIN NORMAL LIMITS			P
COMPLETE CATARACT			1
RETINAL DEGENERATION			1
PHTHISIS BULBI			1
ANIMAL #:	5580	GROUP V	
WITHIN NORMAL LIMITS			P P P
ANIMAL #:	5581	GROUP V	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	5582	GROUP V	
WITHIN NORMAL LIMITS			P
CORNEAL SCAR			2
ANIMAL #:	5583	GROUP V	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	5584	GROUP V	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	5585	GROUP V	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	5586	GROUP V	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	5587	GROUP V	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	5588	GROUP V	
WITHIN NORMAL LIMITS			P
CONJUNCTIVITIS			2
ANIMAL #:	5589	GROUP V	
WITHIN NORMAL LIMITS			P P
ANIMAL #:	5590	GROUP V	
WITHIN NORMAL LIMITS			P
CONJUNCTIVITIS			3

E-1
Appendix E
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Pretest

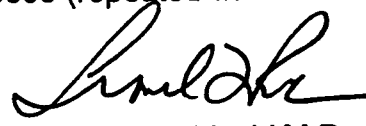
313

February 2, 1994

Pharmaco LSR
Mettlers Road, Box 2360
East Millstone NJ 08875-2360

Re: project J-11 90-3641

Pretest electroretinographic examination of project J-11 90-3641 rats was performed December 17-24, 1992. Low amplitude electroretinograms were recorded from rats 1558, 1560 (repeated with normal results), 1561, 2058, 2556 (repeated with normal results), 2557 (repeated with normal results), 3061 (repeated with normal results), 3557, 3591, 4056 (repeated with normal results), 4058, 4556 (repeated with normal results), 4557 (repeated with normal results), 4561, 4591, 5059 (repeated with normal results), 5559, 5562 and 5592.



Lionel F. Rubin, V.M.D.

E-2
Appendix E (cont.)
LIONEL F. RUBIN, V.M.D.
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February 2, 1994

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Month 3

Re: project J-11 90-3641

Electroretinographic examination of project J-11 90-3641 rats was performed March 30 to April 1, 1993 (month 3). Abnormal electroretinograms were recorded from rats 1059, 1561 (abnormal at pretest examination), 1562, 2559*, 2562, 4056*, 4058 (abnormal at pretest examination), 4557*, 4560, 5056* and 5061. Rats indicated with an asterisk were found (on ophthalmoscopic examination) to have unilateral retinal degeneration in the eye tested electroretinographically. Unilateral retinal degeneration is inconsistent with a toxic etiology. Retinal degeneration had not been ophthalmoscopically visible at the pretest examination.

The following rats had low amplitude electroretinograms at the pre-test examination and are now within normal electroretinographic parameters: 1558, 2058, 3557, 3591 4561, 4591, 5559, 5562 and 5592.

Comparison of a- and b-wave amplitudes* and latencies for each group at this examination compared to the pretest examination indicated:

1) in the males


- a) b-wave amplitudes at each dose level were essentially the same for groups I, II and IV and were increased for groups II and V. There was no indication of dose-related change.
- b) a-wave amplitudes (absolute values) remained essentially the same in three groups, decreased slightly in group IV, and increased slightly in group II. There was no indication of dose-related change.
- c) b-wave latencies remained essentially the same in group IV and increased slightly in all other groups. There was no indication of dose-related change.
- d) a-wave latencies increased in all groups. There was no indication of dose-related change.

2) in the females

- a) b-wave amplitudes at each dose level increased. There was no indication of dose-related change.
- b) a-wave amplitudes (absolute values) at each dose level increased in 4 groups and decreased in group III. There was no indication of dose-related change.
- c) b-wave latencies increased in all groups. There was no indication of dose-related change.
- d) a-wave latencies had increased slightly in all groups. There was no indication of dose-related change.

Therefore, comparison (by group) of the measured parameters failed to indicate an electroretinographic effect attributable to the test compound. There is no indication of compound related electroretinographic abnormality.

Comparison between groups at the 3 month examination indicated b-wave amplitudes were lower in males groups III, IV, and V than in male groups I and II. There was, however, no significant change from the values of each group to its values at the pretest examination.



Lionel F. Rubin, V.M.D.

* a-wave amplitudes are interpreted as absolute numbers.

Month 6

February 2, 1994

Pharmaco LSR
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Re: project J-11 90-3641

Electroretinographic examination of project J-11 90-3641 rats was performed June 29-July 1, 1993 (month 6). Abnormal electroretinograms were recorded from rats 1561, 2559*, 2562*, 3059, 3557, 4056, 4059, 4557, 5056* and 5562. Rats indicated with an asterisk were found (on ophthalmoscopic examination) to have unilateral retinal degeneration (or its sequela, complete cataract) in the eye tested electroretinographically. In rat 4557 the retinal degeneration has become bilateral since the previous ophthalmoscopic examination. Unilateral retinal degeneration is inconsistent with a toxic etiology.

The following rats had low amplitude electroretinograms at the month 3 examination and are now within normal electroretinographic parameters: 1059, 1562, 4058, 4560, 5061.

Comparison of a- and b-wave amplitudes* and latencies for each group at this examination compared to the 3 month examination indicated:

1) in the males

- a) b-wave amplitudes were essentially the same in two groups, had increased in group V and had decreased in groups I and II. There was no indication of dose-related change.
- b) a-wave amplitudes (absolute values) remained essentially the same in group V, and decreased in the other 4 groups. There was no indication of dose-related change.
- c) b-wave latencies remained essentially the same in groups II and V, had increased in groups III and IV and decreased in group I. There was no indication of dose-related change.
- d) a-wave latencies remained essentially the same in four groups and decreased in group V. There was no indication of dose-related change.

2) in the females

- a) b-wave amplitudes in groups IV and V remained essentially the same; mean amplitude increased in group II and decreased in group I and III. There was no indication of dose-related change.
- b) a-wave amplitudes increased in dose levels III and V and decreased in groups I, II and IV. There was no indication of dose-related change.
- c) b-wave latencies remained about the same in groups (I, II and IV). Mean latency decreased in groups III and V. There was no indication of dose-related change.
- d) a-wave latencies increased in group III, remained essentially the same in groups I and II and decreased in groups IV and V. There was no indication of dose-related change.

Therefore, comparison (by group) of the measured parameters failed to indicate an

electroretinographic effect attributable to the test compound. There is no indication of compound related electroretinographic abnormality.



Lionel F. Rubin, V.M.D.

* a-wave amplitudes are interpreted as absolute numbers.

TELEPHONE (610) 520-9430
Month 12

February 9, 1994

Pharmaco LSR
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Re: project J-11 90-3641

Electroretinographic examination of project J-11 90-3641 rats was performed December 29, 1993- January 5, 1994 (1 year). The following rats had low amplitude electroretinograms at the month 6 examination and are now within normal electroretinographic parameters: 3059, 4059. Abnormal electroretinograms were recorded as indicated on the next page.

The incidence of abnormal electroretinograms (whether or not selected for risk) fails to indicate dose related electroretinographic changes.

Comparison (to 6-month values) of a- and b-wave amplitudes (absolute values) and latencies by group at this examination indicated:

1) in the males:

- a) there is no apparent dose-related difference in group mean b-wave amplitude
- b) there is no apparent dose-related difference in group mean a-wave amplitude
- c) there is no apparent dose-related difference in group mean b-wave latency
- d) there is no apparent dose-related difference in group mean a-wave latency (latency is prolonged in control and all dose groups)

2) in the females:

- a) there is no apparent dose-related difference in group mean b-wave amplitude (amplitude had decreased in Groups I, II, III and V, and remained the same in Group IV)
- b) there is no apparent dose-related difference in group mean a-wave amplitude absolute values (amplitude had decreased in Groups I, II, III and V, and increased in Group IV)
- c) there is no apparent dose-related difference in group mean b-wave latency (latency remained the same in all dose groups)
- d) there is no apparent dose-related difference in group mean a-wave latency (latency is prolonged in Groups I, II, III and V, and remained the same in Group IV)

Therefore, comparison (by group) of the measured parameters failed to indicate an electroretinographic effect attributable to the test compound. There is no indication of compound related electroretinographic abnormality.



I. Abnormal electroretinograms

group I	group II	group III	group IV	group V
1061	2061 ^{NR}	3056 ^{NR}	4056 ^{NR}	5056 ^{NR}
1062 ^{NR}		3061 ^{NR}	4062 ^{NR}	5057 ^{NR}
				5061 ^{NR}
				5091
1558	2559 ^{NR}	3557	4557	5560 ^{NR}
1560	2561 ^{NR}	3562	4561 ^{NR}	5562 ^{NR}
1561	2562		4591 ^{NR}	5592

II. Abnormal electroretinograms in eyes at risk (excludes eyes affected with phthisis bulbi)

group I	group II	group III	group IV	group V
1061	2061 ^{NR}	3056 ^{NR}	4056 ^{NR}	5056 ^{NR}
1062 ^{NR}		3061 ^{NR}	4062 ^{NR}	5057 ^{NR}
				5061 ^{NR}
				5091
1558		3557	4557	5560 ^{NR}
1560		3562	4561 ^{NR}	5592
1561				

III. Abnormal electroretinograms in eyes at risk (excludes eyes affected clinically with phthisis bulbi and its sequelae, unilateral focal retinopathy, unilateral retinal degeneration and its sequelae)

group I	group II	group III	group IV	group V
1062 ^{NR}	2061 ^{NR}	3056 ^{NR}	4056 ^{NR}	5057 ^{NR}
		3061 ^{NR}	4062 ^{NR}	5061 ^{NR}
				5091
1558		3557	4561 ^{NR}	5560 ^{NR}
1560		3562		5592
1561				

NR = no recording was obtained when animal was stimulated with white light

Handwritten signature/initials

Appendix E (cont.)

LIONEL F. RUBIN, V.M.D.

1116 SAINT ANDREWS ROAD

BRYN MAWR, PENNSYLVANIA 19010

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Termination

August 9, 1995

Pharmaco LSR
Mettlers Road, Box 2360
East Millstone NJ 08875-2360

Re: study J-11 90-3641

Electroretinograms were recorded from the right eye of 5 study J-11 90-3641 rats from each of the remaining dose levels on December 28 and 29, 1994.

Electroretinograms were judged qualitatively abnormal in rats:

group I	group II	group III	group IV	group V
1015 ^{NR}	2038 ^{NR}	3018 ^{NR}	4013 ^{NR}	-
1043	2045	3028 ^{NR}	4020	
	2054	3035 ^{NR}		
		3041 ^{NR}		
	2501 ^{NR}	3505 ^{NR}	4504 ^{NR}	5514 ^{NR}
	2513 ^{NR}	3511 ^{NR}	4512 ^{NR}	5516 ^{NR}
	2524 ^{NR}	3539 ^{NR}	4554	5543 ^{NR}
	2536 ^{NR}	3542 ^{NR}		

^{NR} = no recording was obtained when animal was stimulated with white light

Therefore, abnormal electroretinograms were obtained from:

group I	2/10	(2/5 males; 0/5 females)
group II	7/10	(3/5 males; 4/5 females)
group III	8/10	(4/5 males; 4/5 females)
group IV	5/10	(2/5 males; 3/5 females)
group V	3/5	(3/5 females)

The number of abnormal electroretinograms of treated rats is greater in each treated group when compared to the untreated group at this time interval, but there is no indication of a dose-related suppression of electroretinographic response. The number of abnormal or non-recordable electroretinograms is high. When one excludes animals in which unilateral disease indicates the animal is not capable of providing a response to stimulation with light (because of the presence clinically of phthisis bulbi and its sequelae,

unilateral focal retinopathy, or unilateral retinal degeneration and its sequelae), there remains no evidence of a dose-response relationship, although the number of abnormal electroretinograms in treated rats exceeds that in untreated rats.

Abnormal electroretinograms in eyes at risk :

group I	1/9	(1/4 males; 0/5 females)
group II	4/8	(2/4 males; 2/4 females)
group III	7/9	(3/4 males; 4/5 females)
group IV	3/8	(1/4 males; 2/4 females)
group V	2/4	(2/4 females)

Electroretinographic and retinal abnormalities are not uncommon in Fischer 344 rats (DiLoreto et al., 1993; Lai et al., 1978; Lai et al., 1979; Lee et al., 1990).

DiLoreto et al. found peripheral retinal degeneration involving the photoreceptor layers and the outer nuclear layer. In male rats, they found the superior peripheral retina underwent a precipitous and complete degeneration between 12 and 18 months, the inferior periphery showing less severe degeneration. Females were less severely affected. This type of degeneration, they claim, is typical of the F344 rat and is not seen in age-matched animals of the Sprague-Dawley strain.

Lai et al. indicate that the numbers of photoreceptor cells in Fischer 344 rats gradually decrease as the rats age. The outer nuclear layer is reduced by one third by 18 months. The decrease of photoreceptor cells is more pronounced in rats housed under a light intensity of 32-ft-c (normal laboratory lighting) than in rats housed under a light intensity of 1 ft-c. Inner and outer segments of surviving photoreceptor cells were morphologically normal. They also found a new form of retinal degeneration in aged Fischer rats characterized by selective degeneration of peripheral retina (similar to DiLoreto et al above). Degeneration was characterized by severe loss of photoreceptor cells in the far peripheral retina. The incidence and severity of peripheral retinal degeneration is an age-related change exaggerated by ambient light.

Lee et al found unilateral retinal and optic nerve lesions developing spontaneously in Fischer rats, in some instances ranging in incidence from above 25% at 26 weeks in rats fed synthetic diets to about 16% in rats fed standard diets. The affected retina is thin and the thinning is confined mainly to inner layers including the outer plexiform layer, inner nuclear layer, inner plexiform layer and ganglion cell layer. Degeneration of the inner nuclear layer, including Müller cells, would affect (suppress) the electroretinogram. This form of retinal degeneration that affects younger rats, and differs from the peripheral retinal degeneration reported in older Fischer rats by Lai et al., which is characterized by a slowly progressive bilateral loss of photoreceptor cells from the peripheral retina without detectable involvement of the optic nerve.

The spontaneous occurrence of retinal thinning and of various retinal diseases in

Fischer F344 rats suffices to explain the high incidence of electroretinographic abnormalities. One would have expected complete extinction of the electroretinogram in a dose-related fashion had the test compound had a significant effect.



Lionel F. Rubin, V.M.D.

REFERENCES

DiLoreto D, del Cerro C, Grover D, Lazar E, del Cerro M: Peripheral, paving stone and cystoid retinal degenerations in the aging Fischer 344 at. Invest Ophthalmol Vis Sci 34(suppl): 1076, 1993.

Lai Y-L, Jacoby RO, Yao PC: Age-related and light-associated retinal changes in Fischer rats. Invest Ophthalmol Vis Sci 17: 634-638, 1978

Lai Y-L, Jacoby RO, Yao PC: Animal model: peripheral retinal degeneration in rats Am J Pathol 97:449-452, 1979

Lee EW, Render JA, Garner CD, Brady AN, Li LC: Unilateral degeneration of retina and optic nerve in Fischer-344 rats. Vet Pathol 27:439-444, 1990

E-11
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Electroretinogram Values
Preface

Electroretinogram results were evaluated by Dr. Lionel Rubin. Preselected animals were examined pretest, Month 3, Month 6, Month 12 and Termination.

Key to Abbreviations

NR = Not Recorded (no discernable response obtained after stimulation with light)
A LAT = A Wave Latency
A AMP = A Wave Amplitude
B LAT = B Wave Latency
B AMP = B Wave Amplitude

Animals excluded from calculation because of extensive unilateral disease, judged incapable of responding to stimulus			
Group	Dose Level (ppm)	Animal Number	Interval
MALES			
I	0	1015	24
II	100/50	2038	24
III	500	3028	24
IV	6000	4013	24
V	12000	5056	12
FEMALES			
II	100/50	2562	3, 6, 12
II	100/50	2559	12
II	100/50	2561	12
II	100/50	2513	24
IV	6000	4557	3, 6, 12
IV	6000	4591	12
IV	6000	4504	24
V	12000	5543	24

E-12
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Electroretinogram Values
Preface (cont.)

Reason for exclusion from calculation				
Group	Dose Level (ppm)	Animal Number	Ocular Abnormality Observed	Interval
MALES				
I	0	1015	cataract	24
II	100/50	2038	glaucoma and complete cataract	24
III	500	3028	extensive cataract	24
IV	6000	4013	complete cataract, unilateral retinopathy	24
V	12000	5056	cataract	12
FEMALES				
II	100/50	2562	phthisis bulbi (3) phthisis bulbi and cataract (6 and 12)	3, 6, 12
II	100/50	2559	complete cataract	6, 12
II	100/50	2561	phthisis bulbi	12
II	100/50	2513	complete cataract	24
IV	6000	4557	complete cataract and retinal degeneration	3, 6, 12
IV	6000	4591	phthisis bulbi	12
IV	6000	4504	extensive cataract	24
V	12000	5543	complete cataract	24

NOTE: A key to statistical analysis is presented in Appendix A, Methodology and References - Statistical Analysis, page A-11 through A-14.

The Group II dose level was reduced on 21 April 1993 (Test Day 113) at the sponsor request, from 100 ppm to 50 ppm.

Mean latencies are calculated using the sum of the responses divided by the number of animals having a measurable response.

Mean amplitudes are calculated using the sum of the responses of the animals judged capable of responding to a stimulus divided by the number of animals judged capable of responding.

E-13
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Mean Electroretinogram Values

Mean Responses - All animals At Risk											
Amplitudes (μ V)											
Group	Dose (ppm)	A-Wave					B-Wave				
MALES											
Stat Symbol		A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	AL-Q+	
Month		P	3	6	12	24	P	3	6	12	24
I	0	107.2	113.5	102.1	75.4	39.7	219.4	223.1	205.4	136.6	136.6
II	100/50	105.1	122.5	93.4	97.5	54.8	181.1	238.9	207.5	177.9	87.9
III	500	109.5	111.0	91.5	62.7	15.9	187.4	178.4	171.2	133.6	24.4*
IV	6000	122.1	103.5	80.8	66.4	37.9	204.7	170.9	186.6	126.4	106.2
V	12000	93.2	91.0	94.0	57.2	a	154.5	149.3	195.5	91.9	a
FEMALES											
Stat Symbols		A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-
I	0	82.9	88.1	84.4	53.6	62.3	135.2	179.9	179.8	112.1	117.5
II	100/50	97.4	118.7	126.3	83.1	19.9	169.1	201.1	262.0	157.7	37.9
III	500	114.6	77.2	86.6	58.0	1.9	138.6	223.0	202.4	122.7	30.4
IV	6000	83.5	103.8	76.8	82.2	38.5	137.9	186.3	191.0	153.5	85.7
V	12000	58.6	95.5	115.0	47.9	25.3	96.4	190.6	200.3	89.3	49.5

* = Statistically significant at $p \leq .05$

CALCULATIONS: Responses/N; N = Total of Animals at Risk in Group. If an animal is a non-responder, Amplitude = 0.

^aValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

E-14
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Mean Electroretinogram Values

Mean Responses - All animals At Risk											
Latencies (msec)											
Group	Dose (ppm)	A-Wave					B-Wave				
MALES											
Stat Symbols		A-L-	K-J-	A-L-	A-L-	A-L-	AL-Q	A-L-	A-L-	A-L-	A-L-
Month		P	3	6	12	24	P	3	6	12	24
I	0	12.0	14.6	13.7	21.3	20.3	54.9	77.7	62.6	72.0	88.0
II	100/50	12.5	16.1	15.1	25.4	40.6	56.6	72.2	74.6	73.7	77.3
III	500	12.2	15.5	14.1	18.1	32.5	45.0	69.5	78.4	80.1	78.5
IV	6000	11.6	13.2	13.1	30.5	26.8	60.5	63.9	74.6	74.2	100.8
V	12000	10.6	16.9	12.6	18.8	a	53.9	77.4	75.6	76.1	a
FEMALES											
Stat Symbols		A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-	A-L-
I	0	12.5	13.9	13.6	18.1	21.8	57.6	84.9	77.7	72.6	64.5
II	100/50	12.4	14.1	12.8	17.3	36.0	51.9	72.3	73.2	67.8	79.5
III	500	11.9	16.1	12.1	16.0	35.5	59.1	85.6	71.7	70.0	105.5
IV	6000	12.1	15.5	13.6	14.0	26.7	56.0	72.9	75.9	76.1	75.3
V	12000	12.4	14.6	12.5	16.5	23.0	52.5	78.0	67.4	65.3	81.0

CALCULATIONS: Responses/N; N = Number of Animals in Group Giving a Measurable Response.

^aValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

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Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Mean Electroretinogram Values

Total Number of Animals at Risk Per Group - Amplitude						
MALES						
Group	Dose	Pretest	Month 3	Month 6	Month 12	Month 24
I	0	7	7	7	7	4
II	100/50	7	7	7	7	4
III	500	7	7	7	7	4
IV	6000	7	7	7	7	4
V	12000	7	7	7	6	
FEMALES						
I	0	7	7	7	7	5
II	100/50	7	7	5	4	4
III	500	7	7	7	7	5
IV	6000	7	6	6	5	5
V	12000	7	7	7	7	4

Total Number of Animals in Group Giving a Measureable Response - Latency						
MALES						
Group	Dose	Pretest	Month 3	Month 6	Month 12	Month 24
I	0	7	7	7	6	3
II	100/50	7	7	7	6	4
III	500	7	7	7	5	1
IV	6000	7	7	7	5	4
V	12000	7	7	7	4	^a
FEMALES						
I	0	7	6	7	7	5
II	100/50	7	6	5	4	1
III	500	7	7	7	6	1
IV	6000	7	5	6	4	3
V	12000	5	7	7	5	2

^aValues were not available at the 24 month (terminal) sacrifice for the males at the 12000 ppm level due to the lack of any survivors in the males at this dose level.

E-16
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Pretest - Males

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1057	15.5	-82.9	40.5	203.4
1058	12.5	-101.7	67.0	191.5
1059	13.5	-168.5	72.0	253.2
1061	9.5	-73.2	48.5	129.8
1062	14.0	-120.9	54.0	153.8
1091	8.5	-58.1	39.5	241.0
1092	10.5	-144.9	62.5	362.9
Mean	12.0	-107.2	54.9	219.4
S.D.	2.6	39.9	12.8	77.0
N	7	7	7	7
Group II - 100 ppm				
2056	10.0	-92.9	56.5	160.5
2058	14.5	-47.3	77.0	7.8
2059	10.0	-119.8	45.0	236.3
2060	12.0	-126.1	46.5	230.0
2061	14.0	-76.9	48.0	164.8
2062	12.8	-120.9	58.0	214.3
2092	14.0	-151.7	65.0	254.2
Mean	12.5	-105.1	56.6	181.1
S.D.	1.9	35.0	11.5	84.3
N	7	7	7	7

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Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Pretest - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3056	12.0	-139.5	39.0	276.8
3057	12.5	-100.7	54.5	206.8
3058	14.5	-97.3	40.5	182.9
3059	11.5	-105.9	48.5	143.7
3060	11.0	-92.2	39.5	134.9
3061	12.0	-153.8	46.8	230.8
3062	12.0	-76.9	46.0	136.0
Mean	12.2	-109.5	45.0	187.4
S.D.	1.1	27.3	5.7	54.1
N	7	7	7	7
Group IV - 6000 ppm				
4056	10.0	-121.5	60.5	236.3
4057	17.0	-164.2	55.5	315.9
4058	9.0	-49.8	55.5	73.4
4059	11.0	-115.4	59.0	174.6
4060	11.5	-128.8	59.0	187.8
4061	13.0	-98.9	70.0	192.3
4062	10.0	-175.8	64.0	252.7
Mean	11.6	-122.1	60.5	204.7
S.D.	2.7	41.9	5.1	75.6
N	7	7	7	7

E-18
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Pretest - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5056	12.5	-169.5	61.5	211.7
5057	8.5	-92.0	50.0	130.2
5058	9.0	-78.8	51.0	153.7
5059	10.5	-67.6	46.5	117.8
5060	9.5	-75.1	55.5	142.2
5061	14.0	-87.9	62.0	142.9
5091	10.0	-81.2	51.0	183.2
Mean	10.6	-93.2	53.9	154.5
S.D.	2.0	34.6	6.0	32.5
N	7	7	7	7

E-19
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Pretest - Females

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1556	15.0	-61.7	56.0	218.8
1557	13.0	-96.6	60.0	181.7
1558	9.5	-30.5	45.0	55.4
1559	13.5	-151.0	55.5	203.2
1560	11.0	-53.2	60.5	130.2
1561	14.5	-120.2	64.0	42.9
1562	11.0	-67.1	62.5	114.2
Mean	12.5	-82.9	57.6	135.2
S.D.	2.0	41.9	6.4	69.7
N	7	7	7	7
Group II - 100 ppm				
2556	10.5	-92.7	57.0	161.7
2557	13.0	-56.6	42.5	111.2
2558	12.0	-75.6	55.5	171.7
2559	13.5	-112.2	48.0	167.8
2560	11.5	-139.0	47.0	169.0
2561	14.0	-137.0	52.0	193.2
2562	12.0	-67.8	61.0	209.0
Mean	12.4	-97.4	51.9	169.1
S.D.	1.2	33.2	6.4	30.5
N	7	7	7	7

E-20
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Pretest - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3557	11.5	-81.0	42.0	52.9
3558	12.0	-159.8	62.0	231.0
3559	10.5	-110.0	79.0	127.6
3560	9.5	-115.6	58.5	240.2
3562	15.5	-175.9	54.0	119.5
3591	8.0	-22.4	67.0	74.9
3592	16.0	-137.3	51.0	124.4
Mean	11.9	-114.6	59.1	138.6
S.D.	3.0	51.6	11.9	71.8
N	7	7	7	7
Group IV - 6000 ppm				
4556	10.5	-35.4	71.0	113.7
4557	10.5	-88.8	61.5	146.3
4558	12.5	-137.1	54.5	209.8
4559	10.5	-105.6	55.0	171.7
4560	11.0	-50.7	52.5	282.2
4561	14.5	-58.5	41.5	41.7
4591	15.0	-108.3	NR	0.0
Mean	12.1	-83.5	56.0	137.9
S.D.	2.0	36.6	9.8	96.7
N	7	7	6	7

E-21
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Pretest - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5556	11.5	-67.6	51.0	86.6
5557	11.0	-69.5	59.5	168.3
5558	10.0	-121.7	41.5	213.7
5559	NR	0.0	NR	0.0
5560	15.0	-76.8	62.5	141.0
5562	14.5	-74.4	48.0	64.9
5592	NR	0.0	NR	0.0
Mean	12.4	-58.6	52.5	96.4
S.D.	2.2	44.0	8.6	82.3
N	5	7	5	7

E-22
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 3 - Males

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1057	16.0	-70.0	90.0	176.1
1058	15.5	-184.6	75.5	330.2
1059	16.5	-83.4	84.5	69.5
1061	14.5	-105.6	66.0	179.5
1062	13.0	-122.7	71.0	252.7
1091	13.5	-99.0	79.0	313.9
1092	13.5	-129.5	78.0	240.0
Mean	14.6	-113.5	77.7	223.1
S.D.	1.4	37.6	8.0	90.0
N	7	7	7	7
Group II - 100 ppm				
2056	15.0	-123.9	66.0	234.2
2058	13.5	-103.7	76.5	188.8
2059	17.5	-133.9	62.5	295.4
2060	14.0	-116.6	86.0	234.9
2061	24.0	-131.8	85.0	207.8
2062	14.5	-82.2	61.5	226.8
2092	14.5	-165.4	68.0	284.6
Mean	16.1	-122.5	72.2	238.9
S.D.	3.7	26.0	10.3	38.6
N	7	7	7	7

E-23

Appendix E (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary AdministrationIndividual Electroretinogram Values
Month 3 - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3056	13.0	-128.3	63.5	151.2
3057	17.0	-155.1	60.5	187.6
3058	16.0	-137.1	67.0	230.7
3059	15.5	-141.5	73.5	152.2
3060	13.0	-53.9	54.0	120.2
3061	18.5	-81.0	85.0	181.2
3062	15.5	-80.0	83.0	225.6
Mean	15.5	-111.0	69.5	178.4
S.D.	2.0	38.7	11.6	40.6
N	7	7	7	7
Group IV - 6000 ppm				
4056	11.5	-66.3	NR	0.0
4057	13.5	-118.1	69.0	130.2
4058	14.0	-49.5	38.5	81.0
4059	14.0	-163.7	61.5	282.7
4060	15.0	-76.8	77.0	208.1
4061	12.5	-106.1	65.0	212.2
4062	12.0	-143.9	72.5	282.4
Mean	13.2	-103.5	63.9	170.9
S.D.	1.3	41.8	13.6	105.6
N	7	7	6	7

E-24
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 3 - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5056	15.0	-83.2	NR	0.0
5057	16.0	-142.7	73.5	140.5
5058	12.5	-111.0	57.0	269.5
5059	16.0	-105.4	82.0	150.5
5060	15.0	-97.6	90.0	210.5
5061	31.0	-37.8	81.0	101.0
5091	13.0	-59.5	81.0	173.2
Mean	16.9	-91.0	77.4	149.3
S.D.	6.4	34.7	11.3	85.1
N	7	7	6	7

E-25
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 3 - Females

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1556	15.0	-188.1	93.5	327.6
1557	11.5	-54.4	85.0	224.6
1558	12.5	-110.2	70.5	227.1
1559	14.5	-101.5	66.0	208.5
1560	15.0	134.6	77.0	202.7
1561	NR	0.0	NR	0.0
1562	15.0	-27.8	117.5	68.8
Mean	13.9	-88.1	84.9	179.9
S.D.	1.8	65.0	18.8	109.6
N	6	7	6	7
Group II - 100 ppm				
2556	14.0	-107.3	94.5	278.1
2557	12.5	-145.9	64.5	233.2
2558	15.0	-131.7	66.0	342.4
2559	13.0	-91.5	68.5	76.6
2560	14.0	-115.4	70.0	208.5
2561	16.0	-238.8	70.0	268.5
2562	NR	0.0	NR	0.0
Mean	14.1	-118.7	72.3	201.0
S.D.	1.3	71.1	11.1	120.7
N	6	7	6	7

E-26
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 3 - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3557	17.5	-77.6	88.5	233.9
3558	15.5	-62.9	88.5	346.6
3559	17.0	-30.2	80.0	118.8
3560	19.0	-84.9	78.0	168.1
3562	16.5	-41.0	99.0	226.6
3591	13.5	-101.0	88.0	184.6
3592	13.5	-142.7	77.0	282.7
Mean	16.1	-77.2	85.6	223.0
S.D.	2.0	37.9	7.8	75.6
N	7	7	7	7
Group IV - 6000 ppm				
4556	18.5	-145.4	69.0	264.9
4557	NR ^a	NR ^a	NR ^a	NR ^a
4558	14.5	-121.0	69.0	188.5
4559	15.0	-67.1	77.5	195.1
4560	NR ^a	NR ^a	NR ^a	NR ^a
4561	15.5	-78.5	75.0	177.3
4591	14.0	-106.8	74.0	105.6
Mean	15.5	-103.8	72.9	186.3
S.D.	1.8	31.7	3.8	56.7
N	5	5	5	5

^aOcular examination indicated this animal was incapable of responding to stimulation with light due to a cataract and retinal degeneration.

E-27
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 3 - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5556	8.0	-95.9	82.5	192.7
5557	14.0	-130.7	75.5	253.4
5558	16.0	-132.9	76.0	212.2
5559	16.0	-45.6	67.5	107.6
5560	16.5	-45.1	74.0	99.5
5562	17.0	-162.4	86.0	287.3
5592	15.0	-56.1	84.5	181.7
Mean	14.6	-95.5	78.0	190.6
S.D.	3.1	47.8	6.6	69.6
N	7	7	7	7

E-28
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 6 - Males

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1057	14.0	-159.8	65.5	333.4
1058	12.5	-147.6	61.5	226.8
1059	14.5	-118.1	72.5	261.5
1061	13.0	-53.7	66.5	112.9
1062	14.0	-75.9	61.0	145.9
1091	15.0	-45.9	57.0	102.0
1092	13.0	-113.7	54.5	255.6
Mean	13.7	-102.1	62.6	205.4
S.D.	0.9	44.7	6.1	86.9
N	7	7	7	7
Group II - 50 ppm				
2056	23.0	-62.9	73.5	175.9
2058	12.5	-89.5	53.0	112.7
2059	13.5	-20.7	96.5	159.3
2060	15.5	-87.6	65.0	193.4
2061	11.5	-100.7	79.5	260.2
2062	14.5	-126.1	88.0	264.9
2092	15.5	-166.3	66.5	286.3
Mean	15.1	-93.4	74.6	207.5
S.D.	3.8	46.0	14.8	64.3
N	7	7	7	7

E-29

Appendix E (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary AdministrationIndividual Electroretinogram Values
Month 6 - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3056	13.0	-86.1	72.5	114.4
3057	14.0	-118.1	63.5	228.3
3058	13.0	-148.3	74.0	231.0
3059	19.0	-88.5	106.5	101.5
3060	11.0	-58.5	79.0	129.3
3061	15.5	-53.7	68.0	139.8
3062	13.5	-87.6	85.0	254.4
Mean	14.1	-91.5	78.4	171.2
S.D.	2.5	32.9	14.2	64.0
N	7	7	7	7
Group IV - 6000 ppm				
4056	12.0	-47.8	59.5	66.6
4057	13.0	-118.8	68.0	225.4
4058	10.0	-55.9	65.0	107.6
4059	14.5	-18.8	113.5	159.5
4060	12.0	-136.3	81.5	313.9
4061	17.0	-106.6	59.0	274.4
4062	13.5	-81.7	75.5	158.8
Mean	13.1	-80.8	74.6	186.6
S.D.	2.2	42.3	19.0	89.0
N	7	7	7	7

E-30

Appendix E (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary AdministrationIndividual Electroretinogram Values
Month 6 - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5056	13.0	-38.3	109.5	35.9
5057	11.0	-84.2	62.5	205.4
5058	12.0	-113.9	68.5	245.6
5059	10.5	-102.2	55.0	195.6
5060	17.0	-152.2	80.5	244.2
5061	10.5	-72.7	76.0	205.4
5091	14.0	-94.6	77.5	236.3
Mean	12.6	-94.0	75.6	195.5
S.D.	2.4	35.4	17.4	73.3
N	7	7	7	7

E-31
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 6 - Females

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1556	11.0	-104.9	68.0	189.0
1557	16.5	-111.2	86.5	194.4
1558	14.0	-91.7	90.0	216.1
1559	15.0	-116.1	84.0	252.9
1560	11.5	-71.7	81.5	185.4
1561	14.0	-39.8	57.0	58.5
1562	13.0	-55.1	77.0	162.4
Mean	13.6	-84.4	77.7	179.8
S.D.	1.9	29.5	11.6	60.6
N	7	7	7	7
Group II - 50 ppm				
2556	13.5	-124.4	78.0	180.7
2557	14.5	-197.8	72.0	381.7
2558	11.0	-111.0	55.0	251.0
2559	NR ^b	NR ^b	NR ^b	NR ^b
2560	11.5	-101.0	78.0	279.5
2561	13.5	-97.1	83.0	217.3
2562	NR ^c	NR ^c	NR ^c	NR ^c
Mean	12.8	-126.3	73.2	262.0
S.D.	1.5	41.4	10.9	76.4
N	5	5	5	5

^bOphthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to a complete cataract.

^cOphthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to a cataract and phthisis bulbi.

E-32
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 6 - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3557	9.0	-37.1	45.0	78.1
3558	12.0	-84.4	84.0	322.9
3559	11.5	-104.2	84.5	242.7
3560	12.5	-65.6	90.0	170.0
3562	14.0	-137.6	69.0	258.1
3591	12.5	-100.0	64.0	192.0
3593	13.5	-77.1	65.5	152.7
Mean	12.1	-86.6	71.7	202.4
S.D.	1.6	31.8	15.6	79.9
N	7	7	7	7
Group IV - 6000 ppm				
4556	12.5	-109.8	74.0	297.1
4557	NR ^a	NR ^a	NR ^a	NR ^a
4558	15.0	-112.7	73.0	147.8
4559	16.0	-56.1	71.5	127.8
4560	12.5	-52.4	88.5	130.2
4561	13.5	-32.4	81.0	137.1
4591	12.0	-97.6	67.5	306.1
Mean	13.6	-76.8	75.9	191.0
S.D.	1.6	34.1	7.6	86.0
N	6	6	6	6

^aOcular examination indicated this animal was incapable of responding to stimulation with light due to a cataract and retinal degeneration.

E-33

Appendix E (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 6 - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5556	14.5	-133.2	78.0	211.7
5557	13.0	-156.1	68.0	311.5
5558	12.5	-212.7	71.5	317.1
5559	14.0	-160.5	72.0	252.0
5560	13.5	-98.8	64.5	169.0
5562	10.0	-30.5	58.5	84.6
5592	10.0	-12.9	59.5	55.9
Mean	12.5	-115.0	67.4	200.3
S.D.	1.8	72.4	7.1	103.3
N	7	7	7	7

E-34

Appendix E (cont.)

A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary AdministrationIndividual Electroretinogram Values
Month 12 - Males

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1057	26.5	-96.3	68.0	157.1
1058	17.5	-138.5	70.5	221.7
1059	37.5	-69.5	83.0	134.2
1061	11.0	-41.7	69.5	76.1
1062	NR	0.0	NR	0.0
1091	17.0	-67.8	67.5	177.8
1092	18.5	-113.9	73.5	189.3
Mean	21.3	-75.3	72.0	136.6
S.D.	9.3	46.2	5.8	75.8
N	6	7	6	7
Group II - 50 ppm				
2056	33.5	-164.4	77.0	235.1
2058	17.5	-163.2	80.5	316.6
2059	32.0	-112.7	77.0	222.7
2060	22.0	-96.3	56.0	153.4
2061	NR	0.0	NR	0.0
2062	31.5	-60.2	81.5	139.3
2092	16.0	-86.3	70.0	178.5
Mean	25.4	-97.5	73.7	177.9
S.D.	7.9	57.8	9.5	98.5
N	6	7	6	7

E-35
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 12 - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3056	NR	0.0	NR	0.0
3057	23.0	-94.6	75.5	195.6
3058	23.0	-61.0	75.5	134.4
3059	18.0	-123.7	98.5	284.9
3060	13.0	-70.0	71.0	95.6
3061	NR	0.0	NR	0.0
3062	13.5	-90.2	80.0	224.6
Mean	18.1	-62.7	80.1	133.6
S.D.	4.9	47.3	10.8	109.7
N	5	7	5	7
Group IV - 6000 ppm				
4056	NR	0.0	NR	0.0
4057	31.0	-80.7	90.0	189.0
4058	28.5	-133.2	77.0	337.3
4059	28.5	-106.6	75.0	211.0
4060	27.5	-83.4	52.5	67.3
4061	37.0	-61.2	76.5	80.0
4062	NR	0.0	NR	0.0
Mean	30.5	-66.4	74.2	126.4
S.D.	3.9	50.7	13.5	124.6
N	5	7	5	7

E-36
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 12 - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5056	NR ^d	NR ^d	NR ^d	NR ^d
5057	NR	0.0	NR	0.0
5058	11.5	-143.2	83.0	294.9
5059	36.0	-85.4	77.5	110.2
5060	15.5	-76.6	82.0	96.3
5061	NR	0.0	NR	0.0
5091	12.0	-38.1	62.0	50.0
Mean	18.8	-57.2	76.1	91.9
S.D.	11.6	55.6	9.7	109.7
N	4	6	4	6

^dOphthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to a cataract.

E-37
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 12 - Females

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1556	27.5	-103.9	63.5	240.7
1557	13.5	-64.2	79.0	148.1
1558	20.0	-26.8	43.0	53.2
1559	16.0	-47.8	81.0	110.7
1560	29.0	-64.9	80.0	36.1
1561	9.0	-29.0	95.5	91.7
1562	12.0	-38.8	66.0	104.2
Mean	18.1	-53.6	72.6	112.1
S.D.	7.7	26.9	16.8	67.8
N	7	7	7	7
Group II - 50 ppm				
2556	15.5	-123.7	82.0	248.8
2557	28.5	-58.3	74.5	80.0
2558	10.5	-72.2	54.5	179.8
2559	NR ^b	NR ^b	NR ^b	NR ^b
2560	14.5	-78.1	60.0	122.2
2561	NR ^e	NR ^e	NR ^e	NR ^e
2562	NR ^c	NR ^c	NR ^c	NR ^c
Mean	17.3	-83.1	67.8	157.7
S.D.	7.8	28.3	12.7	73.2
N	4	4	4	4

^bOphthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to a complete cataract.

^cOphthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to a cataract and phthisis bulbi.

^eOphthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to phthisis bulbi.

E-38
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 12 - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3557	12.5	-31.5	51.5	62.2
3558	13.5	-84.9	74.0	194.4
3559	16.5	-72.4	84.5	95.9
3560	12.5	-105.4	67.5	226.3
3562	NR	0.0	NR	0.0
3591	8.0	-66.1	88.0	197.8
3593	33.0	-45.6	54.5	82.4
Mean	16.0	-58.0	70.0	122.7
S.D.	8.8	35.3	15.1	84.2
N	6	7	6	7
Group IV - 6000 ppm				
4556	15.5	-121.5	70.0	167.3
4557	NR ^a	NR ^a	NR ^a	NR ^a
4558	15.5	-65.9	82.0	112.7
4559	11.5	-144.9	83.5	302.7
4560	13.5	-78.8	69.0	184.6
4561	NR	0.0	NR	0.0
4591	NR ^b	NR ^b	NR ^b	NR ^b
Mean	14.0	-82.2	76.1	153.5
S.D.	1.9	55.9	7.7	110.3
N	4	5	4	5

^aOcular examination indicated this animal was incapable of responding to stimulation with light due to a cataract and retinal degeneration.

^bOcular examination indicated this animal was incapable of responding to stimulation with light due to phthisis bulbi.

E-39
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Month 12 - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5556	9.5	-77.3	68.0	164.2
5557	13.2	-62.9	57.5	105.9
5558	14.5	-119.0	83.5	183.2
5559	30.5	-62.7	62.5	119.5
5560	NR	0.0	NR	0.0
5562	NR	0.0	NR	0.0
5592	14.5	-13.7	55.0	52.0
Mean	16.5	-47.9	65.3	89.3
S.D.	8.1	44.9	11.3	74.1
N	5	7	5	7

E-40
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Termination - Males

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1010	27.0	-42.7	105.5	121.7
1012	22.0	-58.1	78.5	152.0
1015	NR ^e	NR ^e	NR ^e	NR ^e
1024	12.0	-58.1	72.0	156.8
1043	NR	0.0	96.1	116.0
Mean	20.3	-39.7	88.0	136.6
S.D.	7.6	27.5	15.5	20.7
N	3	4	4	4
Group II - 50 ppm				
2038	NR ^f	NR ^f	NR ^f	NR ^f
2044	40.5	-38.1	94.5	146.3
2045	45.0	-51.2	76.5	57.8
2049	41.0	-79.3	59.0	83.7
2054	36.0	-50.5	79.0	63.7
Mean	40.6	-54.8	77.3	87.9
S.D.	3.7	17.4	14.5	40.5
N	4	4	4	4

^eOcular examination indicated this animal was incapable of responding to stimulation with light due to a cataract.

^fOcular examination indicated this animal was incapable of responding to stimulation with light due to glaucoma and a complete cataract.

E-41
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Termination - Males (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3018	NR	0.0	NR	0.0
3023	32.5	-63.7	78.5	97.6
3028	NR ^g	NR ^g	NR ^g	NR ^g
3035	NR	0.0	NR	0.0
3041	NR	0.0	NR	0.0
Mean	32.5	-15.9	78.5	24.4
S.D.	0.0	31.9	0.0	48.8
N	1	4	1	4
Group IV - 6000 ppm				
4013	NR ^h	NR ^h	NR ^h	NR ^h
4020	48.5	-28.1	91.5	62.9
4029	33.0	-41.7	71.0	71.0
4039	13.5	-45.6	125.5	111.5
4050	12.0	-36.1	115.0	179.5
Mean	26.8	-37.9	100.8	106.2
S.D.	17.4	7.6	24.4	53.3
N	4	4	4	4

^gOcular examination indicated this animal was incapable of responding to stimulation with light due to an extensive cataract.

^hOcular examination indicated this animal was incapable of responding to stimulation with light due to a complete cataract and unilateral retinopathy.

E-42
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Termination - Females

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group I - 0 ppm				
1502	14.5	-49.5	86.0	176.8
1503	10.5	-49.8	66.0	89.3
1517	14.5	-61.2	61.5	112.2
1529	32.5	-79.8	47.5	85.9
1554	37.0	-71.2	61.5	123.4
Mean	21.8	-62.3	64.5	117.5
S.D.	12.0	13.3	13.9	36.7
N	5	5	5	5
Group II - 50 ppm				
2501	NR	0.0	NR	0.0
2510	36.0	-79.5	79.5	151.7
2513	NR ^b	NR ^b	NR ^b	NR ^b
2524	NR	0.0	NR	0.0
2536	NR	0.0	NR	0.0
Mean	36.0	19.9	79.5	37.9
S.D.	0.0	39.8	0.0	75.9
N	1	4	1	4

^bOphthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to a complete cataract.

E-43
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Termination - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group III - 500 ppm				
3504	35.5	-9.5	105.5	152.0
3505	NR	0.0	NR	0.0
3511	NR	0.0	NR	0.0
3539	NR	0.0	NR	0.0
3542	NR	0.0	NR	0.0
Mean	35.5	-1.9	105.5	30.4
S.D.	0.0	4.2	0.0	68.0
N	1	5	1	5
Group IV - 6000 ppm				
4504	NR ⁹	0.0	NR ⁹	0.0
4512	NR	0.0	NR	0.0
4517	15.0	-30.0	89.5	107.8
4519	30.5	-89.0	47.5	154.2
4554	34.5	-35.1	89.0	80.7
Mean	26.7	-38.5	75.3	85.7
S.D.	10.3	37.0	24.1	64.7
N	3	5	3	5

⁹Ophthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to an extensive cataract.

E-44
Appendix E (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Individual Electroretinogram Values
Termination - Females (cont.)

Animal Number	A LAT (msec)	A AMP (uV)	B LAT (msec)	B AMP (uV)
Group V - 12000 ppm				
5512	15.0	-41.7	88.0	119.3
5514	NR	0.0	NR	0.0
5516	NR	0.0	NR	0.0
5525	31.0	-59.5	74.0	78.5
5543	NR ^b	NR ^b	NR ^b	NR ^b
Mean	23.0	-25.3	81.0	49.5
S.D.	11.3	30.1	9.9	59.5
N	2	4	2	4

^bOphthalmoscopic examination revealed this animal was incapable of responding to stimulation with light due to a complete cataract.

F-1
Appendix F
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

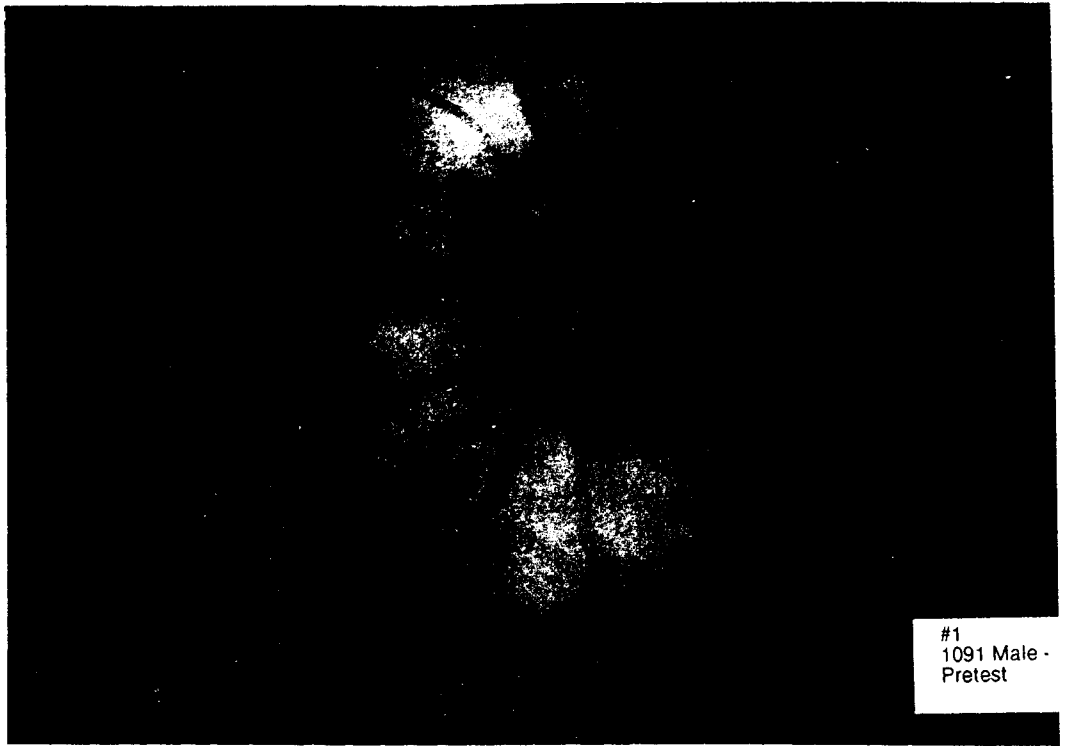
Fundic Photographs							
Slide Number	Animal Number	Group	Dose Level (ppm)	Sex	Eye	Interval	Comments
1	1091	I	0	M	L	Pretest	Normal
2	1091	I	0	M	R	Pretest	Poor quality, light not focused
3	1062	I	0	M	L	Pretest	Normal
4	1062	I	0	M	R	Pretest	Normal
5	1091	I	0	M	L	Month 12	Normal
6	1091	I	0	M	R	Month 12	Normal
7	1062	I	0	M	L	Month 12	Normal
8	1062	I	0	M	R	Month 12	Normal
9	1562	I	0	F	L	Pretest	Normal
10	1562	I	0	F	R	Pretest	Normal
11	1560	I	0	F	L	Pretest	Normal
12	1560	I	0	F	R	Pretest	Normal
13	1562	I	0	F	L	Month 12	Normal
14	1562	I	0	F	R	Month 12	Normal
15	1560	I	0	F	R	Month 12	Normal
16	1560	I	0	F	L	Month 12	Normal
17	5058	V	12000	M	L	Pretest	Normal
18	5058	V	12000	M	R	Pretest	Normal
19	5091	V	12000	M	L	Pretest	Normal
20	5091	V	12000	M	R	Pretest	Normal
21	5058	V	12000	M	L	Month 12	Normal
22	5058	V	12000	M	R	Month 12	Normal
23	5091	V	12000	M	L	Month 12	Normal
24	5091	V	12000	M	R	Month 12	Retinal Pallor, which may be associated with slightly excessive restraint.
25	5556	V	12000	F	L	Pretest	Normal
26	5556	V	12000	F	R	Pretest	Normal
27	5560	V	12000	F	L	Pretest	Normal
28	5560	V	12000	F	R	Pretest	Normal
29	5556	V	12000	F	L	Month 12	Normal
30	5556	V	12000	F	R	Month 12	Normal
31	5560	V	12000	F	L	Month 12	Normal
32	5560	V	12000	F	R	Month 12	Normal

F-2
Appendix F (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Fundic Photographs							
Slide Number	Animal Number	Group	Dose Level (ppm)	Sex	Eye	Interval	Comments
33	1010	I	0	M	R	TERM	Normal
34	1010	I	0	M	L	TERM	Normal
35	4013	IV	6000	M	R	TERM	External photograph fundus not visible.
36	4013	IV	6000	M	L	TERM	Portion of retina obscured.
37	1012	I	0	M	R	TERM	Normal
38	1012	I	0	M	L	TERM	Normal
39	4020	IV	6000	M	R	TERM	Normal
40	4020	IV	6000	M	L	TERM	Normal
41	1015	I	0	M	R	TERM	Normal, slightly out of focus.
42	1015	I	0	M	L	TERM	Normal
43	4029	IV	6000	M	R	TERM	Normal
44	4029	IV	6000	M	L	TERM	Normal
45	1024	I	0	M	R	TERM	Normal
46	1024	I	0	M	L	TERM	Normal
47	4039	IV	6000	M	R	TERM	Normal
48	4039	IV	6000	M	L	TERM	External photograph, fundus not visible.
49	1043	I	0	M	R	TERM	Normal
50	1043	I	0	M	L	TERM	Normal
51	4050	IV	6000	M	R	TERM	Normal
52	4050	IV	6000	M	L	TERM	Normal
53	1502	I	0	F	R	TERM	Normal
54	1502	I	0	F	L	TERM	Normal
55	5512	V	12000	F	R	TERM	Normal, slightly out of focus.
56	5512	V	12000	F	L	TERM	Normal
57	1503	I	0	F	R	TERM	Normal
58	1503	I	0	F	L	TERM	Normal
59	5514	V	12000	F	R	TERM	Normal
60	5514	V	12000	F	L	TERM	Normal
61	1517	I	0	F	R	TERM	Normal
62	1517	I	0	F	L	TERM	Normal, out of focus.
63	5516	V	12000	F	R	TERM	Normal
64	5516	V	12000	F	L	TERM	Normal

F-3
Appendix F (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

Fundic Photographs							
Slide Number	Animal Number	Group	Dose Level (ppm)	Sex	Eye	Interval	Comments
65	1529	I	0	F	R	TERM	Normal
66	5525	V	12000	F	R	TERM	Normal
67	5525	V	12000	F	L	TERM	Normal
68	1554	I	0	F	R	TERM	Normal, slightly out of focus.
69	1554	I	0	F	L	TERM	Normal
70	5543	V	12000	F	R	TERM	Retina appears normal; portion unclear because of anterior disease.
71	5543	V	12000	F	L	TERM	External photograph, fundus not visible.



#1
1091 Male -
Pretest



#2
1091 Male - R
Pretest



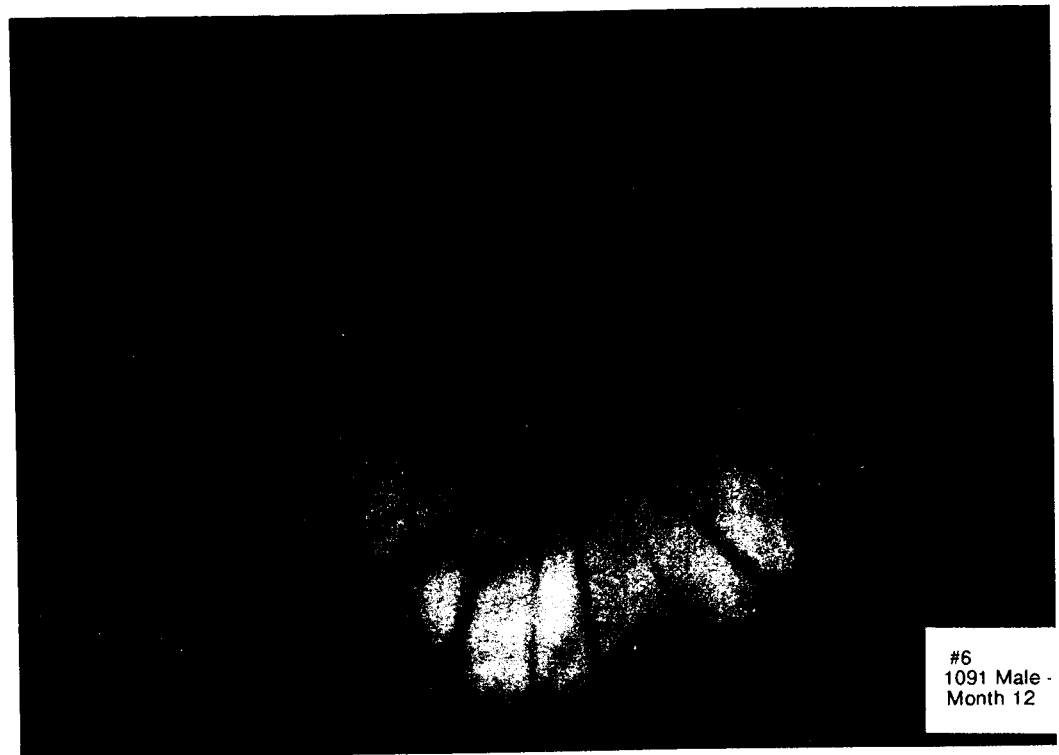
#3
1062 Male - L
Pretest



#4
1062 Male - R
Pretest



#5
1091 Male -
Month 12



#6
1091 Male -
Month 12



#7
1062 Male - L
Month 12



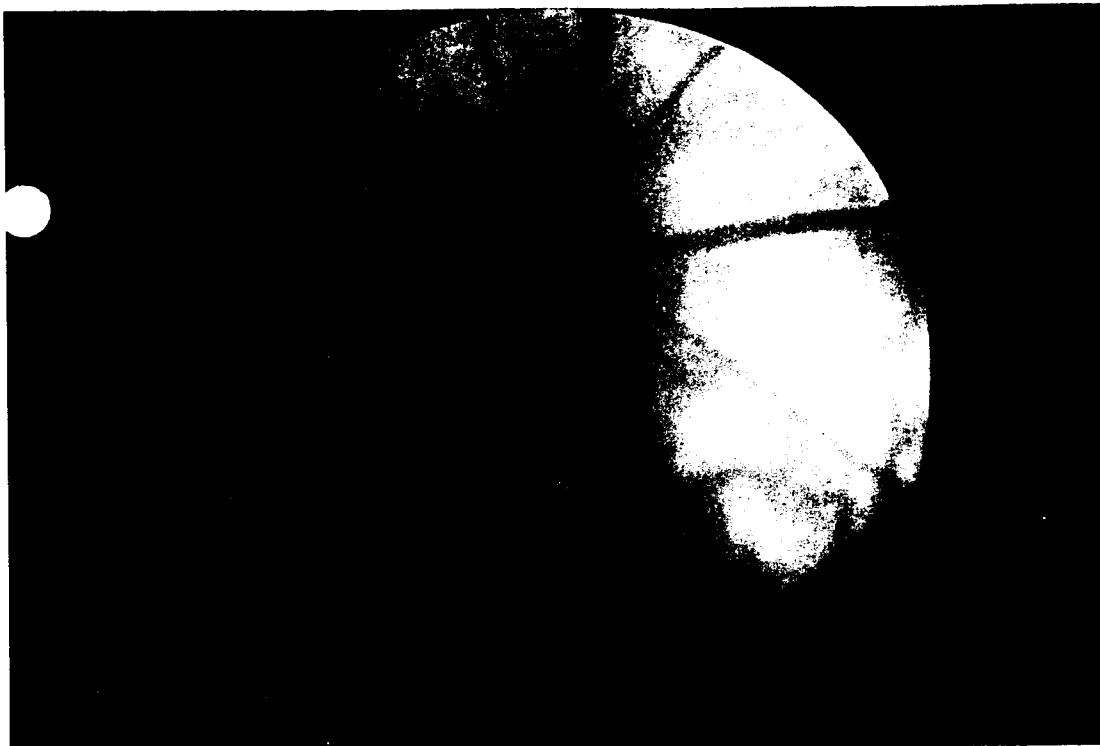
#8
1062 Male - R
Month 12



#9
1562 Female
Pretest



#10
1562 Female - I
Pretest



#11
1560 Female - L
Pretest



#12
1560 Female - R
Pretest



#13
1562 Female
Month 12



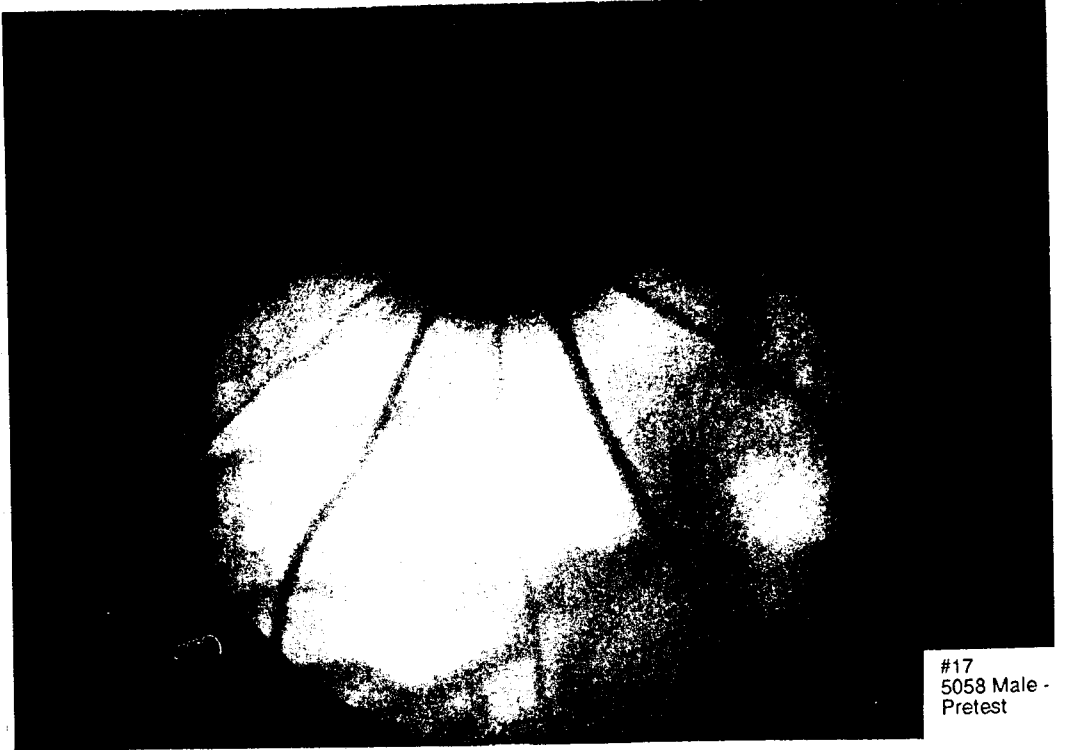
#14
1562 Female -
Month 12



#15
1560 Female - R
Month 12



#16
1560 Female - L
Month 12



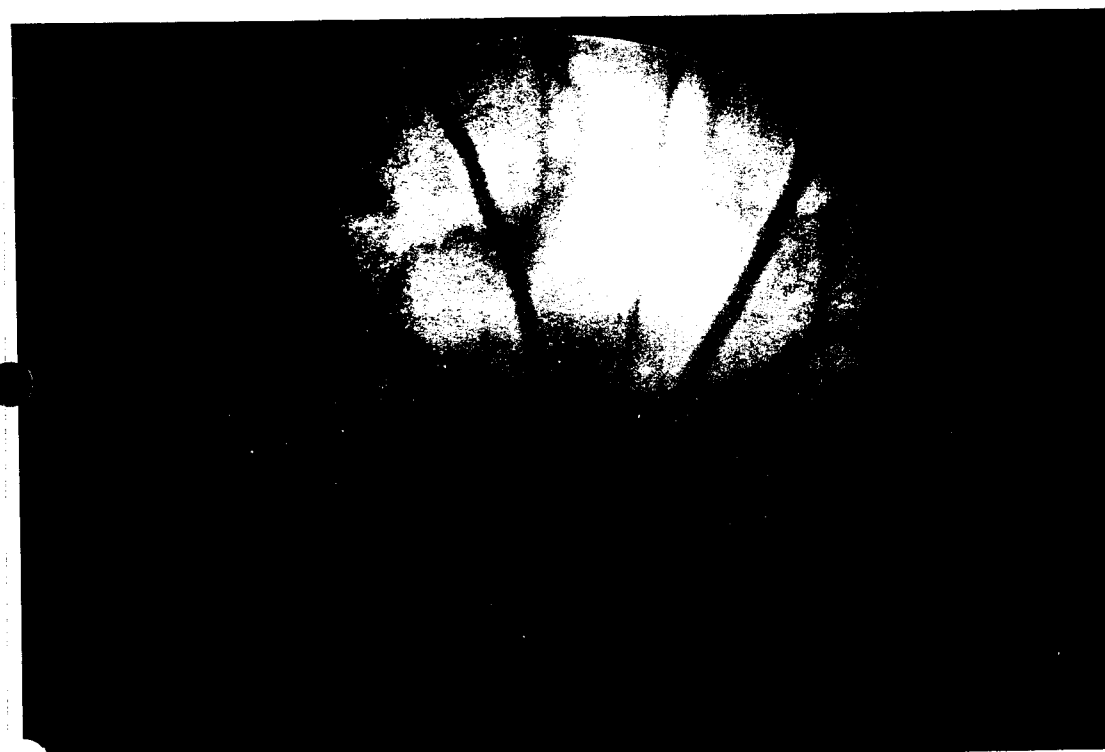
#17
5058 Male -
Pretest



#18
5058 Male - R
Pretest



#19
5091 Male - L
Pretest



#20
5091 Male - R
Pretest



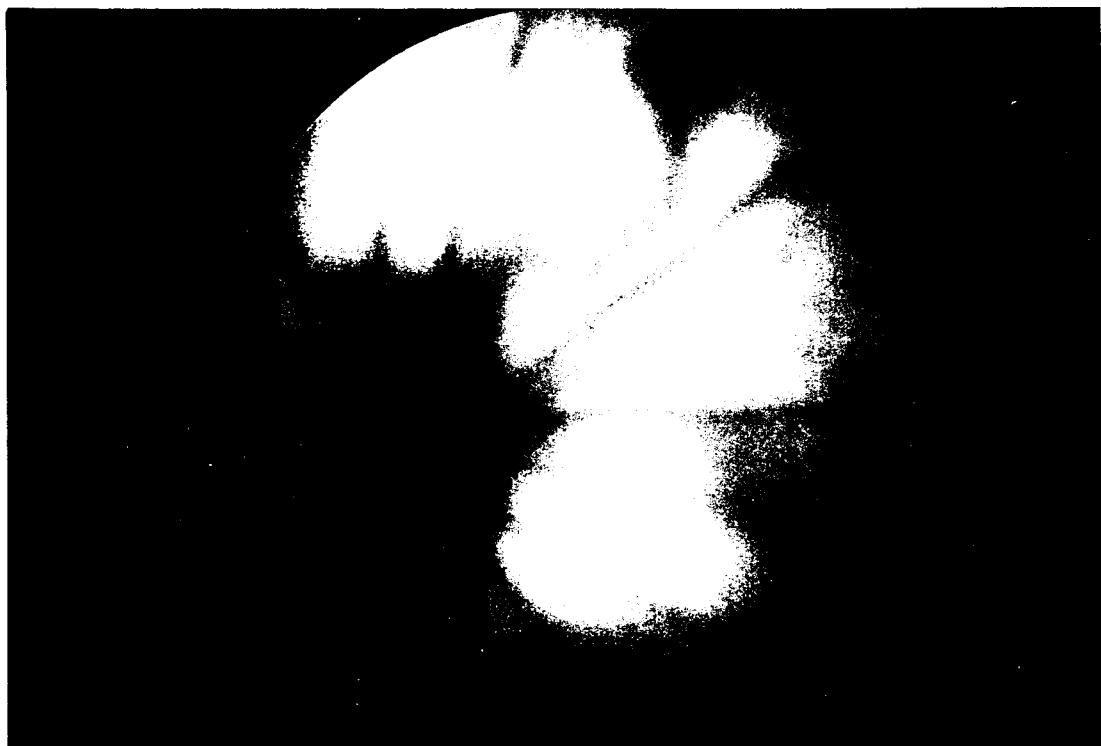
#21
5058 Male - I
Month 12



#22
5058 Male - F
Month 12



#23
5091 Male - L
Month 12



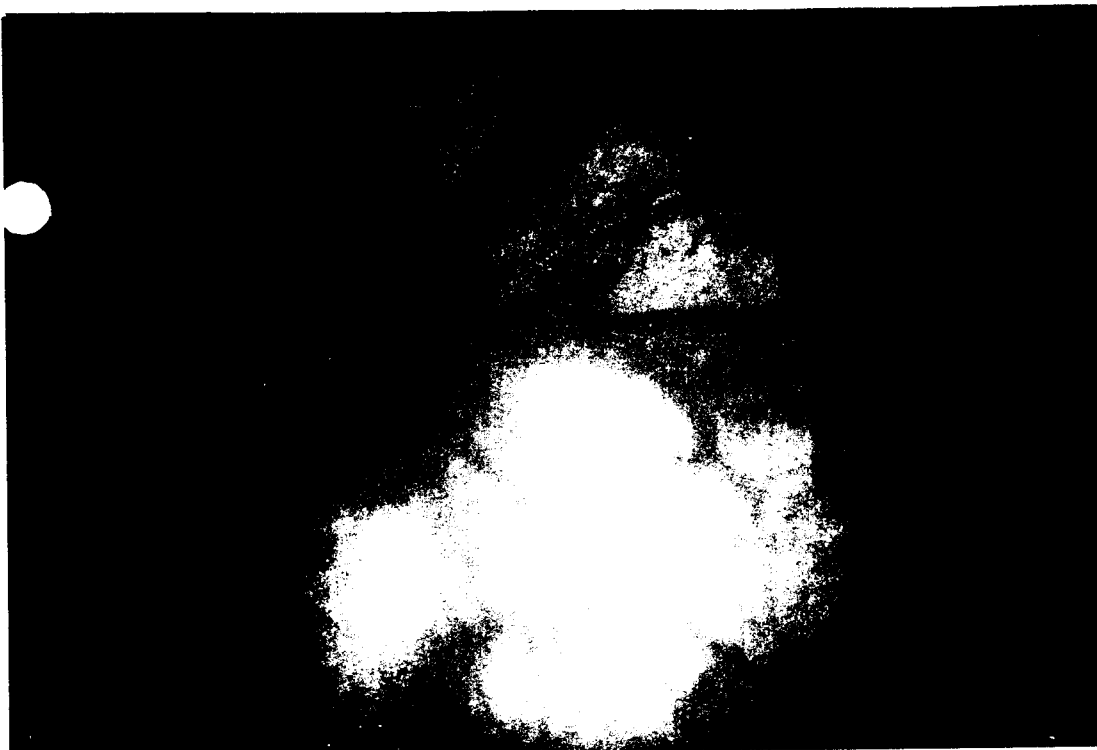
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5091 Male - R
Month 12



#25
5556 Female - L
Pretest



#26
5556 Female -
Pretest



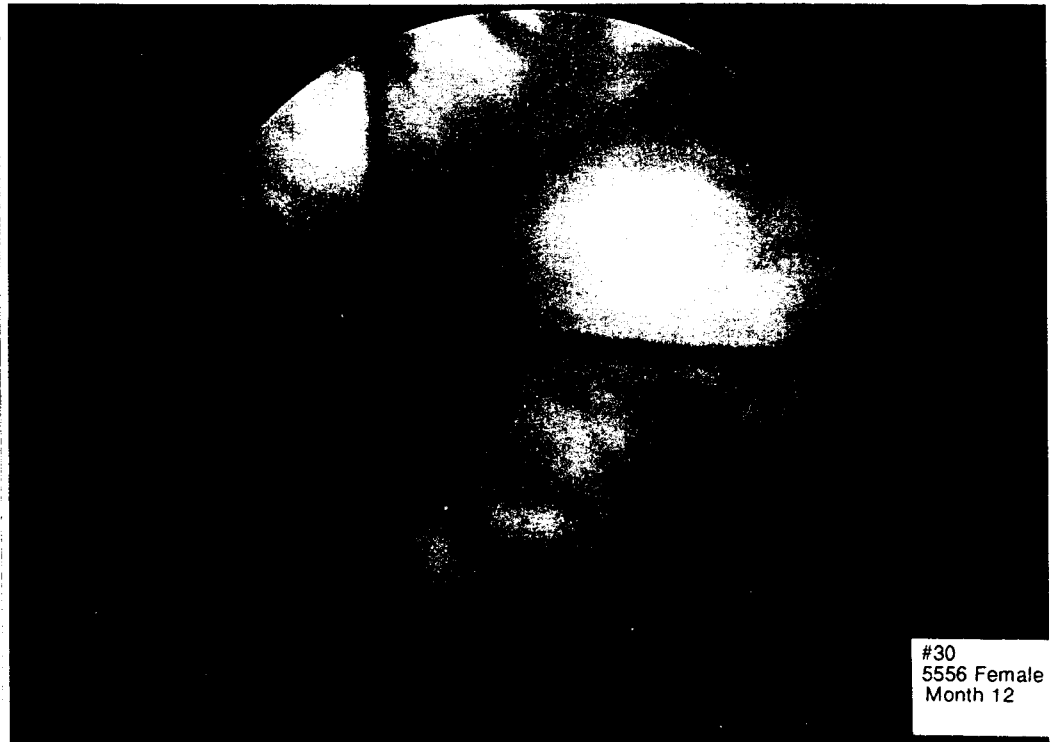
#27
5560 Female - L
Pretest



#28
5560 Female - R
Pretest



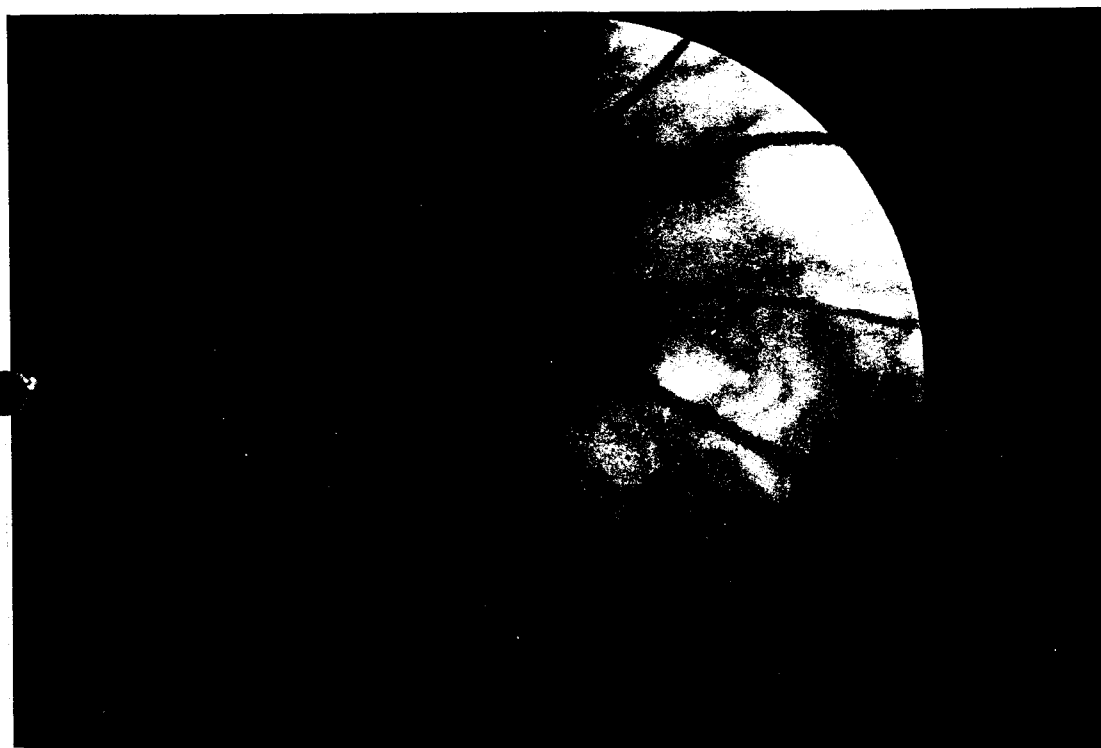
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5556 Female -
Month 12



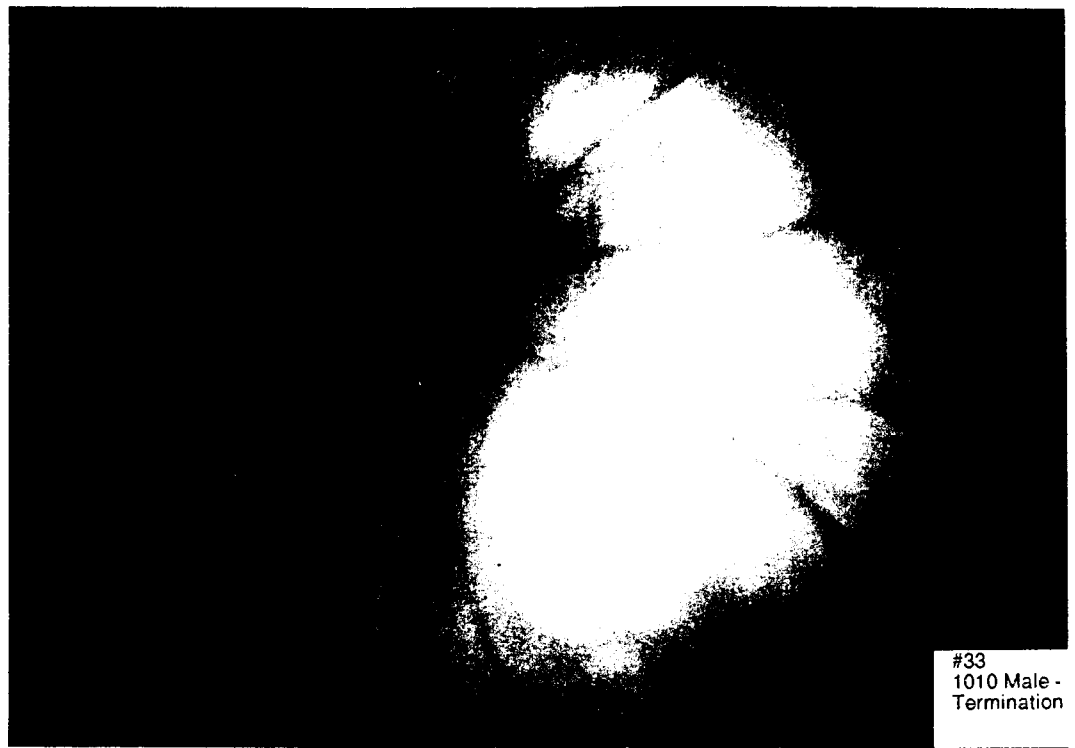
#30
5556 Female
Month 12



#31
5560 Female - L
Month 12



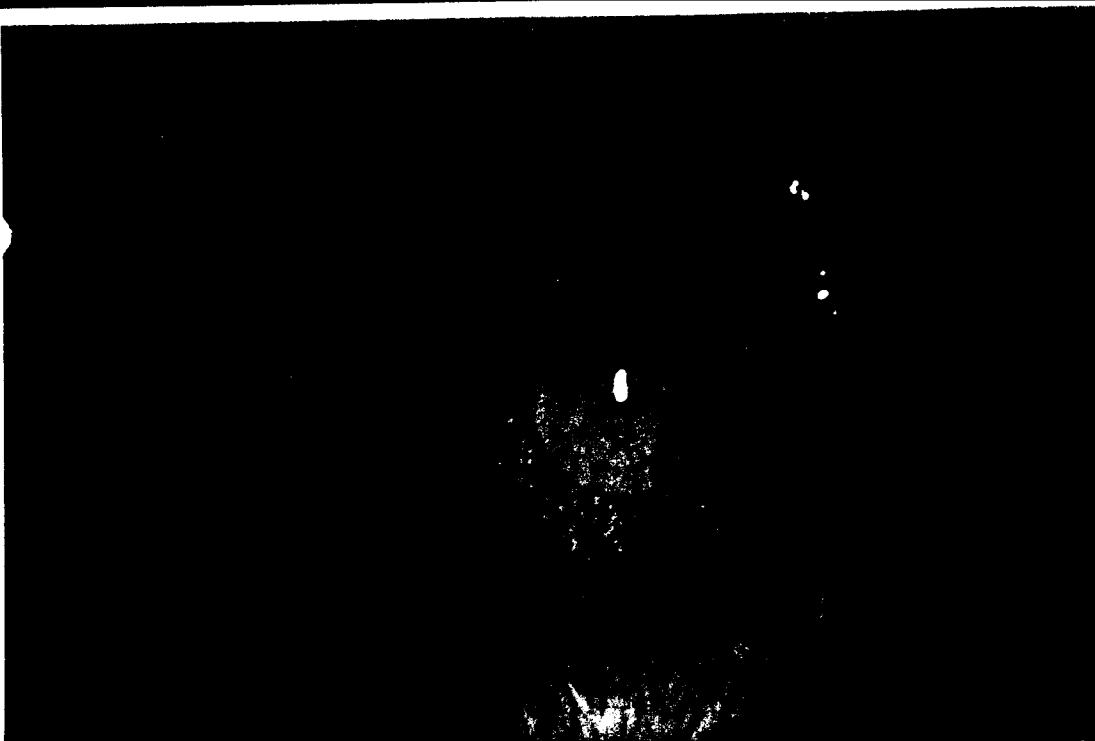
#32
5560 Female - R
Month 12



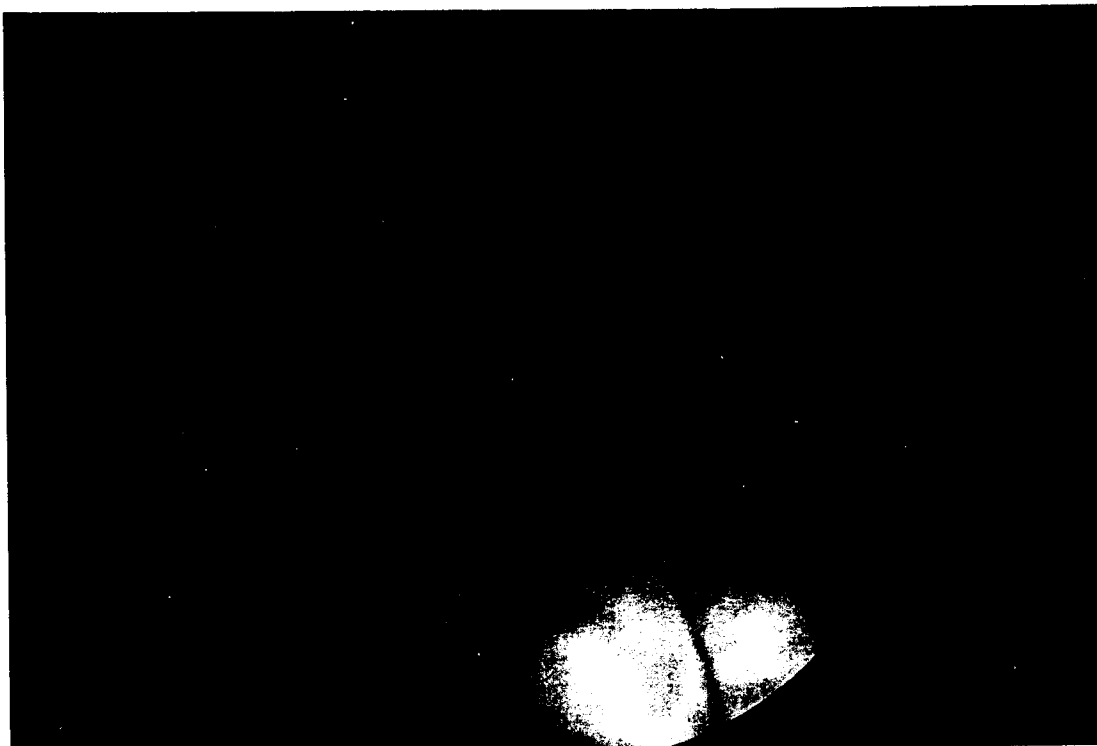
#33
1010 Male -
Termination



#34
1010 Male -
Termination



#35
4013 Male - R
Termination



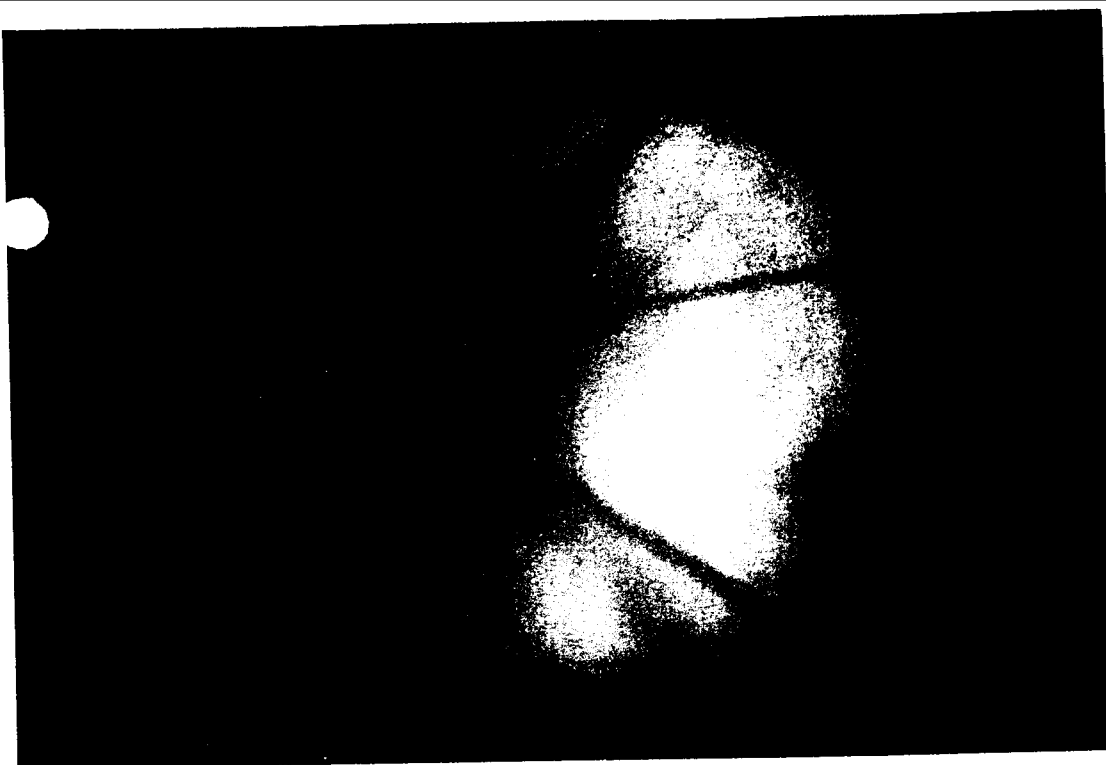
#36
4013 Male - L
Termination



#37
1012 Male - I
Termination



#38
1012 Male -
Termination



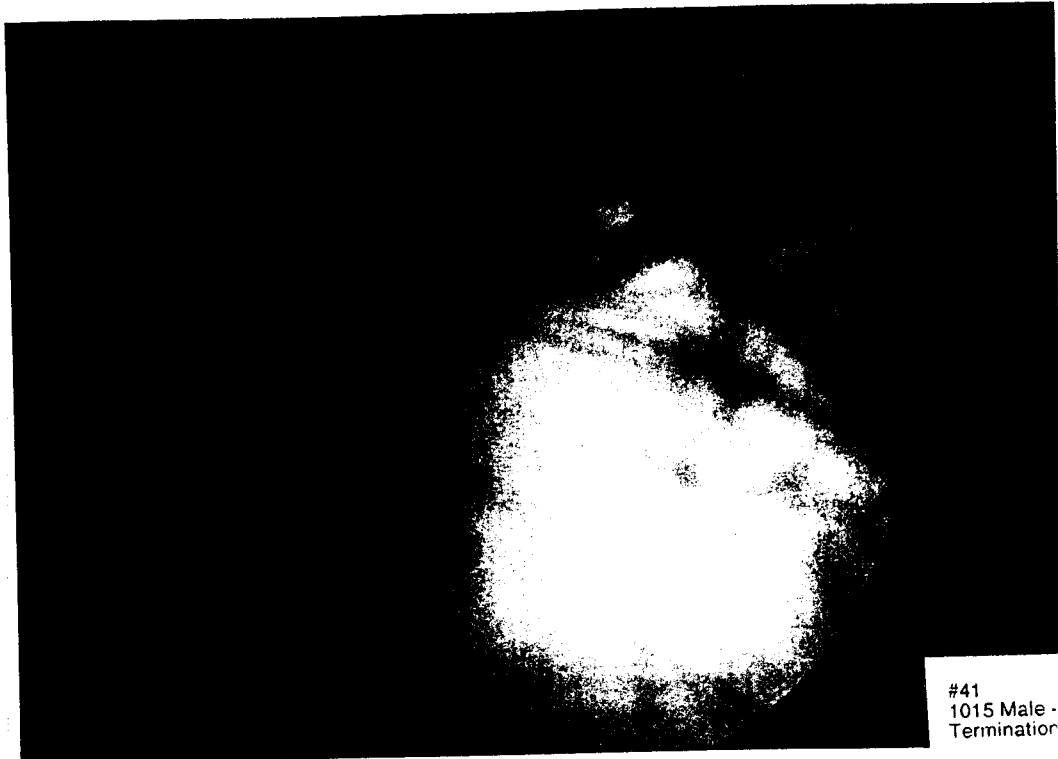
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4020 Male - R
Termination



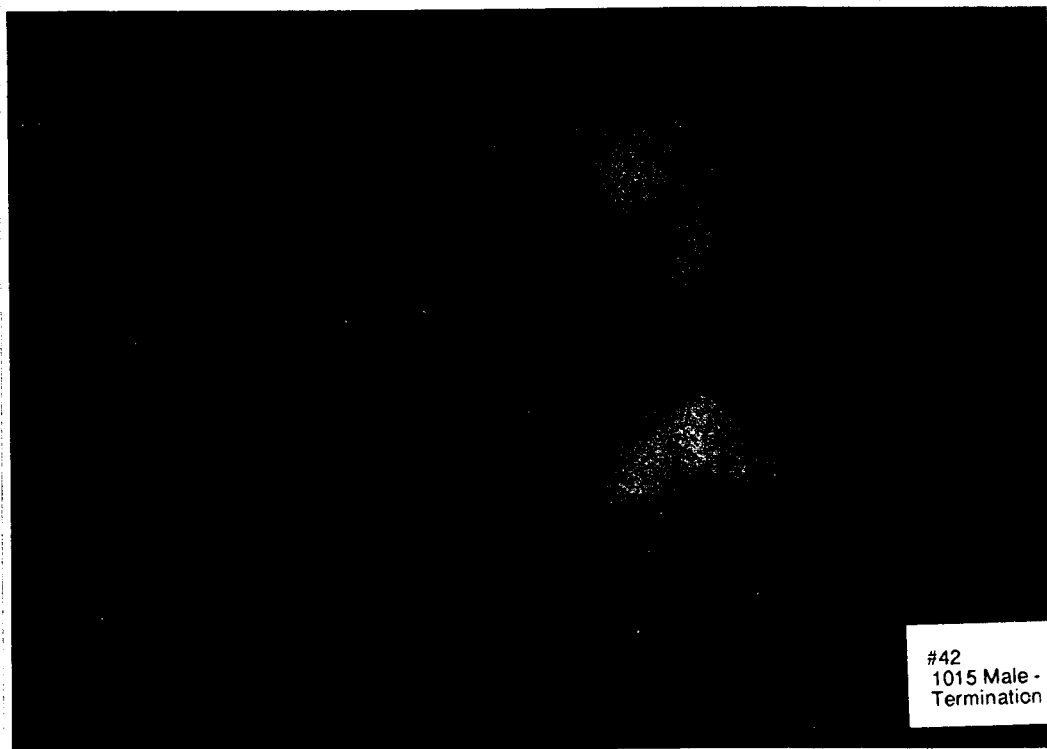
#40
4020 Male - L
Termination

F-23
Appendix F (cont.)
A 24-Month Oral Toxicity/Oncogenicity Study
of Malathion in the Rat via Dietary Administration

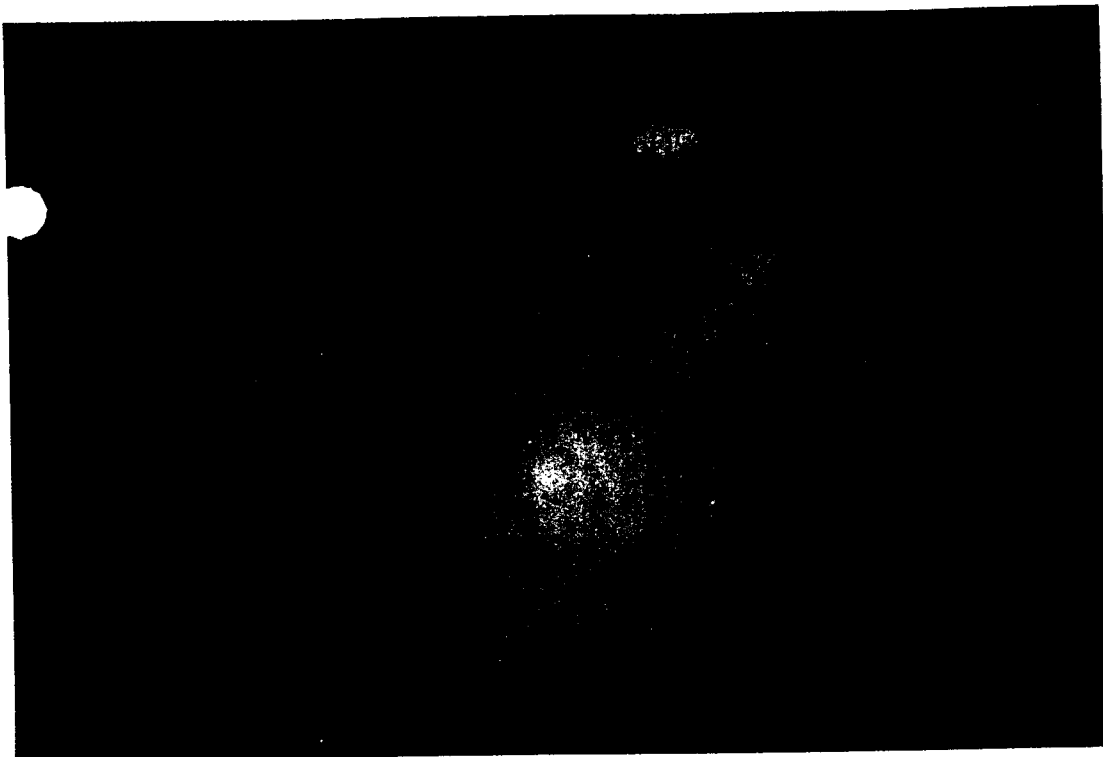
379
90-3641



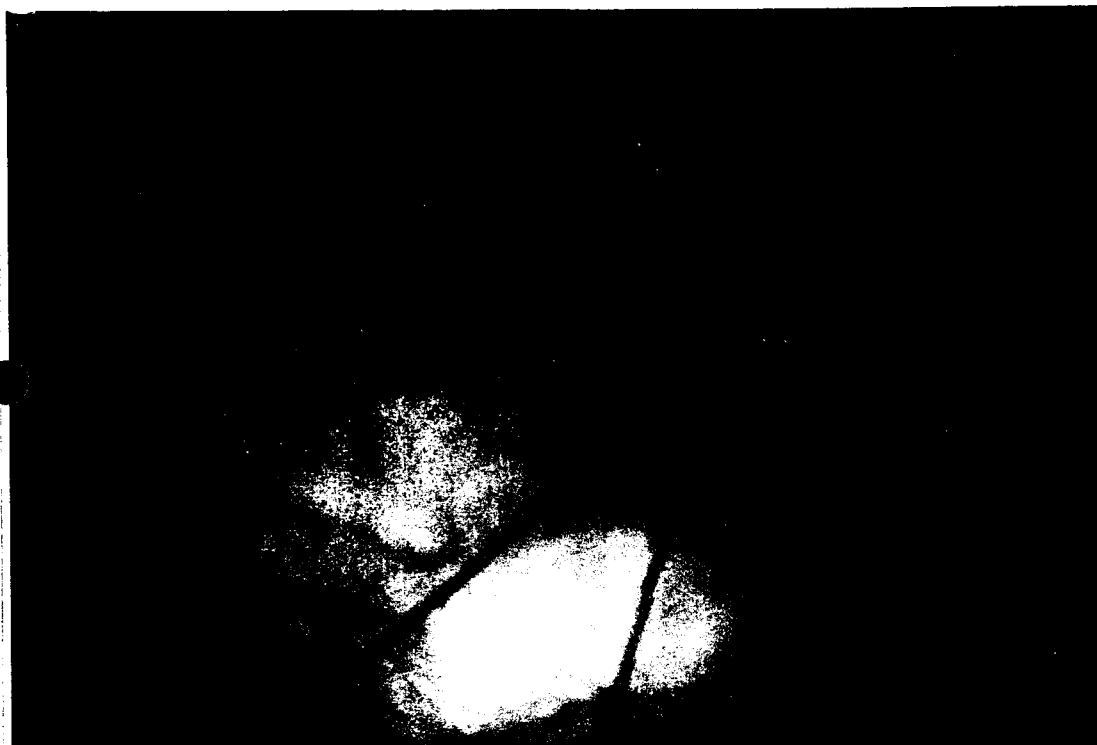
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1015 Male -
Termination



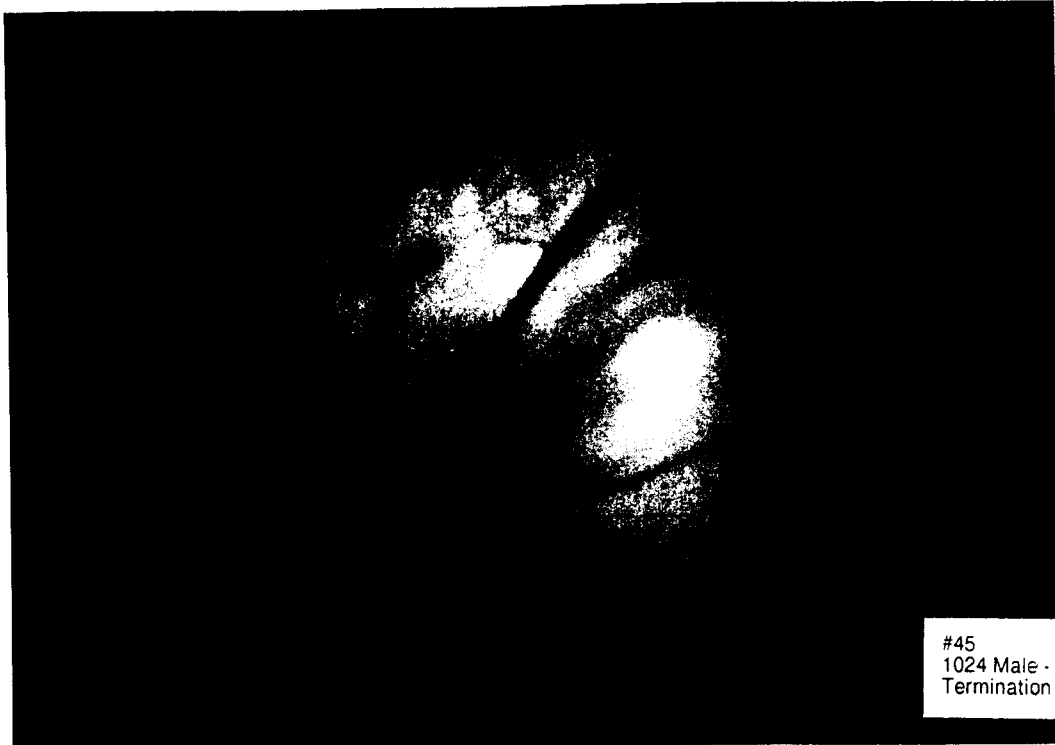
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1015 Male -
Termination



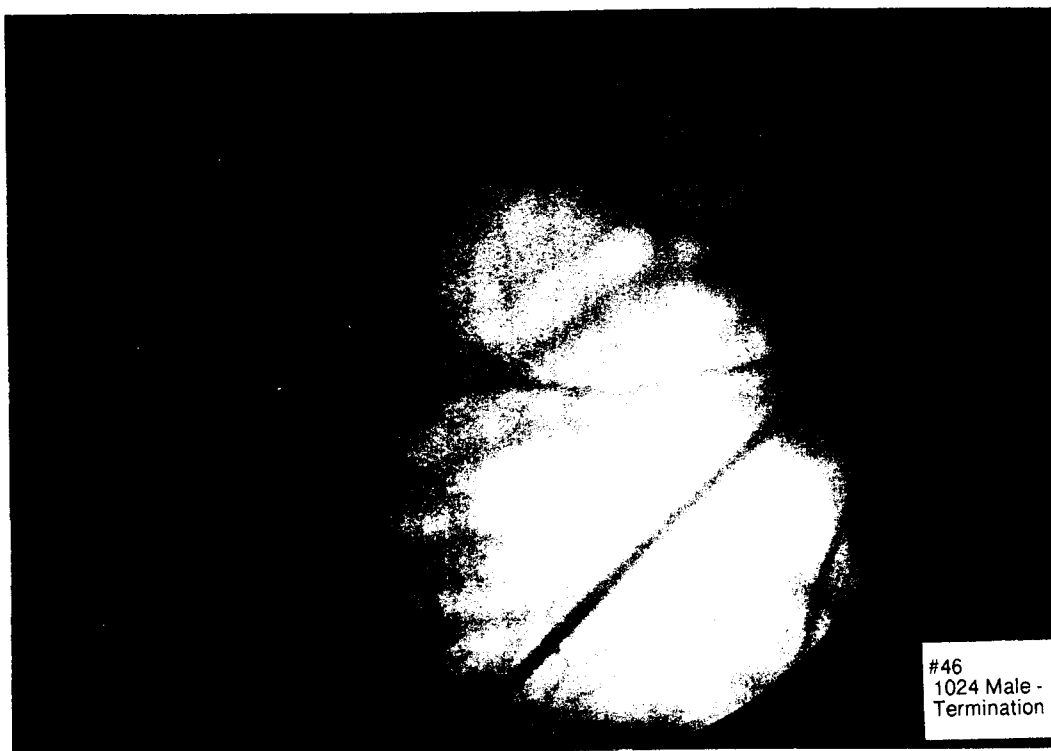
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4029 Male - R
Termination



#44
4029 Male - L
Termination



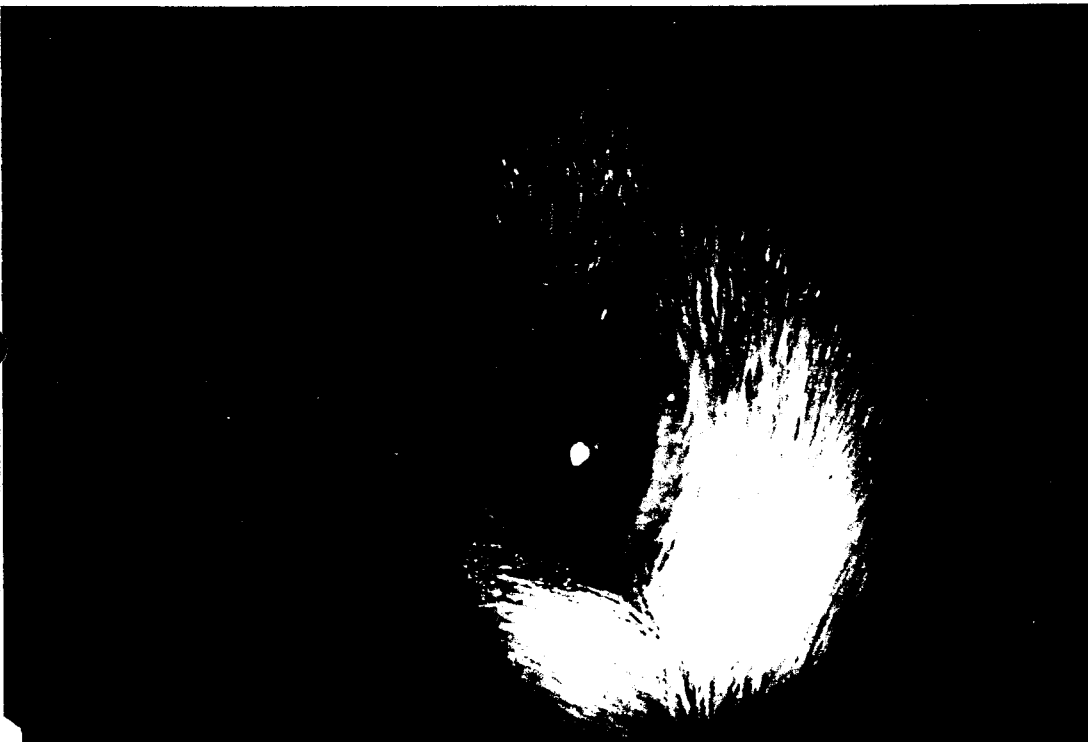
#45
1024 Male - F
Termination



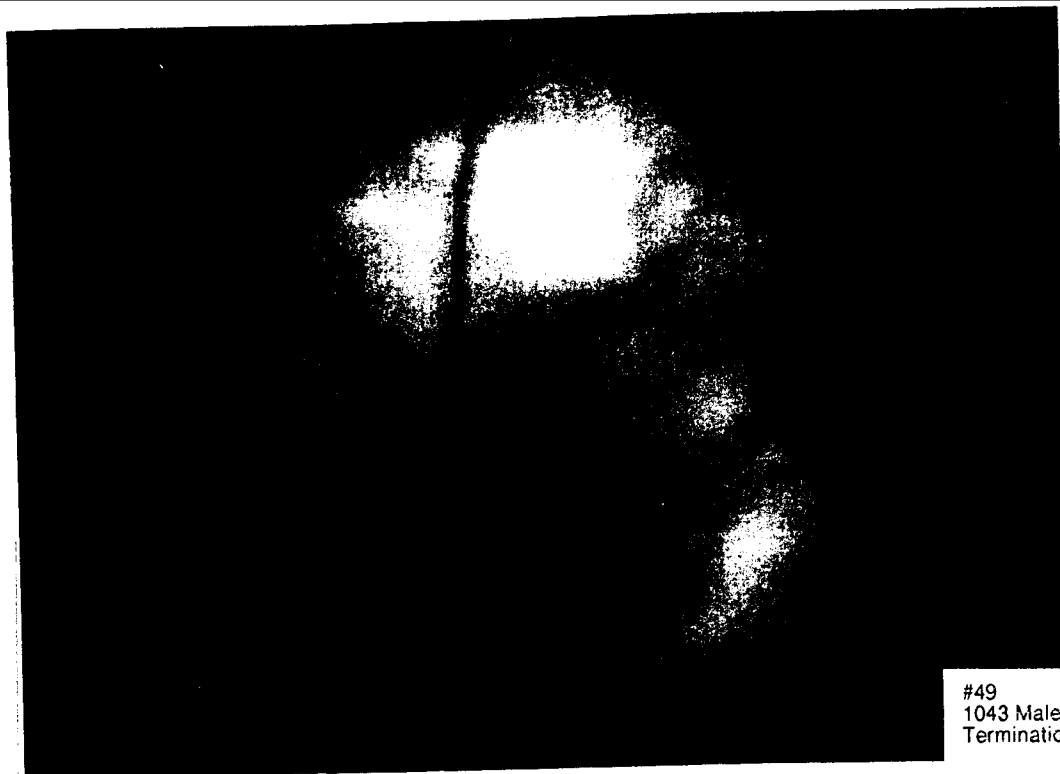
#46
1024 Male - L
Termination



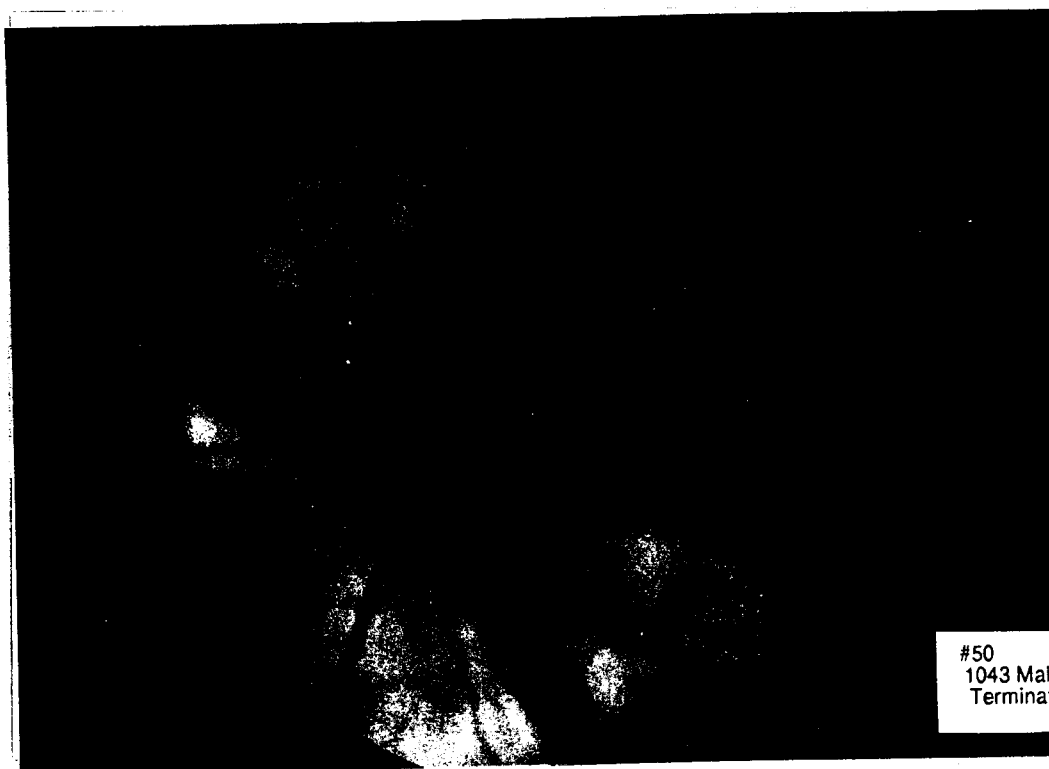
#47
4039 Male - R
Termination



#48
4039 Male - L
Termination



#49
1043 Male
Termination



#50
1043 Male
Termination



#51
4050 Male - R
Termination



#52
4050 Male - L
Termination



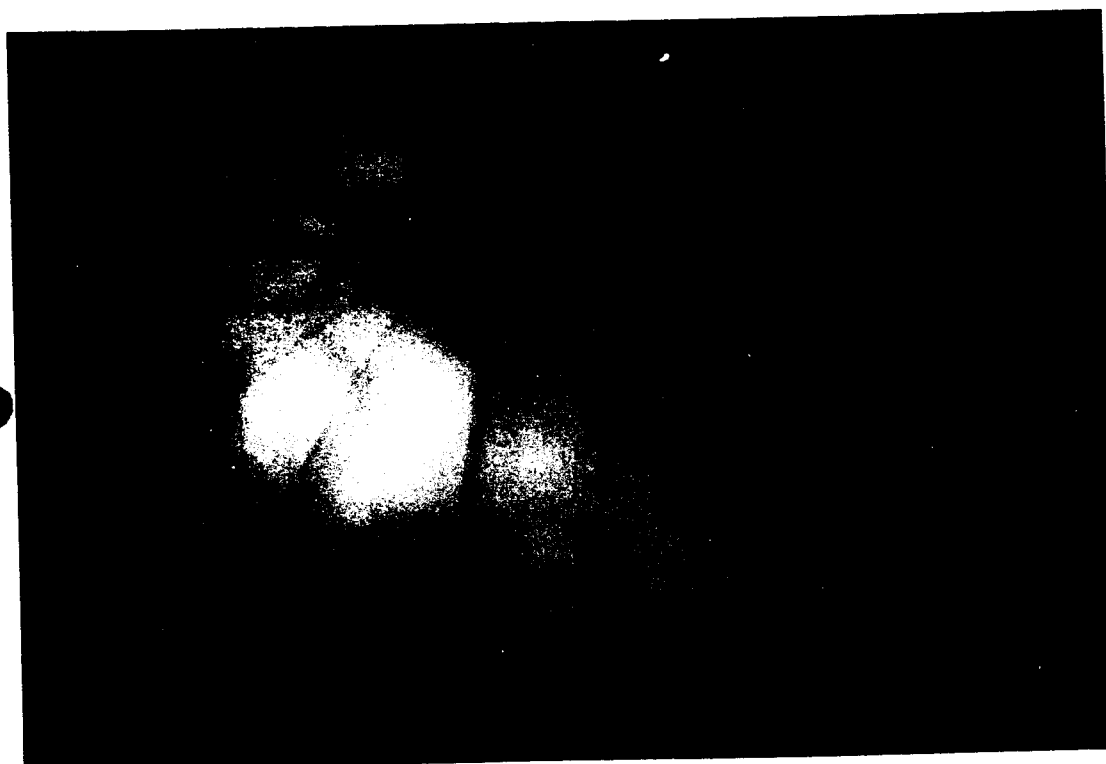
#53
1502 Female
Termination



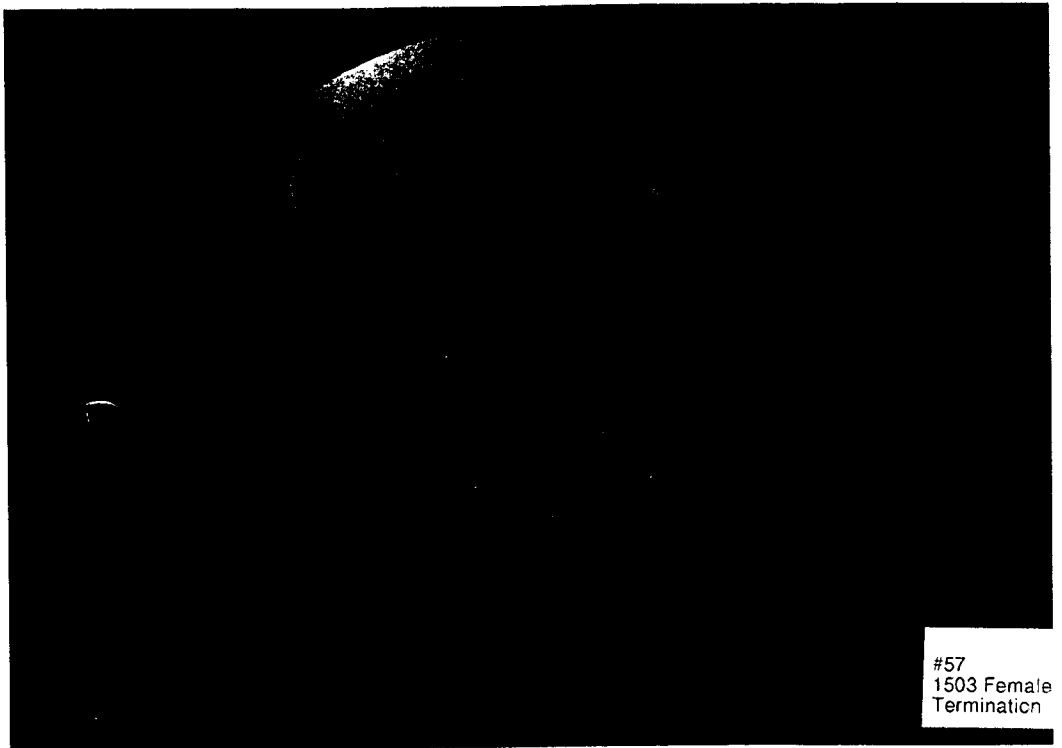
#54
1502 Female
Termination



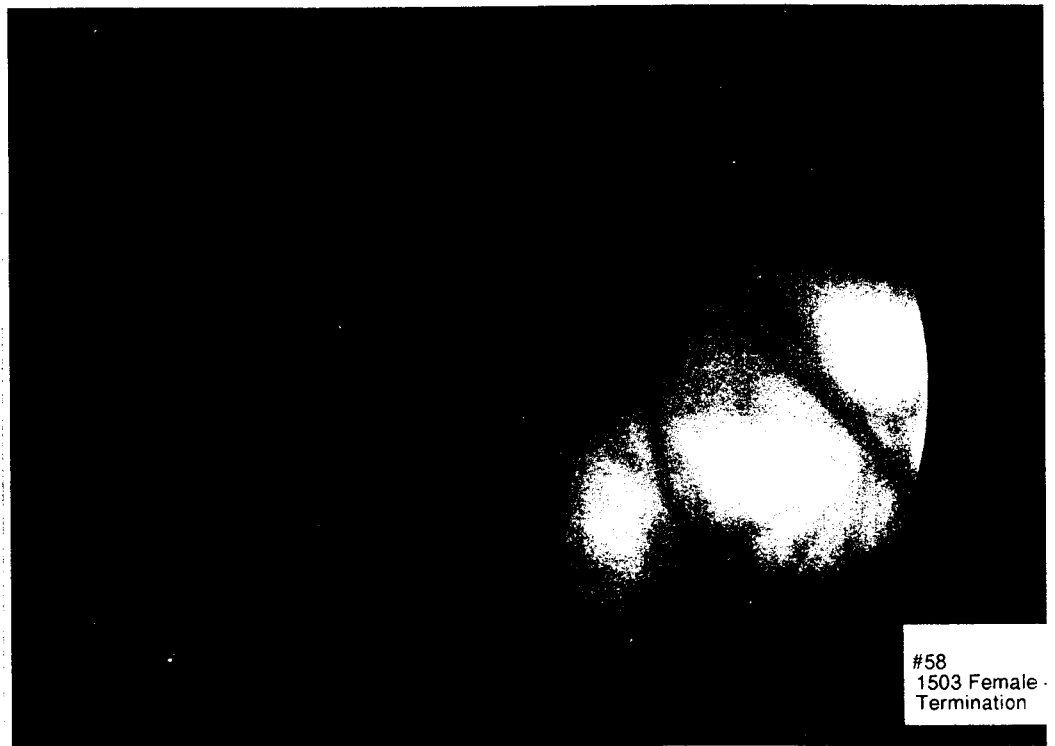
#55
5512 Female - R
Termination



#56
5512 Female - L
Termination



#57
1503 Female
Termination



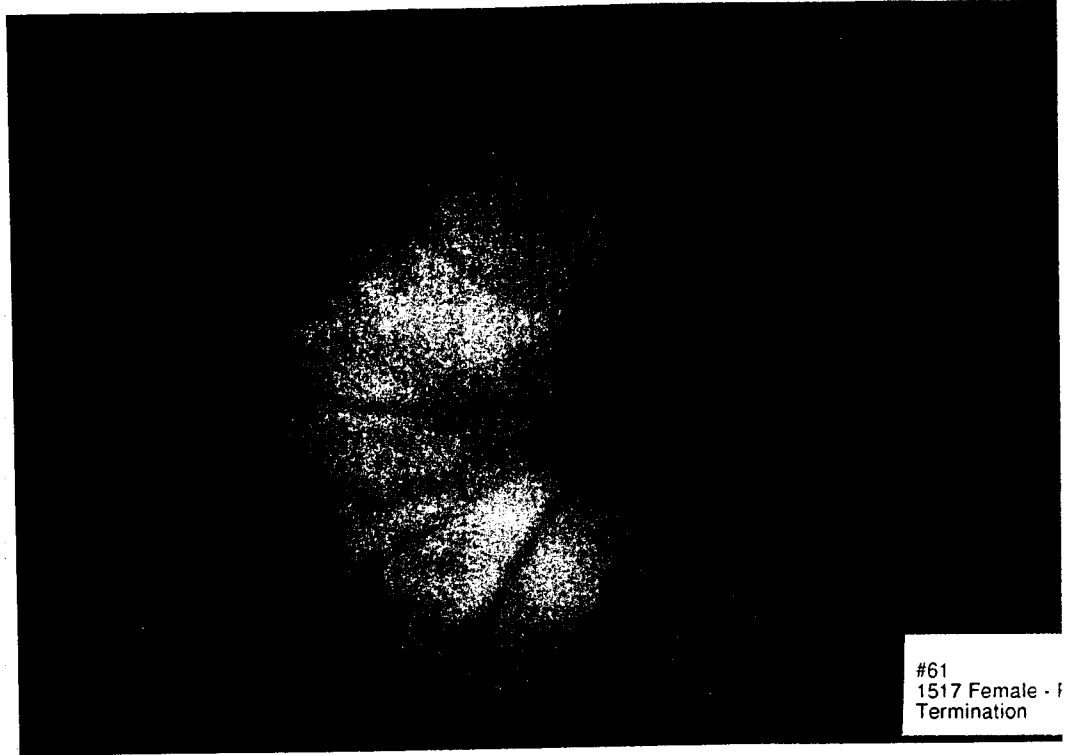
#58
1503 Female
Termination



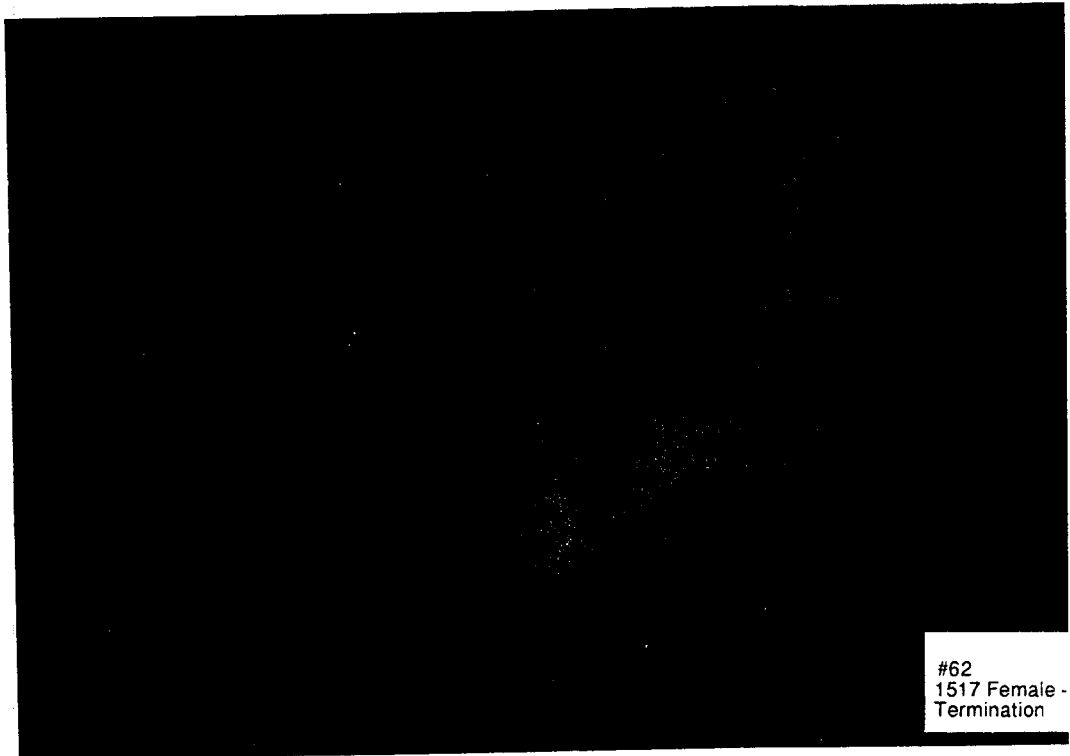
#59
5514 Female - R
Termination



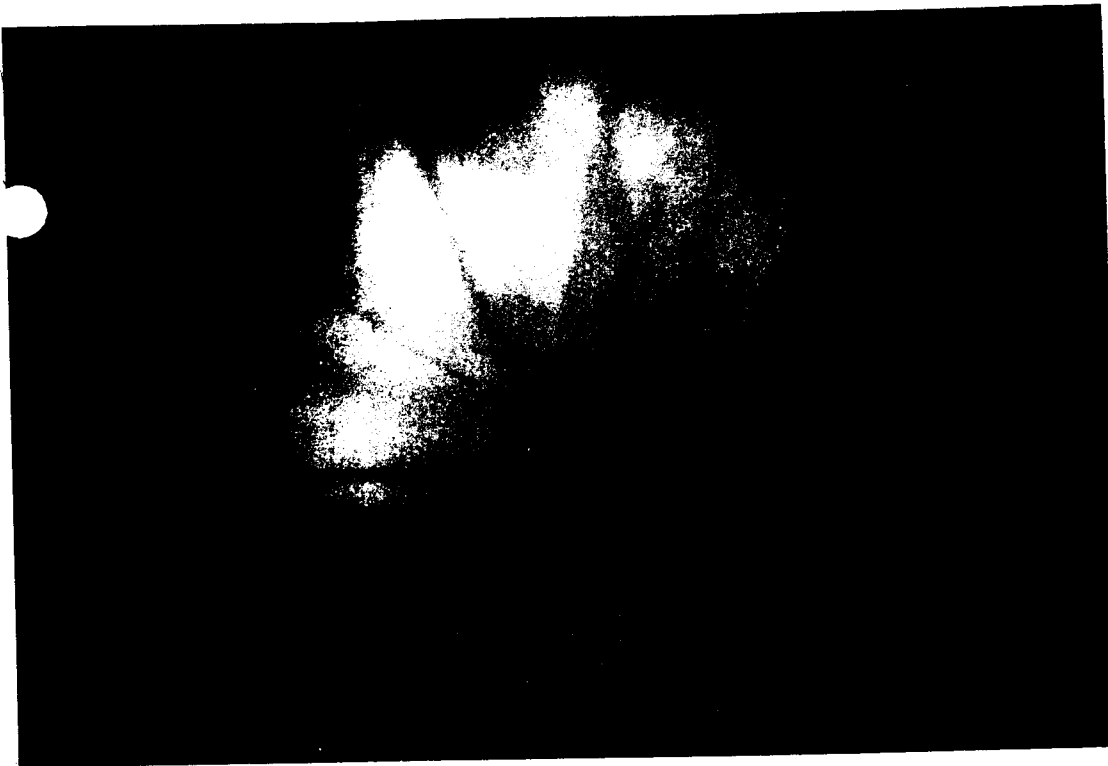
#60
5514 Female - L
Termination



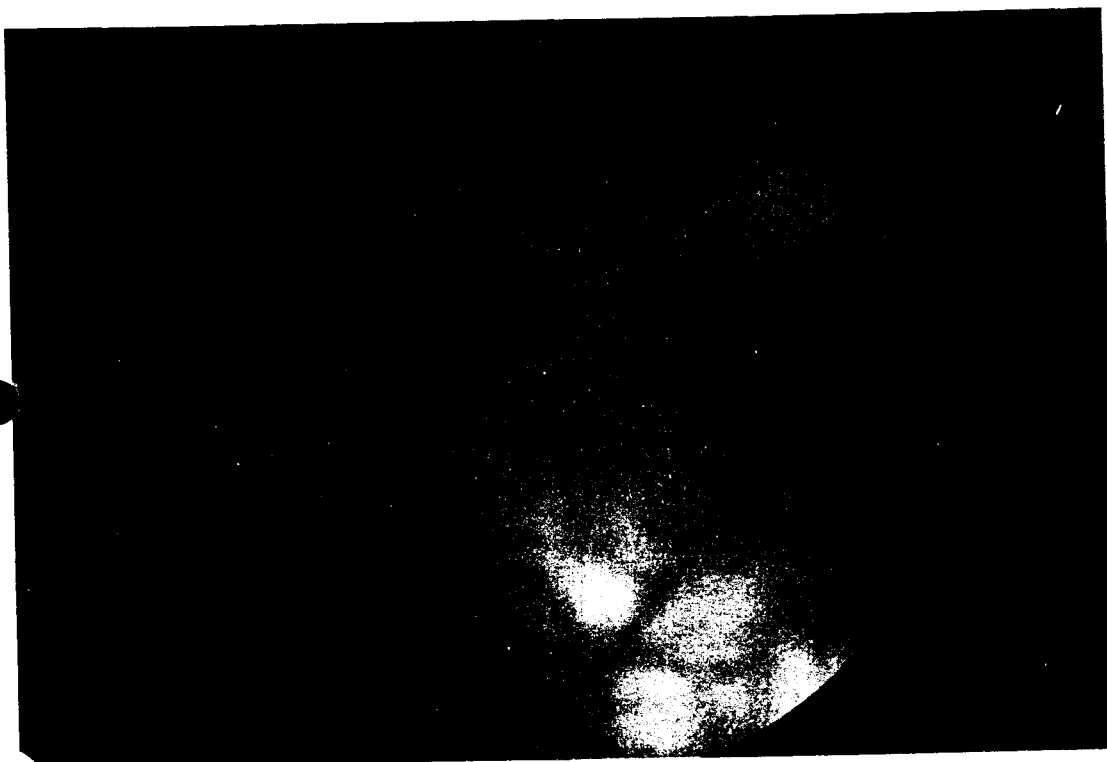
#61
1517 Female - f
Termination



#62
1517 Female -
Termination



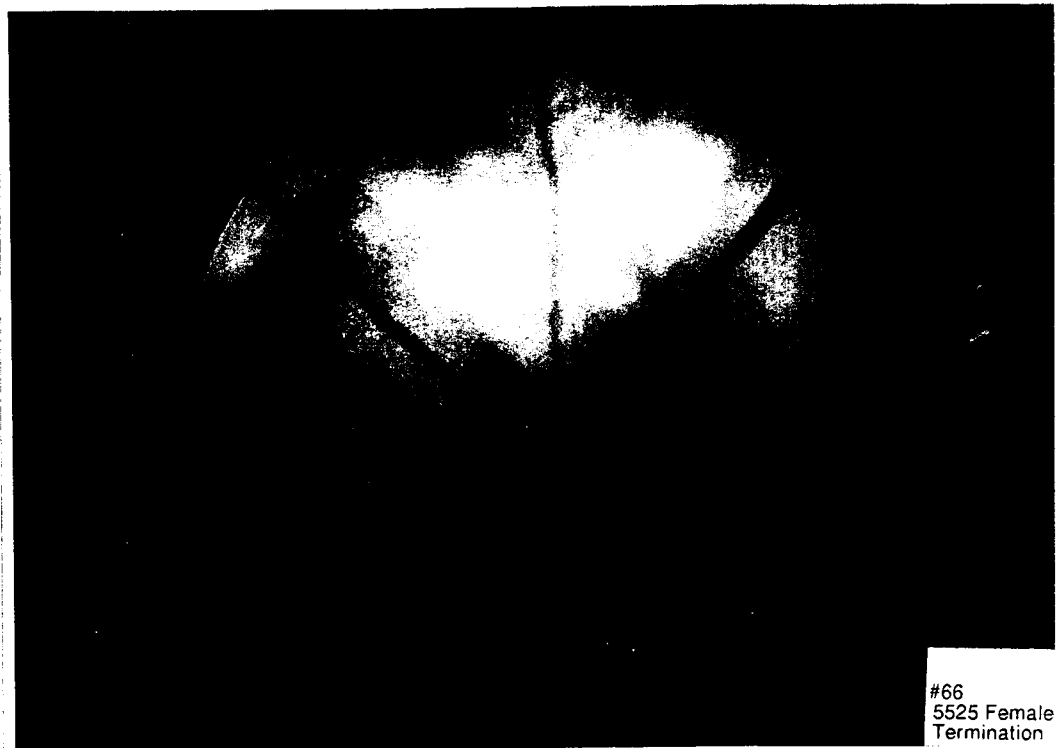
#63
5516 Female - R
Termination



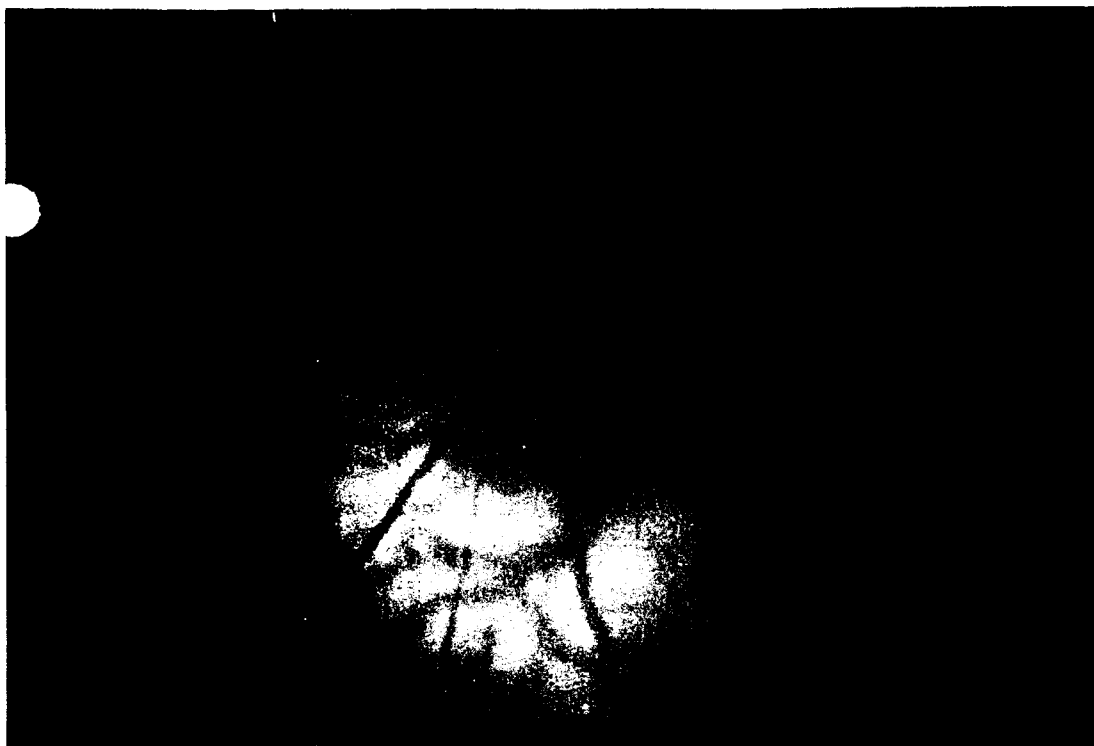
#64
5516 Female - L
Termination



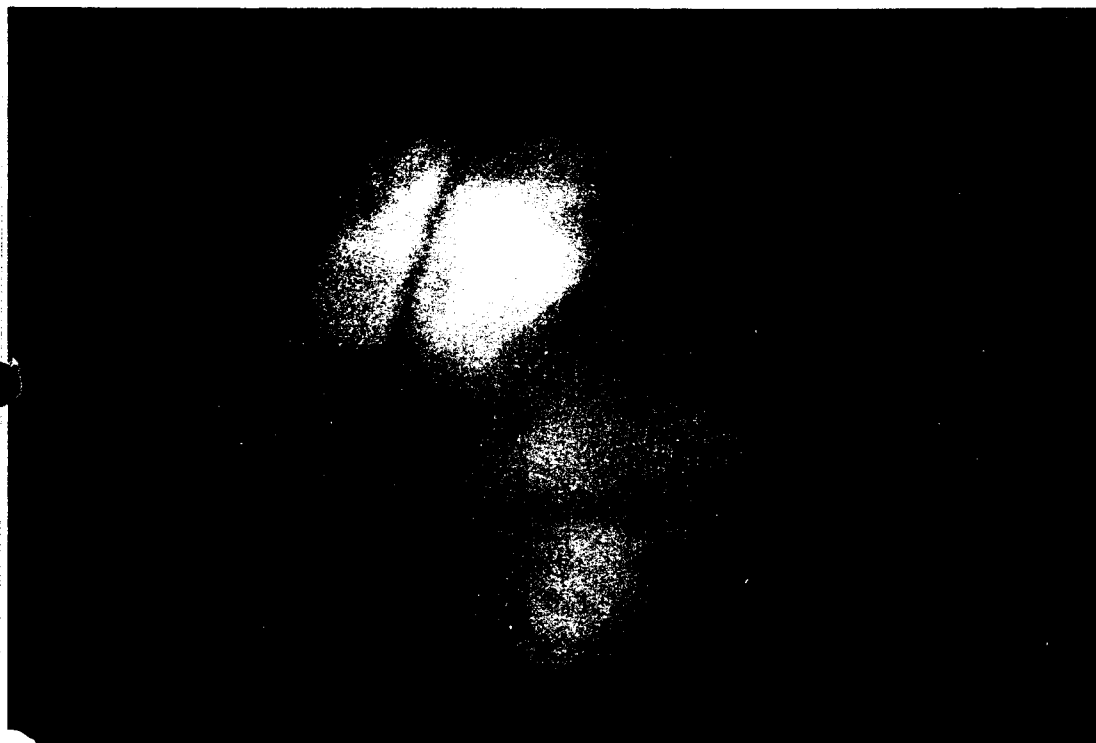
#65
1529 Female
Termination



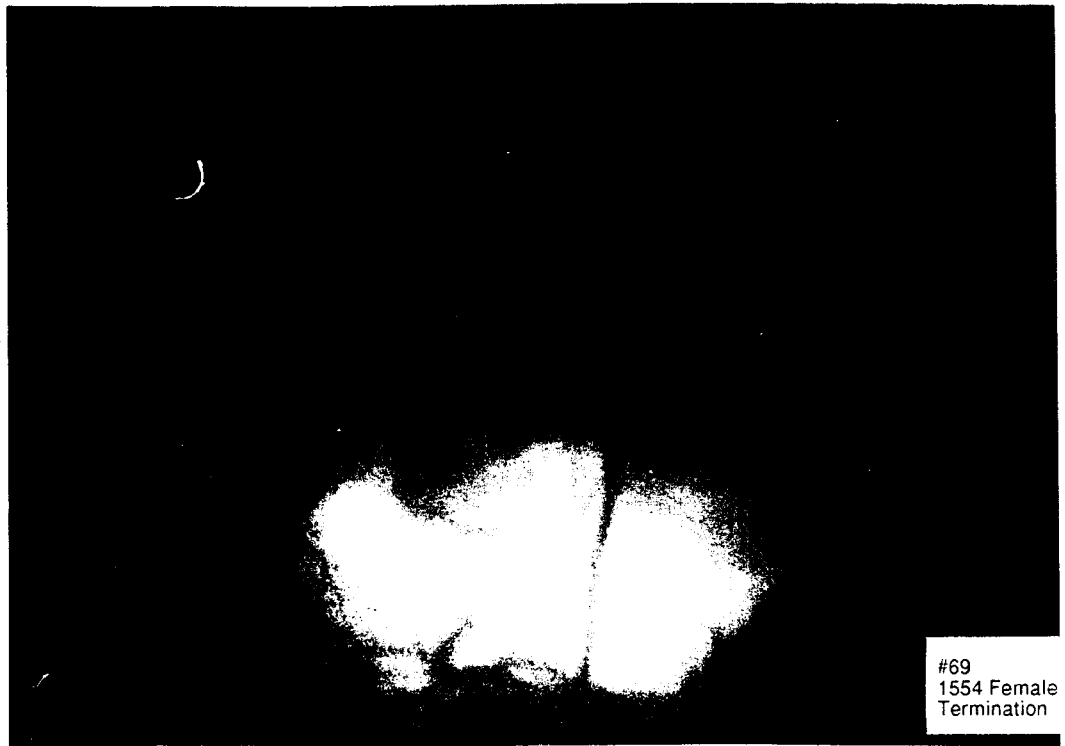
#66
5525 Female
Termination



#67
5525 Female - L
Termination



#68
1554 Female - R
Termination



#69
1554 Female
Termination



#70
5543 Female
Termination



#71
5543 Female-L
Termination