

FINAL REPORT

Study Title

Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats

Test Guideline

OECD Guideline for the Testing of Chemicals, No. 407 (2008)

U.S. EPA. Health Effects Test Guidelines, OPPTS 870.3050 (2000)

Author

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(Study Director)

Study Completed On

05 April 2012
(Final Report)

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Laboratory Project ID

Charles River Laboratories Preclinical Services Protocol Number: TQC00065

STATEMENT OF CONFIDENTIALITY

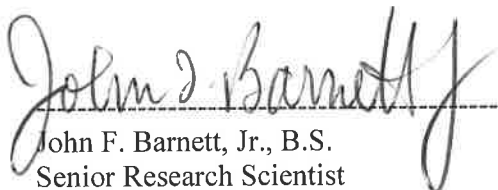
This report contains confidential and proprietary information of Cheminova A/S which must not be disclosed to anyone except the employees of this company or to persons authorized by law or judicial judgment without the expressed and written approval of Cheminova A/S.

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with the Good Laboratory Practice (GLP) regulations of the U.S. Environmental Protection Agency^a and the Organisation for Economic Co-operation and Development^b with the exception that the Benchmark Dose Modeling analysis of cholinesterase data was not designated in the protocol, nor was the Principal Investigator specified in the protocol. The Test Site's quality control procedures, and not Good Laboratory Practice regulations, were applied to these statistical analyses. This exception did not adversely impact the study because this analysis was developed by the Environmental Protection Agency to assist in the analysis of the cholinesterase data.

This final report accurately reflects the raw data obtained during the performance of the study. Deviations from the protocol and standard operating procedures of the Testing Facility are documented in this report and/or the raw data. Those deviations that occurred did not affect the quality or integrity of the study.

Study Director:

 5 Apr 2012
John F. Barnett, Jr., B.S. Date
Senior Research Scientist

-
- a. EPA Good laboratory practice standards. Chapter I Protection of Environment, 40 C.F.R. 160/792. U.S. Environmental Protection Agency.
 - b. OECD Principles of good laboratory practices, [C(97)186/Final] (1998); Environmental Health and Safety Division. OECD Environment Directorate.

QUALITY ASSURANCE STATEMENT

Protocol: TQC00065

This study has been inspected by the QAU to assure conformance with the GLP regulations US Environmental Protection Agency, Good Laboratory Practice Regulations, Chapter I Protection of Environment, 40 C.F.R. 160/792 and Organisation for Economic Co-operation and Development (1998), The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final. Reports were submitted in accordance with SOPs as follows.

QAU INSPECTION DATES

Dates of Inspection	Phase(s) Inspected	<u>Dates Findings Submitted to:</u>	
		Study Director	Study Director Management
05-06 OCT 2010	Protocol	06 OCT 2010	06 OCT 2010
15 OCT 2010	Protocol Amendment 1	15 OCT 2010	15 OCT 2010
09 NOV 2010	Protocol Amendment 2	09 NOV 2010	09 NOV 2010
10 DEC 2010	Protocol Amendment 3	10 DEC 2010	10 DEC 2010
20 DEC 2010	Protocol Amendment 4	20 DEC 2010	20 DEC 2010
26 JAN 2011	Protocol Amendment 5	26 JAN 2011	26 JAN 2011
20 JAN 2012	Protocol Amendment 6	20 JAN 2012	20 JAN 2012
18 OCT 2010	Diet Test Substance Preparation	20 OCT 2010	20 OCT 2010
18 OCT 2010	Detailed Clinical Observations	18 OCT 2010	18 OCT 2010
15 NOV 2010	Diet Test Substance Administration	19 NOV 2010	19 NOV 2010
17 NOV 2010	Cholinesterase Assay	19 NOV 2010	19 NOV 2010
17 NOV 2010	Necropsy	17 NOV 2010	17 NOV 2010

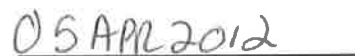
QUALITY ASSURANCE STATEMENT (Continued)**QAU INSPECTION DATES**

		<u>Dates Findings Submitted to:</u>	
		Study Director	Study Director Management
Dates of Inspection	Phase(s) Inspected	Study Director	Study Director Management
02-03 DEC 2010	In-Life Data	03 DEC 2010	03 DEC 2010
02-03 DEC 2010 05 JAN 2011	Necropsy Data	03 DEC 2010 05 JAN 2011	03 DEC 2010 05 JAN 2011
03 DEC 2010	Formulation Data	03 DEC 2010	03 DEC 2010
20-22 DEC 2010	Cholinesterase Data	22 DEC 2010	22 DEC 2010
04-05 JAN 2011 17 JAN 2011	Methods	05 JAN 2011 17 JAN 2011	05 JAN 2011 17 JAN 2011
05 JAN 2011	Tables	05 JAN 2011	05 JAN 2011
18 JAN 2011	Results	18 JAN 2011	18 JAN 2011
19 JAN 2011	Summary	19 JAN 2011	19 JAN 2011
29 Mar 2012	Revised Report	29 Mar 2012	29 Mar 2012
05 Apr 2012	Final Report	05 Apr 2012	05 Apr 2012

The Final Report has been reviewed to assure that it accurately describes the materials and methods, and that the reported results accurately reflect the raw data.



Stacy Wilson, BA. RQAP-GLP, LATG
Senior Quality Assurance Auditor
Charles River Laboratories
Preclinical Services, Pennsylvania



Date

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1. ABSTRACT^a

The purpose of this study was to provide information on possible adverse effects on Crl:CD(SD) rats resulting from repeated exposure to Malathion Technical over a 28-day exposure period. The study was designed to provide information that can be used in the selection of dosage levels for subsequent studies. The requirements of the Organisation for Economic Co-operation and Development and the U.S. Environmental Protection Agency were used as the basis for the study design; however, not all of parameters mentioned in the guidelines were included in the study design.

Seventy-five male and 75 female rats were assigned to five dosage groups (15 rats per sex per group). Diets (PMI[®] Certified Rodent Diet[®] #5002) were prepared on a weekly basis to administer Malathion Technical at concentrations corresponding to target dose levels of approximately 0 (Carrier Control) ppm, 100 ppm, 500 ppm, 5000 ppm and 10000 ppm (Groups I through V, respectively). A constant concentration of the test substance in the diet was offered to the rats, and the mg/kg bw/day dosages consumed were calculated and presented for periods corresponding to body weight and feed consumption observations. Prepared diets were available *ad libitum* beginning on day 1 of study (DS 1) for 28 consecutive days.

The following evaluations were conducted: viability, clinical observations, detailed clinical observations, body weights and body weight gains, feed consumption values, necropsy observations, kidney and liver organ weights, brain and red blood cell (RBC) cholinesterase activity and histopathology.

On DS 29, all rats were anesthetized under isoflurane/oxygen and following blood collection from the vena cava, were sacrificed by an injection of sodium pentobarbital into the inferior vena cava. Red blood cell (RBC) and brain cholinesterase levels were evaluated at the Testing Facility. All rats were examined for gross lesions, and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed. The nasal passages, the nasal cavity and neck with associated organs and tissues were also examined. The liver and kidney were excised and weighed for all rats. The liver, kidney, nasal cavity and turbinates, as well as gross lesions were collected for all animals, retained in neutral buffered 10% formalin. All gross lesions, as well as livers, kidneys and the nasal cavity and turbinates from the 0 (Carrier Control) and the 10000 ppm exposure groups were examined histopathologically. Rats were then discarded without further evaluation.

-
- a. Detailed descriptions of all procedures used in the conduct of this study are provided in the appropriate sections of this report and in the attached protocol (APPENDIX 1, PROTOCOL AND PROTOCOL AMENDMENTS). Deviations from the Protocol and the Standard Operating Procedures of the Testing Facility are available in APPENDIX 2 and/or in the raw data.

Consumed dosage levels for the rats for the entire exposure period (calculated as DSs 1 to 28) are tabulated below. The highest weekly consumed dosages occurred during the first week of exposure.

Consumed Dosages (mg/kg bw/day)		
Concentration in Diet (ppm)	Male Rats	Female Rats
100	9.2	9.4
500	46.1	47.4
5000	457.5	461.3
10000	947.8	910.1

All male and female rats survived until scheduled sacrifice.

There were no test substance-related adverse clinical signs or detailed clinical observations observed in male and female rats during the 28-day exposure period.

At 5000 and 10000 ppm, body weight gain was statistically significantly decreased in male rats on DSs 22 to 28. In male rats at 10000 ppm, body weights and body weight gains were reduced or statistically significantly reduced at all intervals following the initiation of exposure.

In male rats at 10000 ppm, absolute feed consumption was statistically significantly decreased during the first week of exposure. There were also statistically significantly increased relative feed consumption values in the 10000 ppm male rats on DSs 8 to 15 and 15 to 22. Absolute and relative feed consumption values were also statistically significantly decreased in female rats at 10000 ppm on DSs 22 to 28.

Feed efficiency was statistically significantly decreased in male rats at 10000 ppm during the entire exposure period and during the first week of exposure.

At scheduled euthanasia, no adverse necropsy observations were identified.

At 5000 and 10000 ppm, there were statistically significant increases in liver weights (both male and female rats) and kidney weights (male rats at 10000 ppm only). These changes in organ weights were not associated with any microscopic findings.

Microscopic findings were present in the nasal cavity of male and female rats at 10000 ppm (depletion of goblet cells and olfactory epithelial hyperplasia).

Female rats had statistically significantly reduced RBC cholinesterase levels in all exposure groups (ranging from 13.8% to 91.6% inhibition compared with controls) and statistically significantly reduced brain cholinesterase levels at 5000 and 10000 ppm (25.0% and 47.8% inhibition compared with controls, respectively). Male rats had statistically significantly reduced brain and RBC cholinesterase levels in the 500, 5000 and 10000 ppm exposure groups (for brain, ChE levels were 7.2%, 21.5% and 21.2% inhibition compared with controls, respectively; for RBC ChE, levels were 22.3%, 82.6% and 88.6% inhibition compared with controls, respectively).

2. DISCUSSION AND CONCLUSION

Based on the results of this study, dosages of 0, 100, 500, 5000 and 10000 ppm of Malathion Technical in the diet were selected in consultation with the Sponsor for the 90-day toxicity study in rats.

Body weight gains were reduced in male rats at 5000 ppm and body weights, body weight gains and terminal body weights were reduced in male rats at 10000 ppm. Feed consumption values were also reduced in male and female rats at 10000 ppm.

As summarized in the table below, in male rats at 10000 ppm body weight and body weight change values were statistically significant throughout exposure period; however, the difference in the absolute feed consumption value was only significant during the first week of exposure. The decreased feed consumption value during the first week of exposure may be an indication of an initial taste aversion of Malathion Technical in the diet. The initial body weight decrease during the first week of exposure may have resulted in the overall body weight changes that occurred because the reductions occurred during the growth period.

Body Weight and Food Consumption Data from Male Rats at 10000 ppm						
Week	1	8	15	22	28	Overall (1-28)
Body Weight	165	203**	261**	308**	340**	--
Body Weight Change	--	38**	58	47*	32*	175**
Absolute Food Consumption (g/day)	--	20**	24	26	24	23
Relative Food Consumption (g/kg/day)	--	115	106*	90*	76	94
Feed Efficiency (Daily Body Weight Change/ Daily Food Consumption)	--	26.4**	33.6	26.4	21.4	27.1*

* Significantly different from the carrier control group value ($p \leq 0.05$).

** Significantly different from the carrier control group value ($p \leq 0.01$).

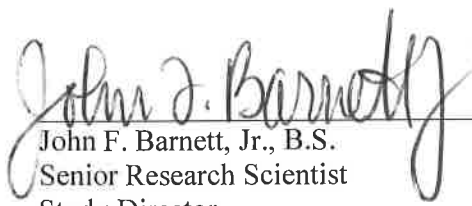
At 5000 and 10000 ppm, there were organ weight increases in the liver (males and females) and kidneys (males only at 10000 ppm). These increases are considered to reflect the metabolic changes occurring in the rats resulting from the continual exposure to Malathion Technical. They were not considered to be adverse as they did not appear

to produce any microscopic findings in either organ. Microscopic findings were present in the nasal cavity of the 10000 ppm (depletion of goblet cells and olfactory epithelial hyperplasia) in both male and female rats. These local findings are considered to be the result of continued nasal exposure to Malathion Technical in the diet.


Red blood cell cholinesterase inhibition was observed at all exposure levels in female rats and at the 500 ppm and greater exposure levels in male rats. The reduction observed in female rats at 100 ppm was considered minor (13.8% inhibition compared with controls) and not toxicologically relevant. Brain cholinesterase levels were also statistically significantly reduced at ≥ 500 ppm exposure levels in male rats and at 5000 and 10000 ppm in female rats.

Based on the results of this study, the no-observed-adverse-effect-level (NOAEL) for general toxicity was 100 ppm.

Based on benchmark dose (BMD) modeling, the estimated dosage level for a 20% inhibition (BMD₂₀) of RBC cholinesterase activity (the most sensitive endpoint) was 45.6 mg/kg bw/day for male rats and 42.9 mg/kg bw/day for female rats. The lowest BMDL₂₀ value (lowest 95th percentile confidence limit) was 37.7 mg/kg bw/day for male rats and 34.6 mg/kg bw/day for female rats. The brain BMD₁₀ estimates were 215.8 mg/kg bw/day (BMDL₁₀ = 145.1 mg/kg bw/day) for male rats and 159.2 mg/kg bw/day (BMDL₁₀ = 135.3 mg/kg bw/day) for female rats.

 5 Apr 2012
John F. Barnett, Jr., B.S. Date
Senior Research Scientist
Study Director

This report has been reviewed for scientific content. The signature below indicates a concurrence with the Study Director's interpretation of these data as presented in this report.

 5 APR - 2012
Alan M. Hoberman, Ph.D., DABT, Fellow ATS Date
Executive Director, Site Operations and Toxicology
Testing Facility Management

3. DESCRIPTION OF TEST PROCEDURES

3.1. Conduct of Study

3.1.1. Sponsor

Cheminova A/S, P.O. Box 9, DK-7620 Lemvig, DENMARK

3.1.2. Testing Facility

Charles River Laboratories Preclinical Services, 905 Sheehy Drive, Building A,
Horsham, PA 19044, USA

3.1.3. Study Number

TQC00065

3.1.4. Purpose of the Study

The purpose of this study was to provide information on possible adverse effects on Crl:CD(SD) rats resulting from repeated exposure to Malathion Technical over a 28-day exposure period. The study was designed to provide information that can be used in the selection of dosage levels for subsequent studies.

3.1.5. Study Design

The requirements of the Organisation for Economic Co operation and Development⁽¹⁾ and the U.S. Environmental Protection Agency⁽²⁾ were used as the basis for study design; however, not all parameters mentioned in the guidelines were included in the study design.

3.1.6. Ownership of the Study

The Sponsor owns the study. All raw data, analyses, reports and preserved tissues are the property of the Sponsor.

3.1.7. Study Monitor

M. Jensen
Cheminova A/S

3.1.8. Study Director

John F. Barnett, Jr., B.S. (Senior Research Scientist)
Address as cited previously for Testing Facility.

3.1.9. Technical Performance**3.1.9.1. Charles River Laboratories, Preclinical Services, Pennsylvania**

Matthew J. Vaneman, B.S. (Director of Operations)
Jason R. Hanna, B.A. (Study Supervisor)
Andrea M. Sweeney, B.S. (Research Technician)
Nicole E. Cochran, B.S. (Necropsy Technician)
Melissa A. Snyder, B.S. (Research Associate)
Julian Gulbinski, III, B.S., M.B.A. (Senior Manager Laboratory Sciences) -
Cholinesterase Analyses
Jason Sarsoza, B. Sc. (Principal Investigator; Research Scientist) - Dose Formulation
Analyses

3.1.9.2. Charles River Laboratories Pathology Associates, Illinois

Carol J. Detrisac, DVM, PhD, DACVP (Principal Investigator) -
Histopathological evaluation

3.1.10. Report Preparation

John F. Barnett, Jr., B.S.
Megan R. Lawhead, M.A. (Study Coordinator)
Tina M. Fedorak, B.S. (Study Coordinator)

3.1.11. Report Review

Alan M. Hoberman, Ph.D., DABT, Fellow ATS (Executive Director, Site Operations and
Toxicology)

3.1.12. Date Protocol Signed

11 October 2010

3.1.13. Dates of Technical Performance

Rat Arrival and Experimental Start Date (OECD)	12 OCT 2010
Experimental Start Date (EPA)	19 OCT 2010
Experimental Completion/Termination Date	21 MAR 2012

3.1.13.1. Replicate 1 - Male Rats

Exposure Period (DS 1 through 28)	19 OCT 2010 - 15 NOV 2010
Scheduled Sacrifice and Cholinesterase Evaluation (DS 29)	16 NOV 2010

3.1.13.2. Replicate 2 - Female Rats

Exposure Period (DS 1 through 28)
Scheduled Sacrifice and Cholinesterase
Evaluation (DS 29)

20 OCT 2010 - 16 NOV 2010
17 NOV 2010

3.1.14. Records Maintained

The original protocol, amendments, and report, raw data and reserve samples of the bulk test substance, corn oil and each lot of the carrier are retained in the archives of the Testing Facility. Any preserved tissues are retained in the archives of the Testing Facility one year after delivery of the final report, after which time the Sponsor will decide their final disposition. Unused prepared diets were discarded at the Testing Facility. Backup samples were discarded at the Testing Facility prior to issuance of the final report. Disposition of the remaining bulk test substance was documented in the raw data after consultation with the Sponsor^a.

All slides, residual wet tissue, blocks, histology data and the report were returned to Charles River Laboratories, Preclinical Services, Pennsylvania, USA for archiving at the completion of the study.

a. See APPENDIX 2 (DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY).

3.2. Test Substance, Corn Oil and Carrier Information

Test Substance Information			
Name: Malathion Technical ^a		Description:	Light, yellow liquid
Storage: Refrigerated (2°C to 8°C), protected from light		Supplier:	Sponsor
Batch Number	CAS Number	Date Received	Expiration Date
D2014-OSJ-MLT-01-S	121-75-5	05 AUG 2010	28 SEP 2013

Corn Oil Information		
Name: Corn Oil ^b		Description: Yellow liquid
Storage: Room temperature		Supplier: Charkit Chemical Corporation, South Norwalk, CT, USA
Lot Number	Date Received	Expiration Date
J-145	09 JUN 2009	06 APR 2011

Carrier Information				
Name	Lot Number	Supplier	Storage Condition	Expiration Date
PMI [®] Certified Rodent Meal	JUN 30 10 1B AUG 02 10 2B	Animal Specialties and Provisions, LLC ^c	Room temperature	30 DEC 2010 02 FEB 2011

- Malathion is synonymous with Malathion (CHA 300) and Fyfanon[®] Technical. The test substance was spiked with relevant impurities to the specification limit (see CofA in Appendix 3).
- The corn oil served to minimize the dust production during diet preparation and usage.
- Animal Specialties and Provisions, LLC, Quakertown, PA, USA

Sampling			
Bulk Test Substance Reserve			
Sample Size: 5 mL			
Date Sampled	Storage Conditions		Date Archived
25 OCT 2010	Refrigerated, protected from light		18 NOV 2010
Bulk Corn Oil Reserve			
Sample Size: 5 mL			
Date Sampled	Storage Conditions		Date Archived
08 NOV 2010	Room temperature		16 NOV 2010
Bulk Carrier Reserve			
Sample Size: 125 g			
Lot Number	Date Sampled	Storage Conditions	Date Archived
JUN 30 10 1B	08 NOV 2010	Room temperature	16 NOV 2010
AUG 02 10 2B	25 OCT 2010		18 NOV 2010

Concentration and Homogeneity ^a				
Sample Size: 25 g				
Date Sampled	Date Transferred	Transfer Conditions	Storage Conditions	Purpose
18 OCT 2010	19 OCT 2010	Refrigerated on cold packs, protected from light	Refrigerated, protected from light	H, C
25 OCT 2010	26 OCT 2010			C
08 NOV 2010	08 NOV 2010			C

- a. Quadruplicate samples for homogeneity analysis were taken from the top, middle and bottom of each concentration from the first preparation on the day prepared. All samples were transferred to the onsite analytical laboratory at the Testing Facility and a duplicate set of samples from each quadruplicate set was analyzed for homogeneity according to a validated method (analytical procedure MALA02). The mean concentration result of the homogeneity analysis for each level was also used to verify the concentrations for week 1. Duplicate samples were taken for concentration analysis on each day of preparation from each concentration. All samples from weeks 2 and 4 were transferred to the analytical laboratory at the Testing Facility. One sample of each set was analyzed in duplicate for concentration according to a validated method (analytical procedure MALA02). All remaining samples were retained at the Testing Facility as backup samples. Additional concentration samples (25 g) were taken at each diet preparation for possible concentration verification and stored refrigerated, protected from light. Disposition of the additional concentration samples was documented in the raw data.

C - Concentration

H - Homogeneity

3.2.1. Special Handling Instructions

Double nitrile gloves, full faced positive pressure hood, appropriate eye protection and Tyvek[®] suit were worn during formulation preparation and dosage administration. The bulk test substance was handled in a chemical fume hood. Gloves were washed with soap and water or sprayed with an appropriate cleaning solution prior to removal and then disposed of in a biohazard container. For all other study activities, standard safety precautions (gloves, dust-mist/HEPA-filtered mask, appropriate eye protection and protective clothing) were followed.

3.2.2. Analysis of Activity/Purity

The test substance was considered 96% active/pure for the purpose of dosage calculations. Since the completion of the testing phase of the study, the Sponsor has confirmed that the purity of the test substance was 95.8% w/w (see APPENDIX 3), which was a little lower than the preliminary purity value of 96% based on non-GLP analyses that is included in the study protocol (APPENDIX 1, Attachment 2). Therefore, during the course of the study, the test substance concentrations were 0.2% lower than intended. This minor difference did not impact the validity or integrity of the study.

Information to document or certify the identity, composition, strength, stability and activity/purity of the test substance was provided by the Sponsor to the Testing Facility. A Certificate of Analysis is available in APPENDIX 3.

The Study Director was not aware of any potential contaminants likely to have been present in the carrier or corn oil that would have interfered with the results of this study. A Certificate of Analysis for the corn oil is available in APPENDIX 3.

3.3. Test Substance Preparation and Storage Conditions

Formulations (diets) were prepared once weekly at the Testing Facility and were stored refrigerated (2°C to 8°C) until use.

3.4. Test System

3.4.1. Species/Strain

Crl:CD(SD) Rat

3.4.2. Supplier (Source)

Charles River Laboratories, Inc., Kingston, NY, USA

3.4.3. Sex

Male and female

3.4.4. Rationale for Test System

The Crl:CD(SD) rat was selected as the Test System because it is one mammalian species accepted for use in toxicity studies and it has been widely used throughout industry for toxicity evaluations.

3.4.5. Test System Data

Approximate Date of Birth	07 SEP 2010
Approximate Age at Arrival	36 days

3.4.5.1. Male Rats

Number of Rats Acclimated	80
Number of Rats Assigned to Study	75
Weight (g) the Day after Arrival	90 - 123
Weight (g) at Study Assignment	114 - 142

3.4.5.2. Female Rats

Number of Rats Acclimated	80
Number of Rats Assigned to Study	75
Weight (g) the Day after Arrival	80 - 109
Weight (g) at Study Assignment	93 - 125

3.4.6. Method of Randomization

Upon arrival, rats were assigned to individual housing on the basis of computer-generated random units. After acclimation, rats were selected for study on the basis of physical appearance and body weights recorded during acclimation. The rats were assigned to five dosage groups (Groups I through V), based on computer-generated (weight-ordered) randomization procedures. In order to accommodate the necropsy schedule, rats in the main study were randomly assigned to two replicates by sex that began exposure and were sacrificed over two consecutive days. Rats not assigned to study were humanely sacrificed.

3.4.7. System of Identification

Male and female rats were assigned temporary numbers at receipt and given permanent identification numbers when assigned to the study before the first day of exposure. Rats were permanently identified using Monel[®] self-piercing ear tags.

3.5. Husbandry**3.5.1. Research Facility Registration**

USDA Registration No. 14-R-0144 under the Animal Welfare Act, 7 U.S.C. 2131 *et seq.*

3.5.2. Study Room

The study room was maintained under conditions of positive airflow relative to a hallway and independently supplied with a minimum of ten changes per hour of 100% fresh air that had been passed through 99.97% HEPA filters. Room temperature and humidity were monitored constantly throughout the study. Room temperature was targeted at 66°F to 77°F (19°C to 25°C); relative humidity was targeted at 30% to 70%^a.

3.5.3. Housing

Rats were individually housed in stainless steel, wire-bottomed cages. All cage sizes and housing conditions were in compliance with the *Guide for the Care and Use of Laboratory Animals*⁽³⁾.

3.5.4. Light

An automatically controlled 12-hours light:12-hours dark fluorescent light cycle was maintained. Each dark period began at 1900 hours (\pm 30 minutes).

3.5.5. Sanitization

Cage pan liners were changed at least three times weekly. Cages were changed approximately every other week.

3.5.6. Diet

During the acclimation period, rats were given *ad libitum* access to Certified Rodent Diet[®] #5002 (PMI[®] Nutrition International, St. Louis, MO, USA) in individual feeders.

During the exposure period, rats were given *ad libitum* access to either Certified Rodent Diet[®] #5002 (PMI[®] Nutrition International) only (carrier control group [Group I]) or test diets prepared using Certified Rodent Diet[®] and the test substance (Groups II through V).

3.5.7. Diet Analysis

Analyses were routinely performed by the feed supplier. No contaminants at levels exceeding the maximum concentration limits for certified feed or deviations from expected nutritional requirements were detected by these analyses. Copies of the results of the feed analyses are available in the raw data and in APPENDIX 4.

The Study Director was not aware of any potential contaminants likely to have been present in the feed that would have interfered with the results of this study.

a. See APPENDIX 4 (ENVIRONMENTAL AND HUSBANDRY REPORTS) and APPENDIX 2.

3.5.8. Enrichment

Chewable Nylabones[®] were supplied to all rats during the course of the study. Analyses for possible contamination were conducted on each lot of Nylabones[®] and were documented in the raw data and in APPENDIX 4.

The Study Director was not aware of any potential contaminants likely to have been present in the enrichment devices that would have interfered with the results of this study.

3.5.9. Water

Local water that had been processed by passage through a reverse osmosis membrane (R.O. water) was available to the rats *ad libitum* from an automatic watering access system. Chlorine was added to the processed water as a bacteriostat.

3.5.10. Water Analysis

The processed water is analyzed twice annually for possible chemical contamination (Lancaster Laboratories, Lancaster, PA, USA) and monthly for possible bacterial contamination (QC Laboratories, Southampton, PA, USA). Copies of the results of the water analyses are available in the raw data and in APPENDIX 4.

The Study Director was not aware of any potential contaminants likely to have been present in the water that would have interfered with the results of this study.

3.6. Methods

3.6.1. Dosage Administration

Dosage Group	Number of Rats Per Sex	Concentration (ppm)	Assigned Rat Numbers	
			Male Rats	Female Rats
I	15	0 (Carrier Control)	216 - 230	316 - 330
II	15	100	231 - 245	331 - 345
III	15	500	261 - 275	361 - 375
IV	15	5000	201 - 215	301 - 315
V	15	10000	246 - 260	346 - 360

- a. The test substance was considered 96% pure for the purpose of dosage calculations. See (APPENDIX 1, Attachment 2).

3.6.2. Rationale for Dosage Selection

Dosage levels were selected by the Sponsor on the basis of previous studies conducted with the test substance.

The highest dosage level was expected to induce toxicity but not death or severe suffering. The descending sequence of the lower dosage levels were selected for the purpose of demonstrating any dosage-related response, with no adverse effects expected at the lowest level.

3.6.3. Route and Rationale for Route of Administration

The oral (diet) route was selected for use because it is a possible route of human exposure.

3.6.4. Method and Frequency of Administration

A constant concentration of the test substance in the diet was offered to the rats, and the mg/kg bw/day dosages consumed were calculated and presented for periods corresponding to body weight and feed consumption observations. A carrier control and four test diet concentrations were given to the rats. Rats were given continual access to the test substance in the diet for 28 consecutive days. The first day of test diet exposure for each replicate was considered DS 1.

3.6.5. Method of Study Performance

Rats were observed for viability at least twice each day of the study and for clinical observations and general appearance twice during the acclimation period. The rats were also examined for clinical observations and general appearance daily during the exposure period.

Detailed clinical observations were recorded once before the first day of exposure and once weekly until scheduled sacrifice. The detailed clinical observations were conducted by an observer unaware of the group assignment of the rat.

Body weights were recorded twice during the acclimation period and daily during the exposure period. A terminal body weight was recorded on the day sacrifice occurred. Feed consumption values were recorded twice during the acclimation period and daily during the exposure period. A feed left value was recorded on the day before sacrifice.

3.6.6. Cholinesterase Assay^a

On DS 29, whole blood samples (2.0 to 3.0 mL each) were collected from each rat.

Prior to blood collection, syringes were flushed with EDTA to prevent clotting. Blood was collected under isoflurane/oxygen anesthesia from the inferior vena cava (the rats were in the isoflurane/oxygen for no longer than 5 minutes prior to blood collection). The time for each blood collection was between 7 and 10 seconds. The blood was transferred into EDTA-coated (lavender-top) tubes and the tubes were stored under cold packs on a tilter until processing and were analyzed for RBC cholinesterase levels at the Testing Facility.

After blood sample collection and sacrifice, brains were excised, placed into a weigh boat on wet ice and weighed. The brains were then placed into a 50 mL conical tube containing approximately 15 mL of saline and were maintained on wet ice until processing and were analyzed for cholinesterase levels at the Testing Facility.

All processed samples were held on wet ice or refrigerated until assayed. The blood and brain samples were analyzed for cholinesterase levels at the Testing Facility on the same day that they were collected, according to the Study Specific Procedure located in APPENDIX 1, Attachment 5. RBC and brain samples were processed and assayed as soon as possible, with the experimental target that samples be analyzed within 60 minutes of sacrifice^a.

Following analysis, samples were retained refrigerated or on wet ice until transferred to frozen (-15°C to -30°C) storage. These samples were discarded prior to issuance of the final report. Disposition of these samples was documented in the raw data.

3.6.7. Gross Necropsy

On DS 29, rats were anesthetized under isoflurane/oxygen, and following blood collection from the vena cava, were subsequently sacrificed by an injection of sodium pentobarbital into the inferior vena cava. Rats were evaluated as described in Section 3.6.6 (Cholinesterase Assay).

Rats were examined for gross lesions, and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed on all rats. In addition, the nasal passages, the nasal cavity and neck with associated organs and tissues were examined. The liver and kidney were excised and weighed. Animal identification, gross lesions, liver, kidney and nasal cavity were collected and retained in neutral buffered 10% formalin for possible histological examination.

a. See APPENDIX 2 (DEVIATIONS).

Tissues that include the nasal cavity and turbinates from male and female rats assigned to the 0 (Carrier Control) and 10000 ppm (Groups I and V, respectively) were shipped under ambient conditions to Charles River Laboratories, Pathology Associates, Maryland, USA for histopathological evaluations. The tissues were trimmed, embedded in paraffin, sectioned, mounted on glass slides and stained with hematoxylin and eosin. The nasal tissues were trimmed consistent with the procedures described by Young⁽⁴⁾. In addition to the four routine sections delineated by Young⁽⁴⁾, the most rostral section of the nose, to include nares, were also examined microscopically. Histopathological examinations were performed on rats assigned to the 0 (Carrier Control) and 10000 ppm exposure groups.

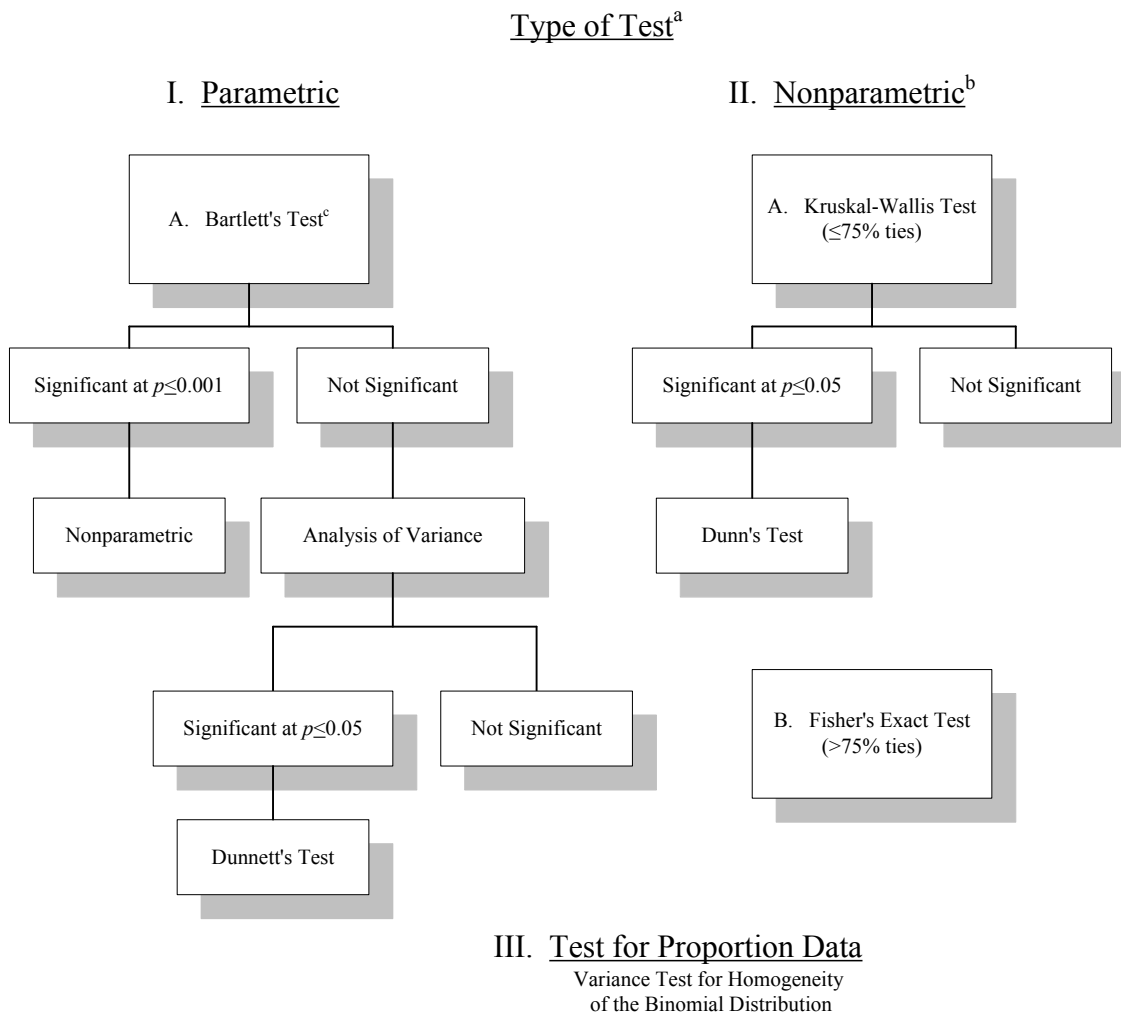
In addition, the remaining tissues from male and female rats assigned to the 0 (Carrier Control) and 10000 ppm (Groups I and V, respectively) were shipped under ambient conditions from the Testing Facility to Charles River Laboratories, Pathology Associates, Maryland, USA for histopathological evaluations. The livers and kidneys were routinely processed, embedded in paraffin, sectioned at approximately 5 microns and stained with hematoxylin and eosin. Histopathological examinations were performed on rats assigned to the 0 (Carrier Control) and 10000 ppm exposure groups.

Results of the histopathological evaluations are available in APPENDIX 5.

3.6.8. Data Collection and Statistical Analyses

Data generated during the course of this study were recorded either by hand or using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System*, *TotalChrom*[®], Version 6.2.1 (for HPLC) *Softmax*[®] *PRO* (for UV/VIS on Softmax) and *SPECTRAmax* 190. All data were tabulated, summarized and statistically analyzed using the *Argus Automated Data Collection and Management System*, *SoftMax*[®] *PRO* 4.0, *Microsoft*[®] *Excel* [part of *Microsoft*[®] Office 2003 (or later versions)], *Quattro Pro* 8 and *The SAS System* (version 6.12).

Averages and percentages were calculated.



-
- a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
 - b. Proportion data are not included in this category.
 - c. Test for homogeneity of variance.

Clinical observations and other proportional data were analyzed, using the Variance Test for Homogeneity of the Binomial Distribution⁽⁵⁾.

Continuous data (e.g., body weights, body weight changes, feed consumption values and organ weights) were analyzed, using Bartlett's Test of Homogeneity of Variances⁽⁶⁾ and the Analysis of Variance⁽⁷⁾, when appropriate [i.e., Bartlett's Test was not significant ($p > 0.001$)]. If the Analysis of Variance was significant ($p \leq 0.05$), Dunnett's Test⁽⁸⁾ was used to identify the statistical significance of the individual groups. If the Analysis of Variance was not appropriate [i.e., Bartlett's Test was significant ($p \leq 0.001$)], the Kruskal-Wallis Test⁽⁹⁾ was used, when less than or equal to 75% ties were present. In cases where the Kruskal-Wallis Test was statistically significant ($p \leq 0.05$), Dunn's Method of Multiple Comparisons⁽¹⁰⁾ was used to identify the statistical significance of the individual groups. If there were greater than 75% ties, Fisher's Exact Test⁽¹¹⁾ was used to analyze the data.

Count data were evaluated, using the procedures described above for the Kruskal-Wallis Test⁽⁹⁾.

Cholinesterase values for RBC and brains were evaluated as separate dependent variables in one-way analyses of variance (ANOVA)⁽⁷⁾ at each combination of sex (male and female). In the event that the ANOVA was significant ($p \leq 0.05$), Dunnett's test⁽⁸⁾ was used to identify the statistical significance of the individual groups.

4. RESULTS

4.1. Analytical Results (APPENDIX 6)

Preparations of Malathion Technical in the diet were analyzed by high-performance liquid chromatography with ultraviolet detection (HPLC-UV) using a validated method (Charles River Study No. TQC00067DX). The dietary preparations used for the first exposure were 0.5%, -0.7%, -2.4% and -0.4% of the target concentrations for the 100 ppm, 500 ppm, 5000 ppm and 10000 ppm preparations, respectively. The relative standard deviations for the sample averages from the top, middle and bottom were 2.1%, 1.9%, 0.4% and 1.2% for the 100 ppm, 500 ppm, 5000 ppm and 10000 ppm preparations, respectively. The dietary preparations for week 2 of the study were 0.2%, -1.9%, 1.5% and 3.5% of the target concentrations for the 100 ppm, 500 ppm, 5000 ppm and 10000 ppm preparations, respectively. The end of study dietary preparations were 5.2%, 0.5%, 0.9% and -4.9% of the target concentrations for the 100 ppm, 500 ppm, 5000 ppm and 10000 ppm preparations, respectively.

Stability data for prepared test substance formulations (diets) bracketing the range of concentrations used on study was determined in Charles River Laboratories study number TQC00067DX. In this study, Malathion Technical was found to be stable in the diet following storage at 20°C to 25°C, protected from light (for at least 22 days) and at 2°C to 8°C, protected from light (for at least 22 days).

4.2. Consumed Dosages (Summaries - Tables 1 and 2)

The average daily consumed Malathion Technical dosages (calculated between DSs 1 to 28) as well as the highest weekly dosages for the rats in each of the groups are summarized in the following table.

Mean Consumed Dosages Levels (mg/kg bw/day)

Dosage Levels (ppm)	Males		Females	
	Exposure Period (DSs 1-28)	Maximum Weekly Value (Week)	Exposure Period (DSs 1-28)	Maximum Weekly Value (Week)
100	9.2	11.9 (1)	9.4	11.6 (1)
500	46.1	60.2 (1)	47.4	56.9 (1)
5000	457.5	604.2 (1)	461.3	576.6 (1)
10000	947.8	1150.5 (1)	910.1	1136.9 (1)

**4.3. Mortality and Clinical and Detailed Clinical Observations
(Summaries - Tables 3 through 6; Individual Data - Tables 23 through 26)**

All male and female rats survived until scheduled sacrifice.

All clinical observations were considered unrelated to the test substance because: 1) the incidences were not statistically significant or biologically important; 2) the observations occurred in only one or two rats in a particular dosage group; and/or 3) the observations occurred only in the Carrier Control exposure group. The clinical observations included a scab on the head, neck and/or back; an abrasion on the neck; sparse hair coat on the head or limbs; displaced pupil in the right or left eye; chromodacryorrhea; localized alopecia on the head or limbs; chromorhinorrhea; urine stained abdominal fur; bent tail; enophthalmos; microphthalmia; and mild dehydration (based on skin turgor).

**4.4. Body Weights and Body Weight Changes
(Figures 1 and 2; Summaries - Tables 7 through 10; Individual Data - Tables 27 and 28)**

At 5000 and 10000 ppm, body weight gain was statistically significantly decreased ($p \leq 0.05$) in male rats on DSs 22 to 28 in comparison with the Carrier Control group values. In male rats at 10000 ppm, body weights and body weight gains were reduced or statistically significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) at all intervals following the initiation of exposure in comparison with the Carrier Control group value.

Body weights and body weight gains were unaffected by exposure to up to 500 ppm dietary concentrations of Malathion Technical in male rats and up to 10000 ppm in female rats. In the 5000 ppm exposure group, body weight gain was statistically significantly increased ($p \leq 0.05$) in female rats on DSs 1 to 8 in comparison with the Carrier Control group value. This difference was not considered to be test substance-related because it was a single occurrence and it did not persist throughout the exposure period.

In male rats, body weight gains for the entire exposure period (calculated as DSs 1 to 28) at 100, 500, 5000 and 10000 ppm were 98.7%, 100.4%, 92.0% and 80.5%, respectively, as compared with the Carrier Control group value. Body weight gains in female rats for the entire exposure period at 100, 500, 5000 and 10000 ppm were 106.3%, 97.8%, 106.0% and 91.4%, respectively, as compared with the Carrier Control group value.

4.5. Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values and Feed Efficiency
(Summaries - Tables 11 through 16; Individual Data - Tables 29 and 30)

At 10000 ppm, the absolute feed consumption value was statistically significantly decreased ($p \leq 0.01$) in male rats during the first week of exposure in comparison with the Carrier Control group values. The relative feed consumption values were statistically significantly increased ($p \leq 0.05$) in male rats on DSs 8 to 15 and 15 to 22 in comparison with the Carrier Control group values. The absolute and relative feed consumption values were also statistically significantly decreased ($p \leq 0.05$) in female rats at 10000 ppm on DSs 22 to 28 in comparison with the Carrier Control group values.

Feed efficiency was statistically significantly decreased ($p \leq 0.01$) in male rats at 10000 ppm during DSs 1 to 8 and when calculated for the entire exposure period (DSs 1 to 28) in comparison with the Carrier Control group values.

Absolute and relative feed consumption values and feed efficiency were unaffected by exposure to up to 5000 ppm dietary concentrations of Malathion Technical. In the 5000 ppm exposure group, the feed efficiency values were statistically significantly increased ($p \leq 0.05$) in female rats on DSs 1 to 8 and statistically significantly decreased ($p \leq 0.05$) in male rats on DSs 15 to 22 in comparison with the Carrier Control group values. These differences were not considered to be test substance-related because they were single occurrences and they did not persist throughout the exposure period.

4.6. Necropsy Observations
(Summaries - Tables 17 and 18; Individual Data - Tables 31 and 32)

There were no test substance-related necropsy observations in the exposure groups. One male rat in the Carrier Control group was observed with a tan area on the right kidney and one female rat in the 5000 ppm exposure group was observed with slight dilation of the pelvis in the right kidney.

4.7. Brain Cholinesterase Activity
(Summaries - Tables 19 and 20; Individual Data - Tables 33 and 34)

As summarized in Text Table 1, male rats at dosages of 500, 5000 and 10000 ppm and female rats at 5000 and 10000 ppm had statistically significantly reduced ($p \leq 0.05$ to $p \leq 0.01$) brain cholinesterase activity as compared with the Carrier Control group values.

Text Table 1: Malathion Technical Brain Cholinesterase Levels			
Group	Dosage (ppm)	Mean ChE ChE U/G \pm S.D. (n)	Percent Inhibition Compared with Controls
Male Rats			
I	0 (Carrier Control)	13.314 \pm 0.981 (15)	--
II	100	12.959 \pm 0.881 (15)	2.7%
III	500	12.355 \pm 0.793 (15)*	7.2%
IV	5000	10.458 \pm 1.026 (15)**	21.5%
V	10000	10.494 \pm 1.381 (15)**	21.2%
Female Rats			
I	0 (Carrier Control)	13.642 \pm 0.962 (15)	--
II	100	13.437 \pm 1.151 (15)	1.5%
III	500	13.007 \pm 0.683 (15)	4.7%
IV	5000	10.226 \pm 0.466 (15)**	25.0%
V	10000	7.119 \pm 2.186 (15)**	47.8%

* Significantly different from the Carrier Control group value ($p \leq 0.05$).

** Significantly different from the Carrier Control group value ($p \leq 0.01$).

4.8. Red Blood Cell (RBC) Cholinesterase Activity (Summaries - Tables 21 and 22; Individual Data - Tables 35 and 36)

As summarized in Text Table 2, female rats had statistically significantly reduced ($p \leq 0.01$) RBC cholinesterase activity in all exposure groups, while male rats had statistically significantly reduced ($p \leq 0.01$) RBC cholinesterase levels in the 500, 5000 and 10000 ppm exposure groups in comparison with the Carrier Control group values. The reduction observed in female rats at 100 ppm was considered minor and not toxicologically relevant because it is less than 20% of the Carrier Control group value.

Text Table 2: Malathion Technical RBC Cholinesterase Activity			
Group	Dosage (ppm)	Mean ChE ChE U/mL \pm S.D. (n)	Percent Inhibition Compared with Controls
Male Rats			
I	0 (Carrier Control)	1.447 \pm 0.190 (15)	--
II	100	1.389 \pm 0.181 (15)	4.0%
III	500	1.124 \pm 0.199 (15)**	22.3%
IV	5000	0.254 \pm 0.070 (13) ^{a**}	82.6%
V	10000	0.165 \pm 0.088 (12) ^{a**}	88.6%
Female Rats			
I	0 (Carrier Control)	1.518 \pm 0.189 (15)	--
II	100	1.324 \pm 0.119 (15)**	13.8%
III	500	1.078 \pm 0.182 (15)**	29.0%
IV	5000	0.259 \pm 0.110 (11) ^{a**}	82.9%
V	10000	0.128 \pm 0.058 (10) ^{a**}	91.6%

** Significantly different from the Carrier Control group value ($p \leq 0.01$).

a. Excludes rats that had values that did not meet the acceptability or reproducibility criteria.

4.8.1. Benchmark Dose Modeling (Appendix 7)

Benchmark dose (BMD) modeling was applied to the data using an exponential model recommended by the U.S. EPA, which provided an adequate fit to the data. The estimated dosage level for a 20% inhibition (BMD₂₀) of RBC cholinesterase activity (the most sensitive endpoint) was 45.6 mg/kg bw/day for male rats and 42.9 mg/kg bw/day for female rats. The lowest BMDL₂₀ value (lowest 95th percentile confidence limit) was 37.7 mg/kg bw/day for male rats and 34.6 mg/kg bw/day for female rats. The brain BMD₁₀ estimates were 215.8 mg/kg bw/day (BMDL₁₀ = 145.1 mg/kg bw/day) for male rats and 159.2 mg/kg bw/day (BMDL₁₀ = 135.3 mg/kg bw/day) for female rats.

4.9. Histopathological Evaluations (APPENDIX 5)

4.9.1. Organ Weight Changes

The absolute and relative (% body weight and % brain weight) weight of the liver was statistically significantly increased ($p \leq 0.05$ to $p \leq 0.01$) in male and female rats at 5000 and 10000 ppm in comparison with the Carrier Control group value. In male rats at 5000 and 10000 ppm, the relative (% body weight) weight of the paired kidneys was statistically significantly increased ($p \leq 0.01$) in comparison with the Carrier Control group value. In female rats at 5000 and 10000 ppm, the relative (% body weight and % brain weight) weights of the paired kidneys were increased or statistically significantly increased ($p \leq 0.01$) in comparison with the Carrier Control group value.

4.9.2. Histopathology

Microscopic findings related to exposure to the test substance were present at 10000 ppm and were present in nose, level 2 (goblet cell depletion) and nose, levels 3, 4 and 5 (olfactory hyperplasia).

Minimal to marked depletion of the goblet cells was also noted on the nasal septum of nose, level 2, in the rats at 10000 ppm. Small numbers of cells with abundant non-staining cytoplasm were also interspersed where there was depletion of goblet cells.

Minimal to moderate hyperplasia of olfactory epithelium was also noted at nose, levels 3, 4 and 5, and consisted of increased numbers of nuclei. The hyperplasia was judged to be minimal when there was preservation of the nuclear free layer, mild when there was loss of the nuclear free layer and moderate when the olfactory epithelium had no nuclear free layer and the surface of the normally straight lining was undulating.

Minimal and mild hepatocellular degeneration, a combination of cellular hypertrophy and clumping of basophilic material in the cytoplasm, was present in two male livers at 10000 ppm. This finding may have been related to the increases in organ weight, but due to the small number of male rats affected, this change was considered equivocal.

5. DISCUSSION AND CONCLUSION

Based on the results of this study, dosages of 0, 100, 500, 5000 and 10000 ppm of Malathion Technical in the diet were selected in consultation with the Sponsor for the 90-day toxicity study in rats.

Repeated oral exposure to Malathion Technical via the diet at exposure levels as high as 10000 ppm for 28 consecutive days did not cause any adverse clinical signs in male or female rats.

Body weight gains were reduced in male rats at 5000 ppm and body weights, body weight gains and terminal body weights were reduced in male rats at 10000 ppm. Feed consumption values were also reduced in male and female rats at 10000 ppm.

In male rats at 10000 ppm, body weight and body weight change values were statistically significant throughout the exposure period; however, the difference in the absolute feed consumption value was only significant during the first week of exposure. The decreased feed consumption value during the first week of exposure may be an indication of an initial taste aversion of Malathion Technical in the diet. The initial body weight decrease during the first week of exposure may have resulted in the overall body weight changes that occurred because the reductions occurred during the growth period.

At 5000 and 10000 ppm, there were organ weight increases in the liver (males and females) and kidneys (males only at 10000 ppm). These increases are considered to reflect the metabolic changes occurring in the rats resulting from the continual exposure to Malathion Technical. They were not considered to be adverse as they did not appear to produce any significant microscopic findings in either organ. Microscopic findings were present in the nasal cavity of the 10000 ppm (depletion of goblet cells and olfactory epithelial hyperplasia) in both male and female rats. These local findings are considered to be the result of continued nasal exposure to Malathion Technical in the diet.

Red blood cell cholinesterase inhibition was observed at all exposure levels in female rats and at the 500 ppm and greater exposure levels in male rats. The reduction observed in female rats at 100 ppm was considered minor (13.8% inhibition compared with controls) and not toxicologically relevant. Brain cholinesterase levels were also statistically significantly reduced at the 500 ppm and greater exposure levels in male rats and at 5000 and 10000 ppm in female rats.

Based on the results of this study, the no-observed-adverse-effect-level (NOAEL) for general toxicity was 100 ppm.

Based on benchmark dose (BMD) modeling, the estimated dosage level for a 20% inhibition (BMD₂₀) of RBC cholinesterase activity (the most sensitive endpoint) was 45.6 mg/kg bw/day for male rats and 42.9 mg/kg bw/day for female rats. The lowest BMDL₂₀ value (lowest 95th percentile confidence limit) was 37.7 mg/kg bw/day for male rats and 34.6 mg/kg bw/day for female rats. The brain BMD₁₀ estimates were 215.8 mg/kg bw/day (BMDL₁₀ = 145.1 mg/kg bw/day) for male rats and 159.2 mg/kg bw/day (BMDL₁₀ = 135.3 mg/kg bw/day) for female rats.

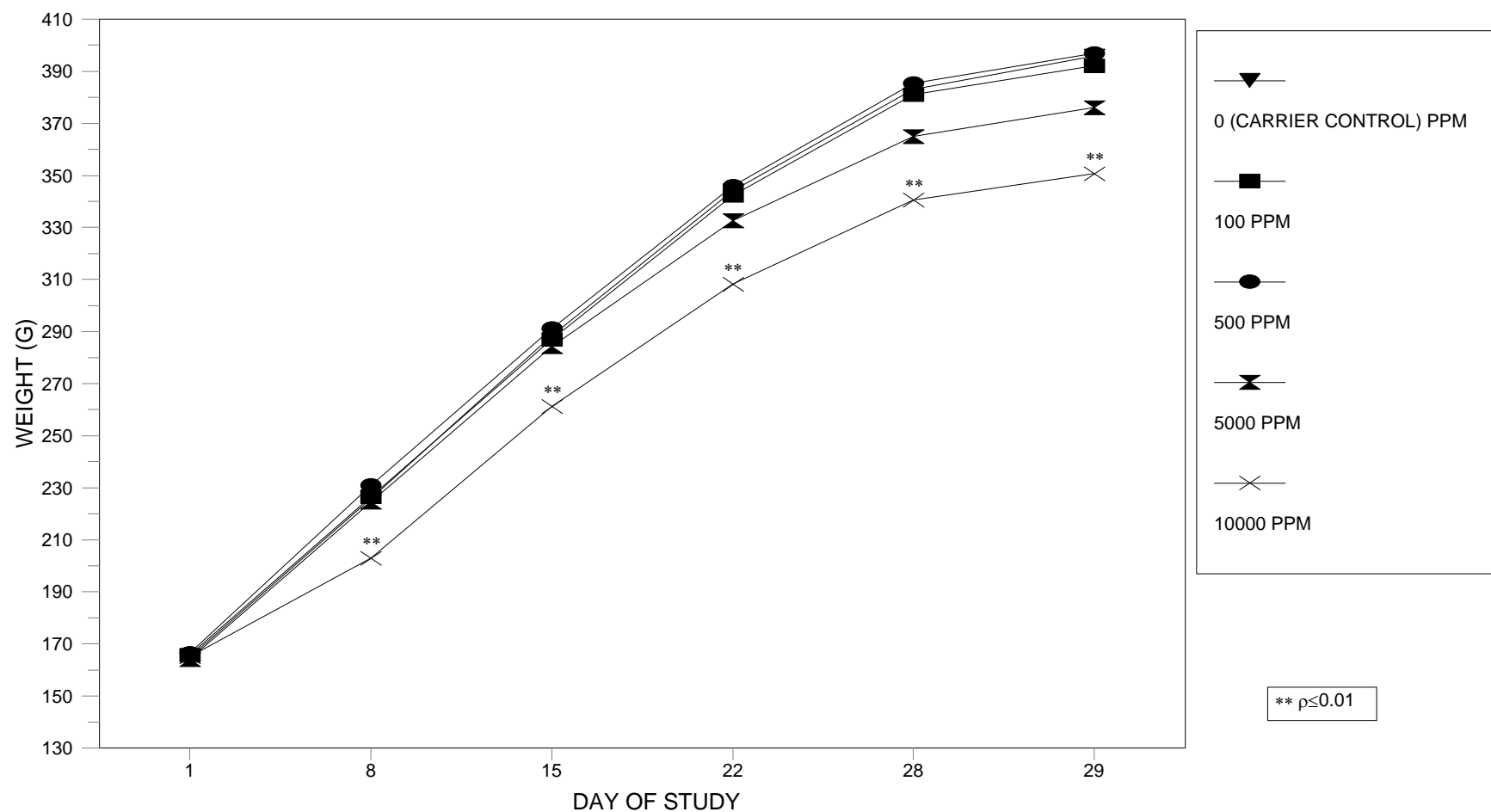
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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

BODY WEIGHTS - MALE RATS

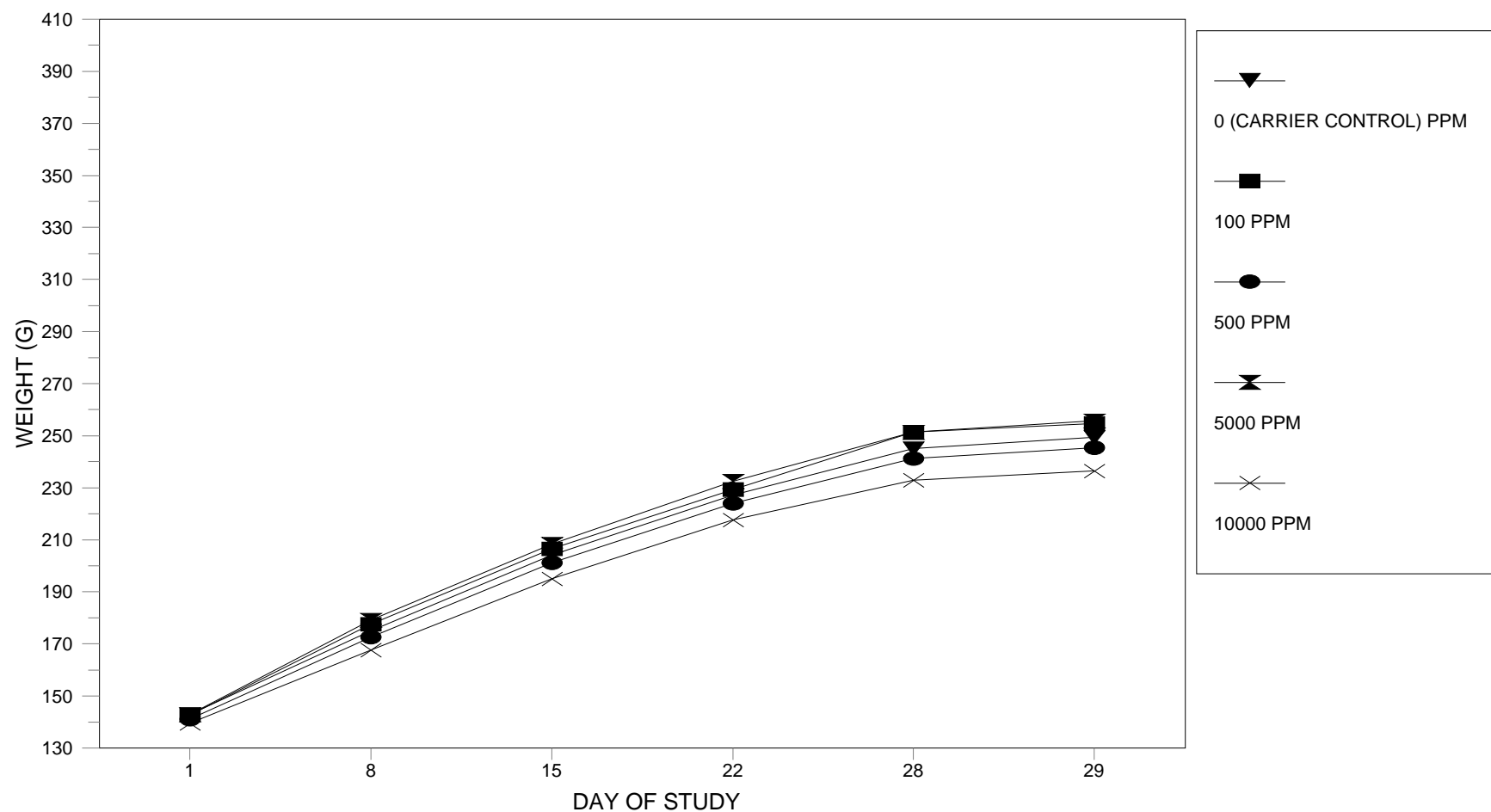
Figure 1



PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

BODY WEIGHTS - FEMALE RATS

Figure 2



PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 1 (PAGE 1): CONSUMED DOSAGES (MG/KG/DAY) - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a	I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	15	15	15	15	15
DIETARY DOSAGE (MG/KG/DAY)					
DAYS 1 - 8	MEAN±S.D. 0.0 ± 0.0	11.9 ± 0.6	60.2 ± 2.6	604.2 ± 34.3	1150.5 ± 119.2
DAYS 8 - 15	MEAN±S.D. 0.0 ± 0.0	10.0 ± 0.5	49.4 ± 2.5	502.3 ± 34.2	1063.7 ± 110.1
DAYS 15 - 22	MEAN±S.D. 0.0 ± 0.0	8.5 ± 0.5	42.6 ± 2.9	421.3 ± 26.9	907.1 ± 73.5
DAYS 22 - 28	MEAN±S.D. 0.0 ± 0.0	7.5 ± 0.4	37.9 ± 2.4	359.3 ± 25.5	764.5 ± 62.9
DAYS 1 - 28	MEAN±S.D. 0.0 ± 0.0	9.2 ± 0.4	46.1 ± 2.4	457.5 ± 25.8	947.8 ± 74.2

DAYS = DAYS OF STUDY

[] = NUMBER OF VALUES AVERAGED

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Excludes a value that appeared incorrectly recorded.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 2 (PAGE 1): CONSUMED DOSAGES (MG/KG/DAY) - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a	I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	15	15	15	15	15
DIETARY DOSAGE (MG/KG/DAY)					
DAYS 1 - 8	MEAN±S.D. 0.0 ± 0.0 [14]b	11.6 ± 0.6	56.9 ± 3.1	576.6 ± 48.1 [14]b	1136.9 ± 99.8
DAYS 8 - 15	MEAN±S.D. 0.0 ± 0.0	9.9 ± 0.4	49.6 ± 4.0	482.3 ± 33.2	962.7 ± 55.4
DAYS 15 - 22	MEAN±S.D. 0.0 ± 0.0 [14]b	8.8 ± 0.5	44.0 ± 3.5	428.8 ± 28.7	845.8 ± 34.1
DAYS 22 - 28	MEAN±S.D. 0.0 ± 0.0	8.1 ± 0.5 [14]b	41.3 ± 5.6	385.2 ± 17.7	747.0 ± 27.5
DAYS 1 - 28	MEAN±S.D. 0.0 ± 0.0	9.4 ± 0.4 [14]b	47.4 ± 3.6	461.3 ± 26.5	910.1 ± 41.2

DAYS = DAYS OF STUDY

[] = NUMBER OF VALUES AVERAGED

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Excludes values that appeared incorrectly recorded.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 3 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) ^a	I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
MAXIMUM POSSIBLE INCIDENCE	435/ 15	435/ 15	435/ 15	435/ 15	435/ 15
MORTALITY	0	0	0	0	0
HEAD, NECK AND/OR BACK: SCAB	13/ 1	22/ 3	51/ 3	0/ 0	2/ 1
NECK: ABRASION	0/ 0	3/ 1	9/ 2	0/ 0	1/ 1
SPARSE HAIR COAT: TOTAL	1/ 1	9/ 1	3/ 1	0/ 0	0/ 0
HEAD	1/ 1	0/ 0	3/ 1	0/ 0	0/ 0
LIMB(S)	0/ 0	9/ 1	0/ 0	0/ 0	0/ 0
LEFT EYE: DISPLACED PUPIL	0/ 0	16/ 1	0/ 0	0/ 0	0/ 0
CHROMODACRYORRHEA	0/ 0	8/ 1	0/ 0	0/ 0	0/ 0
LOCALIZED ALOPECIA: HEAD	0/ 0	2/ 1	0/ 0	0/ 0	0/ 0
CHROMORHINORRHEA	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.

MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION

a. Rats were given continual access to the carrier control or test substance in the diet.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 4 (PAGE 1): DETAILED CLINICAL OBSERVATIONS - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a	I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
MORTALITY	0	0	0	0	0
<u>PREEXPOSURE:</u>					
MAXIMUM POSSIBLE INCIDENCE	15/ 15	15/ 15	15/ 15	15/ 15	15/ 15
DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL	15/ 15	15/ 15	15/ 15	15/ 15	15/ 15
<u>EXPOSURE PERIOD:</u>					
MAXIMUM POSSIBLE INCIDENCE	60/ 15	60/ 15	60/ 15	60/ 15	60/ 15
DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL	57/ 15	56/ 15	50/ 14	60/ 15	58/ 15
DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL	3/ 2	4/ 2	10/ 4	0/ 0	2/ 2
HEAD, NECK AND/OR BACK: SCAB	3/ 2	0/ 0	7/ 3	0/ 0	1/ 1
URINE-STAINED ABDOMINAL FUR	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
TAIL BENT	0/ 0	0/ 0	3/ 1	0/ 0	0/ 0
LEFT EYE: DISPLACED PUPIL	0/ 0	3/ 1	0/ 0	0/ 0	0/ 0
CHROMODACRYORRHEA	0/ 0	2/ 1	0/ 0	0/ 0	0/ 0
SPARSE HAIR COAT: LIMB(S)	0/ 0	2/ 1	0/ 0	0/ 0	0/ 0
LOCALIZED ALOPECIA: HEAD	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.

MAXIMUM POSSIBLE INCIDENCE = (WEEKS x RATS)/NUMBER OF RATS EXAMINED PER GROUP

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION

a. Rats were given continual access to the carrier control or test substance in the diet.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 5 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) ^a	I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
MAXIMUM POSSIBLE INCIDENCE	435/ 15	435/ 15	435/ 15	435/ 15	435/ 15
MORTALITY	0	0	0	0	0
HEAD OR BACK: SCAB	15/ 1	0/ 0	16/ 1	15/ 3	0/ 0
SPARSE HAIR COAT: LIMB(S)	13/ 1	10/ 1	12/ 2	0/ 0	0/ 0
LOCALIZED ALOPECIA: LIMB(S)	0/ 0	0/ 0	6/ 1	0/ 0	0/ 0
RIGHT EYE: DISPLACED PUPIL	29/ 1	27/ 1	0/ 0	0/ 0	0/ 0
ENOPHTHALMOS	0/ 0	29/ 1	0/ 0	0/ 0	0/ 0
MICROPTHALMIA	29/ 1	0/ 0	0/ 0	0/ 0	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.

MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION

a. Rats were given continual access to the carrier control or test substance in the diet.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 6 (PAGE 1): DETAILED CLINICAL OBSERVATIONS - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) ^a	I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
MORTALITY	0	0	0	0	0
<u>PREEXPOSURE:</u>					
MAXIMUM POSSIBLE INCIDENCE	15/ 15	15/ 15	15/ 15	15/ 15	15/ 15
DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL	13/ 13	14/ 14	15/ 15	15/ 15	15/ 15
DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL	2/ 2	1/ 1	0/ 0	0/ 0	0/ 0
RIGHT EYE: DISPLACED PUPIL	1/ 1	1/ 1	0/ 0	0/ 0	0/ 0
ENOPHTHALMOS	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
HEAD: SCAB	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0
MICROPHTHALMIA	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.

MAXIMUM POSSIBLE INCIDENCE = (WEEKS x RATS)/NUMBER OF RATS EXAMINED PER GROUP

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION

a. Rats were given continual access to the carrier control or test substance in the diet.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 6 (PAGE 2): DETAILED CLINICAL OBSERVATIONS - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) ^a	I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
MORTALITY	0	0	0	0	0
<u>EXPOSURE PERIOD:</u>					
MAXIMUM POSSIBLE INCIDENCE	60/ 15	60/ 15	60/ 15	60/ 15	60/ 15
DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL	50/ 14	50/ 14	50/ 15	54/ 15	58/ 15
DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL	10/ 3	10/ 3	10/ 4	6/ 4	2/ 1
HEAD, NECK AND/OR BACK: SCAB	2/ 1	0/ 0	1/ 1	5/ 3	2/ 1
SPARSE HAIR COAT: TOTAL	3/ 1	3/ 1	5/ 3	1/ 1	0/ 0
BACK	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
LIMB(S)	3/ 1	3/ 1	5/ 3	0/ 0	0/ 0
LOCALIZED ALOPECIA: TOTAL	1/ 1	0/ 0	2/ 1	0/ 0	0/ 0
LIMB(S)	0/ 0	0/ 0	2/ 1	0/ 0	0/ 0
HEAD	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0
BACK: ABRASION	0/ 0	0/ 0	2/ 1	0/ 0	0/ 0
RIGHT EYE: DISPLACED PUPIL	4/ 1	4/ 1	0/ 0	0/ 0	0/ 0
ENOPHTHALMOS	0/ 0	4/ 1	0/ 0	0/ 0	0/ 0
TAIL BENT	0/ 0	3/ 1	0/ 0	0/ 0	0/ 0
MICROPHTHALMIA	4/ 1	0/ 0	0/ 0	0/ 0	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.

MAXIMUM POSSIBLE INCIDENCE = (WEEKS x RATS)/NUMBER OF RATS EXAMINED PER GROUP

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION

a. Rats were given continual access to the carrier control or test substance in the diet.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 7 (PAGE 1): BODY WEIGHTS - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED		N	15	15	15	15
BODY WEIGHT (G)						
DAY	1	MEAN±S.D.	164.9 ± 10.1	165.7 ± 9.3	166.4 ± 10.4	164.2 ± 10.6
DAY	8	MEAN±S.D.	225.7 ± 13.4	226.5 ± 10.8	230.9 ± 15.5	224.5 ± 14.5
DAY	15	MEAN±S.D.	288.5 ± 19.2	287.1 ± 12.2	291.3 ± 21.3	284.3 ± 19.0
DAY	22	MEAN±S.D.	344.1 ± 23.2	342.4 ± 15.5	345.9 ± 30.2	332.6 ± 25.9
DAY	28	MEAN±S.D.	383.1 ± 26.8	381.0 ± 18.5	385.4 ± 36.0	364.9 ± 32.3
DAY	29	MEAN±S.D.	395.9 ± 27.3	392.1 ± 18.7	396.9 ± 38.1	376.1 ± 34.3

DAY = DAY OF STUDY

a. Rats were given continual access to the carrier control or test substance in the diet.

** Significantly different from the carrier control group value (p≤0.01).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 8 (PAGE 1): BODY WEIGHT CHANGES - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
BODY WEIGHT CHANGE (G)						
DAYS 1 - 8	MEAN±S.D.	+60.7 ± 6.2	+60.8 ± 3.2	+64.5 ± 6.2	+60.3 ± 5.3	+38.0 ± 9.2**
DAYS 8 - 15	MEAN±S.D.	+62.9 ± 7.6	+60.6 ± 3.9	+60.4 ± 7.4	+59.7 ± 6.9	+58.2 ± 8.6
DAYS 15 - 22	MEAN±S.D.	+55.5 ± 6.7	+55.3 ± 4.8	+54.7 ± 11.9	+48.3 ± 11.9	+47.1 ± 9.1*
DAYS 22 - 28	MEAN±S.D.	+39.1 ± 7.3	+38.6 ± 5.5	+39.5 ± 7.7	+32.3 ± 9.2*	+32.3 ± 9.4*
DAYS 1 - 28	MEAN±S.D.	+218.2 ± 22.2	+215.3 ± 13.7	+219.0 ± 29.7	+200.7 ± 28.0	+175.6 ± 27.3**

DAYS = DAYS OF STUDY

a. Rats were given continual access to the carrier control or test substance in the diet.

* Significantly different from the carrier control group value ($p \leq 0.05$).

** Significantly different from the carrier control group value ($p \leq 0.01$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 9 (PAGE 1): BODY WEIGHTS - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED		N	15	15	15	15
BODY WEIGHT (G)						
DAY 1	MEAN±S.D.	142.9 ± 9.0	142.7 ± 10.0	141.2 ± 7.6	142.9 ± 9.1	139.5 ± 9.7
DAY 8	MEAN±S.D.	175.0 ± 11.3	177.5 ± 13.2	172.6 ± 11.2	179.2 ± 11.5	167.7 ± 13.1
DAY 15	MEAN±S.D.	204.2 ± 15.4	206.5 ± 16.0	201.1 ± 12.7	208.3 ± 18.1	195.1 ± 19.9
DAY 22	MEAN±S.D.	227.1 ± 19.9	229.4 ± 18.7	223.9 ± 14.9	232.5 ± 21.8	217.6 ± 25.7
DAY 28	MEAN±S.D.	245.1 ± 19.6	251.4 ± 23.2	241.3 ± 19.1	251.3 ± 25.6	232.9 ± 28.9
DAY 29	MEAN±S.D.	249.3 ± 21.2	254.8 ± 25.8	245.5 ± 19.5	255.8 ± 26.5	236.5 ± 30.5

DAY = DAY OF STUDY

a. Rats were given continual access to the carrier control or test substance in the diet.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 10 (PAGE 1): BODY WEIGHT CHANGES - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) ^a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
BODY WEIGHT CHANGE (G)						
DAYS 1 - 8	MEAN±S.D.	+32.1 ± 4.6	+34.9 ± 4.7	+31.4 ± 5.4	+36.3 ± 5.8*	+28.2 ± 5.1
DAYS 8 - 15	MEAN±S.D.	+29.2 ± 8.7	+28.9 ± 4.6	+28.5 ± 3.9	+29.1 ± 8.3	+27.4 ± 8.5
DAYS 15 - 22	MEAN±S.D.	+22.9 ± 7.1	+22.9 ± 5.1	+22.9 ± 3.9	+24.1 ± 6.4	+22.5 ± 6.7
DAYS 22 - 28	MEAN±S.D.	+18.0 ± 2.8	+22.0 ± 6.0	+17.4 ± 6.8	+18.8 ± 5.4	+15.3 ± 3.9
DAYS 1 - 28	MEAN±S.D.	+102.3 ± 15.4	+108.7 ± 16.5	+100.1 ± 14.2	+108.4 ± 20.8	+93.5 ± 21.9

DAYS = DAYS OF STUDY

a. Rats were given continual access to the carrier control or test substance in the diet.

* Significantly different from the carrier control group value (p≤0.05).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 11 (PAGE 1): ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
FEED CONSUMPTION (G/DAY)						
DAYS 1 - 8	MEAN±S.D.	23.1 ± 1.4	23.5 ± 1.2	24.1 ± 2.2	23.4 ± 1.9	20.5 ± 2.4**
DAYS 8 - 15	MEAN±S.D.	25.7 ± 1.5	25.7 ± 1.9	25.9 ± 2.5	25.7 ± 2.5	24.7 ± 2.6
DAYS 15 - 22	MEAN±S.D.	26.8 ± 2.2	26.9 ± 2.1	27.2 ± 3.2	26.1 ± 2.6	26.1 ± 2.3
DAYS 22 - 28	MEAN±S.D.	27.0 ± 1.8	27.3 ± 2.4	27.8 ± 3.3	25.2 ± 3.0	24.9 ± 2.9 [14]b
DAYS 1 - 28	MEAN±S.D.	25.6 ± 1.6	25.8 ± 1.8	26.2 ± 2.7	25.1 ± 2.3	23.9 ± 2.1

DAYS = DAYS OF STUDY

[] = NUMBER OF VALUES AVERAGED

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Excludes a value that appeared incorrectly recorded.

** Significantly different from the carrier control group value ($p \leq 0.01$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 12 (PAGE 1): RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
FEED CONSUMPTION (G/KG/DAY)						
DAYS 1 - 8	MEAN±S.D.	117.7 ± 5.2	119.3 ± 5.8	120.3 ± 5.2	120.8 ± 6.9	115.0 ± 11.9
DAYS 8 - 15	MEAN±S.D.	99.7 ± 4.7	99.7 ± 5.5	98.8 ± 4.9	100.5 ± 6.8	106.4 ± 11.0*
DAYS 15 - 22	MEAN±S.D.	84.6 ± 6.2	84.9 ± 4.7	85.1 ± 5.8	84.3 ± 5.4	90.7 ± 7.4* [14]b
DAYS 22 - 28	MEAN±S.D.	74.2 ± 4.0	75.1 ± 4.6	75.8 ± 4.9	71.9 ± 5.1	76.4 ± 6.3
DAYS 1 - 28	MEAN±S.D.	91.2 ± 4.6	92.0 ± 4.2	92.2 ± 4.7	91.5 ± 5.2	94.8 ± 7.4

DAYS = DAYS OF STUDY

[] = NUMBER OF VALUES AVERAGED

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Excludes a value that appeared incorrectly recorded.

* Significantly different from the carrier control group value ($p \leq 0.05$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 13 (PAGE 1): FEED EFFICIENCY - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED		15	15	15	15	15
FEED EFFICIENCY (%) b						
DAYS 1 - 8	MEAN±S.D.	37.4 ± 2.4	37.0 ± 1.6	38.2 ± 2.0	36.8 ± 1.5	26.4 ± 5.3**
DAYS 8 - 15	MEAN±S.D.	34.9 ± 3.3	33.7 ± 2.3	33.3 ± 2.6	33.1 ± 2.0	33.6 ± 3.3
DAYS 15 - 22	MEAN±S.D.	29.5 ± 3.1	29.4 ± 1.9	28.4 ± 4.5	26.1 ± 5.0*	26.4 ± 4.3
DAYS 22 - 28	MEAN±S.D.	24.1 ± 4.4	23.6 ± 2.9	23.6 ± 3.4	21.0 ± 4.5	[14] c 21.4 ± 5.4
DAYS 1 - 28	MEAN±S.D.	31.6 ± 2.7	30.9 ± 1.7	30.9 ± 2.6	29.5 ± 2.3	27.1 ± 3.5**

DAYS = DAYS OF STUDY

[] = NUMBER OF VALUES AVERAGED

a. Rats were given continual access to the carrier control or test substance in the diet.

b. FEED EFFICIENCY = ((AVERAGE DAILY BODY WEIGHT CHANGE)/(AVERAGE DAILY FOOD CONSUMPTION)) * 100

c. Excludes a value that appeared incorrectly recorded.

* Significantly different from the carrier control group value (p≤0.05).

** Significantly different from the carrier control group value (p≤0.01).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 14 (PAGE 1): ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED		N	15	15	15	15
FEED CONSUMPTION (G/DAY)						
DAYS 1 - 8	MEAN±S.D.	17.8 ± 1.4 [14]b	18.6 ± 1.2	18.0 ± 1.5	18.5 ± 1.4 [14]b	17.2 ± 1.6
DAYS 8 - 15	MEAN±S.D.	18.6 ± 1.8	18.9 ± 1.0	18.5 ± 1.6	18.7 ± 2.1	17.6 ± 2.1
DAYS 15 - 22	MEAN±S.D.	18.8 ± 2.3 [14]b	19.3 ± 1.7	18.7 ± 2.1	19.0 ± 2.0	17.5 ± 2.2
DAYS 22 - 28	MEAN±S.D.	18.9 ± 2.1	19.6 ± 1.8 [14]b	19.2 ± 2.9	18.6 ± 1.8	16.8 ± 1.9*
DAYS 1 - 28	MEAN±S.D.	18.6 ± 1.8	19.0 ± 1.3 [14]b	18.6 ± 1.9	18.7 ± 1.7	17.3 ± 1.8

DAYS = DAYS OF STUDY

[] = NUMBER OF VALUES AVERAGED

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Excludes values that appeared incorrectly recorded.

* Significantly different from the carrier control group value ($p \leq 0.05$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 15 (PAGE 1): RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
FEED CONSUMPTION (G/KG/DAY)						
DAYS 1 - 8	MEAN±S.D.	112.3 ± 6.1 [14]b	115.5 ± 5.6	113.9 ± 6.2	115.3 ± 9.6 [14]b	113.7 ± 10.0
DAYS 8 - 15	MEAN±S.D.	97.8 ± 6.1	99.0 ± 4.3	99.2 ± 8.0	96.4 ± 6.6	96.3 ± 5.5
DAYS 15 - 22	MEAN±S.D.	87.1 ± 6.0 [14]b	88.5 ± 5.2	88.0 ± 7.1	85.8 ± 5.7	84.6 ± 3.4
DAYS 22 - 28	MEAN±S.D.	80.1 ± 4.7	81.2 ± 4.9 [14]b	82.7 ± 11.3	77.0 ± 3.5	74.7 ± 2.8*
DAYS 1 - 28	MEAN±S.D.	93.3 ± 4.9	94.7 ± 3.8 [14]b	94.9 ± 7.2	92.3 ± 5.3	91.0 ± 4.1

DAYS = DAYS OF STUDY

[] = NUMBER OF VALUES AVERAGED

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Excludes values that appeared incorrectly recorded.

* Significantly different from the carrier control group value ($p \leq 0.05$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 16 (PAGE 1): FEED EFFICIENCY - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED		15	15	15	15	15
FEED EFFICIENCY (%) b						
DAYS 1 - 8	MEAN±S.D.	25.3 ± 2.8 [14] c	26.7 ± 2.7	24.8 ± 3.1	27.9 ± 3.1* [14] c	23.3 ± 3.2
DAYS 8 - 15	MEAN±S.D.	22.2 ± 4.9	21.8 ± 2.8	22.0 ± 3.3	21.8 ± 4.3	21.8 ± 5.0
DAYS 15 - 22	MEAN±S.D.	17.3 ± 4.2 [14] c	16.9 ± 3.4	17.3 ± 2.5	18.0 ± 4.0	18.0 ± 3.8
DAYS 22 - 28	MEAN±S.D.	16.0 ± 2.8	18.9 ± 3.9 [14] c	14.8 ± 4.6	16.7 ± 4.0	15.0 ± 2.7
DAYS 1 - 28	MEAN±S.D.	20.3 ± 1.8	21.3 ± 2.2 [14] c	19.8 ± 1.8	21.3 ± 2.7	19.8 ± 3.1

DAYS = DAYS OF STUDY

[] = NUMBER OF VALUES AVERAGED

a. Rats were given continual access to the carrier control or test substance in the diet.

b. FEED EFFICIENCY = ((AVERAGE DAILY BODY WEIGHT CHANGE)/(AVERAGE DAILY FOOD CONSUMPTION)) * 100

c. Excludes values that appeared incorrectly recorded.

* Significantly different from the carrier control group value (p≤0.05).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 17 (PAGE 1): NECROPSY OBSERVATIONS - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS EXAMINED b	N	15	15	15	15	15
MORTALITY	N	0	0	0	0	0
APPEARED NORMAL	N	14	15	15	15	15
KIDNEYS: RIGHT, TAN AREA	N	1	0	0	0	0

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Refer to the individual clinical observations table (Table 23) for external observations confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 18 (PAGE 1): NECROPSY OBSERVATIONS - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS EXAMINED b	N	15	15	15	15	15
MORTALITY	N	0	0	0	0	0
APPEARED NORMAL	N	15	15	15	14	15
KIDNEYS: RIGHT, PELVIS, SLIGHT DILATION	N	0	0	0	1	0

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Refer to the individual clinical observations table (Table 25) for external observations confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 19 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALE RATS

DOSAGE GROUP		I	II	III	IV	V
CONCENTRATION (PPM) ^a		0 (CARRIER CONTROL)	100	500	5000	10000
RATS TESTED	N	15	15	15	15	15
BRAIN WEIGHT (G)	MEAN±S.D.	1.934 ± 0.107	1.931 ± 0.098	1.972 ± 0.092	1.950 ± 0.088	1.894 ± 0.082
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	13.314 ± 0.981	12.959 ± 0.881	12.355 ± 0.793*	10.458 ± 1.026**	10.494 ± 1.381**
% CONTROL	%	-	97.3	92.8	78.5	78.8

a. Rats were given continual access to the carrier control or test substance in the diet.

* Significantly different from the carrier control group value ($p \leq 0.05$).

** Significantly different from the carrier control group value ($p \leq 0.01$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 20 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
CONCENTRATION (PPM) ^a		0 (CARRIER CONTROL)	100	500	5000	10000
RATS TESTED	N	15	15	15	15	15
BRAIN WEIGHT (G)	MEAN±S.D.	1.882 ± 0.078	1.856 ± 0.072	1.868 ± 0.072	1.868 ± 0.056	1.850 ± 0.085
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	13.642 ± 0.962	13.437 ± 1.151	13.007 ± 0.683	10.226 ± 0.466**	7.119 ± 2.186**
% CONTROL	%	-	98.5	95.3	75.0	52.2

a. Rats were given continual access to the carrier control or test substance in the diet.

** Significantly different from the carrier control group value ($p \leq 0.01$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 21 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - MALE RATS

DOSAGE GROUP		I	II	III	IV	V
CONCENTRATION (PPM) ^a		0 (CARRIER CONTROL)	100	500	5000	10000
RATS TESTED	N	15	15	15	15	15
INCLUDED IN ANALYSES	N	15	15	15	13b	12b
CHOLINESTERASE LEVELS (UNITS/ML) MEAN±S.D.		1.447 ± 0.190	1.389 ± 0.169	1.124 ± 0.199**	0.254 ± 0.070**	0.165 ± 0.088**
% CONTROL	%	-	96.0	77.7	17.6	11.4

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Excludes rats that had values that did not meet the acceptability or reproducibility criteria.

** Significantly different from the carrier control group value ($p \leq 0.01$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 22 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - FEMALE RATS

DOSAGE GROUP		I	II	III	IV	V
CONCENTRATION (PPM) ^a		0 (CARRIER CONTROL)	100	500	5000	10000
RATS TESTED	N	15	15	15	15	15
INCLUDED IN ANALYSES	N	15	15	15	11b	10b
CHOLINESTERASE LEVELS (UNITS/ML) MEAN±S.D.		1.518 ± 0.189	1.324 ± 0.119**	1.078 ± 0.182**	0.259 ± 0.110**	0.128 ± 0.058**
% CONTROL	%	-	87.2	71.0	17.1	8.4

a. Rats were given continual access to the carrier control or test substance in the diet.

b. Excludes rats that had values that did not meet the acceptability or reproducibility criteria.

** Significantly different from the carrier control group value ($p \leq 0.01$).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 23 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP I		0 (CARRIER CONTROL) PPM
RAT #		DESCRIPTION
216		NO ADVERSE FINDINGS
217		NO ADVERSE FINDINGS
218		NO ADVERSE FINDINGS
219		NO ADVERSE FINDINGS
220	DS(2- 5)	HEAD: SCAB (0.3 CM X 0.3 CM)
	DS(6)	SPARSE HAIR COAT: HEAD
	DS(21- 29)	BACK: SCAB (1.0 CM X 0.7 CM) a
221		NO ADVERSE FINDINGS
222		NO ADVERSE FINDINGS
223		NO ADVERSE FINDINGS
224		NO ADVERSE FINDINGS
225		NO ADVERSE FINDINGS
226		NO ADVERSE FINDINGS
227		NO ADVERSE FINDINGS
228		NO ADVERSE FINDINGS
229		NO ADVERSE FINDINGS
230		NO ADVERSE FINDINGS

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

a. Observation confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 23 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP II		100 PPM
RAT #		DESCRIPTION
231		NO ADVERSE FINDINGS
232		NO ADVERSE FINDINGS
233	DS(3- 13)	HEAD: SCAB (0.5 CM X 0.3 CM)
	DS(7- 8)	LOCALIZED ALOPECIA: HEAD
234	DS(4- 6)	HEAD: SCAB (DID NOT EXCEED 0.3 CM IN DIAMETER)
	DS(14- 29)	LEFT EYE: DISPLACED PUPIL a
	DS(19- 26)	CHROMODACRYORRHEA
	DS(21- 29)	SPARSE HAIR COAT: LIMB(S)a
	DS(26)	CHROMORHINORRHEA
235		NO ADVERSE FINDINGS
236		NO ADVERSE FINDINGS
237		NO ADVERSE FINDINGS
238		NO ADVERSE FINDINGS
239		NO ADVERSE FINDINGS
240		NO ADVERSE FINDINGS
241		NO ADVERSE FINDINGS
242		NO ADVERSE FINDINGS
243	DS(19- 21)	NECK: ABRASION (0.5 CM X 0.2 CM)
	DS(22- 29)	NECK: SCAB (0.3 CM X 0.8 CM)a
244		NO ADVERSE FINDINGS
245		NO ADVERSE FINDINGS

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

a. Observation confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 23 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP III		500 PPM
RAT #		DESCRIPTION
261	DS (13- 17)	NECK: ABRASION (0.2 CM IN DIAMETER)
	DS (18- 29)	NECK: SCAB (DID NOT EXCEED 0.5 CM IN DIAMETER) a
262		NO ADVERSE FINDINGS
263		NO ADVERSE FINDINGS
264		NO ADVERSE FINDINGS
265		NO ADVERSE FINDINGS
266		NO ADVERSE FINDINGS
267		NO ADVERSE FINDINGS
268		NO ADVERSE FINDINGS
269		NO ADVERSE FINDINGS
270		NO ADVERSE FINDINGS
271		NO ADVERSE FINDINGS
272	DS (2- 16)	HEAD: SCAB (DID NOT EXCEED 0.5 CM IN DIAMETER)
	DS (14- 29)	NECK: SCAB (1.0 CM X 0.3 CM) a
	DS (15- 18)	NECK: ABRASION (0.5 CM IN DIAMETER)
	DS (19- 29)	NECK: SCAB (0.5 CM IN DIAMETER) a
	DS (20- 26)	HEAD: SCAB (0.2 CM X 0.3 CM)
	DS (21)	HEAD: SCAB (0.3 CM IN DIAMETER)
273		NO ADVERSE FINDINGS
274	DS (2- 5)	HEAD: SCAB (0.2 CM IN DIAMETER)
	DS (6- 8)	SPARSE HAIR COAT: HEAD
	DS (7- 13)	HEAD: SCAB (0.5 CM IN DIAMETER)
275		NO ADVERSE FINDINGS

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

a. Observation confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 23 (PAGE 4): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP IV		5000 PPM
RAT #	DESCRIPTION	
201	NO ADVERSE FINDINGS	
202	NO ADVERSE FINDINGS	
203	NO ADVERSE FINDINGS	
204	NO ADVERSE FINDINGS	
205	NO ADVERSE FINDINGS	
206	NO ADVERSE FINDINGS	
207	NO ADVERSE FINDINGS	
208	NO ADVERSE FINDINGS	
209	NO ADVERSE FINDINGS	
210	NO ADVERSE FINDINGS	
211	NO ADVERSE FINDINGS	
212	NO ADVERSE FINDINGS	
213	NO ADVERSE FINDINGS	
214	NO ADVERSE FINDINGS	
215	NO ADVERSE FINDINGS	

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE
DS = DAY OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 23 (PAGE 5): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP V		10000 PPM
RAT #		DESCRIPTION
246		NO ADVERSE FINDINGS
247		NO ADVERSE FINDINGS
248		NO ADVERSE FINDINGS
249		NO ADVERSE FINDINGS
250		NO ADVERSE FINDINGS
251	DS(27- 28)	NECK: SCAB (0.2 CM X 0.3 CM)
	DS(29)	NECK: ABRASION (0.2 CM X 0.3 CM) a
252	DS(2- 3)	DEHYDRATION - MILD b
253		NO ADVERSE FINDINGS
254	DS(2- 3)	DEHYDRATION - MODERATE b
	DS(4- 6)	DEHYDRATION - MILD b
255	DS(3- 5)	DEHYDRATION - MILD b
256	DS(2- 3)	DEHYDRATION - MILD b
257		NO ADVERSE FINDINGS
258		NO ADVERSE FINDINGS
259	DS(2- 5)	DEHYDRATION - MILD b
260	DS(2- 5)	DEHYDRATION - MILD b

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

- a. Observation confirmed at necropsy.
- b. Dehydration was verified using a skin turgor test; this test is only conducted on rats based on other clinical signs and/or a reduction in body weight/feed consumption. Therefore, this clinical observation was not summarized or statistically analyzed.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 24 (PAGE 1): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP I		0 (CARRIER CONTROL) PPM
RAT #		DESCRIPTION
216	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
217	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
218	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
219	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
220	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 2)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(3- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(3- 4)	BACK: SCAB (1.0 CM X 0.7 CM)
221	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
222	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
223	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
224	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
225	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
226	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
227	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
228	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 2)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(3)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(3)	BACK: SCAB (0.4 CM IN DIAMETER)
	WS(4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
229	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
230	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE
WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 24 (PAGE 2): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP II		100 PPM
RAT #		DESCRIPTION
231	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
232	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
233	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(1)	LOCALIZED ALOPECIA: HEAD
	WS(2- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
234	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(2- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(2- 4)	LEFT EYE: DISPLACED PUPIL
	WS(3- 4)	CHROMODACRYORRHEA
	WS(3- 4)	SPARSE HAIR COAT: LIMB(S)
235	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
236	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
237	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
238	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
239	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
240	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
241	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
242	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
243	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
244	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
245	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE
 WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 24 (PAGE 3): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP III		500 PPM
RAT #		DESCRIPTION
261	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 2)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(3- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(3- 4)	NECK: SCAB (0.7 CM X 0.4 CM)
262	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
263	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
264	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
265	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
266	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
267	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
268	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
269	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
270	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
271	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(2- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(2- 4)	TAIL BENT
272	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(1- 4)	HEAD: SCAB (DID NOT EXCEED 0.5 CM IN DIAMETER)
	WS(2- 4)	NECK: SCAB(S) (DID NOT EXCEED 1.0 CM X 0.4 CM)
	WS(3- 4)	BACK: SCAB (0.6 CM X 0.2 CM)
273	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
274	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(1)	HEAD: SCAB (0.5 CM IN DIAMETER)
	WS(2- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
275	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE
WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 24 (PAGE 4): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP IV		5000 PPM
RAT #		DESCRIPTION
201	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
202	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
203	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
204	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
205	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
206	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
207	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
208	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
209	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
210	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
211	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
212	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
213	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
214	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
215	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE
 WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 24 (PAGE 5): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP V		10000 PPM
RAT #		DESCRIPTION
246	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
247	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
248	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 3)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(4)	URINE-STAINED ABDOMINAL FUR
249	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
250	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 3)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(4)	BACK: SCAB (0.4 CM IN DIAMETER)
251	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
252	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
253	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
254	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
255	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
256	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
257	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
258	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
259	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
260	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE
WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 25 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP I		0 (CARRIER CONTROL) PPM
RAT #		DESCRIPTION
316		NO ADVERSE FINDINGS
317		NO ADVERSE FINDINGS
318	DS(17- 29)	SPARSE HAIR COAT: LIMB(S) a
319	DS(1- 5)	HEAD: SCAB (DID NOT EXCEED 0.3 CM X 0.1 CM)
	DS(7- 16)	HEAD: SCAB (0.3 CM IN DIAMETER)
320		NO ADVERSE FINDINGS
321		NO ADVERSE FINDINGS
322	DS(1- 29)	MICROPTHALMIA a
	DS(1- 29)	RIGHT EYE: DISPLACED PUPIL a
323		NO ADVERSE FINDINGS
324		NO ADVERSE FINDINGS
325		NO ADVERSE FINDINGS
326		NO ADVERSE FINDINGS
327		NO ADVERSE FINDINGS
328		NO ADVERSE FINDINGS
329		NO ADVERSE FINDINGS
330		NO ADVERSE FINDINGS

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

a. Observation confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 25 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP II		100 PPM
RAT #		DESCRIPTION
331	DS (1- 16)	RIGHT EYE: DISPLACED PUPIL
	DS (1- 29)	ENOPHTHALMOS a
	DS (19- 29)	RIGHT EYE: DISPLACED PUPIL a
332		NO ADVERSE FINDINGS
333		NO ADVERSE FINDINGS
334	DS (20- 29)	SPARSE HAIR COAT: LIMB(S) a
335		NO ADVERSE FINDINGS
336		NO ADVERSE FINDINGS
337		NO ADVERSE FINDINGS
338		NO ADVERSE FINDINGS
339		NO ADVERSE FINDINGS
340		NO ADVERSE FINDINGS
341		NO ADVERSE FINDINGS
342		NO ADVERSE FINDINGS
343		NO ADVERSE FINDINGS
344		NO ADVERSE FINDINGS
345		NO ADVERSE FINDINGS

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

a. Observation confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 25 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP III		500 PPM
RAT #		DESCRIPTION
361		NO ADVERSE FINDINGS
362		NO ADVERSE FINDINGS
363		NO ADVERSE FINDINGS
364		NO ADVERSE FINDINGS
365		NO ADVERSE FINDINGS
366	DS (14- 25)	BACK: SCAB (DID NOT EXCEED 0.7 CM X 0.3 CM)
	DS (21- 29)	BACK: SCAB (DID NOT EXCEED 0.9 CM X 0.4 CM) a
367		NO ADVERSE FINDINGS
368		NO ADVERSE FINDINGS
369	DS (19- 23)	SPARSE HAIR COAT: LIMB(S)
	DS (24- 29)	LOCALIZED ALOPECIA: LIMB(S) a
370		NO ADVERSE FINDINGS
371		NO ADVERSE FINDINGS
372		NO ADVERSE FINDINGS
373		NO ADVERSE FINDINGS
374	DS (23- 29)	SPARSE HAIR COAT: LIMB(S) a
375		NO ADVERSE FINDINGS

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

a. Observation confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 25 (PAGE 4): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP IV		5000 PPM
RAT #		DESCRIPTION
301	DS(5- 11)	HEAD: SCAB (1.0 CM X 0.4 CM)
302	DS(12- 13)	HEAD: SCAB (0.2 CM IN DIAMETER)
303		NO ADVERSE FINDINGS
304		NO ADVERSE FINDINGS
305		NO ADVERSE FINDINGS
306		NO ADVERSE FINDINGS
307		NO ADVERSE FINDINGS
308		NO ADVERSE FINDINGS
309		NO ADVERSE FINDINGS
310		NO ADVERSE FINDINGS
311		NO ADVERSE FINDINGS
312		NO ADVERSE FINDINGS
313		NO ADVERSE FINDINGS
314	DS(14)	BACK: SCAB (1.0 CM X 0.3 CM)
	DS(21- 25)	BACK: SCAB (1.0 CM X 0.4 CM)
315		NO ADVERSE FINDINGS

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 25 (PAGE 5): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP V		10000 PPM
RAT #		DESCRIPTION
346		NO ADVERSE FINDINGS
347		NO ADVERSE FINDINGS
348	DS(2- 4)	DEHYDRATION - MILD a
349		NO ADVERSE FINDINGS
350	DS(2- 4)	DEHYDRATION - MILD a
351		NO ADVERSE FINDINGS
352	DS(3- 4)	DEHYDRATION - MILD a
353		NO ADVERSE FINDINGS
354		NO ADVERSE FINDINGS
355		NO ADVERSE FINDINGS
356		NO ADVERSE FINDINGS
357		NO ADVERSE FINDINGS
358		NO ADVERSE FINDINGS
359		NO ADVERSE FINDINGS
360		NO ADVERSE FINDINGS

CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

DS = DAY OF STUDY

- a. Dehydration was verified using a skin turgor test; this test is only conducted on rats based on other clinical signs and/or a reduction in body weight/feed consumption. Therefore, this clinical observation was not summarized or statistically analyzed.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 26 (PAGE 1): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP I		0 (CARRIER CONTROL) PPM
RAT #		DESCRIPTION
316	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
317	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
318	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(2- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(2- 4)	SPARSE HAIR COAT: LIMB(S)
319	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	PREEEXPOSURE	HEAD: SCAB (0.3 CM X 0.1 CM)
	WS(1- 3)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(1- 2)	HEAD: SCAB (0.3 CM X 0.1 CM)
	WS(3)	LOCALIZED ALOPECIA: HEAD
	WS(4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
320	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
321	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
322	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	PREEEXPOSURE	RIGHT EYE: DISPLACED PUPIL
	PREEEXPOSURE	MICROPHthalmia
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(1- 4)	RIGHT EYE: DISPLACED PUPIL
	WS(1- 4)	MICROPHthalmia
323	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
324	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
325	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
326	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
327	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
328	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
329	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
330	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 26 (PAGE 2): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP II		100 PPM
RAT #		DESCRIPTION
331	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	PREEXPOSURE	RIGHT EYE: DISPLACED PUPIL
	PREEXPOSURE	ENOPHTHALMOS
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS (1- 4)	RIGHT EYE: DISPLACED PUPIL
	WS (1- 4)	ENOPHTHALMOS
332	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
333	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
334	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (2- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS (2- 4)	SPARSE HAIR COAT: LIMB(S)
335	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
336	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
337	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
338	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
339	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
340	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
341	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
342	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
343	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (2- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS (2- 4)	TAIL BENT
344	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
345	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE
WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 26 (PAGE 3): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP III		500 PPM
RAT #	DESCRIPTION	
361	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
362	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 2)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(3- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(3- 4)	SPARSE HAIR COAT: LIMB(S)
363	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
364	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
365	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
366	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(2- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(2)	BACK: SCAB (0.7 CM IN DIAMETER)
	WS(3- 4)	BACK: ABRASION(S) (DID NOT EXCEED 1.1 CM X 0.5 CM)
367	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
368	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
369	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(2- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(2)	SPARSE HAIR COAT: LIMB(S)
	WS(3- 4)	LOCALIZED ALOPECIA: LIMB(S)
370	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
371	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
372	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
373	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
374	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 2)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(3- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(3- 4)	SPARSE HAIR COAT: LIMB(S)
375	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 26 (PAGE 4): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP IV		5000 PPM
RAT #		DESCRIPTION
301	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS (1)	HEAD: SCAB (4.0 CM IN DIAMETER)
	WS (1)	HEAD: SCAB (3.0 CM IN DIAMETER)
	WS (2- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
302	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 2)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (3)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS (3)	SPARSE HAIR COAT: BACK
	WS (4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
303	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
304	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
305	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS (1)	HEAD: SCAB (0.2 CM IN DIAMETER)
	WS (2- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
306	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
307	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
308	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
309	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
310	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
311	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
312	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
313	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
314	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (2- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS (2- 4)	BACK: SCAB(S) (DID NOT EXCEED 1.0 CM X 0.3 CM)
315	PREEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS (1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE

WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 26 (PAGE 5): DETAILED CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP V		10000 PPM
RAT #		DESCRIPTION
346	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
347	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
348	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
349	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
350	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
351	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
352	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
353	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
354	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
355	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
356	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
357	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 2)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(3- 4)	DETAILED CLINICAL OBSERVATIONS WERE NOT NORMAL
	WS(3- 4)	NECK: SCAB (0.3 CM IN DIAMETER)
358	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
359	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
360	PREEEXPOSURE	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL
	WS(1- 4)	DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL

DETAILED CLINICAL OBSERVATIONS APPEARED NORMAL UNLESS NOTED OTHERWISE
WS = WEEK OF STUDY

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP I												
	0 (CARRIER CONTROL) PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
216	146.	152.	160.	172.	176.	184.	191.	201.	206.	215.	220.	232.	240.
217	182.	192.	204.	216.	221.	236.	248.	256.	270.	282.	293.	303.	318.
218	162.	171.	180.	192.	196.	205.	212.	221.	229.	239.	245.	254.	262.
219	167.	174.	179.	194.	195.	205.	214.	218.	231.	240.	247.	254.	262.
220	150.	160.	170.	186.	192.	200.	210.	216.	226.	235.	246.	255.	263.
221	182.	192.	204.	221.	219.	235.	246.	248.	261.	269.	278.	288.	298.
222	163.	170.	180.	196.	200.	210.	221.	229.	237.	244.	254.	263.	274.
223	163.	171.	184.	199.	202.	211.	219.	226.	233.	240.	248.	255.	260.
224	159.	167.	179.	194.	197.	208.	219.	225.	237.	243.	254.	262.	270.
225	172.	179.	188.	205.	205.	220.	226.	231.	244.	250.	262.	267.	276.
226	164.	171.	183.	197.	197.	204.	215.	221.	229.	238.	248.	259.	268.
227	173.	183.	194.	205.	208.	217.	228.	231.	244.	251.	263.	270.	279.
228	159.	166.	176.	185.	189.	196.	205.	211.	221.	230.	240.	247.	258.
229	171.	177.	186.	200.	202.	212.	220.	229.	240.	250.	258.	265.	274.
230	161.	167.	178.	191.	197.	206.	216.	222.	231.	238.	247.	257.	268.
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
216	249.	257.	268.	272.	282.	291.	296.	309.	316.	322.	327.	330.	345.
217	328.	340.	352.	361.	374.	381.	395.	404.	415.	425.	436.	443.	455.
218	268.	276.	285.	294.	306.	313.	320.	328.	334.	342.	350.	354.	361.
219	272.	278.	290.	299.	306.	313.	323.	329.	335.	342.	349.	354.	362.
220	274.	283.	291.	302.	308.	315.	324.	334.	341.	350.	357.	361.	375.
221	306.	315.	326.	336.	344.	350.	359.	363.	369.	375.	384.	386.	390.
222	286.	292.	302.	311.	318.	325.	334.	343.	352.	358.	364.	368.	375.
223	272.	276.	286.	290.	298.	304.	308.	318.	324.	330.	335.	338.	344.
224	280.	287.	282.	295.	307.	316.	325.	332.	339.	347.	360.	364.	366.
225	285.	295.	300.	308.	317.	323.	329.	337.	344.	348.	357.	359.	366.
226	276.	280.	292.	297.	307.	313.	319.	328.	334.	340.	345.	352.	355.
227	290.	297.	310.	315.	326.	332.	337.	347.	349.	359.	363.	371.	374.
228	267.	277.	286.	294.	302.	310.	318.	324.	329.	344.	347.	354.	359.
229	281.	290.	296.	303.	313.	319.	327.	335.	338.	351.	356.	361.	368.
230	278.	285.	294.	304.	313.	322.	329.	337.	342.	353.	360.	363.	368.

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP I			0 (CARRIER CONTROL) PPM
	DAY 27	28	29	
216	345.	356.	360.	
217	460.	469.	484.	
218	369.	375.	389.	
219	371.	375.	390.	
220	380.	391.	400.	
221	397.	398.	404.	
222	379.	385.	397.	
223	354.	352.	366.	
224	381.	385.	398.	
225	377.	379.	391.	
226	365.	366.	382.	
227	386.	388.	401.	
228	369.	370.	389.	
229	376.	380.	394.	
230	376.	378.	394.	

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP II												
	100 PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
231	145.	153.	165.	178.	182.	192.	204.	206.	218.	225.	237.	243.	250.
232	173.	182.	192.	206.	211.	217.	228.	233.	245.	250.	255.	266.	273.
233	165.	175.	183.	196.	202.	210.	220.	226.	238.	245.	254.	262.	270.
234	171.	180.	186.	195.	203.	214.	223.	232.	243.	256.	263.	274.	281.
235	152.	159.	170.	181.	186.	195.	205.	211.	219.	229.	237.	245.	253.
236	174.	180.	192.	206.	209.	219.	231.	235.	244.	253.	262.	271.	280.
237	158.	165.	174.	188.	189.	198.	206.	211.	221.	228.	238.	246.	254.
238	170.	176.	187.	201.	205.	216.	224.	228.	239.	246.	256.	263.	272.
239	158.	164.	177.	190.	194.	202.	213.	221.	230.	238.	248.	259.	269.
240	175.	182.	192.	206.	208.	220.	232.	236.	250.	255.	267.	271.	282.
241	162.	172.	184.	195.	197.	208.	217.	222.	230.	240.	249.	258.	266.
242	173.	180.	192.	204.	210.	222.	231.	241.	253.	260.	269.	279.	288.
243	162.	171.	179.	190.	198.	206.	213.	223.	229.	239.	247.	256.	269.
244	174.	181.	191.	203.	208.	216.	224.	234.	240.	248.	255.	264.	271.
245	174.	181.	192.	205.	209.	219.	233.	239.	253.	259.	270.	279.	288.
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
231	264.	269.	278.	287.	298.	304.	310.	321.	326.	336.	346.	350.	355.
232	282.	287.	298.	304.	312.	319.	327.	334.	338.	348.	355.	360.	368.
233	279.	286.	297.	302.	313.	320.	326.	334.	340.	349.	357.	360.	364.
234	290.	297.	310.	321.	328.	338.	347.	358.	363.	373.	380.	388.	394.
235	259.	268.	276.	282.	288.	294.	300.	308.	314.	321.	328.	332.	338.
236	287.	293.	306.	313.	314.	326.	334.	341.	347.	352.	363.	366.	372.
237	259.	268.	275.	281.	291.	297.	306.	315.	320.	327.	329.	337.	342.
238	280.	287.	296.	304.	313.	322.	327.	335.	340.	347.	355.	361.	366.
239	275.	283.	296.	301.	312.	319.	327.	332.	340.	347.	358.	361.	365.
240	292.	296.	303.	317.	326.	333.	337.	347.	355.	364.	372.	377.	386.
241	278.	284.	295.	304.	312.	321.	328.	334.	341.	346.	351.	356.	361.
242	301.	310.	320.	325.	337.	344.	354.	358.	372.	378.	387.	396.	401.
243	276.	286.	294.	304.	312.	319.	327.	335.	339.	348.	356.	362.	370.
244	281.	290.	297.	305.	311.	319.	328.	336.	343.	351.	354.	359.	366.
245	298.	303.	313.	321.	328.	334.	343.	350.	358.	368.	376.	378.	386.

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 4): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP II			100 PPM
	DAY 27	28	29	
231	364.	370.	379.	
232	378.	383.	394.	
233	373.	380.	388.	
234	402.	407.	419.	
235	344.	349.	359.	
236	382.	381.	397.	
237	348.	350.	365.	
238	375.	378.	389.	
239	374.	375.	387.	
240	398.	403.	412.	
241	371.	371.	386.	
242	409.	415.	431.	
243	370.	379.	389.	
244	371.	378.	385.	
245	388.	396.	401.	

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 5): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP III												
	500 PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
261	146.	154.	164.	177.	182.	190.	201.	209.	217.	227.	235.	242.	250.
262	175.	185.	198.	214.	217.	228.	240.	246.	259.	264.	273.	279.	288.
263	164.	172.	182.	198.	200.	211.	219.	228.	238.	245.	253.	261.	268.
264	164.	172.	183.	198.	202.	213.	224.	231.	242.	249.	260.	267.	277.
265	150.	159.	168.	180.	184.	193.	205.	206.	215.	223.	231.	239.	246.
266	181.	189.	202.	218.	224.	235.	247.	254.	270.	277.	287.	294.	304.
267	163.	174.	185.	199.	204.	213.	225.	229.	236.	246.	255.	262.	274.
268	168.	172.	185.	199.	203.	212.	222.	228.	239.	247.	255.	261.	272.
269	165.	174.	185.	198.	204.	213.	224.	231.	238.	246.	255.	262.	274.
270	175.	184.	193.	208.	212.	224.	234.	242.	250.	256.	265.	275.	282.
271	162.	168.	178.	191.	196.	203.	211.	216.	228.	233.	242.	249.	259.
272	170.	178.	190.	201.	209.	216.	229.	237.	248.	258.	266.	275.	284.
273	156.	162.	169.	180.	186.	193.	199.	209.	215.	220.	226.	234.	238.
274	179.	190.	202.	214.	222.	231.	247.	249.	264.	274.	283.	292.	305.
275	178.	189.	199.	217.	221.	232.	241.	248.	263.	270.	281.	288.	297.
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
261	260.	268.	278.	287.	296.	302.	311.	321.	326.	334.	344.	355.	355.
262	297.	304.	311.	318.	327.	336.	342.	352.	358.	369.	371.	378.	386.
263	276.	282.	287.	290.	294.	302.	305.	309.	314.	318.	325.	328.	336.
264	289.	294.	303.	313.	321.	330.	340.	350.	358.	367.	376.	381.	390.
265	253.	257.	265.	271.	277.	285.	292.	297.	304.	311.	313.	319.	321.
266	315.	323.	333.	344.	354.	361.	370.	376.	384.	393.	404.	406.	415.
267	289.	297.	308.	321.	332.	341.	348.	356.	361.	373.	384.	385.	393.
268	283.	286.	298.	302.	312.	321.	328.	337.	337.	345.	351.	354.	359.
269	284.	291.	304.	310.	321.	334.	342.	348.	359.	365.	373.	380.	389.
270	291.	296.	305.	312.	318.	325.	331.	336.	344.	346.	356.	355.	362.
271	267.	271.	282.	289.	298.	302.	309.	317.	321.	330.	336.	339.	346.
272	298.	304.	311.	319.	328.	337.	348.	351.	355.	370.	373.	380.	390.
273	248.	258.	262.	266.	272.	275.	282.	289.	291.	297.	304.	309.	312.
274	316.	324.	333.	344.	354.	363.	374.	384.	394.	406.	413.	412.	427.
275	310.	314.	328.	336.	343.	352.	362.	374.	383.	390.	400.	404.	412.

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 6): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP III			500 PPM
	DAY 27	28	29	
261	365.	374.	378.	
262	392.	396.	408.	
263	339.	343.	348.	
264	399.	402.	411.	
265	327.	332.	343.	
266	426.	428.	445.	
267	405.	410.	426.	
268	368.	368.	377.	
269	400.	402.	414.	
270	371.	374.	384.	
271	354.	358.	369.	
272	388.	401.	415.	
273	317.	323.	337.	
274	434.	442.	456.	
275	421.	428.	443.	

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 7): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP IV 5000 PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
201	145.	148.	157.	169.	175.	184.	192.	200.	210.	216.	226.	234.	239.
202	181.	188.	201.	213.	215.	228.	243.	247.	259.	270.	276.	287.	295.
203	165.	170.	177.	192.	195.	208.	217.	225.	237.	246.	254.	258.	267.
204	169.	170.	182.	199.	203.	215.	228.	235.	247.	255.	270.	277.	287.
205	151.	155.	167.	178.	185.	196.	204.	213.	224.	234.	240.	248.	258.
206	178.	178.	192.	209.	213.	227.	237.	247.	254.	266.	272.	286.	294.
207	165.	166.	180.	194.	197.	208.	220.	229.	243.	246.	263.	269.	279.
208	171.	169.	183.	200.	203.	214.	225.	234.	245.	253.	262.	266.	276.
209	154.	154.	167.	176.	181.	191.	199.	208.	220.	226.	235.	242.	250.
210	178.	182.	192.	211.	211.	225.	237.	243.	258.	268.	279.	288.	294.
211	159.	164.	176.	185.	190.	203.	208.	215.	223.	233.	239.	249.	257.
212	164.	170.	181.	193.	198.	208.	217.	223.	231.	241.	250.	253.	263.
213	156.	162.	173.	187.	189.	198.	210.	216.	226.	234.	245.	253.	259.
214	171.	174.	184.	197.	200.	210.	216.	222.	232.	237.	247.	252.	259.
215	156.	158.	170.	183.	184.	195.	203.	211.	221.	229.	237.	241.	252.
RAT #	DOSAGE GROUP IV 5000 PPM												
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
201	249.	259.	267.	278.	287.	296.	304.	315.	325.	331.	334.	340.	346.
202	303.	311.	325.	331.	339.	351.	358.	368.	375.	383.	393.	401.	401.
203	274.	280.	286.	292.	298.	301.	306.	307.	309.	314.	319.	319.	324.
204	298.	307.	315.	326.	333.	343.	350.	354.	362.	369.	375.	381.	386.
205	266.	274.	287.	292.	299.	312.	316.	321.	329.	336.	347.	346.	352.
206	303.	314.	321.	330.	337.	344.	350.	356.	361.	367.	374.	375.	386.
207	288.	295.	305.	314.	321.	329.	336.	346.	352.	362.	365.	372.	376.
208	282.	291.	300.	308.	314.	321.	328.	332.	339.	348.	357.	358.	363.
209	255.	266.	270.	276.	285.	293.	299.	305.	316.	323.	326.	332.	340.
210	305.	312.	322.	336.	345.	350.	362.	363.	370.	381.	387.	391.	394.
211	262.	271.	278.	285.	287.	291.	296.	302.	306.	311.	316.	321.	323.
212	267.	273.	279.	284.	293.	298.	303.	312.	316.	323.	329.	331.	340.
213	270.	276.	287.	293.	302.	307.	320.	325.	330.	341.	346.	358.	362.
214	263.	269.	276.	282.	288.	293.	296.	300.	303.	310.	313.	322.	324.
215	259.	266.	271.	275.	280.	287.	290.	291.	296.	298.	301.	302.	302.

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 8): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP IV			5000 PPM
	DAY 27	28	29	
201	354.	357.	373.	
202	414.	419.	433.	
203	329.	334.	343.	
204	395.	402.	415.	
205	361.	366.	371.	
206	386.	389.	402.	
207	386.	388.	398.	
208	366.	369.	381.	
209	346.	351.	363.	
210	401.	406.	413.	
211	328.	332.	340.	
212	345.	344.	362.	
213	372.	378.	399.	
214	328.	333.	341.	
215	304.	305.	308.	

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 9): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP V 10000 PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
246	144.	140.	147.	157.	158.	169.	178.	183.	190.	195.	202.	208.	216.
247	175.	175.	182.	194.	196.	204.	216.	219.	230.	238.	243.	237.	250.
248	162.	154.	160.	172.	177.	185.	196.	202.	208.	218.	226.	232.	239.
249	164.	161.	170.	179.	186.	193.	198.	205.	215.	222.	232.	240.	250.
250	160.	150.	152.	164.	164.	179.	192.	198.	209.	221.	231.	239.	251.
251	179.	175.	179.	187.	188.	195.	211.	217.	227.	237.	249.	256.	266.
252	163.	155.	166.	176.	176.	176.	182.	186.	197.	204.	214.	223.	228.
253	172.	170.	180.	196.	201.	211.	221.	227.	239.	247.	254.	263.	273.
254	158.	150.	152.	165.	164.	173.	183.	189.	198.	206.	215.	221.	229.
255	173.	173.	179.	186.	187.	199.	209.	216.	227.	235.	247.	252.	260.
256	160.	150.	155.	164.	173.	178.	188.	194.	200.	209.	217.	221.	235.
257	168.	157.	159.	171.	180.	187.	198.	205.	213.	222.	228.	233.	240.
258	160.	149.	142.	143.	146.	154.	166.	178.	186.	196.	206.	212.	223.
259	168.	160.	166.	177.	186.	196.	208.	218.	228.	236.	246.	254.	264.
260	169.	166.	167.	176.	179.	192.	203.	208.	219.	228.	237.	241.	252.
RAT #	DOSAGE GROUP V 10000 PPM												
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
246	223.	229.	234.	240.	246.	251.	253.	259.	262.	267.	274.	276.	281.
247	262.	269.	279.	283.	295.	301.	309.	315.	321.	325.	330.	342.	344.
248	249.	257.	261.	269.	276.	281.	291.	293.	296.	303.	307.	315.	318.
249	257.	266.	274.	281.	289.	295.	307.	311.	320.	325.	332.	335.	342.
250	261.	272.	276.	286.	294.	302.	310.	314.	324.	326.	338.	341.	349.
251	276.	280.	294.	303.	310.	319.	324.	334.	336.	347.	351.	358.	364.
252	238.	245.	253.	261.	268.	274.	280.	285.	293.	295.	299.	306.	309.
253	280.	292.	301.	311.	315.	325.	331.	339.	345.	351.	362.	366.	375.
254	241.	243.	253.	258.	263.	270.	278.	285.	291.	297.	299.	302.	308.
255	269.	276.	289.	299.	308.	316.	325.	329.	332.	347.	352.	361.	365.
256	241.	249.	257.	265.	272.	280.	282.	283.	285.	289.	292.	297.	300.
257	242.	245.	252.	254.	254.	263.	264.	272.	277.	279.	282.	286.	290.
258	233.	245.	253.	258.	270.	278.	287.	296.	303.	312.	316.	323.	329.
259	277.	281.	294.	303.	311.	318.	326.	331.	334.	346.	357.	363.	364.
260	259.	269.	274.	279.	284.	290.	297.	301.	306.	309.	318.	318.	320.

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 27 (PAGE 10): BODY WEIGHTS - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP V			10000 PPM
	DAY 27	28	29	
246	284.	285.	291.	
247	352.	358.	374.	
248	325.	327.	334.	
249	350.	355.	365.	
250	351.	359.	375.	
251	373.	380.	392.	
252	320.	322.	334.	
253	379.	386.	389.	
254	315.	317.	324.	
255	374.	376.	388.	
256	300.	299.	309.	
257	296.	296.	304.	
258	339.	342.	354.	
259	370.	376.	383.	
260	328.	331.	345.	

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP I												
	0 (CARRIER CONTROL) PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
316	132.	134.	138.	143.	150.	156.	155.	162.	167.	170.	171.	178.	183.
317	156.	157.	159.	168.	178.	184.	185.	185.	196.	204.	212.	213.	218.
318	142.	142.	145.	152.	159.	167.	168.	170.	177.	183.	186.	191.	193.
319	149.	154.	162.	167.	174.	176.	182.	186.	190.	193.	198.	205.	208.
320	135.	138.	141.	145.	156.	159.	160.	160.	166.	175.	176.	178.	186.
321	160.	164.	174.	176.	176.	185.	192.	196.	201.	199.	208.	216.	222.
322	139.	144.	148.	153.	160.	166.	165.	169.	174.	180.	180.	184.	190.
323	140.	145.	150.	156.	160.	162.	165.	173.	174.	177.	180.	183.	186.
324	128.	131.	138.	145.	150.	154.	154.	159.	163.	168.	168.	171.	177.
325	149.	152.	157.	166.	170.	176.	172.	178.	182.	188.	190.	192.	199.
326	140.	147.	153.	160.	166.	173.	182.	181.	189.	196.	200.	206.	209.
327	144.	147.	154.	160.	163.	166.	172.	176.	182.	182.	186.	194.	195.
328	135.	140.	146.	149.	155.	154.	160.	162.	165.	166.	171.	175.	177.
329	152.	156.	164.	169.	173.	178.	182.	188.	187.	193.	201.	204.	204.
330	142.	149.	156.	159.	163.	168.	171.	180.	177.	182.	189.	194.	195.
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
316	183.	188.	192.	196.	196.	199.	205.	208.	210.	211.	215.	219.	220.
317	231.	236.	235.	234.	237.	249.	251.	254.	255.	254.	265.	266.	269.
318	200.	200.	205.	208.	207.	217.	218.	223.	225.	226.	232.	234.	239.
319	209.	218.	222.	224.	226.	235.	239.	241.	244.	254.	258.	258.	260.
320	193.	195.	196.	203.	209.	211.	211.	216.	222.	225.	228.	234.	237.
321	223.	222.	227.	232.	236.	242.	247.	254.	257.	267.	267.	271.	271.
322	194.	200.	201.	202.	209.	214.	215.	216.	220.	225.	227.	229.	229.
323	190.	190.	193.	198.	199.	204.	209.	212.	211.	214.	217.	222.	220.
324	182.	185.	187.	187.	194.	199.	201.	197.	199.	206.	214.	212.	208.
325	202.	204.	204.	206.	219.	213.	217.	213.	217.	228.	225.	222.	223.
326	221.	224.	227.	234.	238.	244.	247.	251.	263.	261.	263.	270.	272.
327	202.	204.	207.	211.	217.	218.	223.	226.	230.	231.	234.	240.	243.
328	178.	183.	188.	187.	188.	191.	195.	197.	199.	207.	206.	206.	208.
329	206.	209.	214.	211.	214.	223.	224.	222.	228.	235.	232.	232.	240.
330	200.	205.	209.	210.	212.	217.	219.	219.	227.	233.	231.	234.	239.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP I			0 (CARRIER CONTROL) PPM
	DAY 27	28	29	
316	220.	227.	237.	
317	270.	270.	277.	
318	244.	243.	250.	
319	267.	268.	272.	
320	241.	243.	250.	
321	266.	273.	278.	
322	232.	236.	236.	
323	224.	227.	237.	
324	213.	221.	223.	
325	225.	233.	234.	
326	274.	282.	293.	
327	243.	246.	250.	
328	210.	220.	224.	
329	242.	243.	236.	
330	241.	245.	243.	

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP II												
	100 PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
331	126.	128.	137.	142.	146.	148.	155.	158.	160.	161.	167.	174.	178.
332	152.	157.	167.	171.	170.	175.	181.	184.	185.	195.	201.	209.	207.
333	143.	147.	156.	160.	165.	170.	170.	174.	177.	181.	184.	185.	194.
334	137.	142.	147.	151.	156.	161.	164.	167.	170.	176.	180.	186.	186.
335	137.	141.	147.	153.	160.	162.	169.	173.	175.	179.	183.	190.	195.
336	158.	163.	170.	174.	183.	188.	188.	199.	204.	210.	212.	218.	222.
337	132.	134.	141.	147.	151.	153.	156.	159.	164.	165.	168.	175.	178.
338	147.	151.	158.	164.	168.	172.	175.	181.	184.	186.	188.	197.	200.
339	130.	136.	142.	145.	147.	154.	158.	163.	163.	169.	173.	176.	178.
340	153.	159.	164.	171.	171.	178.	181.	188.	186.	193.	200.	202.	201.
341	138.	144.	152.	156.	163.	170.	174.	178.	181.	189.	192.	194.	198.
342	145.	150.	158.	162.	168.	172.	180.	184.	190.	190.	196.	204.	212.
343	136.	142.	149.	152.	160.	167.	168.	172.	179.	184.	186.	192.	197.
344	158.	163.	172.	176.	185.	189.	194.	203.	205.	210.	214.	222.	229.
345	148.	152.	158.	163.	168.	174.	176.	180.	184.	186.	192.	196.	194.
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
331	178.	186.	189.	193.	195.	202.	205.	207.	211.	216.	216.	221.	222.
332	216.	221.	227.	231.	228.	238.	244.	244.	242.	248.	254.	254.	257.
333	196.	199.	201.	200.	207.	212.	212.	210.	218.	220.	220.	220.	219.
334	192.	199.	203.	203.	208.	216.	217.	217.	225.	231.	235.	234.	239.
335	195.	202.	210.	212.	212.	222.	224.	224.	226.	236.	239.	237.	237.
336	232.	232.	232.	237.	242.	252.	251.	253.	254.	269.	270.	272.	277.
337	178.	182.	188.	191.	191.	196.	198.	201.	200.	207.	209.	212.	212.
338	203.	206.	208.	217.	218.	224.	225.	227.	232.	240.	240.	242.	244.
339	184.	188.	192.	190.	198.	202.	202.	202.	208.	214.	214.	212.	220.
340	209.	214.	214.	216.	220.	221.	226.	228.	230.	233.	236.	239.	240.
341	201.	206.	208.	216.	219.	221.	224.	227.	233.	236.	235.	241.	245.
342	211.	219.	223.	224.	227.	235.	240.	244.	240.	246.	254.	255.	252.
343	201.	202.	206.	214.	214.	215.	222.	226.	226.	224.	230.	235.	233.
344	229.	238.	245.	250.	251.	260.	270.	272.	275.	282.	290.	293.	296.
345	201.	203.	206.	207.	211.	215.	216.	218.	221.	226.	228.	229.	233.

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 4): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP II			100 PPM
	DAY 27	28	29	
331	225.	230.	231.	
332	261.	267.	280.	
333	227.	229.	234.	
334	245.	249.	250.	
335	243.	247.	250.	
336	278.	284.	290.	
337	215.	221.	222.	
338	251.	256.	260.	
339	225.	230.	224.	
340	247.	251.	248.	
341	248.	248.	260.	
342	261.	270.	279.	
343	235.	244.	244.	
344	301.	308.	312.	
345	236.	237.	238.	

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 5): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP III												
	500 PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
361	135.	140.	147.	154.	159.	162.	166.	170.	176.	176.	180.	186.	193.
362	152.	159.	166.	170.	172.	170.	179.	185.	189.	186.	196.	198.	205.
363	140.	143.	150.	156.	161.	160.	167.	171.	175.	178.	178.	187.	190.
364	151.	154.	164.	171.	181.	183.	188.	193.	198.	203.	209.	214.	220.
365	132.	136.	143.	149.	155.	157.	162.	168.	172.	174.	179.	186.	192.
366	151.	159.	165.	166.	172.	179.	182.	183.	190.	195.	198.	201.	208.
367	141.	144.	145.	153.	157.	159.	163.	164.	171.	174.	176.	176.	180.
368	144.	151.	153.	159.	166.	172.	173.	181.	183.	184.	190.	194.	198.
369	133.	139.	146.	148.	153.	157.	160.	160.	164.	168.	173.	171.	179.
370	148.	151.	158.	164.	167.	169.	174.	179.	184.	187.	188.	195.	201.
371	139.	146.	152.	155.	163.	167.	169.	169.	174.	180.	182.	182.	190.
372	146.	152.	155.	165.	172.	175.	175.	178.	185.	190.	192.	195.	193.
373	135.	136.	142.	146.	152.	153.	153.	157.	162.	164.	162.	168.	173.
374	143.	147.	152.	159.	168.	173.	173.	178.	185.	192.	189.	193.	199.
375	128.	129.	135.	137.	143.	149.	149.	153.	158.	164.	168.	169.	174.
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
361	194.	197.	200.	202.	209.	212.	215.	210.	221.	222.	230.	225.	233.
362	205.	213.	216.	221.	218.	231.	237.	238.	237.	247.	249.	251.	250.
363	192.	196.	196.	204.	209.	210.	209.	215.	220.	222.	223.	230.	232.
364	221.	226.	234.	238.	237.	241.	249.	253.	254.	262.	267.	270.	271.
365	192.	201.	201.	205.	205.	214.	221.	221.	222.	230.	232.	232.	235.
366	213.	216.	216.	222.	226.	228.	232.	235.	240.	238.	243.	249.	251.
367	185.	189.	193.	192.	196.	200.	205.	206.	206.	213.	213.	214.	214.
368	203.	205.	213.	214.	219.	222.	226.	228.	229.	235.	237.	236.	236.
369	186.	190.	188.	195.	200.	200.	196.	200.	203.	204.	204.	210.	211.
370	204.	203.	207.	212.	215.	216.	215.	220.	227.	229.	230.	229.	236.
371	196.	200.	202.	208.	212.	213.	214.	218.	224.	221.	221.	228.	230.
372	203.	209.	211.	214.	220.	223.	226.	225.	230.	235.	241.	243.	244.
373	176.	178.	185.	191.	194.	191.	199.	203.	204.	202.	209.	214.	215.
374	204.	209.	209.	214.	220.	225.	229.	232.	237.	240.	242.	243.	244.
375	178.	184.	188.	188.	195.	200.	203.	206.	205.	208.	211.	215.	218.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 6): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP III			500 PPM
	DAY 27	28	29	
361	232.	232.	233.	
362	258.	262.	261.	
363	233.	233.	243.	
364	275.	281.	290.	
365	237.	246.	246.	
366	250.	251.	264.	
367	218.	223.	222.	
368	241.	250.	253.	
369	212.	212.	217.	
370	239.	243.	240.	
371	228.	230.	238.	
372	251.	258.	258.	
373	217.	220.	230.	
374	250.	258.	262.	
375	220.	221.	225.	

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 7): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP IV 5000 PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
301	125.	131.	136.	143.	152.	157.	163.	168.	170.	171.	174.	179.	180.
302	152.	159.	164.	167.	177.	184.	188.	193.	199.	202.	211.	219.	222.
303	141.	146.	150.	158.	164.	167.	171.	175.	178.	184.	187.	189.	193.
304	146.	151.	158.	165.	171.	176.	176.	180.	182.	187.	188.	196.	200.
305	129.	128.	138.	141.	148.	149.	152.	158.	160.	161.	162.	169.	171.
306	156.	164.	170.	179.	185.	191.	197.	203.	210.	217.	223.	230.	235.
307	137.	140.	146.	153.	157.	160.	163.	169.	176.	183.	182.	191.	197.
308	146.	149.	159.	166.	168.	172.	178.	181.	177.	186.	190.	196.	199.
309	135.	137.	145.	150.	158.	161.	170.	175.	179.	184.	189.	198.	202.
310	151.	154.	161.	165.	164.	166.	175.	175.	178.	178.	178.	188.	194.
311	137.	140.	147.	152.	158.	164.	165.	173.	178.	184.	187.	189.	198.
312	150.	152.	159.	166.	172.	176.	182.	186.	190.	192.	196.	200.	205.
313	138.	142.	146.	152.	159.	165.	168.	173.	177.	182.	182.	187.	192.
314	150.	154.	160.	164.	174.	181.	183.	187.	198.	206.	209.	213.	220.
315	150.	152.	160.	168.	174.	180.	184.	192.	195.	203.	205.	211.	214.
	DAY 14	15	16	17	18	19	20	21	22	23	24	25	26
301	181.	188.	191.	193.	194.	200.	202.	204.	205.	211.	215.	216.	213.
302	226.	230.	237.	240.	244.	251.	254.	261.	263.	266.	273.	276.	278.
303	200.	203.	205.	207.	213.	216.	219.	220.	222.	228.	230.	229.	233.
304	201.	201.	208.	208.	208.	207.	213.	217.	216.	214.	219.	224.	220.
305	174.	174.	176.	182.	187.	191.	189.	194.	199.	201.	201.	206.	208.
306	240.	247.	246.	252.	258.	262.	268.	267.	272.	277.	284.	286.	287.
307	200.	201.	210.	215.	220.	222.	223.	229.	232.	237.	236.	237.	240.
308	200.	207.	211.	209.	213.	220.	225.	222.	227.	235.	235.	235.	237.
309	204.	211.	216.	220.	222.	227.	234.	234.	233.	243.	243.	247.	244.
310	193.	193.	202.	205.	205.	205.	211.	216.	218.	217.	222.	225.	225.
311	200.	206.	206.	210.	217.	220.	223.	224.	225.	230.	236.	238.	238.
312	204.	211.	216.	219.	218.	226.	230.	232.	230.	236.	241.	240.	237.
313	196.	202.	203.	208.	212.	217.	217.	219.	225.	228.	230.	229.	229.
314	227.	228.	233.	239.	247.	251.	252.	258.	263.	266.	266.	275.	278.
315	222.	223.	230.	238.	245.	249.	245.	249.	257.	261.	262.	265.	270.

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 8): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP IV			5000 PPM
	DAY 27	28	29	
301	219.	223.	225.	
302	283.	289.	298.	
303	235.	240.	250.	
304	221.	226.	232.	
305	213.	214.	216.	
306	290.	297.	302.	
307	245.	251.	251.	
308	243.	246.	240.	
309	250.	261.	263.	
310	224.	228.	236.	
311	240.	245.	256.	
312	245.	247.	251.	
313	231.	239.	244.	
314	281.	281.	290.	
315	274.	282.	283.	

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 9): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP V 10000 PPM												
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
346	127.	125.	133.	134.	143.	147.	149.	154.	155.	160.	164.	164.	166.
347	155.	153.	160.	166.	173.	178.	177.	183.	191.	198.	200.	203.	211.
348	135.	133.	141.	146.	157.	164.	165.	168.	176.	183.	190.	191.	199.
349	144.	139.	146.	154.	161.	163.	174.	176.	186.	187.	194.	201.	206.
350	128.	126.	129.	136.	138.	140.	145.	146.	149.	151.	153.	155.	162.
351	157.	154.	161.	167.	177.	184.	187.	194.	202.	208.	212.	219.	229.
352	135.	136.	139.	144.	150.	150.	157.	160.	163.	163.	168.	175.	180.
353	150.	148.	154.	160.	166.	172.	181.	180.	187.	193.	197.	202.	205.
354	131.	129.	140.	144.	153.	154.	160.	166.	170.	172.	178.	182.	188.
355	142.	140.	146.	150.	157.	160.	162.	168.	170.	172.	173.	179.	185.
356	131.	129.	136.	141.	148.	149.	151.	154.	162.	166.	165.	174.	178.
357	148.	145.	148.	153.	159.	166.	170.	178.	181.	185.	187.	188.	193.
358	132.	130.	137.	139.	145.	145.	150.	153.	154.	157.	158.	164.	165.
359	142.	139.	144.	152.	157.	162.	166.	170.	175.	183.	183.	184.	190.
360	135.	133.	140.	143.	152.	155.	159.	165.	170.	172.	173.	178.	184.
DAY 14	15	16	17	18	19	20	21	22	23	24	25	26	
346	168.	171.	173.	175.	181.	180.	180.	182.	187.	188.	186.	191.	190.
347	216.	225.	231.	235.	238.	243.	250.	255.	256.	258.	260.	268.	275.
348	205.	207.	212.	217.	224.	228.	229.	235.	240.	243.	243.	250.	254.
349	212.	214.	216.	222.	228.	231.	232.	237.	244.	249.	248.	249.	252.
350	163.	166.	166.	168.	172.	176.	179.	178.	180.	184.	188.	189.	189.
351	230.	232.	240.	247.	252.	251.	259.	267.	266.	266.	274.	280.	276.
352	181.	182.	190.	193.	195.	194.	196.	198.	203.	204.	203.	202.	207.
353	208.	210.	214.	217.	222.	225.	226.	231.	231.	239.	237.	242.	241.
354	191.	195.	199.	203.	204.	209.	212.	215.	216.	221.	226.	226.	223.
355	187.	189.	192.	197.	198.	203.	201.	203.	206.	211.	211.	213.	214.
356	179.	183.	187.	192.	196.	194.	200.	204.	210.	210.	213.	216.	220.
357	197.	200.	200.	202.	207.	211.	214.	218.	217.	219.	221.	226.	228.
358	167.	168.	172.	175.	176.	173.	175.	180.	183.	184.	183.	185.	187.
359	193.	196.	200.	200.	205.	209.	212.	213.	216.	222.	221.	221.	221.
360	188.	188.	189.	193.	199.	200.	202.	202.	209.	213.	214.	212.	216.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 28 (PAGE 10): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP V		
	10000 PPM		
	DAY 27	28	29
346	194.	194.	203.
347	277.	278.	285.
348	256.	258.	265.
349	260.	262.	266.
350	190.	194.	202.
351	279.	285.	295.
352	211.	214.	213.
353	245.	249.	249.
354	229.	234.	241.
355	216.	218.	217.
356	220.	225.	233.
357	230.	231.	237.
358	192.	195.	194.
359	231.	234.	227.
360	219.	223.	221.

DAY = DAY OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 1): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP I														0 (CARRIER CONTROL) PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14														
216		21.	19.	23.	22.	21.	20.	24.	20.	23.	22.	27.	24.	24.														
217		24.	23.	24.	25.	27.	26.	28.	26.	29.	28.	27.	29.	29.														
218		22.	21.	22.	23.	21.	21.	25.	22.	24.	22.	25.	24.	25.														
219		21.	20.	22.	22.	22.	23.	20.	26.	25.	23.	25.	23.	25.														
220		22.	22.	23.	22.	23.	23.	25.	22.	25.	26.	26.	25.	27.														
221		25.	26.	27.	24.	26.	27.	24.	26.	26.	26.	28.	29.	27.														
222		23.	24.	26.	26.	24.	24.	28.	26.	28.	27.	29.	29.	29.														
223		22.	24.	24.	26.	23.	24.	27.	25.	28.	24.	27.	24.	26.														
224		21.	22.	21.	25.	23.	22.	25.	24.	24.	24.	25.	26.	26.														
225		24.	22.	24.	23.	25.	21.	24.	25.	25.	25.	24.	28.	26.														
226		23.	22.	23.	20.	21.	23.	23.	21.	25.	24.	25.	25.	26.														
227		25.	24.	21.	24.	22.	22.	23.	24.	24.	25.	25.	25.	27.														
228		22.	21.	21.	21.	20.	22.	24.	21.	24.	25.	25.	26.	25.														
229		21.	22.	21.	22.	24.	21.	25.	25.	25.	25.	25.	28.	25.														
230		24.	23.	25.	23.	23.	23.	25.	30.	26.	26.	26.	28.	29.														
RAT #	DOSAGE GROUP I														0 (CARRIER CONTROL) PPM													
	DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27														
216		26.	25.	25.	26.	25.	23.	27.	25.	24.	23.	24.	26.	20.														
217		30.	30.	27.	31.	29.	31.	30.	31.	31.	32.	31.	32.	27.														
218		24.	26.	27.	28.	26.	27.	28.	25.	28.	28.	25.	27.	26.														
219		23.	26.	25.	25.	25.	25.	26.	23.	25.	27.	24.	26.	24.														
220		28.	24.	27.	24.	27.	25.	27.	26.	27.	26.	26.	30.	26.														
221		28.	27.	28.	28.	27.	29.	30.	25.	29.	26.	28.	24.	27.														
222		29.	35.	33.	31.	30.	31.	31.	31.	33.	31.	29.	29.	27.														
223		26.	26.	27.	27.	26.	26.	29.	29.	31.	29.	25.	26.	27.														
224		25.	10.	27.	26.	26.	26.	27.	24.	26.	27.	25.	24.	24.														
225		29.	25.	26.	28.	28.	24.	27.	26.	27.	27.	25.	27.	27.														
226		24.	27.	25.	27.	25.	25.	27.	26.	27.	27.	25.	25.	25.														
227		28.	27.	25.	26.	25.	25.	28.	23.	26.	24.	25.	26.	25.														
228		28.	24.	26.	27.	27.	27.	27.	26.	30.	26.	27.	27.	27.														
229		26.	26.	26.	26.	27.	30.	27.	17.	28.	28.	25.	30.	25.														
230		28.	30.	30.	31.	32.	28.	30.	29.	29.	25.	25.	28.	29.														

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 2): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP I	0 (CARRIER CONTROL) PPM
DAYS 27 - 28		
216	28.	
217	34.	
218	26.	
219	27.	
220	29.	
221	26.	
222	32.	
223	27.	
224	26.	
225	27.	
226	27.	
227	27.	
228	26.	
229	29.	
230	30.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 3): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP II														100 PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14														
231		23.	22.	23.	24.	23.	23.	24.	24.	23.	25.	24.	24.	26.														
232		24.	21.	23.	23.	21.	22.	23.	22.	24.	22.	26.	24.	27.														
233		24.	21.	23.	24.	22.	22.	26.	24.	25.	25.	24.	26.	24.														
234		24.	22.	23.	26.	25.	24.	28.	26.	29.	28.	29.	29.	28.														
235		23.	22.	21.	24.	22.	22.	26.	22.	25.	23.	25.	25.	23.														
236		23.	24.	25.	26.	26.	25.	25.	27.	26.	27.	28.	27.	26.														
237		20.	21.	21.	22.	20.	20.	22.	22.	21.	23.	22.	24.	22.														
238		24.	23.	24.	26.	23.	26.	26.	30.	29.	28.	26.	30.	31.														
239		23.	25.	22.	24.	23.	24.	27.	24.	24.	26.	26.	27.	26.														
240		25.	24.	25.	24.	24.	25.	25.	27.	27.	28.	24.	29.	29.														
241		23.	21.	22.	23.	22.	24.	23.	21.	24.	23.	24.	26.	25.														
242		24.	23.	24.	24.	23.	24.	27.	24.	26.	25.	26.	29.	27.														
243		23.	23.	23.	23.	24.	19.	27.	20.	25.	24.	25.	29.	24.														
244		22.	23.	21.	24.	23.	21.	24.	22.	23.	23.	23.	24.	24.														
245		25.	24.	25.	25.	25.	24.	28.	27.	26.	27.	28.	29.	28.														
	DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27														
231		27.	24.	25.	25.	26.	25.	28.	25.	27.	26.	23.	25.	26.														
232		24.	23.	25.	24.	26.	26.	25.	24.	26.	27.	24.	28.	28.														
233		28.	24.	26.	26.	27.	26.	27.	26.	28.	28.	26.	27.	28.														
234		29.	30.	29.	30.	30.	30.	31.	30.	31.	29.	31.	31.	27.														
235		27.	23.	24.	23.	25.	23.	24.	25.	25.	22.	22.	25.	21.														
236		28.	29.	28.	26.	30.	27.	29.	28.	27.	29.	42.	a	28.														
237		25.	22.	23.	23.	25.	23.	26.	23.	24.	22.	22.	25.	22.														
238		30.	28.	27.	28.	29.	39.	32.	29.	28.	28.	28.	31.	28.														
239		28.	28.	27.	28.	28.	27.	28.	28.	28.	26.	26.	28.	27.														
240		25.	27.	30.	29.	30.	28.	31.	30.	29.	31.	29.	31.	32.														
241		26.	27.	27.	27.	27.	27.	25.	26.	28.	26.	24.	25.	25.														
242		31.	27.	24.	29.	28.	30.	26.	31.	27.	29.	30.	27.	28.														
243		30.	24.	28.	27.	27.	28.	27.	27.	27.	26.	27.	26.	24.														
244		27.	24.	26.	23.	26.	25.	27.	25.	26.	25.	24.	25.	25.														
245		30.	28.	28.	27.	27.	30.	28.	27.	30.	28.	26.	30.	27.														

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Spilled feed precluded the calculation of this value.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 4): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP II	100 PPM
DAYS 27 - 28		
231	27.	
232	30.	
233	28.	
234	32.	
235	26.	
236	31.	
237	24.	
238	32.	
239	27.	
240	30.	
241	26.	
242	30.	
243	28.	
244	26.	
245	30.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 5): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP III														500 PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14														
261		21.	22.	22.	22.	22.	22.	25.	21.	25.	24.	23.	24.	26.														
262		25.	27.	26.	28.	26.	27.	28.	27.	26.	25.	27.	30.	27.														
263		21.	22.	22.	23.	23.	22.	24.	24.	23.	23.	24.	23.	24.														
264		22.	22.	22.	25.	23.	22.	26.	25.	25.	26.	25.	27.	27.														
265		21.	20.	21.	21.	21.	23.	21.	23.	23.	23.	23.	25.	24.														
266		24.	25.	26.	26.	26.	26.	27.	26.	24.	27.	26.	27.	27.														
267		24.	24.	24.	25.	24.	25.	25.	22.	25.	25.	25.	27.	29.														
268		21.	23.	23.	24.	24.	24.	23.	24.	25.	24.	23.	28.	26.														
269		23.	23.	26.	24.	24.	24.	27.	21.	25.	23.	24.	29.	25.														
270		28.	25.	28.	27.	28.	25.	30.	27.	30.	26.	26.	a	29.														
271		20.	20.	22.	24.	20.	22.	22.	21.	23.	22.	24.	25.	25.														
272		24.	23.	24.	24.	23.	25.	27.	24.	28.	26.	25.	27.	29.														
273		21.	19.	22.	22.	20.	21.	25.	20.	25.	21.	22.	24.	22.														
274		28.	25.	27.	28.	28.	28.	28.	33.	32.	30.	31.	33.	33.														
275		26.	25.	28.	28.	25.	26.	27.	28.	27.	29.	27.	30.	30.														
	DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27														
261		25.	26.	25.	27.	26.	27.	27.	24.	27.	28.	27.	25.	26.														
262		30.	27.	27.	28.	29.	27.	30.	28.	31.	27.	27.	30.	26.														
263		26.	21.	21.	22.	25.	21.	22.	21.	22.	22.	21.	23.	21.														
264		29.	27.	28.	28.	26.	29.	28.	28.	30.	29.	27.	29.	29.														
265		22.	24.	25.	24.	24.	25.	23.	24.	24.	23.	24.	24.	22.														
266		28.	26.	28.	28.	27.	28.	27.	28.	26.	30.	25.	29.	27.														
267		27.	27.	29.	29.	28.	29.	29.	26.	30.	31.	26.	30.	29.														
268		23.	27.	25.	26.	27.	25.	27.	24.	25.	28.	24.	25.	26.														
269		27.	26.	25.	27.	28.	26.	29.	29.	27.	27.	28.	29.	29.														
270		28.	35.	31.	28.	28.	50.b	29.	29.	30.	28.	25.	42.	30.														
271		25.	25.	26.	26.	26.	26.	26.	26.	26.	27.	26.	26.	26.														
272		29.	27.	26.	26.	29.	29.	27.	28.	30.	27.	27.	30.	26.														
273		27.	22.	24.	23.	23.	23.	25.	25.	25.	23.	24.	23.	21.														
274		35.	33.	37.	34.	36.	35.	35.	34.	39.	34.	32.	36.	32.														
275		30.	30.	29.	29.	31.	30.	36.	34.	30.	31.	31.	35.	31.														

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Spilled feed precluded the calculation of this value.

b. Value appeared incorrectly recorded and was excluded from summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 6): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP III	500 PPM
DAYS 27 - 28		
261	30.	
262	29.	
263	24.	
264	29.	
265	25.	
266	29.	
267	31.	
268	24.	
269	28.	
270	30.	
271	27.	
272	30.	
273	27.	
274	35.	
275	36.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 7): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP IV 5000 PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14
201		14.	20.	20.	23.	23.	20.	24.	21.	21.	24.	25.	21.	25.
202		21.	25.	24.	25.	26.	26.	28.	25.	27.	25.	29.	26.	26.
203		20.	22.	23.	23.	24.	22.	27.	24.	26.	25.	26.	24.	25.
204		a	a	30.	22.	27.	27.	26.	29.	29.	34.	28.	30.	32.
205		20.	25.	25.	25.	26.	24.	26.	29.	27.	24.	28.	28.	28.
206		20.	26.	28.	29.	26.	26.	30.	24.	31.	27.	31.	30.	28.
207		16.	25.	24.	26.	26.	27.	28.	28.	26.	31.	27.	30.	28.
208		17.	25.	24.	26.	26.	25.	27.	27.	27.	26.	24.	26.	23.
209		15.	23.	22.	23.	22.	21.	27.	24.	25.	25.	24.	25.	25.
210		20.	23.	25.	25.	26.	26.	25.	26.	26.	28.	29.	25.	29.
211		17.	23.	21.	24.	24.	19.	23.	22.	23.	22.	23.	25.	22.
212		20.	21.	21.	22.	23.	20.	23.	20.	24.	23.	22.	24.	21.
213		19.	24.	23.	25.	22.	23.	27.	24.	25.	24.	26.	25.	25.
214		20.	23.	23.	25.	22.	21.	23.	23.	22.	25.	23.	23.	22.
215		17.	22.	22.	a	20.	21.	24.	22.	24.	22.	22.	26.	23.
RAT #	DOSAGE GROUP IV 5000 PPM													
	DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27
201		25.	25.	26.	27.	27.	27.	19.	37.	27.	27.	27.	26.	25.
202		28.	29.	27.	27.	28.	26.	30.	29.	28.	30.	26.	27.	27.
203		29.	22.	26.	26.	24.	25.	24.	22.	22.	20.	19.	21.	20.
204		32.	31.	34.	30.	33.	29.	32.	29.	30.	29.	29.	26.	29.
205		29.	28.	27.	26.	31.	27.	27.	29.	28.	31.	23.	26.	29.
206		32.	28.	30.	29.	28.	29.	28.	26.	27.	27.	27.	30.	23.
207		29.	27.	28.	29.	28.	27.	29.	27.	27.	27.	27.	27.	27.
208		26.	27.	26.	28.	27.	26.	25.	25.	25.	27.	23.	26.	21.
209		26.	24.	26.	24.	28.	25.	25.	27.	27.	26.	25.	27.	25.
210		27.	29.	30.	29.	30.	29.	25.	27.	30.	28.	25.	25.	26.
211		24.	22.	23.	21.	21.	21.	23.	21.	20.	22.	21.	19.	20.
212		22.	21.	22.	23.	23.	22.	24.	22.	23.	24.	22.	22.	22.
213		26.	27.	25.	26.	25.	19.	37.	26.	29.	27.	28.	27.	21.
214		24.	23.	24.	23.	25.	24.	22.	21.	23.	23.	23.	23.	22.
215		26.	23.	22.	24.	24.	22.	21.	32.	22.	19.	19.	19.	18.

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Spilled feed precluded the calculation of this value.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 8): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP IV	5000 PPM
DAYS 27 - 28		
201	26.	
202	29.	
203	24.	
204	31.	
205	29.	
206	27.	
207	29.	
208	26.	
209	26.	
210	28.	
211	23.	
212	21.	
213	36.	
214	25.	
215	21.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 9): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP V														10000 PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14		14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27
246		12.	19.	21.	23.	21.	22.	22.	21.	22.	20.	22.	22.	20.		23.	22.	22.	21.	22.	22.	20.	22.	22.	22.	22.	20.	
247		14.	22.	23.	23.	23.	21.	24.	24.	23.	21.	15.	21.	23.		24.	23.	23.	21.	22.	23.	23.	23.	23.	23.	23.	23.	
248		13.	20.	20.	22.	22.	22.	23.	21.	24.	23.	23.	24.	24.		25.	24.	25.	24.	25.	26.	24.	24.	24.	24.	24.	24.	
249		25.	22.	26.	24.	25.	21.	24.	25.	22.	26.	25.	27.	24.		28.	27.	28.	26.	27.	28.	27.	27.	27.	27.	27.	27.	
250		11.	17.	18.	19.	25.	25.	28.	25.	30.	34.	32.	35.	30.		36.	35.	36.	34.	35.	36.	35.	35.	35.	35.	35.	35.	
251		13.	17.	17.	19.	21.	25.	26.	25.	24.	27.	26.	27.	26.		28.	27.	28.	26.	27.	28.	27.	27.	27.	27.	27.	27.	
252		23.	22.	26.	25.	21.	21.	22.	28.	24.	24.	26.	26.	26.		29.	28.	29.	27.	28.	29.	28.	28.	28.	28.	28.	28.	
253		18.	23.	25.	28.	25.	24.	26.	26.	27.	22.	27.	28.	26.		30.	29.	30.	28.	29.	30.	29.	29.	29.	29.	29.	29.	
254		18.	17.	19.	22.	22.	20.	23.	25.	25.	24.	25.	24.	27.		31.	30.	31.	29.	30.	31.	30.	30.	30.	30.	30.	30.	
255		58.a	18.	20.	19.	21.	20.	21.	23.	22.	24.	22.	24.	25.		32.	31.	32.	30.	31.	32.	31.	31.	31.	31.	31.	31.	
256		16.	18.	20.	25.	20.	23.	27.	22.	24.	23.	23.	26.	23.		33.	32.	33.	31.	32.	33.	32.	32.	32.	32.	32.	32.	
257		10.	13.	18.	24.	22.	22.	24.	22.	24.	21.	21.	22.	20.		34.	33.	34.	32.	33.	34.	33.	33.	33.	33.	33.	33.	
258		6.	5.	7.	15.	17.	21.	25.	19.	25.	24.	23.	24.	22.		35.	34.	35.	33.	34.	35.	34.	34.	34.	34.	34.	34.	
259		8.	15.	19.	23.	23.	24.	27.	25.	23.	24.	25.	24.	28.		36.	35.	36.	34.	35.	36.	35.	35.	35.	35.	35.	35.	
260		12.	17.	17.	23.	26.	25.	27.	24.	26.	26.	24.	34.	28.		37.	36.	37.	35.	36.	37.	36.	36.	36.	36.	36.	36.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Value appeared incorrectly recorded and was excluded from summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 29 (PAGE 10): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - MALE RATS

RAT #	DOSAGE GROUP V	10000 PPM
DAYS 27 - 28		
246	21.	
247	21.	
248	24.	
249	32.	
250	37.	
251	28.	
252	26.	
253	29.	
254	23.	
255	24.	
256	20.	
257	24.	
258	26.	
259	24.	
260	25.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 1): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP I														0 (CARRIER CONTROL) PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14														
316		17.	15.	19.	17.	16.	15.	17.	18.	15.	15.	19.	17.	18.														
317		19.	17.	21.	20.	19.	22.	15.	21.	24.	24.	21.	21.	25.														
318		16.	15.	17.	16.	17.	19.	14.	18.	17.	17.	19.	16.	18.														
319		22.	19.	20.	19.	17.	22.	34.a	21.	17.	20.	23.	20.	b														
320		18.	16.	18.	18.	17.	18.	14.	19.	20.	17.	18.	20.	21.														
321		22.	22.	22.	15.	20.	23.	17.	21.	17.	23.	22.	22.	21.														
322		19.	18.	19.	18.	18.	17.	16.	18.	19.	17.	17.	19.	18.														
323		18.	18.	20.	16.	16.	18.	19.	18.	18.	16.	18.	19.	17.														
324		18.	18.	19.	17.	16.	16.	15.	18.	16.	17.	15.	19.	19.														
325		18.	18.	21.	16.	18.	23.	15.	17.	18.	17.	19.	19.	16.														
326		20.	20.	21.	19.	20.	23.	15.	21.	21.	22.	21.	19.	22.														
327		15.	15.	17.	16.	15.	18.	12.	16.	15.	15.	18.	16.	18.														
328		18.	18.	19.	16.	15.	19.	15.	17.	16.	18.	18.	16.	17.														
329		18.	20.	20.	16.	17.	21.	18.	16.	19.	22.	20.	18.	20.														
330		20.	19.	19.	18.	18.	21.	19.	17.	18.	22.	21.	19.	21.														
RAT #	DOSAGE GROUP I														0 (CARRIER CONTROL) PPM													
	DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27														
316		14.	19.	19.	17.	16.	19.	17.	17.	b	19.	19.	19.	14.														
317		23.	23.	19.	20.	26.	24.	23.	22.	19.	24.	23.	25.	22.														
318		16.	18.	18.	14.	20.	18.	17.	18.	16.	18.	18.	17.	20.														
319		21.	21.	21.	17.	22.	22.	21.	19.	23.	21.	20.	21.	23.														
320		18.	18.	21.	22.	20.	17.	20.	21.	22.	18.	23.	20.	24.														
321		13.	22.	23.	22.	22.	24.	22.	22.	27.	21.	26.	19.	15.														
322		19.	17.	17.	20.	18.	19.	15.	18.	21.	19.	16.	17.	17.														
323		15.	17.	20.	18.	17.	20.	18.	18.	18.	16.	19.	19.	17.														
324		17.	18.	14.	18.	17.	17.	14.	12.	19.	19.	16.	13.	15.														
325		18.	17.	15.	19.	14.	20.	13.	15.	19.	14.	18.	13.	16.														
326		21.	21.	23.	23.	24.	20.	21.	25.	25.	19.	23.	22.	23.														
327		15.	15.	17.	17.	18.	17.	16.	18.	20.	14.	19.	19.	17.														
328		17.	18.	16.	16.	17.	19.	16.	16.	21.	15.	17.	14.	17.														
329		17.	19.	15.	17.	22.	18.	14.	45.a	22.	18.	15.	19.	20.														
330		21.	19.	19.	18.	21.	21.	15.	21.	23.	19.	17.	20.	22.														

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Value appeared incorrectly recorded and was excluded from summarization and statistical analyses.

b. Spilled feed precluded the calculation of this value.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 2): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP I	0 (CARRIER CONTROL) PPM
DAYS 27 - 28		
316	19.	
317	16.	
318	14.	
319	23.	
320	17.	
321	19.	
322	19.	
323	16.	
324	18.	
325	17.	
326	22.	
327	15.	
328	19.	
329	17.	
330	18.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 3): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP II														100 PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14														
331		18.	18.	18.	17.	18.	19.	15.	18.	16.	18.	20.	20.	16.														
332		21.	21.	20.	15.	17.	20.	17.	17.	20.	21.	22.	19.	22.														
333		21.	20.	19.	18.	19.	18.	18.	18.	17.	20.	18.	18.	18.														
334		18.	17.	17.	17.	16.	17.	15.	16.	18.	19.	19.	18.	20.														
335		19.	17.	19.	18.	16.	21.	15.	19.	17.	18.	20.	20.	16.														
336		21.	21.	19.	19.	20.	20.	20.	20.	20.	20.	19.	10.	32.														
337		17.	16.	18.	15.	14.	18.	15.	17.	15.	16.	19.	17.	16.														
338		21.	18.	20.	18.	17.	19.	17.	19.	17.	18.	21.	19.	20.														
339		19.	19.	17.	15.	18.	20.	17.	18.	20.	19.	18.	16.	19.														
340		21.	19.	21.	18.	18.	22.	19.	16.	20.	21.	21.	18.	21.														
341		19.	18.	19.	18.	19.	20.	17.	17.	20.	19.	17.	19.	19.														
342		19.	19.	21.	19.	17.	22.	18.	20.	18.	21.	23.	20.	20.														
343		19.	29.	15.	17.	17.	26.	17.	19.	18.	18.	19.	19.	20.														
344		20.	20.	21.	20.	17.	20.	19.	18.	19.	19.	23.	21.	18.														
345		20.	19.	20.	18.	18.	20.	17.	19.	21.	19.	20.	19.	21.														
	DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27														
331		19.	20.	19.	17.	20.	20.	18.	17.	21.	17.	19.	15.	20.														
332		20.	22.	23.	17.	22.	29.	25.	19.	23.	21.	21.	18.	22.														
333		20.	16.	16.	17.	19.	18.	15.	17.	19.	18.	14.	15.	19.														
334		19.	20.	17.	20.	21.	19.	18.	20.	23.	21.	18.	19.	23.														
335		19.	20.	20.	16.	21.	19.	18.	15.	23.	17.	18.	15.	20.														
336		18.	19.	20.	19.	24.	20.	18.	17.	24.	20.	22.	21.	19.														
337		17.	19.	17.	15.	18.	17.	17.	13.	19.	16.	18.	15.	16.														
338		18.	17.	21.	18.	20.	18.	18.	19.	22.	18.	18.	18.	22.														
339		19.	20.	17.	21.	20.	19.	15.	19.	22.	18.	14.	20.	22.														
340		22.	21.	18.	22.	21.	21.	19.	20.	23.	20.	18.	20.	24.														
341		19.	17.	20.	20.	19.	17.	19.	19.	21.	16.	19.	20.	19.														
342		21.	21.	19.	21.	23.	22.	22.	18.	12.	30.	21.	19.	22.														
343		16.	18.	20.	18.	17.	19.	19.	16.	17.	18.	18.	19.	16.														
344		21.	23.	21.	21.	24.	24.	21.	23.	25.	22.	23.	19.	23.														
345		19.	19.	17.	20.	21.	19.	19.	28.	22.	19.	17.	20.	29.														

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 4): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP II	100 PPM
DAYS 27 - 28		
331	17.	
332	27.	
333	16.	
334	20.	
335	17.	
336	20.	
337	17.	
338	21.	
339	21.	
340	21.	
341	17.	
342	22.	
343	18.	
344	22.	
345	46.a	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Value appeared incorrectly recorded and was excluded from summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 5): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP III														500 PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14														
361		20.	18.	18.	18.	18.	20.	15.	17.	17.	16.	18.	20.	17.														
362		21.	20.	19.	17.	14.	22.	18.	21.	16.	a	22.	21.	19.														
363		17.	17.	17.	17.	13.	19.	15.	17.	17.	14.	19.	17.	16.														
364		24.	22.	23.	22.	21.	23.	18.	23.	21.	23.	22.	22.	21.														
365		18.	18.	20.	17.	17.	19.	18.	19.	18.	19.	19.	19.	17.														
366		21.	19.	17.	18.	18.	20.	15.	20.	18.	18.	17.	18.	20.														
367		18.	15.	18.	16.	15.	17.	13.	15.	17.	18.	15.	16.	19.														
368		20.	17.	19.	17.	18.	18.	18.	19.	16.	18.	16.	19.	18.														
369		18.	18.	16.	16.	16.	16.	13.	15.	16.	17.	14.	18.	18.														
370		19.	18.	21.	16.	15.	22.	17.	20.	19.	17.	21.	20.	20.														
371		21.	19.	20.	18.	18.	18.	14.	19.	20.	18.	16.	20.	19.														
372		20.	20.	22.	19.	19.	19.	17.	19.	18.	19.	19.	16.	20.														
373		20.	18.	19.	17.	16.	17.	16.	21.	16.	15.	17.	18.	18.														
374		19.	18.	20.	19.	19.	19.	19.	21.	21.	17.	20.	21.	21.														
375		18.	16.	15.	15.	16.	17.	15.	16.	18.	17.	16.	16.	17.														
	DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27														
361		17.	16.	16.	19.	20.	17.	13.	18.	21.	15.	16.	19.	20.														
362		22.	22.	23.	18.	26.	26.	23.	20.	27.	24.	23.	18.	25.														
363		16.	16.	18.	18.	17.	14.	17.	17.	19.	15.	19.	18.	18.														
364		21.	24.	24.	21.	23.	22.	20.	21.	24.	27.	22.	20.	23.														
365		19.	19.	20.	18.	21.	21.	20.	19.	22.	18.	19.	18.	18.														
366		18.	15.	18.	20.	20.	17.	18.	19.	19.	17.	19.	18.	21.														
367		18.	18.	17.	18.	18.	18.	17.	14.	20.	18.	18.	15.	19.														
368		17.	19.	18.	17.	19.	18.	17.	16.	18.	18.	17.	16.	18.														
369		17.	13.	18.	18.	16.	12.	16.	16.	15.	13.	15.	15.	16.														
370		17.	18.	20.	20.	17.	16.	19.	20.	20.	16.	16.	19.	20.														
371		19.	18.	20.	18.	19.	16.	19.	19.	19.	15.	20.	19.	17.														
372		19.	20.	19.	19.	21.	19.	17.	20.	21.	20.	21.	23.	23.														
373		39.	21.	20.	18.	17.	20.	40.b	17.	19.	18.	20.	20.	34.														
374		20.	22.	21.	23.	23.	22.	21.	23.	24.	20.	21.	21.	23.														
375		17.	19.	17.	18.	19.	17.	17.	14.	17.	15.	18.	17.	18.														

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Spilled feed precluded the calculation of this value.

b. Value appeared incorrectly recorded and was excluded from summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 6): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP III	500 PPM
DAYS 27 - 28		
361	15.	
362	23.	
363	14.	
364	21.	
365	20.	
366	14.	
367	17.	
368	19.	
369	11.	
370	18.	
371	14.	
372	25.	
373	34.	
374	24.	
375	14.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 7): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP IV 5000 PPM													
DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14	
301	24.	20.	22.	20.	18.	22.	19.	19.	16.	17.	18.	16.	16.	
302	19.	20.	20.	21.	19.	22.	19.	22.	19.	23.	23.	20.	a	
303	19.	17.	21.	17.	19.	21.	17.	19.	19.	18.	19.	19.	20.	
304	18.	22.	22.	19.	18.	20.	68.b	20.	19.	17.	20.	20.	19.	
305	12.	20.	18.	18.	14.	18.	16.	16.	15.	15.	17.	16.	16.	
306	21.	19.	23.	19.	20.	23.	19.	19.	22.	22.	23.	20.	23.	
307	18.	18.	19.	16.	16.	19.	16.	20.	20.	18.	21.	19.	21.	
308	17.	19.	20.	16.	16.	21.	17.	14.	17.	18.	17.	16.	17.	
309	16.	18.	19.	18.	16.	22.	17.	18.	18.	21.	21.	19.	18.	
310	17.	17.	19.	13.	14.	19.	14.	15.	15.	14.	18.	18.	15.	
311	16.	18.	18.	17.	17.	17.	18.	19.	17.	18.	18.	19.	19.	
312	15.	18.	22.	17.	17.	19.	16.	18.	16.	18.	17.	18.	15.	
313	18.	19.	19.	19.	19.	23.	19.	19.	19.	18.	20.	19.	20.	
314	18.	20.	21.	20.	20.	21.	18.	24.	22.	23.	21.	23.	23.	
315	18.	19.	21.	18.	19.	21.	19.	19.	20.	19.	21.	19.	21.	
DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27	
301	17.	18.	20.	16.	19.	17.	17.	16.	22.	17.	18.	14.	18.	
302	21.	22.	22.	22.	24.	22.	24.	20.	22.	22.	22.	20.	22.	
303	19.	19.	19.	20.	19.	20.	18.	16.	24.	18.	18.	19.	17.	
304	16.	22.	20.	18.	16.	70.b	26.	16.	16.	18.	20.	16.	14.	
305	15.	14.	17.	18.	18.	14.	17.	16.	17.	15.	17.	15.	18.	
306	22.	21.	20.	20.	21.	24.	19.	21.	21.	24.	19.	21.	19.	
307	18.	22.	22.	20.	21.	16.	19.	19.	24.	18.	17.	20.	20.	
308	17.	17.	14.	17.	19.	17.	16.	16.	21.	15.	14.	18.	17.	
309	20.	20.	21.	18.	19.	21.	18.	13.	22.	18.	19.	16.	18.	
310	14.	18.	17.	16.	14.	17.	17.	14.	16.	17.	17.	17.	13.	
311	19.	16.	18.	20.	20.	20.	18.	16.	19.	20.	18.	18.	16.	
312	18.	20.	17.	15.	19.	19.	18.	13.	21.	18.	19.	13.	18.	
313	20.	19.	20.	21.	22.	21.	19.	17.	20.	18.	18.	18.	17.	
314	21.	20.	24.	24.	24.	20.	23.	22.	23.	19.	23.	24.	22.	
315	17.	20.	22.	23.	21.	18.	17.	21.	22.	20.	20.	20.	20.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Spilled feed precluded the calculation of this value.

b. Value appeared incorrectly recorded and was excluded from summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 8): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP IV	5000 PPM
DAYS 27 - 28		
301	17.	
302	21.	
303	17.	
304	17.	
305	14.	
306	19.	
307	19.	
308	17.	
309	20.	
310	16.	
311	18.	
312	17.	
313	19.	
314	17.	
315	21.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 9): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP V														10000 PPM													
	DAYS	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13	13 - 14														
346		13.	17.	18.	18.	27.	25.	15.	15.	17.	16.	14.	16.	14.														
347		14.	19.	20.	18.	17.	17.	16.	18.	19.	17.	19.	18.	20.														
348		a	19.	20.	21.	20.	19.	16.	20.	21.	21.	18.	20.	21.														
349		15.	17.	20.	18.	16.	21.	17.	19.	19.	20.	20.	19.	21.														
350		13.	16.	18.	14.	15.	17.	14.	15.	15.	16.	14.	17.	15.														
351		13.	20.	21.	21.	20.	22.	20.	22.	20.	21.	23.	24.	21.														
352		11.	22.	25.	17.	16.	20.	16.	18.	15.	19.	20.	18.	18.														
353		10.	19.	21.	20.	20.	23.	16.	21.	19.	20.	19.	20.	18.														
354		13.	18.	20.	20.	17.	22.	17.	19.	17.	19.	20.	17.	17.														
355		10.	16.	18.	16.	16.	17.	16.	15.	16.	15.	17.	17.	16.														
356		13.	15.	17.	16.	15.	15.	14.	18.	16.	13.	18.	17.	15.														
357		14.	15.	20.	19.	18.	21.	19.	19.	19.	18.	17.	17.	18.														
358		10.	16.	18.	15.	14.	18.	16.	13.	15.	13.	16.	16.	16.														
359		12.	17.	18.	18.	16.	20.	17.	16.	19.	17.	13.	17.	18.														
360		10.	14.	a	17.	15.	19.	16.	16.	15.	15.	16.	17.	17.														
RAT #	DOSAGE GROUP V														10000 PPM													
	DAYS	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	25 - 26	26 - 27														
346		16.	15.	16.	16.	14.	12.	16.	15.	15.	12.	15.	15.	16.														
347		21.	20.	20.	19.	21.	21.	20.	18.	18.	18.	22.	22.	20.														
348		20.	17.	20.	22.	20.	18.	20.	21.	22.	17.	20.	21.	19.														
349		18.	17.	20.	19.	21.	19.	17.	19.	21.	19.	18.	16.	20.														
350		15.	12.	15.	16.	17.	15.	14.	13.	17.	15.	16.	13.	13.														
351		18.	23.	23.	23.	19.	22.	23.	19.	10.	31.	22.	21.	18.														
352		15.	21.	20.	18.	14.	15.	18.	17.	19.	13.	13.	18.	18.														
353		27.	21.	19.	17.	19.	43.b	27.	17.	20.	16.	16.	16.	18.														
354		18.	19.	19.	17.	20.	18.	18.	14.	18.	18.	18.	14.	17.														
355		16.	17.	19.	16.	18.	14.	15.	15.	17.	16.	15.	14.	16.														
356		16.	17.	17.	17.	15.	17.	16.	17.	15.	17.	16.	18.	15.														
357		19.	16.	18.	20.	19.	19.	17.	16.	18.	17.	19.	17.	16.														
358		11.	16.	17.	15.	12.	13.	16.	15.	16.	11.	13.	16.	17.														
359		17.	17.	13.	18.	19.	17.	16.	18.	19.	15.	12.	17.	18.														
360		14.	15.	16.	17.	16.	14.	13.	17.	17.	16.	12.	15.	16.														

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Spilled feed precluded the calculation of this value.

b. Value appeared incorrectly recorded and was excluded from summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 30 (PAGE 10): FEED CONSUMPTION VALUES - INDIVIDUAL DATA - FEMALE RATS

RAT #	DOSAGE GROUP V	10000 PPM
DAYS 27 - 28		
346	11.	
347	18.	
348	17.	
349	17.	
350	16.	
351	18.	
352	17.	
353	17.	
354	18.	
355	14.	
356	16.	
357	13.	
358	14.	
359	17.	
360	16.	

DAYS = DAYS OF STUDY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 31 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM)	RAT NUMBER	DAY OF NECROPSY	DAYS OF EXPOSURE	OBSERVATIONS a
I				
0 (CARRIER CONTROL)	216	DS 29	28	ALL TISSUES APPEARED NORMAL.
	217	DS 29	28	ALL TISSUES APPEARED NORMAL.
	218	DS 29	28	ALL TISSUES APPEARED NORMAL.
	219	DS 29	28	ALL TISSUES APPEARED NORMAL.
	220	DS 29	28	ALL TISSUES APPEARED NORMAL.
	221	DS 29	28	ALL TISSUES APPEARED NORMAL.
	222	DS 29	28	KIDNEYS: RIGHT, TAN AREA (0.4 CM X 0.2 CM). ALL OTHER TISSUES APPEARED NORMAL.
	223	DS 29	28	ALL TISSUES APPEARED NORMAL.
	224	DS 29	28	ALL TISSUES APPEARED NORMAL.
	225	DS 29	28	ALL TISSUES APPEARED NORMAL.
	226	DS 29	28	ALL TISSUES APPEARED NORMAL.
	227	DS 29	28	ALL TISSUES APPEARED NORMAL.
	228	DS 29	28	ALL TISSUES APPEARED NORMAL.
	229	DS 29	28	ALL TISSUES APPEARED NORMAL.
	230	DS 29	28	ALL TISSUES APPEARED NORMAL.
II				
100	231	DS 29	28	ALL TISSUES APPEARED NORMAL.
	232	DS 29	28	ALL TISSUES APPEARED NORMAL.
	233	DS 29	28	ALL TISSUES APPEARED NORMAL.
	234	DS 29	28	ALL TISSUES APPEARED NORMAL.
	235	DS 29	28	ALL TISSUES APPEARED NORMAL.
	236	DS 29	28	ALL TISSUES APPEARED NORMAL.
	237	DS 29	28	ALL TISSUES APPEARED NORMAL.
	238	DS 29	28	ALL TISSUES APPEARED NORMAL.
	239	DS 29	28	ALL TISSUES APPEARED NORMAL.
	240	DS 29	28	ALL TISSUES APPEARED NORMAL.
	241	DS 29	28	ALL TISSUES APPEARED NORMAL.
	242	DS 29	28	ALL TISSUES APPEARED NORMAL.
	243	DS 29	28	ALL TISSUES APPEARED NORMAL.
	244	DS 29	28	ALL TISSUES APPEARED NORMAL.
	245	DS 29	28	ALL TISSUES APPEARED NORMAL.

DAYS OF EXPOSURE WERE CALCULATED FROM DAY 1 OF STUDY (FIRST FEED VALUE RECORDED) THROUGH THE DAY BEFORE SACRIFICE
DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table 23) for external observations confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 31 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM)	RAT NUMBER	DAY OF NECROPSY	DAYS OF EXPOSURE	OBSERVATIONS a
III 500	261	DS 29	28	ALL TISSUES APPEARED NORMAL.
	262	DS 29	28	ALL TISSUES APPEARED NORMAL.
	263	DS 29	28	ALL TISSUES APPEARED NORMAL.
	264	DS 29	28	ALL TISSUES APPEARED NORMAL.
	265	DS 29	28	ALL TISSUES APPEARED NORMAL.
	266	DS 29	28	ALL TISSUES APPEARED NORMAL.
	267	DS 29	28	ALL TISSUES APPEARED NORMAL.
	268	DS 29	28	ALL TISSUES APPEARED NORMAL.
	269	DS 29	28	ALL TISSUES APPEARED NORMAL.
	270	DS 29	28	ALL TISSUES APPEARED NORMAL.
	271	DS 29	28	ALL TISSUES APPEARED NORMAL.
	272	DS 29	28	ALL TISSUES APPEARED NORMAL.
	273	DS 29	28	ALL TISSUES APPEARED NORMAL.
	274	DS 29	28	ALL TISSUES APPEARED NORMAL.
	275	DS 29	28	ALL TISSUES APPEARED NORMAL.
IV 5000	201	DS 29	28	ALL TISSUES APPEARED NORMAL.
	202	DS 29	28	ALL TISSUES APPEARED NORMAL.
	203	DS 29	28	ALL TISSUES APPEARED NORMAL.
	204	DS 29	28	ALL TISSUES APPEARED NORMAL.
	205	DS 29	28	ALL TISSUES APPEARED NORMAL.
	206	DS 29	28	ALL TISSUES APPEARED NORMAL.
	207	DS 29	28	ALL TISSUES APPEARED NORMAL.
	208	DS 29	28	ALL TISSUES APPEARED NORMAL.
	209	DS 29	28	ALL TISSUES APPEARED NORMAL.
	210	DS 29	28	ALL TISSUES APPEARED NORMAL.
	211	DS 29	28	ALL TISSUES APPEARED NORMAL.
	212	DS 29	28	ALL TISSUES APPEARED NORMAL.
	213	DS 29	28	ALL TISSUES APPEARED NORMAL.
	214	DS 29	28	ALL TISSUES APPEARED NORMAL.
	215	DS 29	28	ALL TISSUES APPEARED NORMAL.

DAYS OF EXPOSURE WERE CALCULATED FROM DAY 1 OF STUDY (FIRST FEED VALUE RECORDED) THROUGH THE DAY BEFORE SACRIFICE

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table 23) for external observations confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 31 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM)	RAT NUMBER	DAY OF NECROPSY	DAYS OF EXPOSURE	OBSERVATIONS a
V				
10000	246	DS 29	28	ALL TISSUES APPEARED NORMAL.
	247	DS 29	28	ALL TISSUES APPEARED NORMAL.
	248	DS 29	28	ALL TISSUES APPEARED NORMAL.
	249	DS 29	28	ALL TISSUES APPEARED NORMAL.
	250	DS 29	28	ALL TISSUES APPEARED NORMAL.
	251	DS 29	28	ALL TISSUES APPEARED NORMAL.
	252	DS 29	28	ALL TISSUES APPEARED NORMAL.
	253	DS 29	28	ALL TISSUES APPEARED NORMAL.
	254	DS 29	28	ALL TISSUES APPEARED NORMAL.
	255	DS 29	28	ALL TISSUES APPEARED NORMAL.
	256	DS 29	28	ALL TISSUES APPEARED NORMAL.
	257	DS 29	28	ALL TISSUES APPEARED NORMAL.
	258	DS 29	28	ALL TISSUES APPEARED NORMAL.
	259	DS 29	28	ALL TISSUES APPEARED NORMAL.
	260	DS 29	28	ALL TISSUES APPEARED NORMAL.

DAYS OF EXPOSURE WERE CALCULATED FROM DAY 1 OF STUDY (FIRST FEED VALUE RECORDED) THROUGH THE DAY BEFORE SACRIFICE

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table 23) for external observations confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 32 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM)	RAT NUMBER	DAY OF NECROPSY	DAYS OF EXPOSURE	OBSERVATIONS a
I				
0 (CARRIER CONTROL)	316	DS 29	28	ALL TISSUES APPEARED NORMAL.
	317	DS 29	28	ALL TISSUES APPEARED NORMAL.
	318	DS 29	28	ALL TISSUES APPEARED NORMAL.
	319	DS 29	28	ALL TISSUES APPEARED NORMAL.
	320	DS 29	28	ALL TISSUES APPEARED NORMAL.
	321	DS 29	28	ALL TISSUES APPEARED NORMAL.
	322	DS 29	28	ALL TISSUES APPEARED NORMAL.
	323	DS 29	28	ALL TISSUES APPEARED NORMAL.
	324	DS 29	28	ALL TISSUES APPEARED NORMAL.
	325	DS 29	28	ALL TISSUES APPEARED NORMAL.
	326	DS 29	28	ALL TISSUES APPEARED NORMAL.
	327	DS 29	28	ALL TISSUES APPEARED NORMAL.
	328	DS 29	28	ALL TISSUES APPEARED NORMAL.
	329	DS 29	28	ALL TISSUES APPEARED NORMAL.
	330	DS 29	28	ALL TISSUES APPEARED NORMAL.
II				
100	331	DS 29	28	ALL TISSUES APPEARED NORMAL.
	332	DS 29	28	ALL TISSUES APPEARED NORMAL.
	333	DS 29	28	ALL TISSUES APPEARED NORMAL.
	334	DS 29	28	ALL TISSUES APPEARED NORMAL.
	335	DS 29	28	ALL TISSUES APPEARED NORMAL.
	336	DS 29	28	ALL TISSUES APPEARED NORMAL.
	337	DS 29	28	ALL TISSUES APPEARED NORMAL.
	338	DS 29	28	ALL TISSUES APPEARED NORMAL.
	339	DS 29	28	ALL TISSUES APPEARED NORMAL.
	340	DS 29	28	ALL TISSUES APPEARED NORMAL.
	341	DS 29	28	ALL TISSUES APPEARED NORMAL.
	342	DS 29	28	ALL TISSUES APPEARED NORMAL.
	343	DS 29	28	ALL TISSUES APPEARED NORMAL.
	344	DS 29	28	ALL TISSUES APPEARED NORMAL.
	345	DS 29	28	ALL TISSUES APPEARED NORMAL.

DAYS OF EXPOSURE WERE CALCULATED FROM DAY 1 OF STUDY (FIRST FEED VALUE RECORDED) THROUGH THE DAY BEFORE SACRIFICE

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table 25) for external observations confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 32 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM)	RAT NUMBER	DAY OF NECROPSY	DAYS OF EXPOSURE	OBSERVATIONS a
III 500	361	DS 29	28	ALL TISSUES APPEARED NORMAL.
	362	DS 29	28	ALL TISSUES APPEARED NORMAL.
	363	DS 29	28	ALL TISSUES APPEARED NORMAL.
	364	DS 29	28	ALL TISSUES APPEARED NORMAL.
	365	DS 29	28	ALL TISSUES APPEARED NORMAL.
	366	DS 29	28	ALL TISSUES APPEARED NORMAL.
	367	DS 29	28	ALL TISSUES APPEARED NORMAL.
	368	DS 29	28	ALL TISSUES APPEARED NORMAL.
	369	DS 29	28	ALL TISSUES APPEARED NORMAL.
	370	DS 29	28	ALL TISSUES APPEARED NORMAL.
	371	DS 29	28	ALL TISSUES APPEARED NORMAL.
	372	DS 29	28	ALL TISSUES APPEARED NORMAL.
	373	DS 29	28	ALL TISSUES APPEARED NORMAL.
	374	DS 29	28	ALL TISSUES APPEARED NORMAL.
	375	DS 29	28	ALL TISSUES APPEARED NORMAL.
IV 5000	301	DS 29	28	ALL TISSUES APPEARED NORMAL.
	302	DS 29	28	ALL TISSUES APPEARED NORMAL.
	303	DS 29	28	ALL TISSUES APPEARED NORMAL.
	304	DS 29	28	ALL TISSUES APPEARED NORMAL.
	305	DS 29	28	ALL TISSUES APPEARED NORMAL.
	306	DS 29	28	ALL TISSUES APPEARED NORMAL.
	307	DS 29	28	ALL TISSUES APPEARED NORMAL.
	308	DS 29	28	ALL TISSUES APPEARED NORMAL.
	309	DS 29	28	ALL TISSUES APPEARED NORMAL.
	310	DS 29	28	KIDNEYS: RIGHT, PELVIS, SLIGHT DILATION. ALL OTHER TISSUES APPEARED NORMAL
	311	DS 29	28	ALL TISSUES APPEARED NORMAL.
	312	DS 29	28	ALL TISSUES APPEARED NORMAL.
	313	DS 29	28	ALL TISSUES APPEARED NORMAL.
	314	DS 29	28	ALL TISSUES APPEARED NORMAL.
	315	DS 29	28	ALL TISSUES APPEARED NORMAL.

DAYS OF EXPOSURE WERE CALCULATED FROM DAY 1 OF STUDY (FIRST FEED VALUE RECORDED) THROUGH THE DAY BEFORE SACRIFICE

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table 25) for external observations confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 32 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM)	RAT NUMBER	DAY OF NECROPSY	DAYS OF EXPOSURE	OBSERVATIONS a
V				
10000	346	DS 29	28	ALL TISSUES APPEARED NORMAL.
	347	DS 29	28	ALL TISSUES APPEARED NORMAL.
	348	DS 29	28	ALL TISSUES APPEARED NORMAL.
	349	DS 29	28	ALL TISSUES APPEARED NORMAL.
	350	DS 29	28	ALL TISSUES APPEARED NORMAL.
	351	DS 29	28	ALL TISSUES APPEARED NORMAL.
	352	DS 29	28	ALL TISSUES APPEARED NORMAL.
	353	DS 29	28	ALL TISSUES APPEARED NORMAL.
	354	DS 29	28	ALL TISSUES APPEARED NORMAL.
	355	DS 29	28	ALL TISSUES APPEARED NORMAL.
	356	DS 29	28	ALL TISSUES APPEARED NORMAL.
	357	DS 29	28	ALL TISSUES APPEARED NORMAL.
	358	DS 29	28	ALL TISSUES APPEARED NORMAL.
	359	DS 29	28	ALL TISSUES APPEARED NORMAL.
	360	DS 29	28	ALL TISSUES APPEARED NORMAL.

DAYS OF EXPOSURE WERE CALCULATED FROM DAY 1 OF STUDY (FIRST FEED VALUE RECORDED) THROUGH THE DAY BEFORE SACRIFICE

DS = DAY OF STUDY

a. Refer to the individual clinical observations table (Table 25) for external observations confirmed at necropsy.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 33 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP I		0 (CARRIER CONTROL) PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
216	1.745	15.199	
217	1.923	14.218	
218	1.952	13.610	
219	2.044	14.201	
220	1.843	13.279	
221	1.864	11.693	
222	2.072	11.504	
223	1.950	13.734	
224	1.939	13.113	
225	1.823	12.847	
226	1.876	12.544	
227	2.036	12.923	
228	2.107	12.851	
229	2.025	13.914	
230	1.806	14.074	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 33 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP II		100 PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
231	1.775	14.686	
232	1.919	13.623	
233	1.873	12.158	
234	1.825	13.708	
235	1.849	11.997	
236	2.096	12.774	
237	2.036	11.846	
238	2.005	12.608	
239	1.967	13.587	
240	1.902	12.837	
241	2.068	11.852	
242	1.891	12.249	
243	1.959	12.808	
244	2.002	14.179	
245	1.804	13.476	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 33 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP III		500 PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
261	1.814	13.794	
262	1.989	12.175	
263	1.914	11.394	
264	1.980	11.961	
265	1.872	12.877	
266	1.960	12.146	
267	1.918	12.648	
268	1.972	12.822	
269	2.013	12.516	
270	2.074	12.049	
271	2.212	11.102	
272	1.970	11.615	
273	1.899	11.848	
274	1.964	13.936	
275	2.026	12.437	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 33 (PAGE 4): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP IV		5000 PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
201	1.978	11.065	
202	2.028	10.869	
203	1.844	10.458	
204	2.023	9.107	
205	1.859	10.504	
206	2.083	10.303	
207	1.918	9.913	
208	2.071	9.981	
209	1.816	10.290	
210	2.011	8.574	
211	2.018	11.730	
212	1.864	9.528	
213	1.976	10.314	
214	1.909	12.461	
215	1.858	11.772	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 33 (PAGE 5): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP V		10000 PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
246	1.683	11.640	
247	1.901	9.234	
248	1.958	9.424	
249	1.890	9.665	
250	1.866	12.789	
251	1.956	9.430	
252	1.870	10.544	
253	1.921	9.843	
254	1.942	8.845	
255	1.846	9.310	
256	1.879	12.061	
257	1.803	10.251	
258	1.966	9.507	
259	2.037	12.498	
260	1.896	12.369	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 34 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP I		0 (CARRIER CONTROL) PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
316	1.785	14.605	
317	1.873	14.831	
318	1.887	13.605	
319	1.933	14.467	
320	1.882	14.982	
321	1.990	13.580	
322	1.910	13.260	
323	1.993	12.448	
324	1.834	13.915	
325	1.854	12.713	
326	1.888	11.649	
	1.888	11.564a	
327	1.901	13.804	
328	1.692	14.560	
329	1.964	12.774	
330	1.847	13.439	

a. Sample was inadvertently analyzed a second time; value was excluded from summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 34 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP II		100 PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
331	1.845	14.755	
332	1.791	14.935	
333	1.736	14.579	
334	1.818	14.607	
335	1.837	15.187	
336	1.875	13.830	
337	1.775	13.291	
338	1.813	13.090	
339	1.934	12.631	
340	1.890	13.270	
341	1.795	12.554	
342	1.932	11.616	
343	1.923	11.959	
344	2.004	12.273	
345	1.877	12.973	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 34 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP III		500 PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
361	1.837	13.159	
362	1.845	13.242	
363	1.971	13.293	
364	1.995	13.857	
365	1.887	12.627	
366	1.846	14.185	
367	1.727	13.568	
368	1.938	12.501	
369	1.864	12.254	
370	1.900	12.771	
371	1.813	12.102	
372	1.800	12.957	
373	1.819	12.521	
374	1.825	14.004	
375	1.950	12.069	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 34 (PAGE 4): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP IV		5000 PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
301	1.777	11.148	
302	1.919	10.502	
303	1.871	10.123	
304	1.846	9.941	
305	1.832	10.943	
306	1.843	10.155	
307	1.841	10.271	
308	1.928	9.605	
309	1.819	9.539	
310	1.962	9.799	
311	1.861	10.679	
312	1.919	10.221	
313	1.795	10.517	
314	1.953	10.135	
315	1.860	9.819	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 34 (PAGE 5): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP V		10000 PPM	
RAT #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
346	1.632	8.485	
347	1.919	10.933	
348	1.784	9.578	
349	1.964	9.455	
350	1.813	5.335	
351	1.890	9.146	
352	1.878	4.024	
353	1.934	5.987	
354	1.759	7.883	
355	1.821	6.864	
356	1.875	5.068	
357	1.901	8.754	
358	1.792	4.371	
359	1.885	5.779	
360	1.910	5.123	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 35 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP I		0 (CARRIER CONTROL) PPM
RAT #	FINAL CHOLINESTERASE (UNITS/ML)	FOOTNOTE
216	1.181	
217	1.381	
218	1.282	
219	1.635	
220	1.808	
221	1.505	
222	1.583	
223	1.643	
224	1.305	
225	1.217	
226	1.262	
227	1.313	
228	1.495	
229	1.420	
230	1.671	

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 35 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP II		100 PPM	
RAT #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
231	1.294		
232	1.307		
233	1.230		
234	1.442		
235	1.434		
236	1.486		
237	1.811		
238	1.335		
239	1.459		
240	1.432		
241	1.060		
242	1.251		
243	1.300		
244	1.512		
245	1.480		

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 35 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP III		500 PPM	
RAT #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
261	0.687		
262	1.217		
263	1.341		
264	1.242		
265	1.206		
266	0.922		
267	1.193		
268	0.870		
269	1.004		
270	0.971		
271	1.137		
272	1.136		
273	1.170		
274	1.414		
275	1.350		

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 35 (PAGE 4): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP IV		5000 PPM	
RAT #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
201	X		DNR
	X		DNR
	X		DNR
202	X		DNR
	0.379		
203	X		DNR
	0.226a		LOW
	0.215		LOW
204	X		DNR
	0.139a		LOW
	X		DNR
205	0.318		
206	X		DNR
	0.257		
207	0.297		
208	X		DNR
	0.141a		LOW
	0.205		LOW
209	X		DNR
	X		DNR
	X		DNR
210	X		DNR
	X		DNR
	0.218a		LOW
211	X		DNR
	X		DNR
	0.254		

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD (VALUES WERE EXTRAPOLATED); VALUE WAS EXCLUDED FROM SUMMARIZATION AND STATISTICAL ANALYSES

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

a. Extrapolated value was included in summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 35 (PAGE 5): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP IV		5000 PPM	
RAT #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
212	0.247		
213	0.269		
214	X		DNR
	0.219		
215	X		DNR
	0.342		

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD (VALUES WERE EXTRAPOLATED); VALUE WAS EXCLUDED FROM SUMMARIZATION AND STATISTICAL ANALYSES

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

a. Extrapolated value was included in summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 35 (PAGE 6): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP V		10000 PPM	
RAT #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
246	X		DNR
	X		DNR
	0.178a		LOW
247	X		DNR
	0.111		LOW
	X		DNR
248	X		DNR
	X		DNR
	X		DNR
249	X		DNR
	0.108a		LOW
	X		DNR
250	X		DNR
	X		DNR
	X		DNR
251	X		DNR
	X		DNR
	0.131a		LOW
252	X		DNR
	0.135a		LOW
	X		DNR
253	0.201a		LOW
	0.180		LOW
	0.202		LOW
254	X		DNR
	0.093a		LOW
	X		DNR
255	X		DNR
	X		DNR
	0.123a		LOW

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD (VALUES WERE EXTRAPOLATED); VALUE WAS EXCLUDED FROM SUMMARIZATION AND STATISTICAL ANALYSES

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

a. Extrapolated value was included in summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 35 (PAGE 7): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP V		10000 PPM
RAT #	FINAL CHOLINESTERASE (UNITS/ML)	FOOTNOTE
256	X	DNR
	X	DNR
	X	DNR
257	X	DNR
	X	DNR
	0.214a	LOW
258	X	DNR
	0.419	
	X	DNR
259	X	DNR
	X	DNR
	0.147a	LOW
260	X	DNR
	X	DNR
	0.121a	LOW

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD (VALUES WERE EXTRAPOLATED); VALUE WAS EXCLUDED FROM SUMMARIZATION AND STATISTICAL ANALYSES

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

a. Extrapolated value was included in summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 36 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP I		0 (CARRIER CONTROL) PPM
RAT #	FINAL CHOLINESTERASE (UNITS/ML)	FOOTNOTE
316	1.427	
317	1.294	
318	1.352	
319	1.667	
320	1.289	
321	X	DNR
	1.258	
322	1.344	
323	1.667	
324	1.555	
325	1.555	
326	1.620	
327	1.816	
328	1.860	
329	1.560	
330	1.510	

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 36 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP II		100 PPM	
RAT #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
331	1.418		
332	1.238		
333	1.055		
334	1.380		
335	1.471		
336	X		DNR
	1.286		
337	1.285		
338	1.451		
339	1.265		
340	1.448		
341	X		DNR
	1.376		
342	1.251		
343	1.351		
344	1.163		
345	1.429		

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 36 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP III		500 PPM	
RAT #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
361	0.935		
362	0.953		
363	0.915		
364	0.967		
365	1.086		
366	X		DNR
	0.935		
367	0.987		
368	0.968		
369	1.123		
370	1.105		
371	1.539		
372	1.195		
373	1.093		
374	0.968		
375	1.406		

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 36 (PAGE 4): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP IV		5000 PPM
RAT #	FINAL CHOLINESTERASE (UNITS/ML)	FOOTNOTE
301	X	DNR
	X	DNR
	X	DNR
302	X	DNR
	X	DNR
	X	DNR
303	X	DNR
	0.198a	LOW
	X	DNR
304	0.185a	LOW
	X	DNR
	0.194	LOW
305	0.209a	LOW
	X	DNR
	0.200	LOW
306	X	DNR
	X	DNR
	X	DNR
307	X	DNR
	X	DNR
	X	DNR
308	X	DNR
	0.123a	LOW
	0.098	LOW
309	X	DNR
	X	DNR
	0.419	
310	0.273	
311	X	DNR
	X	DNR
	0.234	

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD (VALUES WERE EXTRAPOLATED); VALUE WAS EXCLUDED FROM SUMMARIZATION AND STATISTICAL ANALYSES

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

a. Extrapolated value was included in summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 36 (PAGE 5): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP IV		5000 PPM	
RAT #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
312	0.201		LOW
	X		DNR
	0.244		
313	0.504		
314	0.218		LOW
	0.262		
315	X		DNR
	0.201a		LOW
	0.237		LOW

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD (VALUES WERE EXTRAPOLATED); VALUE WAS EXCLUDED FROM SUMMARIZATION AND STATISTICAL ANALYSES

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

a. Extrapolated value was included in summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 36 (PAGE 6): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP V		10000 PPM
RAT #		FOOTNOTE
346	-0.114	LOW
	X	DNR
	X	DNR
347	X	DNR
	0.073a	LOW
	X	DNR
348	X	DNR
	X	DNR
	X	DNR
349	X	DNR
	X	DNR
	X	DNR
350	X	DNR
	X	DNR
	X	DNR
351	X	DNR
	0.106a	LOW
	X	DNR
352	0.049a	LOW
	X	DNR
	0.086	LOW
353	X	DNR
	X	DNR
	X	DNR
354	X	DNR
	0.104a	LOW
	X	DNR
355	X	DNR
	X	DNR
	0.189a	LOW

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD (VALUES WERE EXTRAPOLATED); VALUE WAS EXCLUDED FROM SUMMARIZATION AND STATISTICAL ANALYSES

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

a. Extrapolated value was included in summarization and statistical analyses.

PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 36 (PAGE 7): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP V		10000 PPM
RAT #		FOOTNOTE
356	X	DNR
	X	DNR
357	0.096a	LOW
	X	DNR
	X	DNR
358	0.155a	LOW
	X	DNR
	X	DNR
359	0.143a	LOW
	X	DNR
	0.117a	LOW
360	X	DNR
	X	DNR
	0.249	

X = SAMPLE RESULTS DID NOT MEET ACCEPTABILITY CRITERIA

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD (VALUES WERE EXTRAPOLATED); VALUE WAS EXCLUDED FROM SUMMARIZATION AND STATISTICAL ANALYSES

DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

a. Extrapolated value was included in summarization and statistical analyses.

APPENDIX 1 - PROTOCOL AND PROTOCOL AMENDMENTS



FINAL PROTOCOL

Charles River Laboratories Study No. TQC00065

**Oral (Diet) Repeated Dose 28-Day Toxicity Study of
Malathion Technical in Rats**

SPONSOR:

Cheminova A/S
P.O. Box 9
DK-7620 Lemvig
DENMARK

PERFORMING LABORATORY:

Charles River Laboratories
Preclinical Services
905 Sheehy Drive, Building A
Horsham, PA 19044
USA

11 October 2010

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1. STUDY NUMBER

TQC00065

2. STUDY TITLE

Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats

3. PURPOSE

The purpose of this study is to provide information on possible adverse effects on Crl:CD(SD) rats resulting from repeated exposure to Malathion Technical over a 28-day exposure period. The study should provide information that can be used in the selection of dosage levels for subsequent studies.

4. TESTING FACILITY

Charles River Laboratories
Preclinical Services
905 Sheehy Drive, Building A
Horsham, PA 19044
USA
Main Tel: 215.443.8710
Fax: 215.443.8587

5. STUDY DIRECTOR

John F. Barnett, Jr., B.S. (Senior Research Scientist)
Address as cited above for Testing Facility.
Direct Tel: 267.532.3750
E-mail: john.barnettjr@crl.com

6. SPONSOR

Cheminova A/S
P.O. Box 9
DK-7620 Lemvig
DENMARK

7. STUDY MONITOR

M. Jensen

8. REGULATORY COMPLIANCE

The requirements of the Organisation for Economic Co-operation and Development¹ and the U.S. Environmental Protection Agency² will be used as the basis for study design.

This study will be conducted in compliance with the Good Laboratory Practice (GLP) regulations of the U.S. Environmental Protection Agency³ and the Organisation for Economic Co-operation and Development⁴.

All changes or revisions of this protocol shall be documented, approved by the Institutional Animal Care and Use Committee, approved and signed by the Study Director and the Sponsor, dated and maintained with the protocol.

The Testing Facility's Quality Assurance Unit (QAU) will audit the protocol, the raw data and the report, and will inspect critical phases of those portions of the study conducted at the Testing Facility in accordance with the Standard Operating Procedures of the Testing Facility.

The final report will include a compliance statement signed by the Study Director that the report accurately reflects the raw data obtained during the performance of the study and that all applicable GLP regulations were followed in the conduct of the study. Should deviations from GLP regulations occur, each will be described in detail, together with how the deviation might affect the quality or integrity of the study.

Should any portion of the study be conducted by a subcontractor or by the Sponsor, the Testing Facility management will ensure that a qualified Principal Investigator is identified by the site conducting that portion of the study. All procedures conducted by the Test Site will be specifically defined by the protocol, or will be described in detail in the Standard Operating Procedures of the Test Site. The QAU for this facility site will

conduct critical phase inspections and audit respective results and reports for that study portion according to the SOPs of that site. Such critical phase inspection reports and report audits will be submitted by the site to the Principal Investigator and the Study Director. The dates of the inspections and report submissions will be incorporated into a QAU Statement generated by that site and provided to the Testing Facility for inclusion in the final report. In addition, this site will provide a statement of GLP compliance, as described above, signed by the Principal Investigator for inclusion in the final report. The archival location of any records generated by this site will be identified in the final report.

The Study Director will notify the Study Monitor of any possible adverse effects as required by law under FIFRA Section 6(a)(2) within 24 hours of obtaining such information.

9. SCHEMATIC OF STUDY DESIGN AND PROPOSED STUDY SCHEDULE

See Attachment 1 to the protocol.

10. TEST SUBSTANCE AND CARRIER

10.1. Identification

10.1.1. Test Substance

Malathion Technical (CHA 300)

Batch Number:	D2014-OSJ-MLT-01-S
Expiration Date:	22 July 2012
Appearance:	Light, yellow liquid
Purity:	96.0% w/w

Documentation or certification of the identity, composition, strength and activity/purity of the test substance is on file at the Testing Facility. This documentation will be included in the final report. The test substance is a marketed product and therefore the method of synthesis information has been documented.

The Study Director is not aware of any potential contaminants likely to be present in the test substance that would interfere with the results of this study. Therefore, no additional analyses are being conducted. A Certificate of Analysis is attached to the protocol (ATTACHMENT 2).

10.1.2. Carrier

The carrier will be the meal form of Certified Rodent Diet[®] #5002 (PMI[®] Nutrition International) containing 5% corn oil to minimize dust production during diet preparation and usage. Results of feed analyses will be included in the raw data.

The Study Director is not aware of any potential contaminants likely to be present in the carrier that could interfere with the results of this study. Therefore, no analyses other than those mentioned in this protocol will be conducted.

10.2. Safety Precautions

Double nitrile gloves, full faced positive pressure hood, appropriate eye protection and Tyvek[®] suit will be worn during formulation preparation and dosage administration. Bulk test substance will be handled in a chemical fume hood. Gloves will be washed with soap and water or sprayed with an appropriate cleaning solution prior to removal and then disposed of in a biohazard container. For all other activities, standard safety precautions will be followed. The Material Safety Data Sheet (MSDS) is attached to the protocol (Attachment 3).

10.3. Storage

Bulk Test Substance:	Refrigerated (2°C to 8°C) and protected from light.
Carrier:	Room Temperature.
Prepared Diets:	Refrigerated (2°C to 8°C) until use.
Corn Oil:	Room Temperature.

11. FORMULATION**11.1. Frequency of Preparation**

Formulations (diets) will be prepared at least weekly at the Testing Facility.

Detailed preparation procedures are attached to this protocol (Attachment 4).

11.2. Adjustment for Activity/Purity

The test substance will be considered 96% active/pure for the purpose of dosage calculations.

11.3. Testing Facility Reserve Samples

The Testing Facility will reserve a sample of approximately 5 mL of each lot of bulk test substance and corn oil, and a sample (125 g) of each lot of the carrier used during the course of the study. Samples will be stored under the previously cited conditions.

12. ANALYSES

Results of required analyses will be provided to the Testing Facility for inclusion in the study report.

Samples additional to those described below may be taken if deemed necessary during the course of the study. Additional analyses, if required, will be documented by protocol amendment.

12.1. Acceptance Criteria

Acceptance criteria for analytical results for each group are defined as follows:

1) concentration results will be considered acceptable if the difference between the actual mean value and the targeted concentration is $\leq 10\%$ for diets; and 2) homogeneity results for a group will be considered acceptable if the relative standard deviation (RSD) for the formulation, calculated as the RSD for the grand mean of the average values for top, middle and bottom locations, is $\leq 5\%$. Results obtained outside of the criteria will be considered Out of Specification (OOS) and procedures for investigation and notification will be followed in the applicable laboratory Standard Operating Procedure covering OOS results.

12.2. Bulk Test Substance Stability

A sample of the bulk test substance will not be retained during the course of this study. Information to document or certify the stability of each lot of the bulk test substance will be provided by the Sponsor to the Testing Facility.

12.3. Analyses of Prepared Formulations

12.3.1. Concentration and Homogeneity

Homogeneity of the prepared diets will be verified during the course of this study according to a validated method (analytical procedure MALA02). Quadruplicate samples (25 g each) will be taken from the top, middle and bottom of each concentration from the first preparation on the day prepared. All samples will be transferred to the

analytical laboratory at the Testing Facility. A duplicate set of samples from each quadruplicate set will be analyzed. The mean concentration result of the homogeneity analysis for each level will also be used to verify the concentrations for Week 1. The remaining samples will be retained refrigerated (2°C to 8°C), protected from light at the Testing Facility as backup samples.

Concentration of the prepared diets will be verified during the course of this study according to a validated method (analytical procedure MALA02). Duplicate samples (25 g each) will be taken on each day of preparation from each concentration. All samples from weeks 2 and 4 will be transferred to the analytical laboratory at the Testing Facility. One sample of each set will be analyzed in duplicate. The remaining samples will be retained refrigerated (2°C to 8°C), protected from light at the Testing Facility as backup samples.

12.3.2. Stability

Stability data for prepared test substance formulations bracketing the range of concentrations will be determined in Charles River Laboratories study number TQC00067DX.

12.4. Transfer Instructions

Concentration and homogeneity samples to be analyzed will be transferred to the analytical laboratory at the Testing Facility on cold packs to:

Principal Investigator: Jason Sarsoza, B.S.
Charles River Laboratories, Preclinical Services, Pennsylvania
905 Sheehy Drive, Building A
Horsham, PA 19044
USA
Tel: 267.532.3771
E-mail:jason.sarsoza@crl.com

The recipient will be notified in advance of sample transfer.

Following the analyses, the remaining dietary extracts from all dosage levels will be retained and stored frozen (at least -20°C), for possible future analyses. Disposition of the dietary extracts will be documented in the raw data.

13. DISPOSITION

Unused prepared diets will be discarded at the Testing Facility. Backup samples will be discarded at the Testing Facility prior to issuance of the final report. Disposition of the remaining bulk test substance and dietary extracts will be documented in the raw data after consultation with the Sponsor.

14. TEST SYSTEM

14.1. Species/Strain and Reason for Selection

The Crl:CD(SD) rat was selected as the Test System because: 1) it is one mammalian species accepted for use in toxicity studies; and 2) it has been widely used throughout industry for toxicity evaluations.

14.2. Number

Initial population acclimated: 80 male and 80 virgin female rats.

Population selected study: 75 male and 75 female rats (fifteen per sex per dosage group).

14.3. Sex

Both male and female rats will be evaluated.

14.4. Body Weight and Age

Male and female rats will be ordered to be approximately 35 days of age at receipt, at which time they will be expected to weight from 80 g to 140 g each. Actual body weights will be recorded the day after receipt and will be documented in the raw data. The weight ranges will be included in the final report.

14.5. Source

Charles River Laboratories, Inc.

The rats will be shipped in filtered cartons by air freight and/or truck from Charles River Laboratories, Inc., to the Testing Facility.

14.6. Identification

Rats are permanently identified using Monel[®] self-piercing ear tags. Male and female rats are assigned temporary numbers at receipt and given unique permanent identification numbers when assigned to the study before the first day of exposure.

15. ANIMAL HUSBANDRY

All cage sizes and housing conditions are in compliance with the *Guide for the Care and Use of Laboratory Animals*⁵.

15.1. Housing

During the acclimation and study periods, the rats will be individually housed in stainless steel, wire-bottomed cages.

15.2. Room Air, Temperature and Humidity

The animal room is independently supplied with at least ten changes per hour of 100% fresh air that has been passed through 99.97% HEPA filters. Room temperature will be maintained at 66°F to 77°F (19°C to 25°C) and monitored constantly. Room humidity will also be monitored constantly and maintained at 30% to 70%.

15.3. Light

An automatically controlled 12-hour light:12-hour dark fluorescent light cycle will be maintained. Each dark period will begin at 1900 hours (\pm 30 minutes). The light cycle may be adjusted by the Study Director or designee if deemed necessary to accommodate scheduled laboratory activities. Any such adjustment will be documented in the raw data.

15.4. Diet

Rats will be given either Certified Rodent Diet[®] #5002 (PMI[®] Nutrition International) only (carrier control group) or test diets prepared using Certified Rodent Diet[®] and the test substance. These will be available *ad libitum* from individual feeders.

15.5. Water

Water will be available *ad libitum* from individual bottles attached to the cages and/or from an automatic watering access system. All water will be from a local source and passed through a reverse osmosis membrane before use. Chlorine will be added to the processed water as a bacteriostat; processed water is expected to contain no more than 1.2 ppm chlorine at the time of analysis. Water is analyzed monthly for possible bacterial contamination and twice annually for possible chemical contamination.

15.6. Enrichment

Chewable Nylabones[®] will be supplied to all rats during the course of the study.

Analyses for possible contamination are conducted on each lot of Nylabones[®] and documented in the raw data.

15.7. Contaminants

The Study Director is not aware of any potential contaminants likely to be present in the certified diet, the drinking water or in the chewable enrichment devices at levels that could interfere with the results of this study. Therefore, no analyses other than those routinely performed by the feed supplier or those mentioned in this protocol will be conducted.

16. RANDOMIZATION AND ACCLIMATION

Upon arrival, rats will be assigned to individual housing on the basis of computer-generated random units. After acclimation, rats will be selected for study on the basis of physical appearance and body weights recorded during acclimation. The rats will be assigned to dosage groups based on computer-generated (weight-ordered) randomization procedures. The weight variation of rats used on study will not exceed $\pm 20\%$ of the mean body weight of each sex (when possible).

In order to accommodate the necropsy schedule, rats will be randomly assigned to two replicates by sex that will begin exposure and be sacrificed on consecutive days.

17. ADMINISTRATION**17.1. Route of Exposure**

The oral (diet) route was selected for use because it is a possible route of human exposure.

17.2. Method and Frequency

A constant concentration of the test substance in the diet will be offered to the rats, and the mg/kg/day dosages consumed will be calculated and presented for periods corresponding to body weight and feed consumption observations.

A carrier control and four test diet concentrations will be given to the rats. Rats will be given continual access to the test substance in the diet for 28 consecutive days. The first day of test diet exposure for each replicate will be day 1 of the study. Test diet concentrations may be adjusted if observed toxicity indicates that it is required.

17.3. Rationale for Dosage Selection

Dosage levels were selected by the Sponsor on the basis of previous studies conducted with the test substance.

The highest dosage level is expected to induce toxicity but not death or severe suffering. The descending sequence of the lower dosage levels were selected for the purpose of demonstrating any dosage-related response, with no adverse effects expected at the lowest level.

17.4. Dosage Levels, Concentrations and Dosage Volumes

Dosage Group	Number of Rats Per Sex	Concentration (ppm)	Batch Number
I	15	0 (Carrier Control)	B-TQC00065-A(Day.Month.Year)
II	15	100	B-TQC00065-B(Day.Month.Year)
III	15	500	B-TQC00065-C(Day.Month.Year)
IV	15	5000	B-TQC00065-D(Day.Month.Year)
V	15	10000	B-TQC00065-E(Day.Month.Year)

The test substance will be considered 96.0% active/pure for the purpose of dosage calculations.

18. TESTS, ANALYSES AND MEASUREMENTS**18.1. Viability**

All Periods: At least twice daily.

18.2. Clinical Observations and/or General Appearance

Acclimation Period: At least weekly.

Exposure Period: Once daily.

Signs of toxicity will be recorded as observed, including the time of onset, degree and duration.

Clinical observations may be recorded more frequently than cited above.

18.3. Detailed Clinical Observations - Male and Female Rats

Once before the first day of exposure and at least once weekly thereafter, detailed clinical observations will be conducted for all male and female rats. The detailed clinical observations will be conducted by an observer unaware of the group assignment of the rat.

18.4. Body Weights

Acclimation Period: At least weekly (not tabulated).

Exposure Period: Weekly and on the day before sacrifice.

Sacrifice: Terminal weight.

18.5. Feed Consumption Values

Acclimation Period: At least once (not tabulated).

Exposure Period: Weekly.

Day before Sacrifice: Feed left recorded.

Feed consumption values may be recorded more frequently if it is necessary to replenish the feed. These intervals will not be tabulated.

19. CHOLINESTERASE ASSAY**19.1. Blood and Brain Sample Collection**

On the day of sacrifice, DS 29, whole blood samples (2 to 3 mLs each) will be collected once from each rat. The time of each blood collection will be recorded in the raw data. Blood will be collected under isoflurane/oxygen anesthesia from the inferior vena cava (the rats will be in the isoflurane/oxygen for no longer than 5 minutes prior to blood collection). The time for each blood collection will be targeted to be ≤ 10 seconds and will be recorded using a stopwatch and documented in the raw data.

Blood samples will be maintained under cold packs on a tilter until being processed at the Testing Facility. The brains will be stored in saline on wet ice until being processed at the Testing Facility. All processed samples will be held on wet ice until assayed.

The blood and brain samples will be analyzed for cholinesterase levels at the Testing Facility the same day that they are collected. RBC and brain samples will be processed and assayed as soon as possible, with the experimental target that samples be analyzed within 60 minutes of sacrifice.

Following analysis, samples will be retained frozen (-15°C to -30°C). These samples will be discarded prior to issuance of the final report. Disposition of these samples will be documented in the raw data.

19.1.1. RBC

Prior to blood collection, syringes will be coated with EDTA to prevent clotting; 2 to 3 mLs of whole blood will be transferred into EDTA-coated (lavender-top) tubes. Blood samples will be stored under cold packs on a tilter until being processed and subsequently analyzed for RBC cholinesterase levels according to the Study Specific Procedure located in ATTACHMENT 5 of the protocol.

19.1.2. Brains

After blood sample collection and sacrifice, the brain will be excised and placed in a weighing boat on wet ice. The brain will be weighed and the weight recorded to three decimal places. The brains will be stored in saline on wet ice until being processed and subsequently analyzed for cholinesterase levels according to the Study Specific Procedure located in ATTACHMENT 5 of the protocol.

20. METHOD OF SACRIFICE

Rats will be anesthetized under the isoflurane/oxygen and following blood collection from the vena cava, subsequently sacrificed by an injection of sodium pentobarbital into the inferior vena cava.

20.1. Scheduled Sacrifice

Rats will be sacrificed on day 29 of study and necropsied as described below in Section 21.

20.2. Rats Found Dead or Unscheduled Sacrifice

Rats that die or are sacrificed before scheduled termination will be examined for the cause of death or condition as soon as possible after the observation is made. When not precluded by autolysis, the heart, lungs, liver, kidneys, stomach and spleen will be retained in neutral buffered 10% formalin for possible histological evaluation. Additional tissues may be retained at the discretion of the Study Director. The rats will be necropsied as described below in Section 21.

21. NECROPSY

Male and female rats will be sacrificed and examined for gross lesions. Gross lesions will be retained in neutral buffered 10% formalin for possible future evaluation. A gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. In addition, the nasal passages, the nasal cavity and neck with associated organs and tissues will be examined.

Representative samples of the tissues identified in the Tissue Collection and Preservation table will be collected from all rats and preserved in 10% neutral buffered formalin for future possible evaluation.

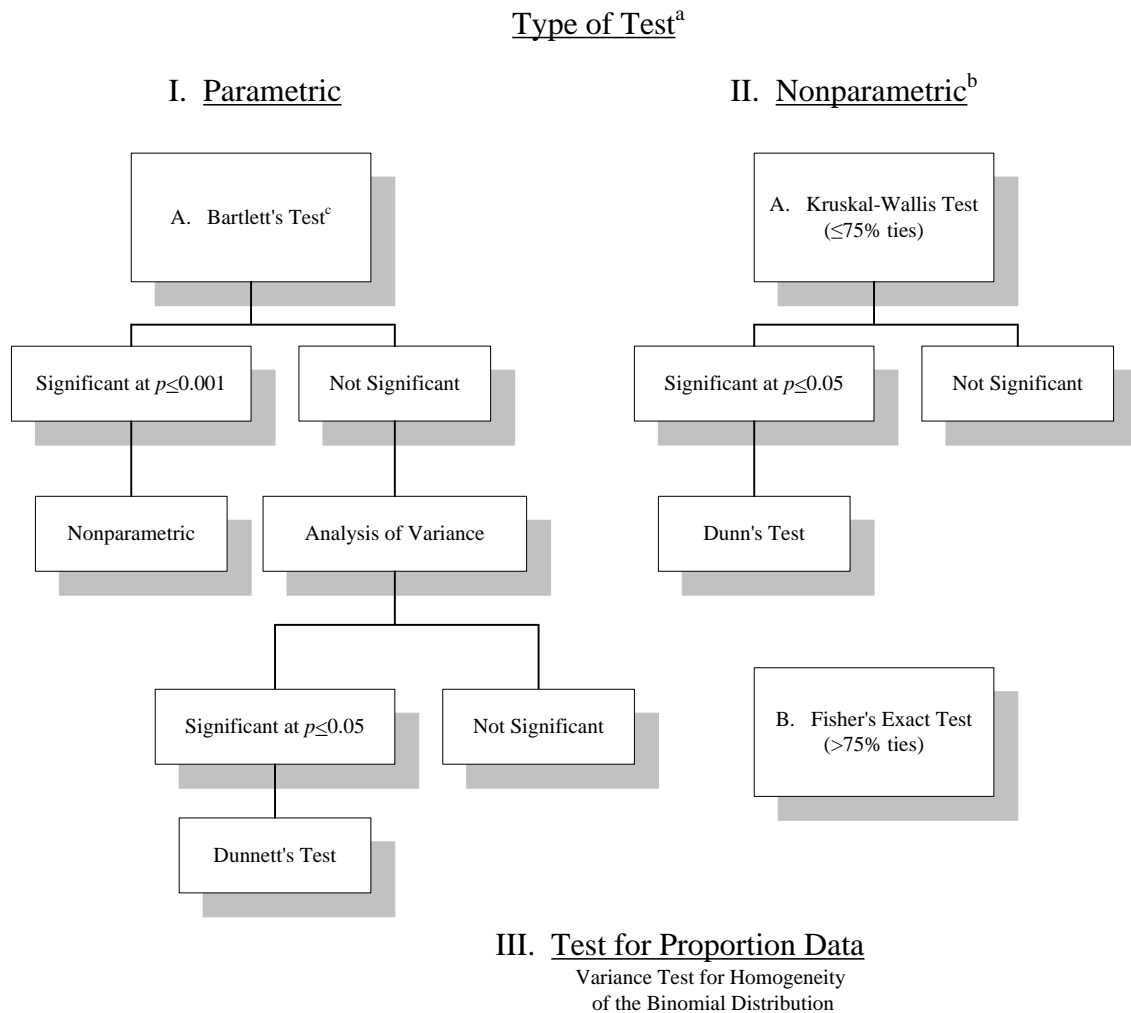
Tissue Collection and Preservation

Tissue	Weigh	Collect	Microscopic Evaluation	Comment
Animal identification	-	X	-	-
Gross lesions/masses	-	X	-	-
Liver	X	X	-	-
Kidney	X	X	-	Paired weight and examination.
Nasal Cavity	-	X	-	Collect with sinuses.

X = procedure to be conducted; - = not applicable.

22. PROPOSED STATISTICAL TESTS

Averages and percentages will be calculated. The following schematic represents the statistical analyses of the data:



-
- a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
 - b. Proportion data are not included in this category.
 - c. Test for homogeneity of variance.

Clinical observations and other proportional data will be analyzed, using the Variance Test for Homogeneity of the Binomial Distribution⁶.

Continuous data (e.g., body weights, body weight changes, feed consumption values and organ weights) will be analyzed, using Bartlett's Test of Homogeneity of Variances⁷ and the Analysis of Variance⁸, when appropriate [i.e., Bartlett's Test was not significant ($p > 0.001$)]. If the Analysis of Variance is significant ($p \leq 0.05$), Dunnett's Test⁹ will be used to identify the statistical significance of the individual groups. If the Analysis of Variance is not appropriate [i.e., Bartlett's Test was significant ($p \leq 0.001$)], the Kruskal-Wallis Test¹⁰ will be used, when less than or equal to 75% ties are present. In cases where the Kruskal-Wallis Test is statistically significant ($p \leq 0.05$), Dunn's Method of Multiple Comparisons¹¹ will be used to identify the statistical significance of the individual groups. If there are greater than 75% ties, Fisher's Exact Test¹² will be used to analyze the data.

Count data will be evaluated, using the procedures described above for the Kruskal-Wallis Test¹⁰.

Cholinesterase values for RBC and brains will be evaluated as separate dependent variables in one-way analyses of variance (ANOVA)⁸ at each combination of sex (male and female). In the event that the ANOVA is significant ($p \leq 0.05$), Dunnett's test⁹ will be used to identify the statistical significance of the individual groups.

Alternate or additional statistical evaluations may be performed if deemed necessary or appropriate following consultation with the Sponsor.

23. DATA ACQUISITION, VERIFICATION AND STORAGE

Data generated during the course of this study will be recorded either by hand or using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System* and/or chart recorders, *TotalChrom*®, Version 6.2.1 (for HLPC) *Softmax*® *PRO* (for UV/VIS on Softmax), and/or SPECTRAmax 190. All data will be tabulated, summarized and/or statistically analyzed using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System*, SoftMax® PRO 4.0, Microsoft® *Excel* [part of Microsoft® Office 2003 (or later versions)], Quattro Pro 8 and/or *The SAS System* (version 6.12).

Records will be reviewed by the Study Director and/or appropriate management personnel within 21 days after generation. All original records will be stored in the archives at the Testing Facility. All raw data will be bound and indexed. The archived raw data will be scanned and retained on CD-ROM in an Adobe® Acrobat PDF file. A copy of all raw data will be supplied to the Sponsor upon request. Preserved tissues will be stored at the Testing Facility at no additional charge for one year after delivery of the final report, after which time the Sponsor will be contacted to determine the disposition of these materials.

24. RECORDS TO BE MAINTAINED

Protocol, Amendments and Deviations.
Test Substance, Carrier and/or Reagent Receipt, Preparation and Use.
Animal Acquisition.
Randomization Schedules.
Supportive Care (if prescribed by Staff Veterinarian).
General Comments.
Clinical Observations and/or General Appearance.
Detailed Clinical Observations.
Body Weights.
Feed Consumption Values.
Blood and Brain Sample Collection and Processing
Cholinesterase Data.
Gross Necropsy Observations.
Organ Weights.
Tissue Sample Collection, Processing and Shipment.
Photographs (if required).
Study Maintenance (room and environmental records).
Feed, Enrichment, and Water Analyses.
Packing and/or Shipment Lists.
Analytical Procedure for Test Substance Analysis.
Analytical Results.

25. KEY PERSONNEL

Executive Director, Site Operations and Toxicology:
Alan M. Hoberman, Ph.D., DABT, Fellow ATS
Study Director and Senior Research Scientist: John F. Barnett, Jr., B.S.
Director of Reproductive and Neurobehavioral Toxicology: Elise M. Lewis, Ph.D.
Director of Operations: Matthew J. Vaneman, B.S.
Associate Director of Regulatory Compliance: Nancy A. Catricks, M.S.
Senior Manager of Study Management: Monica L. Davis, B.S., RQAP-GLP, ALAT
Senior Staff Veterinarian: Dena C. Lebo, V.M.D., Division Veterinarian
Chair, Institutional Animal Care and Use Committee: Joseph W. Lech, B.S., LAT
Consultant, Veterinary Pathology: W. Ray Brown, D.V.M., Ph.D., Diplomate, ACVP
Consultant, Veterinary Pathology: Charles River Laboratories Preclinical Services
Pathology Associates Division

26. FINAL REPORT

The Study Director will provide periodic updates of study progress to the Sponsor. Draft summary tables of unaudited computer-recorded data may accompany these updates. Statistical analyses will not be performed on these interim data.

A comprehensive draft final report will be prepared on completion of the study and will be finalized following consultation with the Sponsor. The report will include the following:

- Summary and Conclusion.
- Experimental Design and Method.
- Evaluation of Test Results.
- Appendices: Figures, Summary and Individual Tables Summarizing the Above Data, Protocol and Associated Amendments and Deviations, Study Director's GLP Compliance Statement, Reports of Supporting Data (if appropriate) and QAU Statement.
- Certificate(s) of Analysis of Test Substance.

The Sponsor will receive an electronic copy of the draft report. A copy of the final report will be provided by e-mail or on CD-ROM in Adobe Acrobat PDF format. The PDF document will be created from native electronic files to the extent possible, including text and tables generated by the Testing Facility. Report components not available in native electronic files and/or original signature pages will be scanned and converted to PDF image files for incorporation. The hard copy of the report with original signatures retained at the Testing Facility will be considered the original.

Study reports should be finalized within six months of submission of the audited draft final report. Two Sponsor-requested revisions to the draft report will be addressed by the Testing Facility at no charge. Additional revisions to the draft report or amendments to the final report may incur additional costs. If the Sponsor has not provided comments to the report within six months of draft submission, the report will be finalized by the Testing Facility.

27. ANIMAL WELFARE

Animal care and use will be in accordance with the Animal Welfare Act regulations (9 CFR, Parts 1, 2 and 3), the conditions specified in the *Guide for the Care and Use of Laboratory Animals*⁵, the relevant SOPs of the Testing Facility, and the protocol. Anticipated or suspected clinical signs and supportive care agreed upon by the Study Director, veterinary staff and Sponsor should these clinical signs be observed are documented in the IACUC proposal for this study.

Adverse observations will be promptly reported to the Study Director and veterinary staff. The veterinarian may make recommendations regarding care of the animal(s) in addition to those already agreed upon and/or alteration of study procedures to ensure the well-being of the animal(s) should unanticipated responses or circumstances occur. All recommendations shall be discussed with the Study Director and the recommendations and subsequent actions properly documented in the study record. Supportive care of the animal(s) may occur without notification of the Sponsor when such supportive care, as determined by the Study Director, does not adversely affect the study objectives.

If the condition of the animal(s) warrants therapeutic intervention or alterations in study procedures above the previously-agreed-upon conditions, the Sponsor will be contacted, whenever possible, to discuss appropriate action. If the condition of the animal(s) is such that immediate measures must be taken to relieve pain and/or distress, the attending veterinarian will attempt to consult the Study Director prior to initiating medical action, but the veterinarian has the authority to act immediately at his/her discretion to address the condition under these circumstances. The Sponsor will be informed by the Study Director of any such event as soon as possible.

28. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STATEMENT

The procedures described in this protocol have been reviewed by the Testing Facility's Institutional Animal Care and Use Committee. All procedures described in this protocol that involve study animals will be conducted in a manner to avoid or minimize discomfort, distress or pain to the animals.

The signature of the Sponsor below is assurance that the study is not an unnecessary duplication of previous work. Documentation for the necessity of this study may be obtained from the Sponsor. No alternative procedures were available to meet the stated purposes of the study.

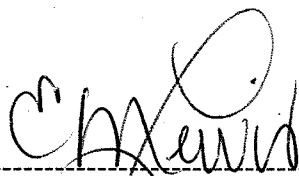
29. REFERENCES

- (1) OECD guideline for the testing of chemicals. Repeated dose 28-day oral toxicity study in rodents, No. 407 section 4 Health Effects (Pink pages); last updated 3 October, 2008. Organisation for Economic Co-operation and Development.
- (2) Health effects test guidelines: Repeated dose 28-day oral toxicity study in rodents, OPPTS 870.3050; July, 2000; Prevention, Pesticides and Toxic Substances. U.S. Environmental Protection Agency.
- (3) EPA Good laboratory practice standards. Chapter I Protection of Environment, 40 C.F.R. 792. U.S. Environmental Protection Agency.
- (4) OECD Principles of good laboratory practices, [C(97)186/Final] (1998); Environmental Health and Safety Division. OECD Environment Directorate.
- (5) Institute of Laboratory Animal Resources Commission on Life Sciences and the National Research Council. *Guide for the care and use of laboratory animals*. Washington (D.C.): National Academy Press; 1996.
- (6) Snedecor GW, Cochran WG. Variance test for homogeneity of the binomial distribution. *Statistical methods. 6th Ed.* Iowa State University Press, Ames; 1967. p. 240-1.
- (7) Sokal RR, Rohlf FJ. Bartlett's test of homogeneity of variances. *Biometry: the principles and practice of statistics in biological research*. San Francisco (CA): Freeman & Co; 1969. p. 370-1.
- (8) Snedecor GW, Cochran WG. Analysis of variance. *Statistical methods. 6th Ed.* Iowa State University Press, Ames; 1967. p. 258-98.
- (9) Dunnett CW. A multiple comparison procedure for comparing several treatments with a control. *J Am Stat Assoc* 1955;50:1096-121.
- (10) Sokal RR, Rohlf FJ. Kruskal-Wallis test. *Biometry: the principles and practice of statistics in biological research*. San Francisco (CA): Freeman & Co; 1969. p. 388-91.
- (11) Dunn OJ. Multiple comparisons using rank sums. *Technometrics* 1964;6(3):241-52.

- (12) Siegel S. The Fisher's exact probability test. *Nonparametric statistics for the behavioral sciences*. New York (NY): McGraw-Hill Co; 1956. p. 96-105.

30. PROTOCOL APPROVAL

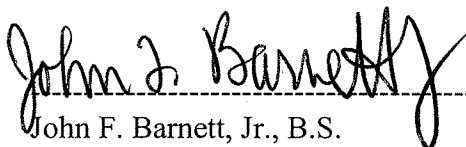
30.1. For the Testing Facility



Elise M. Lewis, Ph.D.
Director of Reproductive and
Neurobehavioral Toxicology

11 Oct 2010

Date




John F. Barnett, Jr., B.S.
Senior Research Scientist
Study Director

11 Oct 2010

Date

30.2. For the Sponsor^a



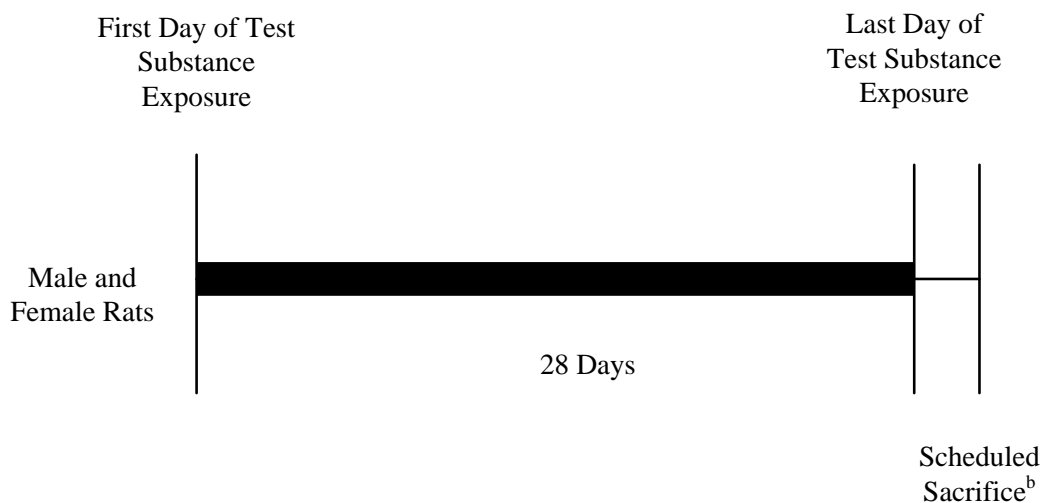
M. Jensen
Study Monitor

11 October 2010

Date

a. Date of Sponsor Approval: 11 October 2010

ATTACHMENT 1 -
SCHEMATIC OF STUDY DESIGN AND PROPOSED STUDY SCHEDULE

STUDY SCHEMATIC**REPEATED DOSE 28-DAY TOXICITY STUDY IN RATS^a****Exposure Period**

- a. For additional details see "Tests, Analyses and Measurements" section of the protocol.
- b. All male and female rats will be sacrificed on day 29 of study and a gross necropsy will be performed.

PROPOSED STUDY SCHEDULE^a

12 OCT 2010	Animal Receipt.
12 OCT 2010	OECD Experimental Start Date.
19 OCT 2010	EPA Experimental Start Date.
19 OCT 2010 - 15 NOV 2010	Exposure Period [Day 1 to 28 of Study - Replicate 1 (Males)].
20 OCT 2010 - 16 NOV 2010	Exposure Period [Day 1 to 28 of Study - Replicate 2 (Females)].
16 NOV 2010	Sacrifice and Cholinesterase Evaluation [Day 29 of Study - Replicate 1 (Males)].
17 NOV 2010	Sacrifice and Cholinesterase Evaluation [Day 29 of Study - Replicate 2 (Females)].
19 JAN 2011	Draft Final Report and Experimental Completion/Termination Date.

a. The study initiation date is the date the Study Director signs the protocol.

**ATTACHMENT 2 -
CERTIFICATE OF ANALYSIS**



TiK/btr

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September 2, 2010

CERTIFICATE OF ANALYSIS

MALATHION TECHNICAL

We, CHEMINOVA A/S, DK-7620 Lemvig, Denmark, do hereby certify that we have analyzed a representative sample of the following material

Malathion Technical
Batch No.: D2014-OSJ-MLT-01-S
CAS No.: 121-75-5

Results:
Malathion: 96%w/w (GC-analysis)

Date of analysis: 22 July 2010.

The expiry date is 22 July 2012 when stored in refrigerator.

CHEMINOVA A/S

A handwritten signature in blue ink, appearing to read 'Tina Kusk', written over a dotted line.

Tina Kusk
Head of Quality Control

**ATTACHMENT 3 -
MATERIAL SAFETY DATA SHEET**



Product no. 300
Product name FYFANON[®] TECHNICAL

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GHB/November 2009
Replaces GHB/August 2008

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SAFETY DATA SHEET

FYFANON[®] TECHNICAL

Revision: Sections containing a revision or new information are marked with a ♣.

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING



Product name **FYFANON[®] TECHNICAL**

Intended use Active ingredient in insecticides

Manufacturer **CHEMINOVA A/S**
P.O. Box 9
DK-7620 Lemvig
Denmark
sds@cheminova.dk

Phone (+45) 97 83 53 53 (24 hr; for emergencies only)

2. ♣ HAZARDS IDENTIFICATION

- 2.1. EU classification Xn;R22 R43 N;R50/53; see 1.5.1.
according to Dir. 67/548/EEC as amended
- CLP classification Acute oral toxicity: Category 4
according to Reg. 1272/2008 as amended Sensitisation – skin: Category 1
Hazards to the aquatic environment: Category acute 1 and chronic 1
- WHO classification Class III: Slightly hazardous
- 2.2. Health hazards (acute and chronic) **Fyfanon[®]** (malathion) is a cholinesterase inhibitor of low toxicity to mammals. However, storage at too high temperatures may induce formation of the much more toxic and synergistic contaminant isomalathion (LD₅₀, oral, rat, 89 mg/kg). Both malathion and isomalathion rapidly enter the body on contact with all skin surfaces and eyes.
- Repeated exposures to cholinesterase inhibitors such as isomalathion may, without warning, cause increased susceptibility to doses of any cholinesterase inhibitor.
- 2.3. Signs and symptoms of cholinesterase inhibition Headache, nausea, vomiting, cramps, weakness, blurred vision, pin-point pupils, tightness in chest, laboured breathing, nervousness, sweating, watering of eyes, drooling or frothing of mouth and nose, muscle spasms and coma.
- 2.4. Environmental hazards The substance is very toxic to aquatic organisms, see section 1.2.



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3. COMPOSITION/INFORMATION ON INGREDIENTS

3.1. Fyfanon®	
CAS name	Butanedioic acid, [(dimethoxyphosphinothioylthio)-, diethyl ester
CAS no.	121-75-5
IUPAC name(s)	Diethyl (dimethoxythiophosphorylthio)succinate
	S-[1,2-bis(Ethoxycarbonyl)ethyl] O,O-dimethyl phosphorodithioate
ISO name/EU name	Malathion
EC no. (EINECS no.)	204-497-7
EU index no.	015-041-00-X
Structural formula	$ \begin{array}{c} \text{CH}_3\text{O} \quad \text{S} \\ \quad \quad \parallel \\ \text{CH}_3\text{O} - \text{P} - \text{S} - \text{CH} - \text{COOC}_2\text{H}_5 \\ \quad \quad \quad \quad \\ \quad \quad \quad \text{CH}_2\text{COOC}_2\text{H}_5 \end{array} $
3.2. Typical content	96 - 97%

4. FIRST AID MEASURES

4.1. Emergency and first aid procedures	
General	<p>If any of the signs of cholinesterase inhibition (see 2.3.) occurs, call a doctor (physician), clinic or hospital immediately. Explain that the victim has been exposed to malathion, an organophosphorus insecticide, and describe his/her condition. Immediately move the victim from the area where malathion is present.</p> <p>Clothing contaminated with material must be removed immediately and all skin washed thoroughly.</p>
Inhalation	If experiencing any discomfort, immediately remove from exposure. Get medical attention immediately if symptoms develop.
Ingestion	Inducing vomiting is not recommended. Rinse mouth and drink water or milk. If vomiting occurs, rinse mouth and drink fluids again. Get medical attention immediately.
Eye contact	Immediately flush with much water or eyewash solution, occasionally opening eyelids, until no evidence of chemical remains. Remove contact lenses after a few minutes and flush again. See physician immediately.
Skin contact	Immediately flush with plenty of water while removing contaminated clothing and footwear. Wash with water and soap. See physician immediately if symptoms develop.
4.2. Note to physician	Fyfanon® (malathion) is a cholinesterase inhibitor affecting the central and peripheral nervous systems producing respiratory depression.
Cholinesterase inhibition – treatment	Decontamination procedures such as whole body washing, gastric lavage and administration of activated charcoal are often required.
	<p>Antidote: If symptoms of cholinesterase inhibition (see 2.3.) are present, administer atropine sulphate, which often is a lifesaving antidote, in large doses, TWO to FOUR mg intravenously or intramuscularly as soon as possible. Repeat at 5 to 10 minute</p>



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intervals until signs of atropinisation appear and maintain full atropinisation until all organophosphate is metabolised.

Obidoxime chloride (Toxogonin), alternatively pralidoxime chloride (2-PAM), may be administered as an adjunct to, but not a substitute for atropine sulphate. Treatment with oxime should be maintained as long as atropine sulphate is administered.

At first sign of pulmonary oedema the patient should be given supplementary oxygen and treated symptomatically.

Relapse can occur after initial improvement.
VERY CLOSE SUPERVISION OF THE PATIENT IS INDICATED FOR AT LEAST 48 HOURS, DEPENDING ON THE SEVERITY OF POISONING.

5. FIRE-FIGHTING MEASURES

- | | |
|---|--|
| 5.1. Extinguishing media and procedure | Dry chemical or carbon dioxide for small fires, water spray or foam for large fires.

Use water spray to keep fire-exposed containers cool. Approach fire from upwind to avoid hazardous vapours and toxic decomposition products. Fight fire from protected location or maximum possible distance. Avoid heavy hose streams. Dike area to prevent water runoff. Firemen should wear self-contained breathing apparatus and protective clothing. |
| 5.2. Hazardous decomposition products in a fire | The essential breakdown products are volatile, toxic, malodorous, irritant and inflammable compounds such as dimethyl sulphide, sulphur dioxide, carbon monoxide, carbon dioxide and phosphorus pentoxide. |
| 5.3. Unusual fire and explosion hazards | See 10.1. |

6. ♣ ACCIDENTAL RELEASE MEASURES

- | | |
|---|--|
| 6.1. Personal protection | Observe all protection and safety precautions when cleaning up spills. Depending on the magnitude of the spill, this may mean wearing respirator, eye protection or face mask, coveralls, protective gloves and boots. See section 8, Personal protection. |
| 6.2. Steps to be taken in case of spill ... | It is recommended to have a predetermined plan for the handling of spills. Empty, closable vessels for the collection of spills should be available.

Stop the source of the spill if safe to do so. Contain the spill to prevent any further contamination of surface, soil or water. Keep unprotected persons away from the spill area. |
| 6.3. Cleaning method | Spills on the floor or other impervious surface should be absorbed onto an absorptive material such as universal binder, hydrated lime, Fuller's earth or other absorbent clays. Collect contaminated absorbent in suitable containers. Rinse area with soda lye and much water. Absorb wash liquid onto suitable absorbent as well and collect in suitable containers. Wash waters must be prevented from |



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entering surface water drains.

Large spills which soak into the ground should be dug up and transferred to suitable containers.

Spills in water should be contained as much as possible by isolation of the contaminated water. The contaminated water must be collected and removed for treatment or disposal. Uncontrolled discharge into water courses must be alerted to the appropriate regulatory body.

- 6.4. Disposal The used containers should be properly closed and labelled. Refer to section 13 for disposal.

7. ♣ HANDLING AND STORAGE

- 7.1. Precautions to be taken in handling In an industrial environment it is recommended to avoid all personal contact with the product, if possible by using closed systems and remote system control. Otherwise the material should preferably be handled by mechanical means. Adequate ventilation or local exhaust ventilation is required. The exhaust gases should be filtered or treated otherwise. For personal protection in this situation, see section 8.
- For its use as a pesticide, first look for precautions and personal protection measures on the officially approved label on the packaging or for other official guidance or policy in force. If these are lacking, see section 8.
- 7.2. Precautions to be taken in storing The product is stable when stored at temperatures not exceeding 20-25°C.
- The product should never be heated above 55°C. Local heating above this temperature should be avoided as well. Protect against strong heat from sunshine or other source, e.g. fire.
- Store in closed, labelled containers. The storage room should be constructed of incombustible material, closed, dry, ventilated and with impermeable floor, without access of unauthorised persons or children. The room should exclusively be used for storage of chemicals. Foodstuffs, drinks, feed or seed should not be present. A warning sign reading "POISON" is recommended. A hand wash station should be available.
- 7.3. Specific use The product is meant for the production of insecticides which may only be used for officially approved applications.
- 7.4. Fire and explosion precautions —

8. ♣ EXPOSURE CONTROLS/PERSONAL PROTECTION

- 8.1. Personal exposure limits
- | | Year |
|--------------------------|---|
| Malathion OSHA (USA) PEL | 2009 TWA 15 mg/m ³ total dust; skin notation |



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ACGIH (USA) TLV	2009	TWA 1 mg/m ³ ; measured as inhalable fraction and vapor Skin notation; BEI
EU, 2000/39/EC as amended	2006	Not established
Germany, MAK	2009	TWA 15 mg/m ³ measured as inhalable fraction of the aerosol Peak level 60 mg/m ³ BAT
HSE (UK) WEL	2007	8-hr TWA 10 mg/m ³ ; skin notation

However, other personal exposure limits defined by local regulations may exist and must be observed.

8.2. Personal protection

When used in a closed system, personal protection equipment will not be required. The following is meant for other situations, when the use of a closed system is not possible, or when it is necessary to open the system. Consider the need to render equipment or piping systems non-hazardous before opening.



Respiratory protection

The product is not likely to present an airborne exposure concern during normal handling, but in the event of discharge of the material which produces a heavy vapour or mist, workers can put on officially approved respiratory protection equipment with a universal filter type including particle filter.



Protective gloves

Wear chemical resistant gloves, such as barrier laminate, butyl rubber, nitrile rubber or viton. The breakthrough times of these materials for malathion are unknown, but it is expected that they will give adequate protection.



Eye protection

Wear safety glasses. It is recommended to have an eye wash fountain immediately available in the workplace when there is a potential for eye contact.



Other protection

Wear appropriate chemical resistant clothing.

8.3. Work/hygienic practices

Persons working with this product for a longer period should have frequent blood tests of their cholinesterase levels. If the cholinesterase level falls below a critical point, no further exposure should be allowed until it has been determined by means of blood tests that the cholinesterase level has returned to normal.

Keep all unprotected persons and children away from working area.

Avoid contact with eyes, skin or clothing. Avoid breathing vapour or spray mist.

Remove contaminated clothing immediately. Wash thoroughly after handling. Before removing gloves, wash them with water and soap. After work, take off all work clothes and footwear. Take a shower, using water and soap. Wear only clean clothes when leaving job. Wash protective clothing and protective equipment with water and soap after each use.



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8.4. Environmental exposure controls Avoid discharge to the environment. See section 13 for disposal.

9. ♣ PHYSICAL AND CHEMICAL PROPERTIES

9.1. Physical state	Liquid
9.2. Colour	Colourless to light yellow or light pink
9.3. Odour	Slightly aromatic odour
9.4. Melting point	< -20°C
9.5. Boiling point	Decomposes; decomposition starts at 174°C. 156 - 157°C at 0.7 mm Hg
9.6. Specific gravity	1.23 g/ml at 20°C
9.7. Vapour pressure	3.4 x 10 ⁻⁶ mm Hg at 25°C 1.4 x 10 ⁻⁴ mm Hg at 45°C
9.8. Viscosity	30.0 cP at 25°C 16.4 cP at 40°C
9.9. Surface tension	Saturated solution in water: 57.8 mN/m at 20°C
9.10. Solubility in water	148.2 mg/l at 25°C
9.11. Solubility in organic solvents	Solubility of malathion at 20°C in: acetone > 250 g/l methanol > 250 g/l ethyl acetate > 250 g/l 1,2-dichloroethane > 250 g/l xylene > 250 g/l heptane 57 - 67 g/l
9.12. Partition coefficient n-octanol/water	K _{ow} = 560; log K _{ow} = 2.75
9.13. pH	When equal amounts of malathion and distilled water are dispersed at 20°C, the pH measured in the water phase is 3.7 - 3.8.
9.14. Flash point	163°C (Pensky-Martens closed tester; see, however, 10.1.)
9.15. Autoignition temperature	278°C
9.16. Explosive properties	Not explosive
9.17. Oxidising properties	Not oxidising

10. ♣ STABILITY AND REACTIVITY

10.1. Thermal decomposition	Malathion will decompose rapidly when heated to temperatures above 140°C, significantly increasing the risk of explosion. Direct local heating such as electric heating or by steam must be avoided. The decomposition is dependent on time as well as temperature due to self-accelerating exothermic and autocatalytic reactions. The reactions involve rearrangements and polymerisation releasing volatile malodorous and inflammable compounds such as dimethyl sulphide and methyl mercaptan.
10.2. Hazardous decomposition products	Storage at too high temperatures may induce formation of the more toxic and synergistic contaminant isomalathion. See also 5.2.
10.3. Materials to avoid	Strong alkalis, amines and strong oxidising compounds. The product can corrode metals. Malathion is rapidly hydrolysed at pH > 7.0.



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11. TOXICOLOGICAL INFORMATION

- | | |
|---|---|
| 11.1. Toxicokinetics, metabolism and distribution | After oral intake, malathion is rapidly absorbed and excreted. The highest concentration was found in the liver, followed by skin, fat, bone and gastrointestinal tract. It is extensively metabolised. There is no evidence of accumulation. |
| 11.2. Acute toxicity | The product is not considered as harmful, neither by inhalation, in contact with skin nor if swallowed. However, it may become harmful after storage at too high temperatures, see 2.2 |
| Route(s) of entry | - ingestion LD ₅₀ , acute oral, rat: approx. 5500 mg/kg |
| | - skin LD ₅₀ , dermal, rat: > 2000 mg/kg |
| | - inhalation LC ₅₀ , inhalation, rat: > 5.2 mg/l/4 h |
| 11.3. Irritancy | The product is slightly irritating to skin and eyes. |
| 11.4. Allergic sensitisation | In animal tests mixed results were obtained:
Magnusson-Kligman maximisation test: positive
Buehler test: negative
Local Lymph Node Assay: negative.
The meaning of these results for humans cannot be fully evaluated. |
| 11.5. Carcinogenicity | IARC evaluation: The available data provide no evidence that malathion is likely to present a carcinogenic risk to humans. |
| 11.6. Effects on reproduction | No effects on fertility are found for malathion in rats and rabbits at maternally non-toxic doses. |
| 11.7. Teratogenicity | No indications of teratogenic (birth defects causing) effects of malathion are found. |
| 11.8. Mutagenicity | Malathion is not mutagenic. |

12. ECOLOGICAL INFORMATION

- | | |
|---------------------------------|---|
| 12.1. Ecotoxicity | Malathion is very toxic to fish, aquatic invertebrates, aquatic life stages of amphibians and insects. It is less toxic to aquatic plants, birds and soil macro- and microorganisms. |
| The ecotoxicity is measured as: | |
| - Fish | Rainbow trout (<i>Oncorhynchus mykiss</i>) 96 h-LC ₅₀ : 0.18 mg/l
37-day NOEC: 21 µg/l |
| - Invertebrates | Daphnids (<i>Daphnia magna</i>) 48 h-EC ₅₀ : 0.72 µg/l
21-day NOEC: 0.06 µg/l |
| - Algae | Green algae (<i>Selenastrum capricornutum</i>) 72-h IC ₅₀ : 4.06 mg/l |
| - Birds | Bobwhite quail (<i>Colinus virginianus</i>) LD ₅₀ : 359 mg/kg
5-day dietary LC ₅₀ : 3497 mg/kg |
| - Earthworms | Mallard duck (<i>Anas platyrhynchos</i>) LD ₅₀ : 1485 mg/kg |
| - Bees | <i>Eisenia foetida foetida</i> 14-day LC ₅₀ : 613 mg/kg soil
Honey bees (<i>Apis mellifera</i>) LD ₅₀ , acute oral: 0.38 µg/bee
LD ₅₀ , topical: 0.27 µg/bee |
| 12.2. Mobility | Under normal conditions malathion is of medium mobility in soil, but is degraded rapidly. |



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- 12.3. Persistence and degradability Malathion is biodegradable, but does not fulfil the criteria for being readily biodegradable. It undergoes rapid degradation in the environment and in waste water treatment plants. No adverse effects are found at concentrations up to 100 mg/l in waste water treatment plants. Degradation occurs both aerobically and anaerobically, mostly biologically.
- Degradation half-lives vary with circumstances, but are usually one to a few days in aerobic soil and water.
- 12.4. Bioaccumulative potential Malathion is not expected to bioaccumulate. It is rapidly metabolised and excreted (with half-life of approx. 3 days). The measured bioconcentration factor (BCF) of malathion is 95 (average for several fish species).

13. ♣ DISPOSAL CONSIDERATIONS

- 13.1. Waste disposal method Waste material that cannot be reused or chemically reprocessed can be disposed of by removal to a licensed chemical destruction plant or by controlled incineration with flue gas scrubbing.
- Malathion can be hydrolysed in water by heating and adjusting the pH (alkaline).
- Do not contaminate water, foodstuffs, feed or seed by storage or disposal.
- 13.2. Container disposal Triple rinse (or equivalent) and offer for recycling or reconditioning. Alternatively, the packaging can be punctured to make it unusable for other purposes and then be disposed of in a sanitary landfill. Controlled incineration with flue gas scrubbing is possible for combustible packaging materials.
- Disposal of waste and packagings must always be in accordance with all applicable local regulations.

14. TRANSPORT INFORMATION

ADR/RID classification

Proper shipping name Environmentally hazardous substance, liquid, n.o.s. (Malathion)
Class 9
UN no. 3082
Packaging group III

IMDG classification

Proper shipping name Environmentally hazardous substance, liquid, n.o.s. (Malathion)
Class 9
UN no. 3082
Packaging group III
Marine pollutant (P/PP) Marine pollutant

IATA/ICAO classification

Proper shipping name Environmentally hazardous substance, liquid, n.o.s. (Malathion)
Class 9
UN no. 3082



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Packaging group III

15. ♣ REGULATORY INFORMATION

15.1. LABELLING IN THE EU

According to Dir. 67/548/EEC as amended

Hazard symbols



Contains Malathion

R-phrases R22-43-50/53: Harmful if swallowed. May cause sensitisation by skin contact. Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

S-phrases S24-37-46-60-61: Avoid contact with skin. Wear suitable gloves. If swallowed, seek medical advice immediately and show this container or label. This material and its container must be disposed of as hazardous waste. Avoid release to the environment. Refer to special instructions/safety data sheets.

Other mentions To avoid risks to man and the environment, comply with the instructions of use.

15.2. GLOBALLY HARMONISED SYSTEM

According to Reg. 1272/2008 as amended

CLP classification Acute oral toxicity: Category 4
Sensitisation – skin: Category 1
Hazards to the aquatic environment: Category acute 1 and chronic 1

CLP labelling

Product identifier Fyfanon® Technical

Contains Malathion

CAS no. 121-75-5

Hazard pictograms required on label



Signal word Warning

Hazard statements H302: Harmful if swallowed.
H317: May cause an allergic skin reaction.
H410: Very toxic to aquatic life with long lasting effects.

Supplementary hazard statement ... EUH401: To avoid risks to human health and the environment, comply with the instructions of use.

Precautionary statements

Prevention P280: Wear protective gloves.



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P273: Avoid release to the environment.

Response P301+P312: IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell.
P302+P352: IF ON SKIN: Wash with plenty of soap and water.
P333+P313: If skin irritation or rash occurs: Get medical advice/attention.

Disposal P501: Dispose of contents/container in accordance with local regulation.

15.3. Regulatory status The product is covered by EU chemical legislation.

16. OTHER INFORMATION

This material should only be used by persons who are made aware of its hazardous properties and have been instructed in the required safety precautions.

The information provided in this safety data sheet is believed to be accurate and reliable, but uses of the product may vary and situations unforeseen by Cheminova A/S may exist. The user of the material has to check the validity of the information under local circumstances.

**ATTACHMENT 4 -
TEST SUBSTANCE PREPARATION PROCEDURES**

ATTACHMENT 4**TEST SUBSTANCE PREPARATION PROCEDURES**

Test Substance: Malathion Technical (CHA 300), batch#: D2014-OSJ-MLT-01-S

Carrier: The meal form of Certified Rodent Diet[®] #5002 (PMI[®] Nutrition International) containing 5% corn oil (the corn oil will serve to minimize the dust production during diet preparation and usage).

A. Purpose:

The purpose of this procedure is to provide a method for the preparation of diet containing the test substance for oral (diet) administration to rats on Study No. TQC00065.

B. General Information:

1. All diet containers will be labeled and color-coded. Each label will specify the study number, test substance or carrier identification, batch number, concentration, dosage level, dosage group, preparation date, expiration date, and storage conditions, as applicable.
2. Formulations (diets) will be prepared at least once weekly at the Testing Facility.
3. Safety:
 - Double nitrile gloves, uniform, goggles or safety glasses with side shields
 - Full-faced Positive-Pressure Hood
 - Tyvek[®] Suit
 - The bulk test substance will be handled inside a chemical fume hood
4. The test substance will be considered 96.0% active/pure for the purpose of dosage calculations.
5. Sampling requirements: Cited in protocol
6. Storage: Cited in protocol

C. Test Substance Diet Preparation (20 kg preparation size per group):

NOTE: Prior to formulation of the test substance diet preparations, remove the bulk container of test substance from storage and allow the test substance to equilibrate to ambient room temperature for at least 30 minutes prior to opening the container.

1. The following steps are completed for each concentration, beginning with the carrier only group (0 ppm) preparation and continuing from the lowest to the highest concentration of the test substance. The carrier only group will be prepared as described below except no test substance will be added (the steps below that apply are: C.1.a, C.1.b, C.1.j through C.1.dd).
 - a. Weigh out the amount of certified rodent diet required to prepare a single concentration (see PREPARATION CALCULATIONS) into an appropriately sized and labeled container. All of the diet used in the subsequent procedure will be taken from this aliquot.
 - b. Check the placement of the intensifier bar in the twin shell blender and ensure that the blender port (bottom) of the twin shell blender is closed then place at least 3 kg of the diet into the twin shell blender.
 - c. Place at least 3 kg of the weighed diet from step C.1.a into a Hobart[®] mixing bowl.
 - d. Add at least 100 g of diet to an appropriately sized mortar.
 - e. Weigh out the required amount of test substance (see PREPARATION CALCULATIONS). Quantitatively transfer the test substance onto the diet in the mortar. Using an appropriately sized pestle grind the diet and test substance together until visually homogeneous.

- f. Transfer the mixture from the mortar to the diet in the Hobart® mixing bowl. Rinse the mortar and pestle with additional diet, as needed, to remove any residue. Transfer all rinses to the Hobart® mixing bowl.
- g. Turn the Hobart® mixer on and mix for at least 15 minutes using an appropriate mixing blade.
- h. Following completion of mixing, turn off the mixer.
- i. Transfer the diet pre-mix to the twin shell blender.
- j. Place at least 3 kg of the weighed diet from step C.1.a into a Hobart® mixing bowl.
- k. Using an appropriately-sized, tared beaker measure 500 g of corn oil (2.5% of the final prep amount).
- l. Quantitatively transfer the corn oil to the Hobart® mixing bowl containing the diet described in step C.1.j above. Rinse any corn oil residue using blank diet.
- m. Turn the Hobart® mixer on and mix for at least 3 minutes using an appropriate mixing blade.
- n. Following completion of mixing, turn off the mixer.
- o. Transfer the diet pre-mix to the twin shell blender.
- p. Place at least 3 kg of the weighed diet from step C.1.a into a Hobart® mixing bowl.
- q. Using an appropriately-sized, tared beaker measure 500 g of corn oil (2.5% of the final prep amount).

- r. Quantitatively transfer the corn oil to the Hobart® mixing bowl containing the diet described in step C.1.p above. Rinse any corn oil residue using blank diet.
- s. Turn the Hobart® mixer on and mix for at least 3 minutes using an appropriate mixing blade.
- t. Following completion of mixing, turn off the mixer.
- u. Transfer the diet pre-mix to the twin shell blender.
- v. Place at least 3 kg of the weighed diet from step C.1.a into a Hobart® mixing bowl.
- w. Turn the Hobart® mixer on and mix for at least 3 minutes using an appropriate mixing blade.
- x. Following completion of mixing, turn off the mixer.
- y. Transfer the diet rinse to the twin shell blender.
- z. Place the remaining weighed diet from step C.1.a into the twin shell blender, then close the twin shell blender. Turn on the twin shell blender and then turn on the intensifier bar. Check for leakage of feed from the lids.
- aa. Run the intensifier bar and blender for at least 15 minutes.
- bb. Following completion of the required mixing time, turn off the intensifier bar and blender.
- cc. Center the collection bag/container under the blender port and collect the prepared diet. If applicable, samples can now be taken.
- dd. Prepared diets will be stored refrigerated to the extent possible until use and maintained at ambient temperature during use. The prepared diets can be used within the established stability parameters.
- ee. Repeat this process (steps C.1.a to C.1.dd) for each concentration

2. Clean the blender and intensifier bar and all other equipment according to Standard Operating Procedures.

Version: TQC00065(07.OCT.2010) # of pages: 5

Calculations
Calculated By: Patrice A Garbely Date: 11 OCT 2010

Calculations
Recalculated
By: [Signature] Date: 11 OCT 2010

Verified and
Approved By: John J. Barnette Date: 11 Oct 2010

ATTACHMENT 5 -
STUDY-SPECIFIC PROCEDURE FOR THE CHOLINESTERASE
EVALUATION OF RAT BRAINS AND RBC

ATTACHMENT 5 -**STUDY-SPECIFIC PROCEDURE FOR
THE CHOLINESTERASE EVALUATION OF RAT BRAINS AND RBC**

Purpose: This Study Specific Procedure describes the steps used to evaluate cholinesterase levels in rat brain tissue and red blood cells.

I. DEFINITIONS AND ABBREVIATIONS

<u>Abbreviation</u>	<u>Definition</u>
0.1M Monobasic	0.1M Monobasic Sodium Phosphate Buffer
0.1M Dibasic	0.1M Dibasic Sodium Phosphate Buffer
pH8 Buffer	0.1M Sodium Phosphate Buffer, pH 8
0.1% Tween [®] Buffer	0.1% Tween [®] in Sodium Phosphate Buffer, pH 8
ACHE	Acetylcholinesterase
ATC	Acetylthiocholine iodide
DTNB	5,5'-dithio-bis (2-nitrobenzoic acid)
RA	Rat Albumin, fraction V
I.D.	Identification – For chemicals in their original container, the ID is the lot number. For reagents prepared in-house, the ID is the identifier.
LLOQ	Lower Limit Of Quantification
LOD	Limit Of Detection
Optical Density	A unit of measure; the relative intensity for a given wavelength of light.
RBC	Red blood cells
ULOQ	Upper Limit Of Quantification
Vmax	Rate of change of the Optical Density (OD) per minute, usually expressed as (milli-OD/min)

II. BACKGROUND

The method for cholinesterase is based on Ellman's method, where one unit of ACHE will hydrolyze one micromole of ATC into choline and acetic acid per minute at pH 8.0, 37°C. Choline then reacts instantaneously with DTNB resulting in a yellow color. A standard curve is prepared with each standard having a different concentration of ACHE. A fixed amount of ATC and DTNB are added to the standards and unknowns. The rate of color change (Vmax) is captured using a microtiter plate reader. The ACHE

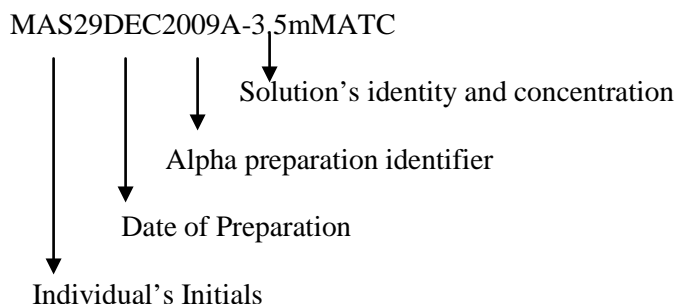
concentration in the unknowns is then back calculated on the standard curve using linear, unweighted regression.

III. PROCEDURE

A. Documentation

1. Reagents and standards are each prepared according to the formulas in Reagent Preparation Procedures and each is given a unique identifier. The identifier includes the initials of the individual preparing the solution, the date of preparation, a letter to indicate a particular preparation and the solution's concentration and identity.

Refer to the following example:



B. Reagent Preparation Documentation

1. Reagent preparation is documented on the Reagent Preparation Form. The complete reagent name and concentration are recorded on the Reagent line (e.g. 3.5mM ATC). The reagent identifier is recorded on the I.D. line. The preparer's initials and the date prepared are entered on the appropriate lines.
2. Each chemical used for the preparation of the reagent is documented in the table. For chemicals in their original container from the manufacturer, the lot number and manufacturer are identified and the I.D. box does not apply. For chemicals prepared in the laboratory (e.g. a stock solution), the reagent I.D. is recorded and the manufacturer and lot number boxes do not apply. NA is entered in each box that does not apply. Refer to the example below:

CHEMICAL	LOT #	MFG	I.D.	AMT
Rat Albumin	123456	Sigma	NA	1g
0.1% Tween [®] buffer	NA	NA	MAS29DEC2009A-Tween [®] buffer	1000 mL

3. Any equipment used in the preparation is recorded. This includes, but is not limited to, pipettes, balances, volumetric flasks and pH meters. The storage conditions of the reagent and an expiration date are assigned. The expiration date is the date of the ingredient with the shortest lifetime
 - a. General reagents expire one month from the time of preparation as long as they are stored refrigerated.
 - b. Critical reagents are only good for the day they are prepared.

C. Sample Processing Documentation

1. Two forms are available for documenting sample processing. The first form, Brain Sample Processing, is for documenting the steps taken in the processing of brains. The second form, Blood Sample Processing, is for documenting steps taken in the processing of blood.
 - a. Brain Sample Processing

The animal number for each sample is recorded in the sample section. The technician(s) performing each activity fill out the corresponding portions of the form.
 - b. Blood Sample Processing

The animal number for each sample is recorded in the sample section. The sample may be processed in the vial in which it came. The technician(s) performing each activity fill out the corresponding portions of the form.

If a blood sample contains a clot, it should be footnoted. The footnote should include information as to whether the removal of the clot resulted in insufficient volume for processing or if there was still sufficient sample to be processed.

D. Run Documentation Form

1. The Run Documentation Form identifies the Run I.D., description, acceptance or failure of each run, the reagents added to each well, the initials and date of the technician performing each analysis.

IV. PREPARATION OF STANDARDS

A. Preparation and Analysis of the Glutathione Reference Solutions

Note: All activities for the preparation of the L-Glutathione are recorded on the GLUTATHIONE PREPARATION form.

1. Prepare a working stock solution of one milli-Molar (mM) L-Glutathione by dissolving $30.73 \pm 2\text{mg}$ of L-Glutathione reduced form, (Sigma G-4251 or equivalent) in 100 mL of pH8 Buffer. Different preparation sizes may be used as long as the proportions remain the same.
2. Prepare a set of L-Glutathione standards according to the table below.

Glutathione Concentration (mMolar)	Reference Solution I.D.	Working Stock Volume (mL)	Volume of pH 8 Buffer (mL)	Final Volume (mL)
1.00	G1	2.00	0.00	2.00
0.90	G2	1.80	0.20	2.00
0.80	G3	1.60	0.40	2.00
0.70	G4	1.40	0.60	2.00
0.60	G5	1.20	0.80	2.00
0.50	G6	1.00	1.00	2.00
0.40	G7	0.800	1.20	2.00
0.30	G8	0.600	1.40	2.00
0.20	G9	0.400	1.60	2.00
0.10	G10	0.200	1.80	2.00

3. Analyze a new empty plate as a “pre-read” plate using an endpoint analysis at a wavelength of 435 nm. This is used as the background to subtract differences between wells.

4. Using the pre-read plate add 10 mcL of each Glutathione reference solution or blank (pH8 buffer) to individual wells. Each concentration of glutathione should have an n=6 and the blanks should have an n=4. Add 250 mcL 0.65 mM DTNB solution and 100 mcL pH 8 buffer to each of the wells.
5. Place the prepared plate into the instrument and set the instrument to incubate for approximately 10 minutes at 37°C. After the incubation, analyze the plate using an endpoint at 435nm.
6. SOFTMax PRO 4.0 prepares a linear least squares regression based on the data collected and generates a slope, intercept, and R² (R squared). The acceptance criteria, the R² value is > 0.975 and the acceptance criteria for the slope is 0.310 OD/10 micromoles +/- 10%. Multiply this slope by 1000 to convert it into mOD/10 mcL for future comparison (i.e. 310 mOD/10 mcL).
7. If either the slope or the R² acceptance criteria are not met, then one replicate from each of the concentrations (no more than 25%) may be excluded (i.e. masked) and the slope and R² recalculated. If, after masking, the slope and/or the R² still do not meet the acceptance criteria, new solution(s) are prepared.

B. Preparation of ACHE Standards

The following procedure is used when preparing ACHE standards. The standards are aliquotted for daily use and stored frozen (at -15°C to -30°C) for up to eight days. Once thawed, aliquots may not be refrozen; standards should be kept cold (refrigerated or on cold packs) while in use and are discarded at the end of each day.

Standards are prepared using two working stock solutions of varying concentration in order to achieve the most accurate standard curves. Standards are to be prepared as needed for each study, high standard curve or low standard curve or both. All activities are recorded on the ACHE STANDARD PREPARATION form.

1. Preparation of ACHE stock solution

- a. Each vial of acetylcholinesterase standard from Sigma Chemical Cat# C2888 comes as a lyophilized dry powder. Each vial is labeled with the mg quantity and the activity associated with each lot of material.
- b. Reconstitute each of three vials with 1.0 mL of R.O. deionized water. Mix by inversion and allow the vials to sit at room temperature for at least 15 minutes.
- c. Pool the solutions from each vial into a 25 mL volumetric flask. Rinse each vial three times with 0.1% Rat Albumin buffer and transfer the rinse aliquot into the same 25 mL volumetric flask. Q.S. to the final required volume with 0.1% Rat Albumin buffer. Mix by inversion.
- d. This stock solution is stable for 6 months from time of preparation at $5^{\circ}\text{C} \pm 3^{\circ}\text{C}$.
- e. Theoretical concentration of each vial is calculated by multiplying the amount of mg solid within the vial by the amount of units/mg solid. This product is then multiplied by three (the # of vials used), then divided by the 25 mL, the final solution volume.

For example: each vial = 1.53 mg solid; each mg = 658 U/mg solid
 $1.53 \text{ mg solid} \times 658 \text{ U/mg solid} = 1006.74 \text{ U/vial}$
 $1006.74 \text{ U/vial} \times 3 \text{ vials} = 3020.22 \text{ U}$
 $3020.22 \text{ U} \div 25 \text{ mL} = 120.8088 \text{ U/mL} = \text{Theoretical Concentration}$

- f. The theoretical concentration calculated will be used to prepare ACHE standards.

2. Working Stocks

Prepare working stock solution A at a concentration of 2.500 U/mL and working stock solution B at a concentration of 2.000 U/mL.

This can be accomplished by multiplying the desired final volume by the

desired working stock concentration, and dividing this product by the manufacturers labeled concentration. This will yield the volume of stock solution needed to make the desired working stock solution. Once the solutions have been prepared, the solutions will be vortex thoroughly.

Example Calculation:

Desired Volume = 25 mL

Desired Working Stock A Concentration = 2.5 U/mL

Prepared solution concentration = 120.8088 U/mL

$25 \text{ mL} \times 2.5 \text{ U/mL} / 120.8 \text{ U/mL} = 0.517 \text{ mL}$

3. Calibration Standards- Low Curve

Prepare a set of standards representing the low concentration calibration curve by pipetting the appropriate amount of working stock into individual volumetric flasks. Bring to volume with 0.1% rat albumin buffer. Mix well. The standards may be aliquotted and stored in vials or tubes for 8 days at -15°C to -30°C. Refer to the table below for standard preparation proportions. The preparation size may be adjusted if necessary to prepare the correct volume needed for each study, as long as the proportions are maintained. If necessary, LB3 may be diluted as needed with 0.1% Rat Albumin buffer in order to expand the range of the standard curve. This will be done to capture the scientifically significant inhibition levels.

Working Stock Solution	Volume of Stock Solution (mL)	Final Volume (mL)	Diluent	Standard I.D.	Target Concentration (U/mL)
Working Stock A	0.600	10.0	0.1% Rat Albumin	LA1	0.150
Working Stock B	0.500	10.0	0.1% Rat Albumin	LB1	0.100
Working Stock A	0.280	10.0	0.1% Rat Albumin	LA2	0.070
Working Stock B	0.250	10.0	0.1% Rat Albumin	LB2	0.050
Working Stock A	0.120	10.0	0.1% Rat Albumin	LA3	0.030
Working Stock B	0.075	10.0	0.1% Rat Albumin	LB3	0.015

4. Calibration Standards- High Curve

Prepare a set of standards representing the high concentration calibration curve by pipetting the appropriate amount of working stock into individual volumetric flasks. Bring to volume with 0.1% Rat Albumin Buffer. Mix well. The standards may be aliquotted and stored in vials or tubes for 8 days at -15°C to -30°C). Refer to the table below for standard preparation proportions. The preparation size may be adjusted if necessary to prepare the correct volume needed for each study, as long as the proportions are maintained. If necessary, HB3 may be diluted as needed with 0.1% Rat Albumin buffer in order to expand the range of the standard curve. This will be done to capture the scientifically significant inhibition levels.

Working Stock Solution	Volume of Stock Solution (mL)	Final Volume (mL)	Diluent	Standard I.D.	Target Concentration (U/mL)
Working Stock A	2.00	5.0	0.1% Rat Albumin	HA1	1.00
Working Stock B	2.00	5.0	0.1% Rat Albumin	HB1	0.80
Working Stock A	1.20	5.0	0.1% Rat Albumin	HA2	0.60
Working Stock B	1.00	5.0	0.1% Rat Albumin	HB2	0.40
Working Stock A	0.40	5.0	0.1% Rat Albumin	HA3	0.20
Working Stock B	0.25	5.0	0.1% Rat Albumin	HB3	0.10

Target values are based on the theoretical values of ACHE. Adjustment to working stock A or working stock B will result in the same target concentrations.

C. Analysis of ACHE Standards

Once the standard solutions have been prepared they are analyzed to determine the actual slope of each standard curve. A new empty plate is used for this analysis. This plate is analyzed as a kinetic analysis at 435 nm for ten minutes at 37°C, see below for the analysis procedure. NOTE: because this analysis is a kinetic analysis no pre-read is needed.

1. 10 mcL of each standard is placed into 6 individual sample wells, each concentration should have an n=6. Add 10 mcL of pH 8 buffer to the plate blanks only; n=2.
2. Add 250 mcL of 0.65 mM DTNB solution to each sample well, plus 4 additional wells to serve as blanks.
3. Place the entire plate in an incubator (e.g., the instrument) at 37°C for approximately 10 minutes.
4. Remove the plate from the incubator and add 100 mcL of 3.5 mM ATC to all wells. Quickly place the plate in the plate reader and run a kinetic analysis for 10 minutes at a wavelength of 435 nm.
5. The instrument will collect the data and prepare a linear least squares regression table and generate a graph, a slope, an intercept and R^2 values. The acceptance criteria for the R^2 result is >0.975 , and the acceptance criteria for the slope is $310 \pm 10\%$.
6. If either the slope or the R^2 acceptance criteria are not met, then no more than 25% of the standards may be excluded (i.e. masked) and the slope and R^2 recalculated. If, after masking, the slope and/or the R^2 still do not meet the acceptance criteria, new standard(s) are prepared.

NOTE: for the analysis of the initial standard curve preparation, the slope of the standard curve may not meet acceptance criteria. This slope will be used only for the purposes of calculating the correction factor. When the adjusted standard curve is prepared using the correction factor, it must meet all acceptance criteria, otherwise it will be re-prepared.

D. Calculating the Correction Factor

In order to determine if the standard curve is producing a reliable result from one batch of standards to another, the slope of the L-Glutathione reference curve is compared to the slope of the enzyme standard curve.

1. The slope from the adjusted L-Glutathione reference curve is divided by the slope from the Acetylcholinesterase curve. If the number is less than 0.95 or greater than 1.05, adjust the stock preparations of Acetylcholinesterase by the calculated correction factor.

If the quotient is equal to or between 0.95 and 1.05, no adjustment to the stock enzyme solution is necessary. If the number is less than 0.95 or greater than 1.05, an adjustment is necessary.

Example:

$$\begin{aligned}\text{Slope of Enzyme} &= 251 \\ \text{Slope of L-Glutathione curve (x1000)} &= 306 \\ 306/251 &= 1.219\end{aligned}$$

Note: At the discretion of the Study Director, additional slope adjustments may be made even if all other criteria are met. This additional adjustment is documented on the ACHE STANDARD PREPARATION form.

2. If the Correction Factor is required, new standards are prepared by adjusting the amount of stock enzyme used by the correction factor.

Example:

The previous example (section IV.B.2.) refers to 0.517 mL of 120.8088 U/mL stock solution for the working stock A. This value is adjusted by the 1.219 correction factor to be 0.630 mL for working stock A. Once the working stock solutions for both "A" and "B" have been adjusted all other dilution ratios are maintained. The new standards are recorded on the ACHE STANDARD PREPARATION form, which has the information for adjustment factor calculation and a place where the adjusted volumes can be calculated.

3. Once adjustments have been made to Working Stock Solution A and B, repeat the preparation of the enzyme standard curve as outlined in Sections IV.B.3. and IV.B.4.

V. SAMPLE PROCESSING

A. Brain Sample Processing

1. The brain is transferred into an individual 15 mL polypropylene tube containing 7.5 mL of chilled 0.1% Tween[®] 80 buffer. The exact amount of buffer used will be documented in the raw data.
2. The brains will be homogenized with an OMNI TH tissue disperser/homogenizer using a 7 mm blade for approximately 1 minute at approximately 80% power or until an even homogenate is obtained. Samples will be kept on wet ice throughout the homogenization process.
3. The homogenate will be continuously mixed on a tube rotator on ice packs for at least five minutes. The time of mixing will be documented in the raw data.
4. The homogenate will be diluted with a secondary dilution factor. The dilution will be performed by pipetting 0.250 mL of homogenate into an individual vial containing 0.750 mL of chilled 0.1% Tween[®] 80 buffer. However, if the diluted homogenate produces a result below the limit of quantification (i.e. “low”), the initial homogenate is to be reanalyzed in order to achieve an acceptable result.
5. If sample results are above the ULOQ or below the LLOQ, the diluted sample may be reanalyzed, the sample may be rediluted using the same dilution ratio or the dilution ratio may be adjusted with the permission of the Study Director. This will be documented in the raw data.
6. Sample results that are labeled by SoftMax as “No Fit” (unable to calculate the Vmax of the sample) will be reanalyzed.
7. Analyze the brain samples using the High Standard Curve according to section VI below. Brain samples may be analyzed no more than three times to achieve an acceptable result; see section VIII.

B. Blood Processing

1. One mL of whole blood will be transferred from the collection tube into an empty labeled vial for processing.
2. Centrifuge the sample for 10 minutes, at 2-8°C, at 2000-2500 rpm.
3. Remove the plasma from the packed red blood cell and discard. Store the packed RBCs at 2-8°C until the sample preparation described below can be performed.
4. The dilution is performed by transferring 0.040 mL of the RBCs into a vial containing 0.560 mL of 0.1% Tween[®] 80 buffer and mix well by inversion.
5. The sample will be sonicated using a Misonix sonicator[®] 3000. The sample will be sonicated for 5 seconds at a power setting of 0.5W (watts).
6. If sample results are above the ULOQ, an additional 1:2 dilution will be performed. If the sample results are below the LLOQ (i.e., “low”), the diluted sample will be reanalyzed for confirmation. If the second analysis confirms the “low” result, the extrapolated value will be used at the discretion of the Study Director. If the second analysis does not confirm the initial “low” result, the sample will be analyzed a third time. This will be documented in the raw data.
7. Sample results that are labeled by SoftMax as “No Fit” (unable to calculate the Vmax of the sample) will be reanalyzed.
8. Analyze the diluted RBC sample using the Low Standard Curve according to section VI below. RBC samples may be analyzed no more than three times to achieve an acceptable result; see section VIII below.

VI. PLATE SET-UP and INSTRUMENT PARAMETERS**A. Plate Set-Up (Note : all samples are to be mixed prior to analysis)**

1. Standards, blanks and test samples are run in duplicate.
2. Place 0.010 mL (10 mcL) of each standard, reagent blank (pH8 buffer), or

prepared test sample into two individual wells. The location of the sample is to be entered into the Softmax[®] template and verified. The Softmax[®] template will include the location of all standards, reagent blanks, and samples (sample addition will be documented on the Run Documentation Form).

3. Place 0.250 mL of 0.65mM DTNB into each well including the reagent blank well. DTNB addition is recorded on the Run Documentation Form.
4. Incubate the plate for approximately 10 minutes at 37°C in the SpectraMax 190. Incubation times are recorded on the Run Documentation Form.
5. The plate is removed from the instrument and 0.100 mL of 3.5mM ATC is added to all wells containing standards, samples, and reagent blanks. All wells will be checked for bubbles prior to returning the plate to the instrument for analysis. The run is then started by activating the READ icon. All sample analysis runs will be initiated within 5 minutes of the end of the pre-run incubation (section VI.A.4). ATC addition will be documented on the Run Documentation Form.

B. Instrument Parameters (Brain and RBC Analysis)

Analysis Parameters for Brain and RBC Samples

PARAMETER	SETTING
Mode:	Kinetic
Run Time:	12 minutes (3 minute lag time)
Intervals:	15 seconds
Detection:	435nm
Auto-mix:	Before first read: Off Between Reads : Off
AutoCalibrate:	On
Strips:	Read entire plate
OD Min:	0.0 (1)
OD Max:	2.0 (1)
Incubator Temperature:	37°
Kinetic Reduction:	Vmax
Data Mode:	Absorbance
Display:	with reduced number

(1) The recommended Min and Max values may change based on response magnitude of response and or baseline drift.

VII. SAMPLE ANALYSIS

- A. Once the samples have been processed, they are analyzed by the SPECTRAmax 190 and recorded using Softmax[®] PRO 4.0 software according to the set-up parameters as outlined in Section VI above.
- B. Softmax[®] PRO 4.0 will automatically add a time and date stamp to each file as part of the file name. This will serve as the unique identifier of each analysis.

VIII. CALCULATIONS & ACCEPTANCE CRITERIA

A. Calculations

1. The kinetics are automatically reduced to a slope or a Vmax as reported by Softmax[®] PRO 4.0. Each plot is manually checked by the operator to ensure good kinetics, (i.e linear). Samples with results that are less than the Lower Limit of Quantification (LLOD) are documented in the raw data as “low”.
2. Softmax[®] PRO 4.0 calculates the actual concentration of the standards from the theoretical concentration in terms of Units per milliliter (U/mL). Theoretical concentrations for the standards are part of the Softmax[®] protocol file. These concentrations are calculated based on dilutions of prepared stocks.
3. Softmax[®] PRO 4.0 computes the un-weighted linear regression, relating the slopes of the standards to their respective enzyme concentrations, with the plate blank used.
4. Softmax[®] PRO 4.0 computes the correlation coefficient for the calibration curve.
5. Softmax[®] PRO 4.0 back calculates the concentration of the standards, determines the regression equation, and calculates the ACHE concentration of the test sample in terms of U/mL of enzyme.
6. All dilution information recorded during the sample preparation will be incorporated into the calculations of the final cholinesterase values.

B. Acceptance Criteria

1. The Correlation Coefficient (R^2) for the standard curve must be no less than 0.975. If the correlation coefficient is less than 0.975, then it is considered a failed run and all samples should be repeated.

2. Standard Curve

Each standard must replicate within $\pm 10\%$. The back-calculated concentrations of the calibration standards must be within $\pm 15\%$ [$\pm 20\%$ for concentrations less than or equal to 0.1 U/mL (high standard curve) or less than or equal to 0.015 U/mL (low standard curve)] of their theoretical concentrations. Standards that do not meet the appropriate criteria may be excluded by masking, as long as no more than 25% of the standards are “masked” (dropped). The LLOQ and ULOQ are then re-defined by *Softmax*[®] Pro according to the remaining standards.

The slope of the standard curve at the 37°C assay temperature will be 310 +/- 10%.

3. Sample Replication:

All samples are analyzed in duplicate. Brain sample duplicates must replicate within 80% of each other in order to be accepted. RBC sample duplicates must replicate within 75% of each other in order to be accepted. Samples that do not meet this criteria are labeled by *Softmax*[®] Pro as “DNR” (Does Not Replicate) and the sample should be reanalyzed. (NOTE: Samples labeled as “No Fit” will also be labeled as “DNR”). Samples should not be repeated more than two additional times (including “No Fits”). If there is insufficient sample to be re-analyzed, then the results are footnoted.

4. Samples that are below the LLOQ, are labeled “low”. Any samples that have been labeled as “low” are to be repeated; these samples should not be analyzed more than three times in total.
5. Samples that are above the ULOQ for the assay are labeled as “high”. Any sample that generates a “high” result may be re-analyzed or diluted as described in section V above, then re-analyzed. Diluted samples which produce unacceptable results may be analyzed up to three times.

IX. DATA COLLECTION AND FINAL REPORTING

A. Data Collection

1. Data Files:

Once a set has been analyzed it is automatically saved into the appropriate study file on the network (see preference function in the edit menu). Once the data file has been saved the file is printed and initialed and dated as raw data.

2. Exported Data:

Once the data has been saved and printed it is exported into an Excel format. This is done by selecting the appropriate *Softmax*[®] file and selecting the export function under the “File” menu. Files are exported as text files with the “Groups” option selected. This provides an excel format which allows for post calculation data to be entered, (e.g., group, age, sex and time variables from the protocol). This information is obtained from the in-life data.

B. Retest Criteria

1. Any initial acceptable sample may be re-tested as long as the rationale for testing is documented in the General Comments and is subsequently approved by the Study Director (retesting is done after an initial result has been acquired, and may be done in addition to the three analyses limit).
2. Any sample that is retested must generate acceptable results (based on SOFTMax[®] PRO 4.0 Acceptance Criteria).
 - a. If the acceptable result is less than or equal to $\pm 25\%$ of the original sample, then the original sample is considered “confirmed” and is used (the second sample result is reported but not used in the group averages).
 - b. If the acceptable result is greater than $\pm 25\%$ of the original sample, then the original sample is considered “contradicted” and a third analysis will be conducted.

- c. If the third analysis is less than or equal to $\pm 25\%$ of the original sample, then the original sample is considered "confirmed" and is used in the group average (the second and third sample results are reported but not used in the group averages). If the third analysis is less than or equal to $\pm 25\%$ of the second analysis, then the second analysis is considered "confirmed" and is used in the group average (the first and the third sample results are reported but not used in the group averages).
- d. If neither the first analysis nor the second analysis is confirmed, then all data will be reported but none of the results from this sample will be used in the group average.

X. REFERENCES

1. Ellman, G.L., Courtney, K.D., Andres, V.Jr. and Featherstone, R.M. (1961). A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochem Pharmac.*, 7, 88-95
2. Lawson, A.A. and Barr, R.D. (1987) Acetylcholinesterase in red blood cells. *American Journal of Hematology*, 26, 101-112.

Prepared by: Melissa A. Snyder Date: 11 OCT 2010

Calculations
Recalculated by: John J. Burnett Date: 11 OCT 2010

Verified and
Approved by: John J. Burnett Date: 11 OCT 2010

REAGENT PREPARATION PROCEDURES

Below lists the general procedures to be followed when preparing reagents for cholinesterase analysis. The preparation size may be adjusted as necessary to prepare the correct volume needed for the assay, as long as the proportions are maintained. All reagents will be stored refrigerated when not in use.

A. PREPARATION OF GENERAL REAGENTS (expiration is one month from prep date)

1. 0.1M DIBASIC SODIUM PHOSPHATE BUFFER

Dissolve 14.2 ± 2 g dibasic sodium phosphate in 1L water.

2. 0.1M MONOBASIC SODIUM PHOSPHATE BUFFER

Dissolve 13.8 ± 2 g monobasic sodium phosphate in 1L water.

3. 0.1M SODIUM PHOSPHATE BUFFER, pH 8

Combine 0.1M dibasic sodium phosphate buffer with 0.1M monobasic sodium phosphate buffer (95:5, v: v).

4. 0.1% TWEEN[®] 80 BUFFER

Transfer 1.0mL Tween[®] 80 into a 1L volumetric flask and bring to volume with 0.1M sodium phosphate buffer, pH 8

5. 0.1% RAT ALBUMIN BUFFER

Dissolve 1g rat albumin, fraction V, in 1L 0.1% Tween[®] 80 buffer.

B. PREPARATION OF CRITICAL REAGENTS (expiration is one day from prep date)

1. 0.65mM DTNB

Dissolve 25.76 ± 2 mg of DTNB for each 100mL of 0.1M of sodium phosphate buffer, pH 8 buffer used. Use a volumetric flask to q.s. to the final volume and mix well.

2. 3.5mM ATC

Dissolve 50.61 ± 2 mg of ATC iodide for each 50 mL of 0.1M of sodium phosphate buffer, pH 8 buffer used. Use a volumetric flask to q.s. to the final volume and mix well.

**Protocol Amendment No. 1****Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion
Technical in Rats****Testing Facility Study No. TQC00065****1. Section 18.4. Body Weights**

Acclimation Period: At least weekly (not tabulated).

Exposure Period: **Daily.**

Sacrifice: Terminal weight.

Justification:

This provides additional assessments of body weights for evaluation.

2. Section 18.5. Feed Consumption Values

Acclimation Period: At least once (not tabulated).

Exposure Period: **Daily.**

Day before Sacrifice: Feed left recorded.

Feed consumption values may be recorded more frequently if it is necessary to replenish the feed. These intervals will not be tabulated.

Justification:

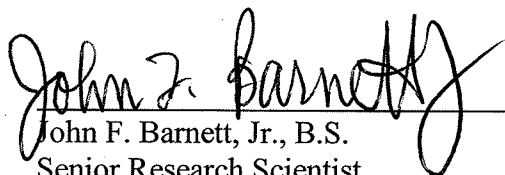
This provides additional assessments of feed consumption values for evaluation.

Protocol Amendment No. 1

Page 2

Testing Facility Study No. TQC00065

Amendment Approval:



John F. Barnett, Jr., B.S.
Senior Research Scientist
Study Director

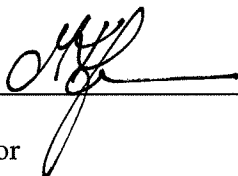
Date:

18 Oct 2010

Protocol Amendment No. 1

Page 3
Testing Facility Study No. TQC00065

Sponsor Approval:

 _____ Date: 11. Nov, 2010
M. Jensen
Study Monitor



Protocol Amendment No. 2

Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats

Testing Facility Study No. TQC00065

1. Section 19.1. Blood and Brain Sample Collection

The second paragraph of this section will be revised as follows:

Blood samples will be maintained under cold packs on a tilter until being processed at the Testing Facility. The brains will be stored in saline on wet ice until being processed at the Testing Facility. All processed samples will be held on wet ice **or refrigerated** until assayed. **Once assayed, samples will be stored refrigerated or on wet ice until transferred to frozen (-15°C to -30°C) storage.**

Justification:

This provides additional suitable holding conditions for processed samples prior to and following assay.

2. Attachment 5 - Study-Specific Procedure for the Cholinesterase Evaluation of Rat Brains and RBC, Preparation of Standards (Section IV), Preparation of ACHE Standards (Step B), Preparation of Ache Stock Solution, Step 1

Step 1 of this section will be replaced with the following text:

1. Preparation of ACHE Stock Solution (if required)

NOTE: If aqueous ACHE is purchased, this step will not be necessary as the aqueous solution will be used as supplied from the manufacturer.

- a. Each vial of acetylcholinesterase standard from Sigma Chemical Cat# C2888 is supplied as a lyophilized dry powder. Each vial is labeled with the mg quantity and the activity associated with each lot of material. The activity per vial will determine the number of vials used for the preparation of the stock solution. The target theoretical final concentration of the stock solution is between 100 U/ml and 200 U/mL, although this may be adjusted as necessary according to the activity level per vial.

- b. Reconstitute the appropriate number of vials in 1.0 mL of R.O. deionized water (per vial). Mix by inversion and allow the vials to sit at room temperature for at least 15 minutes.
- c. Pool the solutions from each vial into a 25 mL volumetric flask. Rinse each vial three times with 0.1% Rat Albumin buffer and transfer the rinses into the same 25 mL volumetric flask. QS to 25 mL with 0.1% Rat Albumin buffer and mix by inversion.
- d. The theoretical concentration of each vial is calculated by multiplying the amount of mg solid in the vial by the number of units/mg solid. This product is then multiplied by the # of vials used, then divided by the 25 mL, (the final volume of the solution).

For example: if each vial contains 1.53 mg solid @ 658 U/mg solid:

$$\begin{aligned} 1.53 \text{ mg solid} \times 658 \text{ U/mg solid} &= 1006.74 \text{ U/vial} \\ 1006.74 \text{ U/vial} \times 3 \text{ vials used} &= 3020.22 \text{ U total} \\ 3020.22 \text{ U} \div 25 \text{ mL} &= 120.8088 \text{ U/mL} = \text{Theoretical} \\ &\text{Concentration} \end{aligned}$$

- e. The stock solution is stable for 6 months from time of preparation when stored refrigerated ($5 \pm 3^\circ\text{C}$).
- f. The calculated theoretical concentration will be used to prepare the ACHE standards.

Justification:

This provides directive for the preparation of the ACHE stock solution based upon the lot and activity level of ACHE obtained from the supplier.

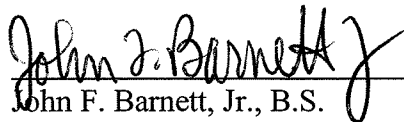
3. Attachment 5 - Study-Specific Procedure for the Cholinesterase Evaluation of Rat Brains and RBC - Sample Processing (Section V), Blood Sample Processing (Step B), Step 3

Remove the plasma from the packed red blood cell and discard. Store the packed RBCs at $2-8^\circ\text{C}$ or on wet ice until the sample preparation described below can be performed.

Justification:

This provides additional suitable holding conditions for processed samples prior to assay.

Amendment Approval:



John F. Barnett, Jr., B.S.
Senior Research Scientist
Study Director


Date: 10 Nov 2010

Protocol Amendment No. 2

Page 4

Testing Facility Study No. TQC00065

Sponsor Approval:



M. Jensen
Study Monitor

Date: 12. Nov, 2010

**Protocol Amendment No. 3****Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion
Technical in Rats****Testing Facility Study No. TQC00065****1. Histopathology (New Section)**

Tissues that include the nasal cavity and turbinates from male and female rats assigned to the 0 (Carrier Control) and 10000 ppm (Groups I and V, respectively) will be shipped (ambient conditions) from the Testing Facility to Charles River Laboratories, Pathology Associates, Maryland, USA for histopathological evaluations. The tissues will be trimmed, embedded in paraffin, sectioned, mounted on glass slides, and stained with Hematoxylin and eosin. The nasal tissue will be trimmed consistent with the procedures described by Young¹.

Histopathological examinations will be performed on rats assigned to the 0 (Carrier Control) and 10000 ppm dosage groups. If lesions attributed to the test substance are observed in the rats exposed to the high test substance concentration, the same organs will be examined histologically in the rats exposed to the lower test substance concentrations. Should results from the control and high dosage groups warrant examination of the lower dosage groups and conduct of the quantitative evaluation, scheduled report dates will be adjusted accordingly. Additional costs will be incurred should these evaluations be required.

Tissues for histological processing will be sent (ambient conditions) to:

Daniel MacDonald
Manager, Archive/Repository
Charles River Laboratories, Pathology Associates, Maryland
15 Worman's Mill Court, Suite I
Frederick, MD 21701 USA
Tel: 301.624.2022
Fax: 301.695.9850
E-Mail: daniel.macdonald@crl.com

The recipient will be notified in advance of sample shipment.

Following histological processing, all slides will be sent to the Principal Investigator, for histopathological evaluation. The Principal Investigator of the evaluation will be Carol J. Detrisac, DVM, PhD, DACVP. Dr. Detrisac's contact information is as follows:

Principal Investigator: Carol J. Detrisac, DVM, PhD, DACVP

Charles River Laboratories, Pathology Associates, Illinois

2255 W. Harrison Street

Chicago, IL 60612

Main Tel: 312.666.1555

Direct Tel: 312.567.4876

Fax: 312.666.1764

Direct Fax: 312.567.4888

E-mail: carol.detrisac@crl.com

The recipient will be notified in advance of sample shipment.

All slides residual wet tissue, blocks, histology data, and the report will be returned to Charles River Laboratories, Preclinical Services, Pennsylvania for archiving at the completion of the study.

Reference:

1. Young, J.T., Histopathologic Examination of the Rat Nasal Cavity. *Fund. Appl. Toxicol.* 1:309-312, 1981

Justification:

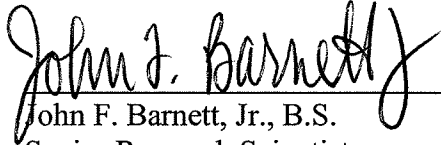
At the request of the Sponsor, histopathological examinations will be performed on the tissues that include the nasal cavity and turbinates.

Protocol Amendment No. 3

Page 3

Testing Facility Study No. TQC00065

Amendment Approval:



John F. Barnett, Jr., B.S.
Senior Research Scientist
Study Director

Date: 10 Dec 2010

Protocol Amendment No. 3

Page 4
Testing Facility Study No. TQC00065

Sponsor Approval:

 _____ Date: 2/12-2010

M. Jensen
Study Monitor



Protocol Amendment No. 4

Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats

Testing Facility Study No. TQC00065

1. Histopathology, and Amendment No. 3

In addition to the four routine sections delineated by Young (see reference in Amendment No. 3), the most rostral section of the nose, to include nares, will also be examined microscopically by the Principal Investigator for histopathology.

Justification:

This provides clarity regarding the histopathological examinations to be performed on the tissues that include the nasal cavity and turbinates.

2. Histopathology, and Amendment No. 3

The remaining tissues from male and female rats assigned to the 0 (Carrier Control) and 10000 ppm (Groups I and V, respectively) will be shipped (ambient conditions) from the Testing Facility to Charles River Laboratories, Pathology Associates, Maryland, USA for histopathological evaluations. The livers and kidneys will be removed and routinely processed, embedded in paraffin, sectioned at approximately 5 microns and stained with hematoxylin and eosin.

Histopathological examinations will be performed on rats assigned to the 0 (Carrier Control) and 10000 ppm exposure groups. If lesions attributed to the test substance are observed in the rats exposed to the high test substance concentration, the same organs will be examined histologically in the rats exposed to the lower test substance concentrations. Should results from the control and high dosage groups warrant examination of the lower dosage groups and conduct of the quantitative evaluation, scheduled report dates will be adjusted accordingly. Additional costs will be incurred should these evaluations be required.

Protocol Amendment No. 4

Page 2

Testing Facility Study No. TQC00065

Tissues for histological processing will be sent (ambient conditions) to:

Daniel MacDonald
Manager, Archive/Repository
Charles River Laboratories, Pathology Associates, Maryland
15 Worman's Mill Court, Suite I
Frederick, MD 21701 USA
Tel: 301.624.2022
Fax: 301.695.9850
E-Mail: daniel.macdonald@crl.com

The recipient will be notified in advance of sample shipment.

Following histological processing, all slides will be sent to the Principal Investigator, for histopathological evaluation. The Principal Investigator of the evaluation will be Carol J. Detrisac, DVM, PhD, DACVP. Dr. Detrisac's contact information is as follows:

Principal Investigator: Carol J. Detrisac, DVM, PhD, DACVP
Charles River Laboratories, Pathology Associates, Illinois
2255 W. Harrison Street
Chicago, IL 60612
Main Tel: 312.666.1555
Direct Tel: 312.567.4876
Fax: 312.666.1764
Direct Fax: 312.567.4888
E-mail: carol.detrisac@crl.com

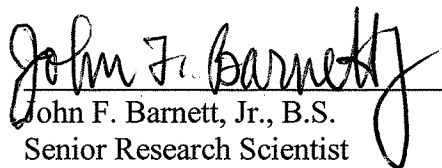
The recipient will be notified in advance of sample shipment.

All slides residual wet tissue, blocks, histology data, and the report will be returned to Charles River Laboratories, Preclinical Services, Pennsylvania for archiving at the completion of the study.

Justification:

This provides directive for the shipment and evaluation of the livers and kidneys.

Amendment Approval:


John F. Barnett, Jr., B.S.
Senior Research Scientist
Study Director


Date: 20 Dec 2010

Protocol Amendment No. 4

Page 4

Testing Facility Study No. TQC00065

Sponsor Approval:



M. Jensen
Study Monitor

Date: 3. jan. 2011



Protocol Amendment No. 5

Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats

Testing Facility Study No. TQC00065

1. Histopathology, and Amendments 3 and 4

All remaining tissues including the nasal cavity and turbinates from male and female rats assigned to the 100 and 500 ppm exposure groups (Groups II and III, respectively) will be shipped (ambient conditions) from the Testing Facility to Charles River Laboratories, Pathology Associates, Maryland, USA for histopathological evaluations. The aforementioned tissues from the Groups II and III will be processed to slides as described in Amendments 3 and 4. The slides in the 100 and 500 ppm exposure groups will be read as detailed in Amendments 3 and 4.

Justification:

Due to histopathologic findings, the nasal cavity and turbinates will be examined.

2. Section 29. References

Reference number 3 will be revised to the following:

- 3) Federal Insecticide, Fungicide and Rodenticide Act/Toxic Substances Control Act (FIFRA/TSCA); Good laboratory practice standards; Final Rule 40 C.F.R Part 160/792; August 17, 1989. U.S. Environmental Protection Agency.**

Justification:

This clarifies the GLP regulations that will be followed during the conduct of the study.

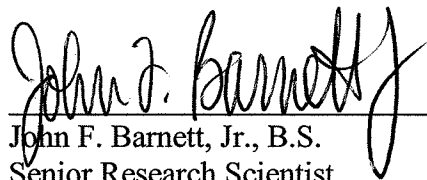
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Protocol Amendment No. 5

Page 2

Testing Facility Study No. TQC00065

Amendment Approval:



John F. Barnett, Jr., B.S.
Senior Research Scientist
Study Director


Date: 26 Jan 2011

Protocol Amendment No. 5

Page 3

Testing Facility Study No. TQC00065

Sponsor Approval:

 _____ Date: 26 jan. 2012

M. Jensen
Study Monitor



Protocol Amendment No. 6

**Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion
Technical in Rats**

Testing Facility Study No. TQC00065

1. Histopathology; Amendments 3, 4 and 5

All remaining tissues, including the nasal cavity and turbinates from male and female rats identified in Amendment 5 (assigned to the 100 and 500 ppm exposure groups [Groups II and III, respectively]) will be retained at the Testing Facility, rather than shipped for analysis. The tissues were archived at the Testing Facility.

Justification:

At the request of the Sponsor, these tissues will not be shipped or microscopically examined.

Amendment Approval:

A handwritten signature in dark ink, appearing to read "John F. Barnett, Jr.", written over a horizontal line.

John F. Barnett, Jr., B.S.
Senior Research Scientist
Study Director

Date: _____

A handwritten date "26 Jan 2012" in dark ink, written over a horizontal line.

Protocol Amendment No. 6

Page 2

Testing Facility Study No. TQC00065

Sponsor Approval:



M. Jensen
Study Monitor

Date: 1 Feb. 2012

**APPENDIX 2 - DEVIATIONS FROM THE PROTOCOL, THE STANDARD
OPERATING PROCEDURES OF THE TESTING FACILITY,
AND GOOD LABORATORY PRACTICES**

DEVIATIONS FROM THE PROTOCOL, STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY, AND GOOD LABORATORY PRACTICES

There were no deviations that affected the outcome or interpretation of this study. All deviations that occurred on this study were incidental in nature as they were documentation or recording errors, minimal excursions from specific data collection endpoints (e.g., temperature or relative humidity range excursions, cholinesterase evaluations, etc.) or minor procedural errors that deviated from original intent of the experimental design. These types of deviations from the protocol had no impact on the study outcome or interpretation of the data because, relative to the total number of rats evaluated and/or the number of data points collected per parameter, the deviations were not significant. Each deviation is listed below.

Disposition

There is no documentation of the disposition of the diet sample extracts from batches TQC00065-AA-1-001-1, TQC00065-AA-1-002, and TQC00065AA-1-003-1. This deviation did not impact the outcome of the study because it is presumed that these samples were discarded and inadvertently not documented.

Animal Husbandry

The sensitivity of the temperature recording equipment is $\pm 3\%$. Deviations are detailed in the following chart. Documentation of all excursions is available in the raw data.

Date(s) of Excursions	Total Duration (hours)	Peak	Duration of Peak (hours)
22 OCT 2010	1	65	1
22 OCT 2010 - 23 OCT 2010	18	64	5
23 OCT 2010 - 24 OCT 2010	10	65	10
25 OCT 2010 - 26 OCT 2010	21	65	21
26 OCT 2010 - 27 OCT 2010	23	64	10
27 OCT 2010 - 28 OCT 2010	23	64	18
31 OCT 2010	12	65	9
01 NOV 2010	8	65	8
03 NOV 2010	14	65	14
04 NOV 2010	11	65	11
04 NOV 2010 - 05 NOV 2010	21	64	2
06 NOV 2010	15	65	15
07 NOV 2010	16	65	16

The sensitivity of the humidity recording equipment is $\pm 3\%$. Deviations are detailed in the following chart. Documentation of all excursions is available in the raw data.

Date	Total Duration (hours)	Minimum/Maximum Humidity (%)	Approximate Duration of Minimum/Maximum Humidity (hours)
13 OCT 2010 - 14 OCT 2010	25	28	17
15 OCT 2010 - 19 OCT 2010	101	25	28

Cholinesterase Evaluations

On 24 September 2010, the AChE stock solution was prepared as a Testing Facility reagent without protocol or Standard Operating Procedure directive. All standard curves prepared from this stock solution met all acceptance criteria. This GLP deviation did not impact the outcome of the study because the appropriate AChE stock solution was prepared and used for the study.

On DS 29 (16 November 2010 and 17 November 2010), transfer of the brains to a 15 mL polypropylene tube for homogenization was not documented. Retained samples were inspected and the tubes were confirmed to be 15 mL polypropylene tubes.

On DS 29 (17 November 2010), the brain sample from female rat 326 in the 0 (Carrier Control) ppm exposure group was inadvertently re-analyzed after an acceptable result had already been obtained.

On DS 29 (16 November 2010 and 17 November 2010), the majority of brain and RBC samples were not analyzed within 60 minutes of sacrifice. The ranges of the time deviated is detailed in the following charts:

Brain Sample	Range of Time Deviated from 60 Minute Allotted Time Window
Male Rats	1 minute to 1 hour and 3 minutes
Female Rats	1 minute to 1 hours and 13 minutes

RBC Sample	Range of Time Deviated from 60 Minute Allotted Time Window
Male Rats	1 minute to 2 hour and 8 minutes
Female Rats	1 minute to 2 hours and 19 minutes

All deviations are documented in the raw data.

APPENDIX 3 - CERTIFICATES OF ANALYSIS



Cheminova A/S
P.O. Box 9
DK-7620 Lemvig
Denmark

Phone (+45) 96 90 96 80
Fax (+45) 96 90 96 91
www.cheminova.com
CVR-No. DK12 76 00 43

Certificate of Analysis

TEM 010-08

Test substance certified:

Test substance:	Malathion Technical fortified			
CHA Code No.:	-			
Batch No.:	D2014-OSJ-MLT-01-S			
Origin of test substance:	<input checked="" type="checkbox"/> Laboratory	<input type="checkbox"/> Pilot plant	<input type="checkbox"/> Commercial	

Analysis:

Content of Malathion:	95.8% w/w
Identified by:	¹ H-NMR and ¹³ C-NMR Spectroscopy, Mass Spectrometry and IR Spectroscopy
Quantified by:	GC (Method VAM 001-02)
Date of analysis:	September 28, 2010

Information of the test substance:

Appearance:	Pale yellowish liquid
Storage:	Refrigerator
Tap density:	Not determined
Expiry date:	September 28, 2013

Information of analyte(s):

Common name:	Malathion
CAS name:	Butanedioic acid ((dimethoxyphosphinothioyl) thio)-, diethyl ester
CAS No.:	121-75-5
Molecular formula:	C ₁₀ H ₁₉ O ₆ PS ₂
Molecular mass:	330.36 g/mol
Structure formula:	

Statement of GLP Compliance

The identification and quantification were performed at Cheminova A/S and conducted according to FIFRA Good Laboratory Practice Standards, 40 CFR Part 160 and the OECD Principles of Good Laboratory Practices.

Date

November 9, 2010

Barbara Hinz

**Charkit Chemical Corporation**

32 Haviland Street, P.O. Box 90, South Norwalk, CT 06854
203-299-3220 • Fax: 203-299-1355
www.charkit.com • e-mail: sales@charkit.com

B 13648941

CERTIFICATE OF ANALYSIS

PRODUCT	Com Oil	Lot #	J-145	
Customer Name	Charkit Chemical Corp.	Date	4/7/2009	Manufacture Date: 4-06-09A
Address	32 Haviland St. South Norwalk, CT 06854			Expiration Date: 4-06-11A

COLOR:	1.5	R	S.F.I @ 10.0 OC	50 F
FLAVOR:	Bland		S.F.I @ 21.1 OC	70 F
FREE FATTY ACIDS:	0.04	%	S.F.I @ 26.7 OC	80 F
PEROXIDE VALUE:	0.5	me/kg	S.F.I @ 33.3 OC	92 F
IODINE VALUE :			S.F.I @ 40.0 OC	104 F
OSI:		hrs	Melting Point	
COLD TEST:		hrs		
MOISTURE:		%		

Additives	
TBHQ	NEG
MS	NEG
S-1	NEG
BHT	NEG

Fatty Acid Profile	
C16:0	%
C18:0	%
C18:1	%
C18:2	%
C18:3	%

EXACT COPY
CC 01 OCT 2010

Official Weighers
and Inspectors For:
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PRODUCTS ASSOCIATION,
PUBLIC WEIGHER,
NATIONAL INSTITUTE OF
OIL PRODUCTS
Chemists:
NATIONAL COTTONSEED
PRODUCTS ASSOCIATION,
NATIONAL OILSEED
PROCESSORS ASSOCIATION
NATIONAL INSTITUTE OF
OILSEED PRODUCTS



THONVILLE LABORATORIES, INC.

Independent & Official Weighers, Samplers, Chemists

P.O. Box 23687
New Orleans, La. 70183-0687, U.S.A.

5440 Pepsi Street
New Orleans, La. 70123

(504) 733-9603

FAX: (504) 733-6457

TELEX: 460114 THION UI

operations@thionvillenola.com

FOSFA International Full Member Analyst
FOSFA International Full Member Superintendent

Referee Chemists:
AMERICAN OIL CHEMISTS'
SOCIETY

Member:
AMERICAN ASSOCIATION
OF CEREAL CHEMISTS
AMERICAN FATS & OILS
ASSOCIATION
AMERICAN INSTITUTE OF
CHEMISTS
N.O. CHAMBER OF
COMMERCE
N.O. BOARD OF TRADE
NATIONAL RENDERERS
ASSOCIATION
AMERICAN PETROLEUM
INSTITUTE

BATON ROUGE
HOUSTON
MOBILE
SAN FRANCISCO
CHICAGO
SAVANNAH
NORFOLK
NEW YORK
CANADA
ROTTERDAM
HAMBURG
ANTWERP
PARIS
LORIENT
BREST
BORDEAUX
ROUEN
GENEVA

BUENOS AIRES
PARAGUAY
SAO PAULO
SANTOS
PARANAGUA
PORTO ALEGRE
RIO GRANDE
RIO DE JANEIRO
ITALY
SPAIN
GREECE
TURKEY
DENMARK
SWEDEN
NORWAY

CERTIFICATE OF ANALYSIS

CHARKIT CHEMICAL CORP.
Norwalk, CT

APRIL 17, 2009

SAMPLE DESCRIBED AS : CORN OIL

IDENTIFIED AS : LOT #J-145; 04/14/09
P.O. #64409

Iodine Value _____ 127.7
Saponification Value _____ 193.0
Unsaponifiable Matter _____ 0.63%
Organic Volatile Matter _____ NONE DETECTED*
*NONE DETECTED = < 10 PPM

HEAVY METALS:

Lead _____ NONE DETECTED**
Mercury _____ NONE DETECTED**
Arsenic _____ NONE DETECTED**
Cadmium _____ NONE DETECTED**
**NONE DETECTED = 0.1 PPM

Benzo (a) Pyrene _____ NONE DETECTED***
***NONE DETECTED = 0.1 PPB

"Based on the above tests, this product is consistent with USP Specifications."

Above results are based upon samples submitted to Thionville Laboratories, Inc., for analysis. Any sample identification is reported as submitted and is not verified by Thionville Laboratories, Inc., as representative of sample.

THONVILLE LABORATORIES, INC.

Shani Jolly
Laboratory Manager

LAB NO. 5717
SJ/em
0417/1031

EXACT COPY
CC 01 OCT 2010

Neither Thionville nor its Officers, Directors or Committee members nor its surveyors, representatives or agents are under any circumstances whatsoever to be held responsible or legally liable for any inaccuracy or error in any report or certificate issued by Thionville or by its surveyors or other agents or employees, or any error of judgment, default, omission, negligence or breach of warranty, either express or implied, including warranty of workmanlike service, arising or allegedly arising out of services of Thionville, its surveyors or other employees, representatives or agents.

APPENDIX 4 - ENVIRONMENTAL AND HUSBANDRY REPORTS

TEMPERATURE AND RELATIVE HUMIDITY REPORTS

A duplicate copy of each tempscribe form was added to the data and the final report because the size of each tempscribe obscured the following information: the technician that completed each form, the technician who reviewed each form, and the date of review.

TEMPSCRIBE FORM

Reviewed by:

Date:

28 Oct 2010

(3) Deviations written. AS 29 Dec 10

31.AUG.2010.T2-12 34B7

④ See attached sheet for complete by. AMK 14 Dec

TEMPSCRIBE FORM

PROTOCOL: <u>TQC00065</u>		ROOM NUMBER: <u>54</u>	TYPE OF RECORD TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE: <u>12 OCT 10 - 19 OCT 10</u>	COMPANY I.D. NUMBER <u>246</u>	SPECIES/STRAIN: <u>NITE</u>	

Copyright © 2005 Dickson

Form completed by (initials/date): ANK-28 Oct 2010

Reviewed by: Chris KaurigaDate: 28 Oct 2010

DODRE2100110

② Humidity out of range. AnK 27 Oct 2010

EXACT COPY

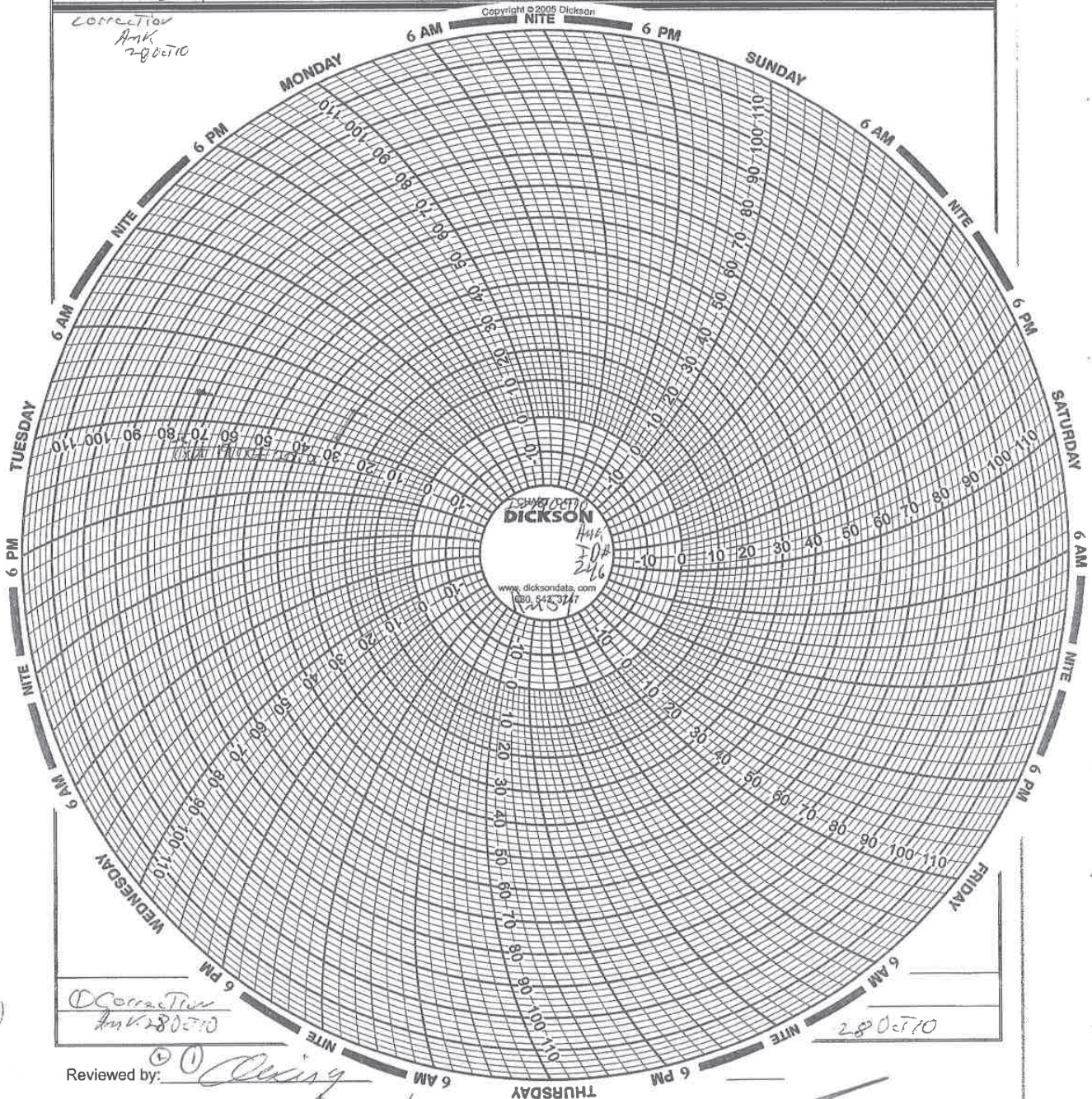
AnK 11 Dec 11

31.AUG.2010.T2-12 34B7

Exact Copy of temperature and humidity data. Header information added per study.

TEMPSCRIBE FORM

PROTOCOL: TQC00065		ROOM NUMBER: Rm 54	TYPE OF RECORD TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input checked="" type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE: 10/27/2010 280-T-10	COMPANY I.D. NUMBER 246	SPECIES/STRAIN: Rat/Crl:CO(50)	



PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD
		Rm 54	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input checked="" type="checkbox"/> °F <input type="checkbox"/>
DATE:	COMPANY I.D. NUMBER	SPECIES/STRAIN:	
11/01/2010 26 OCT 2010	246		

Correction
Amk
28 OCT 10

Form completed by (initials/date): *Amk 28 OCT 10*

Reviewed by:

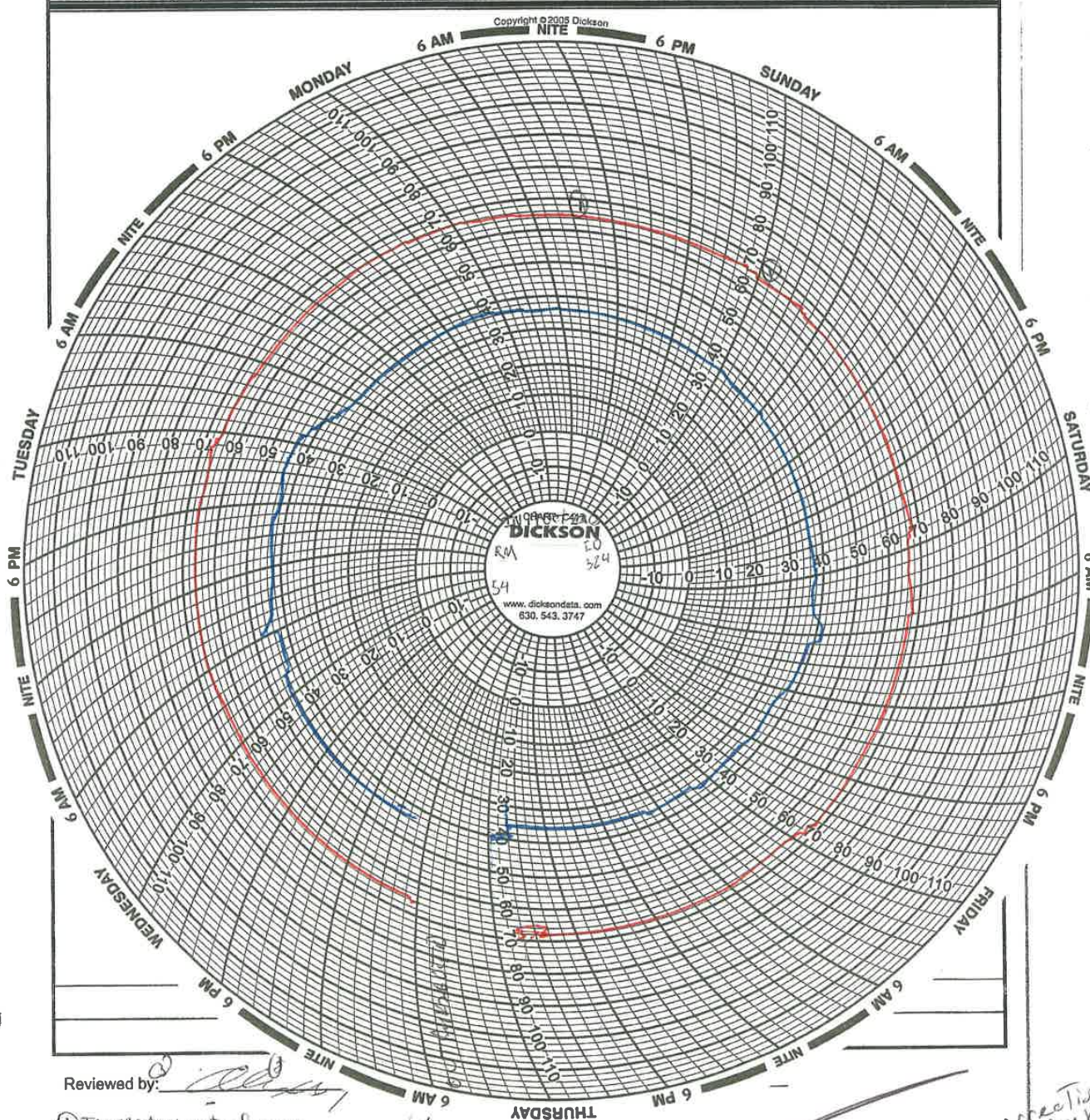
Date: 28 OCT 10

EXACT COPY

31.AUG.2010.T2-12 34B7

TEMPSCRIBE FORM

PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD	
TQ00065		Rm 54	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/>	°C <input type="checkbox"/>
			TEMPERATURE ONLY <input type="checkbox"/>	°F <input checked="" type="checkbox"/>
DATE:	COMPANY I.D. NUMBER	SPECIES/STRAIN:		
05 OCT 2010 TO 26 OCT 2010	324	Rat/Crl: CO(CSD)		



Reviewed by:

- ① Temperature out of range.
Deviation written. Se

CSAP Review w/ SHAN Review 11/9/04

- ③ See attached sheet For Reviewed by: Anil
400cell

31.AUG.2010.T2-12 34B7

EXACT COPY

corrected
AMK
14 Dec 1973

TEMPSCRIBE FORM

PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD
		Rm 54	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE:	COMPANY I.D. NUMBER	SPECIES/STRAIN:	
19 Oct 2010 to 26 Oct 2010	324		

Form completed by (initials/date): Amk 28 Oct 10

Reviewed by: Alvin KaurigaDate: 28 Oct 10

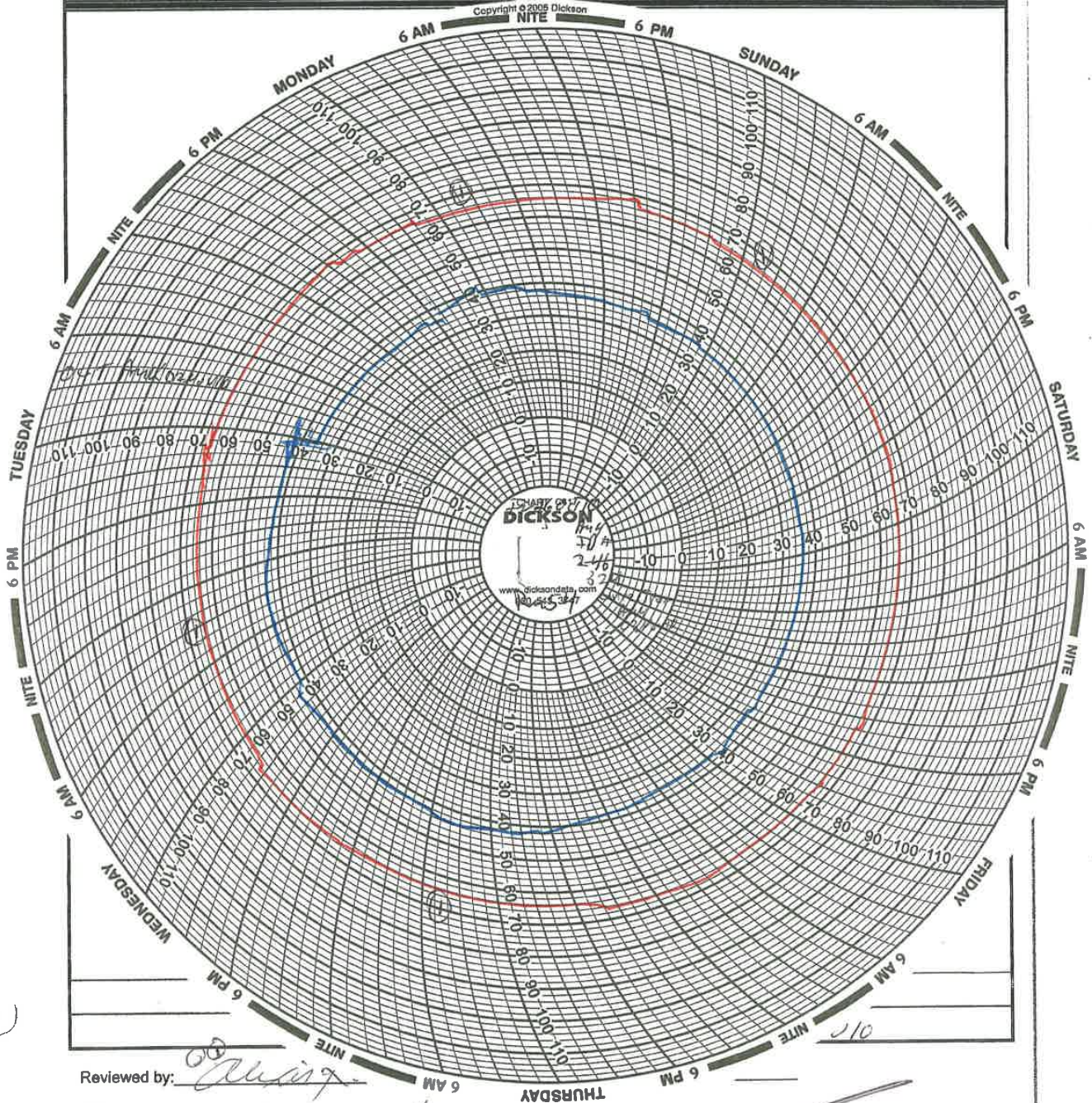
- ① Chart inadvertently placed in wrong date. Tuesday started 19 Oct 2010
 ② Wednesday, ③ Thursday, ④ Friday, ⑤ Saturday, ⑥ Sunday, ⑦ Monday, ⑧ Tuesday, ⑨ Wednesday, ⑩ Thursday, ⑪ Friday, ⑫ Saturday, ⑬ Sunday, ⑭ Monday, ⑮ Tuesday, ⑯ Wednesday, ⑰ Thursday, ⑱ Friday, ⑲ Saturday, ⑳ Sunday, ㉑ Monday, ㉒ Tuesday, ㉓ Wednesday, ㉔ Thursday, ㉕ Friday, ㉖ Saturday, ㉗ Sunday, ㉘ Monday, ㉙ Tuesday, ㉚ Wednesday, ㉛ Thursday, ㉜ Friday, ㉝ Saturday, ㉞ Sunday, ㉟ Monday, ㊱ Tuesday, ㊲ Wednesday, ㊳ Thursday, ㊴ Friday, ㊵ Saturday, ㊶ Sunday, ㊷ Monday, ㊸ Tuesday, ㊹ Wednesday, ㊺ Thursday, ㊻ Friday, ㊼ Saturday, ㊽ Sunday, ㊾ Monday, ㊿ Tuesday, 1 AUG. 2010, T2-12 34B7

EXACT COPY
Amk 14 Dec 11

Exact Copy of temperature and humidity data. Header information added per study.

TEMPSCRIBE FORM

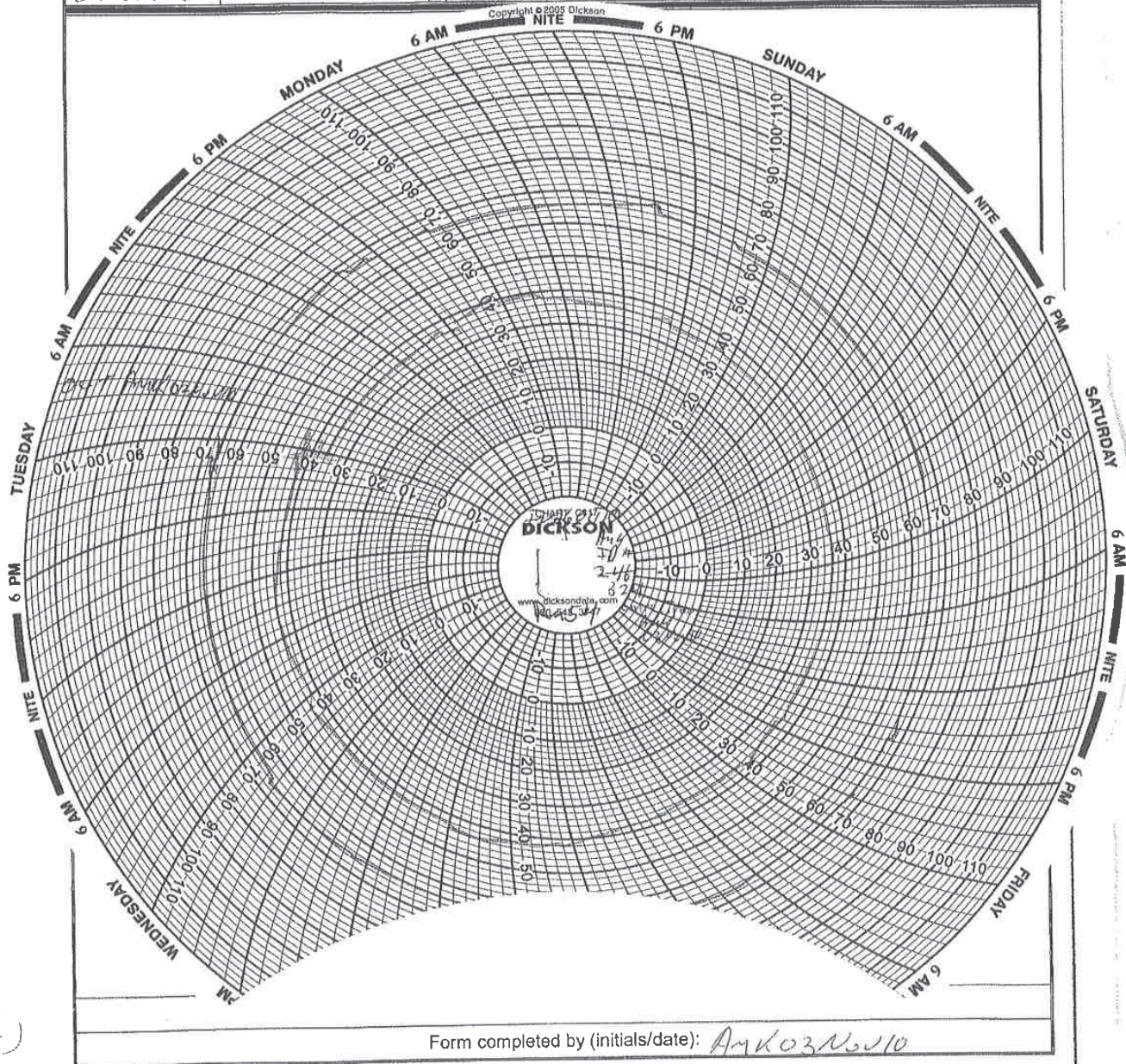
PROTOCOL: TQC00065		ROOM NUMBER: Rm 54	TYPE OF RECORD TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE: 26 Oct 2010 to 02 Nov 2010	COMPANY I.D. NUMBER 324	SPECIES/STRAIN: Rat / Cr1: CD (SD)	

Reviewed by: *[Signature]*① Temperature out of range,
deviation written. AS 39 Dec 10② Set Range - to show review *[Signature]* 900011③ See attached sheet for Reviewed by: *[Signature]* 140011

31.AUG.2010.T2-12 34B7

TEMPSCRIBE FORM

PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD
		Rm 54	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE:	COMPANY I.D. NUMBER	SPECIES/STRAIN:	
26 Oct 2010 to 02 Nov 2010	324		



Reviewed by: Alan Kawiga Date: 03 Nov 10

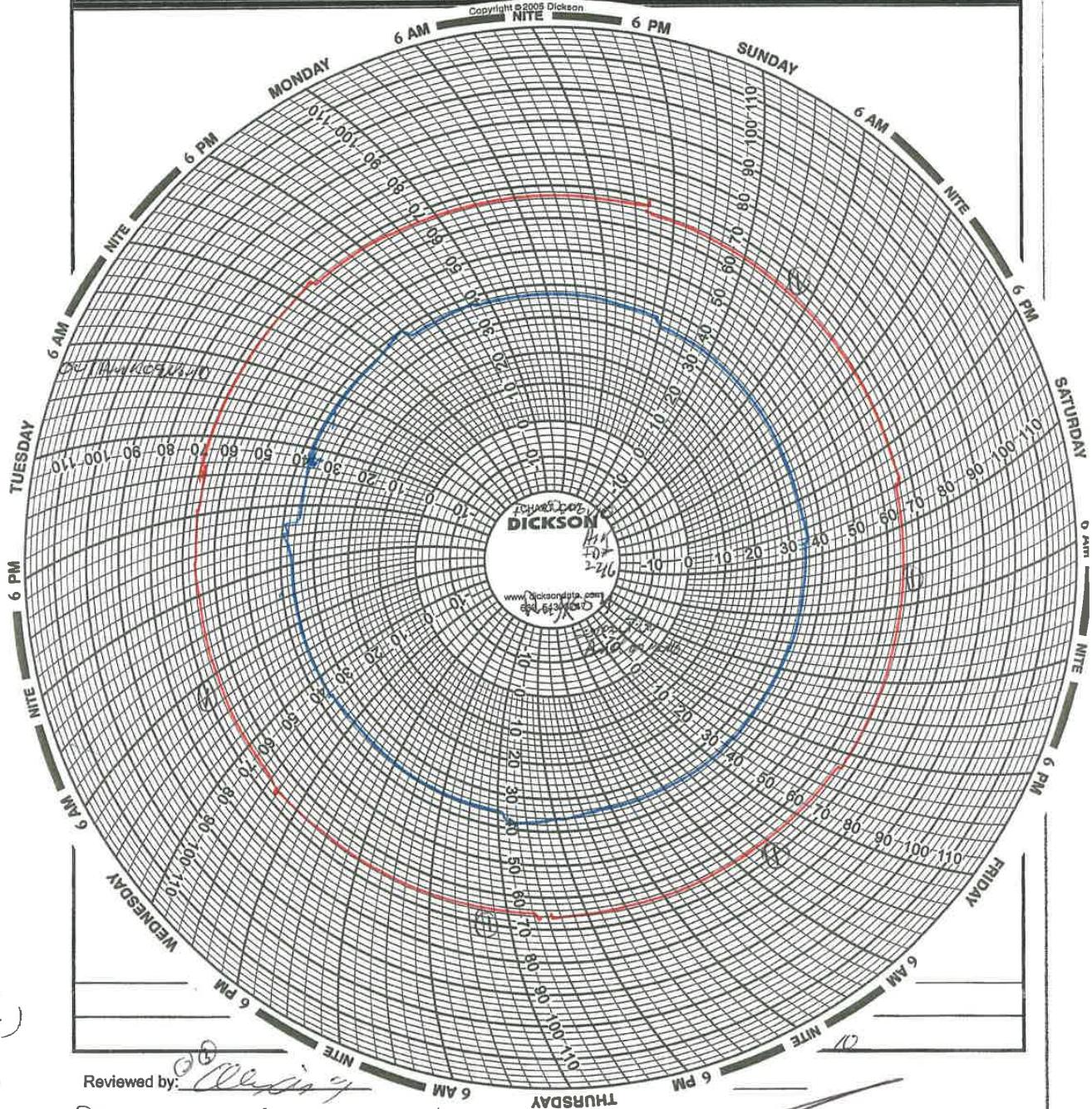
EXACT COPY
Amk 14 Dec 11

31 AUG.2010.T2-12 34B7

Exact copy of temperature and humidity data. Header information added per study.

TEMPSCRIBE FORM

PROTOCOL: TQC00065		ROOM NUMBER: Rm 54	TYPE OF RECORD TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE: 06 Nov 2010 09 Nov 2010	COMPANY I.D. NUMBER 246	SPECIES/STRAIN: Rat/Cr1: CD(SD)	



① Temperature out of range,
Deviation written: AS 39 DEC 10

② Supplied to SMM Animal *[Signature]*

③ See attached sheet for Reviewed by: *[Signature]* 12 Dec 11

31.AUG.2010.T2-12 34B7

PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD	
DATE:		COMPANY I.D. NUMBER:	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> °F	TEMPERATURE ONLY <input type="checkbox"/> °C <input checked="" type="checkbox"/> °F
SPECIES/STRAIN:		Form completed by (initials/date):		

Reviewed by: Alisa Kaurin Date: 09 Nov 10

EXACT COPY 31.AU

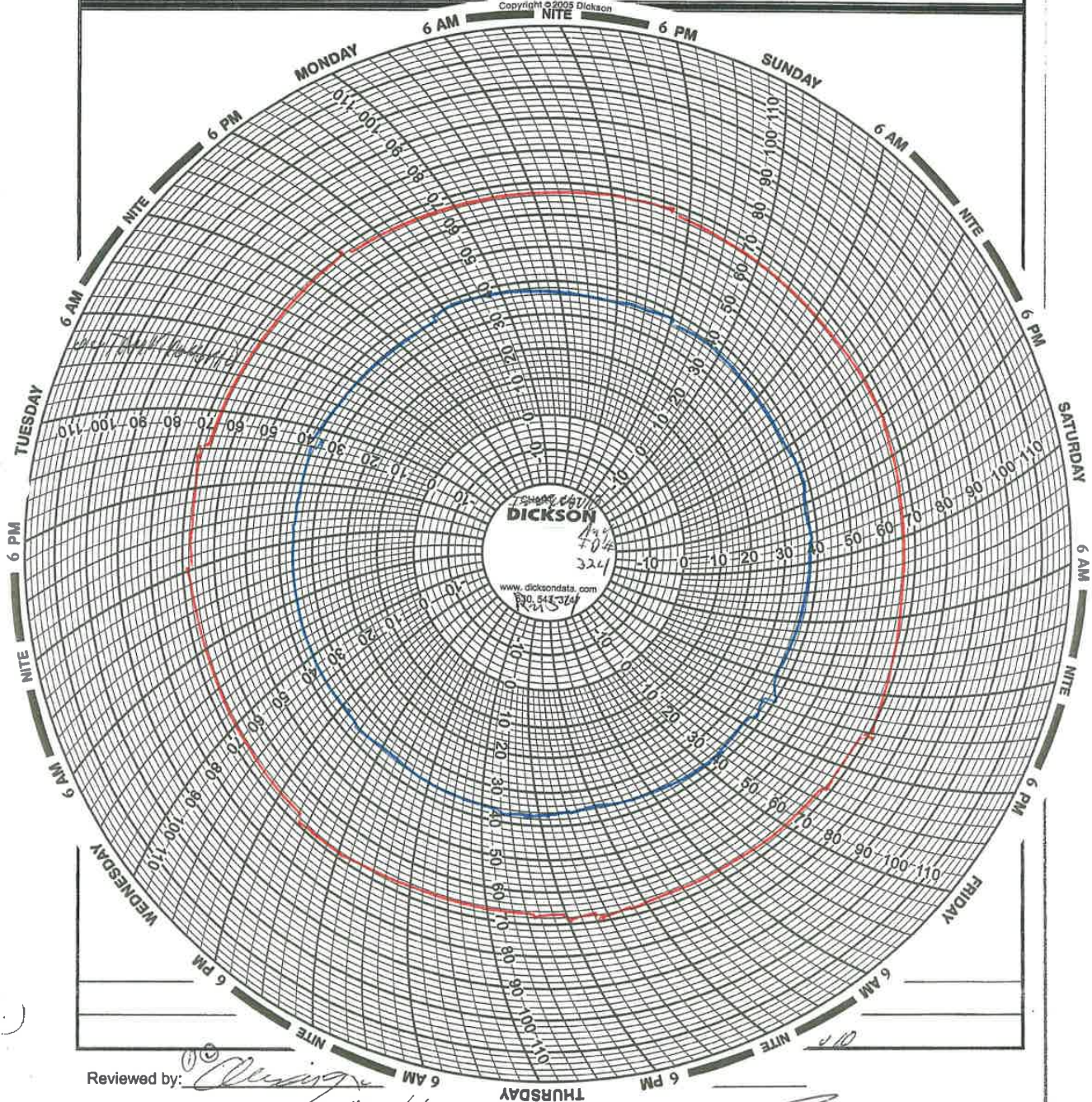
31.AUG.2010.T2-12 34B7

Ans ✓ 14/Dec 11

Exact copy of temperature and humidity data. Header information added per study.

TEMPSCRIBE FORM

PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD
TQC00065		Rm 54	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE:	COMPANY I.D. NUMBER	SPECIES/STRAIN:	
04 AUG 2010 16 AUG 2010	324	Rat/Cr:CD(SD)	

Reviewed by: *[Signature]*

① See attached sheet for review 11/19/11

② See attached sheet for review 12/10/11

Reviewed by: *[Signature]*
③ correction
1/10/11

31.AUG.2010.T2-12 34B7

TEMPSCRIBE FORM

PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD
		Rm 54	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE:	COMPANY I.D. NUMBER	SPECIES/STRAIN:	
08 Nov 2010 16 Nov 2010	324		

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Form completed by (initials/date): Am K 17 Nov 10

Reviewed by: Alvin Kauriga Date: 17 Nov 10

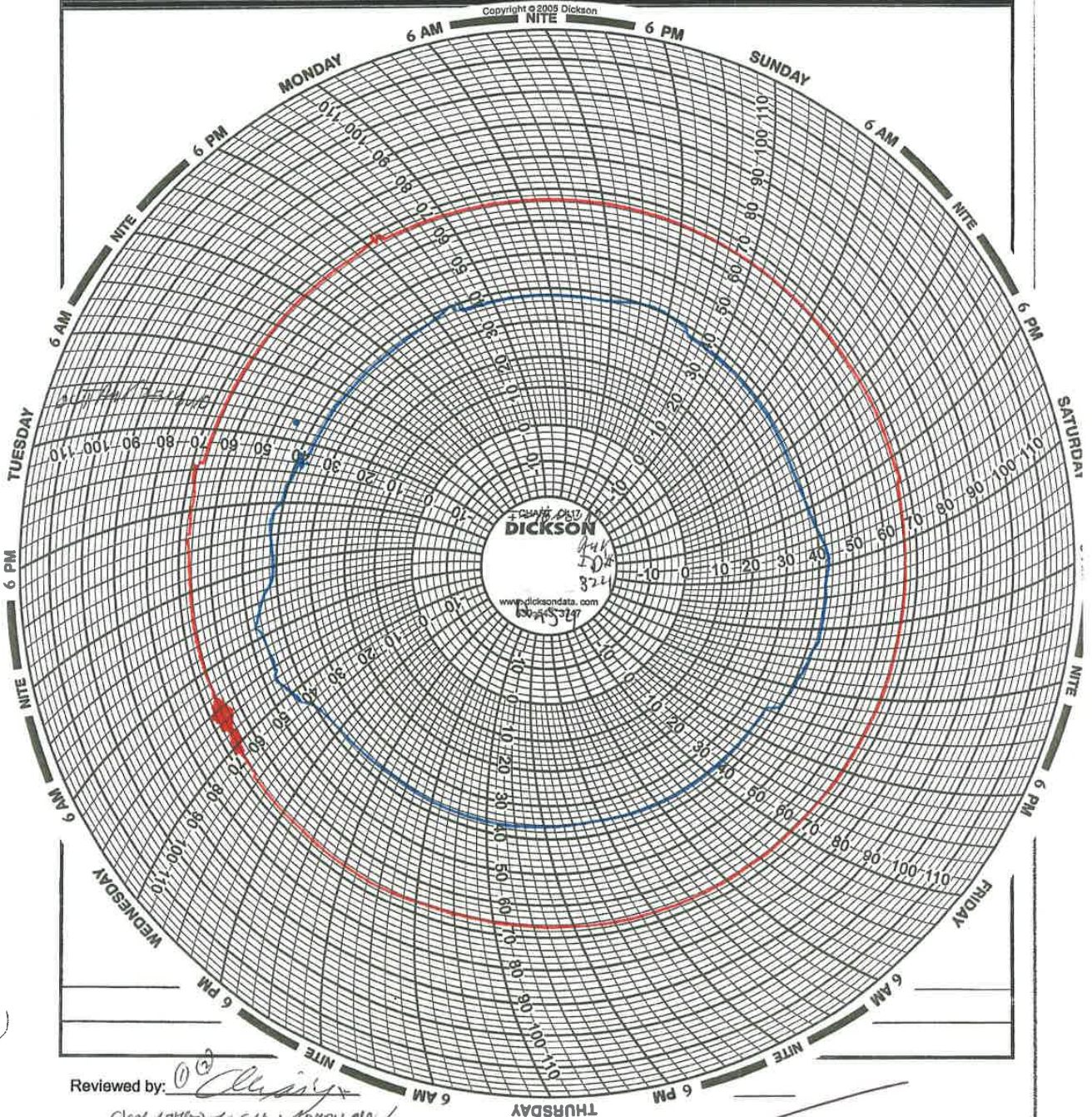
EXACT COPY
Am K 14 Dec 11

31.AUG.2010.T2-12 34B7

Exact Copy of temperature and humidity data. Header information added per study.

TEMPSCRIBE FORM

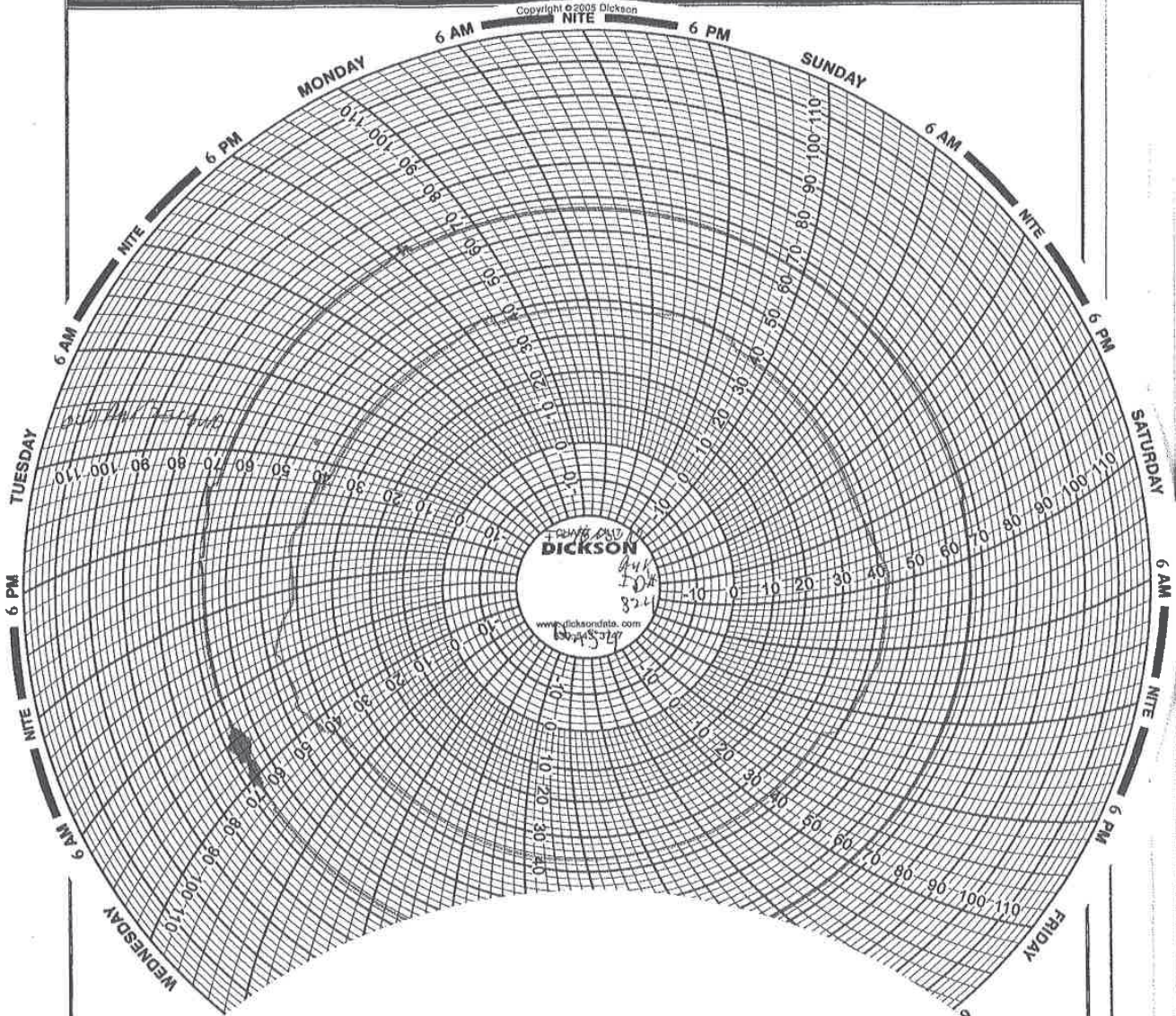
PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD	
TQC00065		Rm 54	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>	
DATE:	COMPANY I.D. NUMBER	SPECIES/STRAIN:		
10/20/2010 23/10/2010	324	Rat / Cr1: CO(50)		



31.AUG.2010.T2-12 34B7

TEMPSCRIBE FORM

PROTOCOL:		ROOM NUMBER:	TYPE OF RECORD
		Rm 54	TEMPERATURE/HUMIDITY <input checked="" type="checkbox"/> °C <input type="checkbox"/> TEMPERATURE ONLY <input type="checkbox"/> °F <input checked="" type="checkbox"/>
DATE:	COMPANY I.D. NUMBER	SPECIES/STRAIN:	
01 Nov 2010 23 Nov 2010	324		

Form completed by (initials/date): Am 23 Nov 10Reviewed by: Chris KavigaDate: 23 Nov 10

EXACT COPY

Am 14 Dec 11

31.AUG.2010.T2-12 34B7

FEED ANALYSES



Return to Certified Analysis Retrieval

Product Code: 5002M
Product Desc: CERTIFIED RODENT DIET MEAL
Lab Number: L1018428-2
Lot Code: JUN 30 10 1B
Entered: 7/26/2010

Assay	Analysis	Units
PROTEIN	22.5	%
FAT (ACID HYDRO)	5.5	%
FIBER (CRUDE)	5.07	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.0546	PPM
CALCIUM	0.8247	%
LEAD	0.21	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.7133	%
SELENIUM	0.371	PPM
Organophosphates	PPM	Organophosphates
Diazinon	LESS THAN 0.02	Disulfoton
Ethion	LESS THAN 0.02	Malathion
Methyl Parathion	LESS THAN 0.02	Parathion
Thimet	LESS THAN 0.02	Trithion
Chlorinated Hydrocarbons and PCB	PPM	Chlorinated Hydrocarbons and PCB
Aldrin	LESS THAN 0.02	Alpha-BHC
Beta-BHC	LESS THAN 0.02	Chlordane
DDE	LESS THAN 0.02	DDT
Delta-BHC	LESS THAN 0.02	Dieldrin
Endrin	LESS THAN 0.02	HCB
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide
Lindane	LESS THAN 0.02	Methoxychlor
Mirex	LESS THAN 0.02	PCB
Thiodan	LESS THAN 0.02	
AFLATOXIN	PPB Aflatoxins	LESS THAN 5

EXACT COPY
L1018428-2

Approved
M. J. W.
06 Aug 2010

No notes.

Approved by: Angela Crutcher

Angela Crutcher

For additional information, please contact:

- 1) Customer Service at (314) 982-1310 -- for assay methodology
- 2) Dr. Kristi Thompson, (765)894-3104 or Dr. Carrie Schultz, (314)974-6529 -- for nutritional interpretation
- 3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed.
The use of the term "Less Than" does not imply that traces of analyte were present.

EXACT COPY
well 23 Mar 2010

Approved
[Signature]
06 Aug 2010



Return to Certified Analysis Retrieval

Product Code: 5002M
 Product Desc: CERTIFIED RODENT DIET MEAL
 Lab Number: L1019196-1
 Lot Code: JUL 15 10 3A
 Entered: 8/9/2010

Assay	Analysis	Units
PROTEIN	21.2	%
FAT (ACID HYDRO)	5.55	%
FIBER (CRUDE)	4.6	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.06	PPM
CALCIUM	0.749	%
LEAD	0.204	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.637	%
SELENIUM	0.362	PPM

Organophosphates	PPM	Organophosphates	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Trithion	LESS THAN 0.02

Chlorinated Hydrocarbons and PCB	PPM	Chlorinated Hydrocarbons and PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
Thiodan	LESS THAN 0.02		

AFLATOXIN	PPB Aflatoxins	LESS THAN 5
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EXACT COPY
TF 234210

Approved
 [Signature]
 29 sep 2010

Certified Papers Retrieval

Page 2 of 2



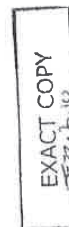
No notes.

Approved by: Angela Crutcher

For additional information, please contact:

- 1) Customer Service at (314) 982-1310 -- for assay methodology
- 2) Dr. Kristi Thompson, (765)894-3104 or Dr. Carrie Schultz, (314)974-6529 -- for nutritional interpretation
- 3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

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Approved
Mitt
29 Sep 2010

1 AUG 10 12



Return to Certified Analysis Retrieval

Product Code: 5002M
 Product Desc: CERTIFIED RODENT DIET MEAL
 Lab Number: L1019865-2
 Lot Code: AUG 02 10 2B
 Entered: 8/18/2010

Assay	Analysis	Units
PROTEIN	21.2	%
FAT (ACID HYDRO)	5.94	%
FIBER (CRUDE)	5.17	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.0946	PPM
CALCIUM	0.826	%
LEAD	0.144	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.6202	%
SELENIUM	0.348	PPM

Organophosphates	PPM	Organophosphates	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Trithion	LESS THAN 0.02

Chlorinated Hydrocarbons and PCB	PPM	Chlorinated Hydrocarbons and PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02
Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
Thiodan	LESS THAN 0.02		

AFLATOXIN	PPB Aflatoxins	LESS THAN 5
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EXACT COPY
 MRL 14 JAN 2011

<http://www.labdiet.com/certified/mys.asp?002.asp>


11/15/2010

Certified Labels Removal

Page 2 of 2

No notes.

Approved by: Angela Crutcher



For additional information, please contact:

- 1) Customer Service at (314) 982-1310 -- for assay methodology
- 2) Dr. Kristi Thompson, (765)894-3104 or Dr. Carrie Schultz, (314)974-6529 -- for nutritional interpretation
- 3) Richmond, IN Manufacturing Plant at (765) 962-9561 -- all other questions

The term "Less Than" is used to signify the lower limit of quantitation of the procedure under the conditions employed.
The use of the term "Less Than" does not imply that traces of analyte were present.

Approved

22 Nov 2010

EXACT COPY
MPL 14 JAN 2011

WATER ANALYSES



QC Laboratories®

Analytical Report



MATTHEW VANEMAN
CHARLES RIVER LABORATORIES, INC.
905 SHEEHY DRIVE
HORSHAM, PA 19044

Regarding:

MATTHEW VANEMAN
CHARLES RIVER LABORATORIES, INC.
905 SHEEHY DRIVE
HORSHAM, PA 19044

Account No: W05899, CHARLES RIVER LABORATORIES, INC.
Project No: W05899, CHARLES RIVER LABORATORIES, INC.

P.O. No: 6600061155
PWSID No:

Inv. No: 1249368

Sample Number L3503244-1 Sample Description
DRINKING WATER - IN VITRO
Received Temp: 34 F Iced (Y/N): Y

Samp. Date/Time/Temp
10/01/10 11:03am NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/01/10 06:52PM ARD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/01/10 05:15PM ARD
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL-FIELD	SM 4500CL G	< 0.02	mg/l	10/01/10 11:06AM JCN

Sample Number L3503244-2 Sample Description
DRINKING WATER - FORMULATION
Received Temp: 34 F Iced (Y/N): Y

Samp. Date/Time/Temp
10/01/10 11:13am NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/01/10 06:52PM ARD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/01/10 05:15PM ARD
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL-FIELD	SM 4500CL G	< 0.02	mg/l	10/01/10 11:15AM JCN

Sample Number L3503244-3 Sample Description
DRINKING WATER - FILL STATION
Received Temp: 34 F Iced (Y/N): Y

Samp. Date/Time/Temp
10/01/10 11:16am NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/01/10 06:52PM ARD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/01/10 05:15PM ARD
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL-FIELD	SM 4500CL G	0.60	mg/l	10/01/10 11:21AM JCN

Approved
11 OCT 2010
Thomas J. Hines, President

Exact copy
TF 23 Nov 10

QC Laboratories

Analytical Report



Account No: W05899, CHARLES RIVER LABORATORIES, INC.
Project No: W05899, CHARLES RIVER LABORATORIES, INC.

P.O. No: 6600061155
PWSID No:

Inv. No: 1249368

Sample Number L3503244-4	Sample Description DRINKING WATER - ANALYTICAL Received Temp: 34 F Iced (Y/N): Y	Samp. Date/Time/Temp 10/01/10 11:18am NA F	Sampled by Customer Sampled	
Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/01/10 06:52PM ARD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/01/10 05:15PM ARD
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL-FIELD	SM 4500CL G	< 0.02	mg/l	10/01/10 11:23AM JCN

Sample Number L3503244-5	Sample Description DRINKING WATER - ROOM 13 RACK 126 Received Temp: 34 F Iced (Y/N): Y	Samp. Date/Time/Temp 10/01/10 11:24am NA F	Sampled by Customer Sampled	
Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/01/10 06:52PM ARD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/01/10 05:15PM ARD
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL-FIELD	SM 4500CL G	0.17	mg/l	10/01/10 11:27AM JCN

Sample Number L3503244-6	Sample Description DRINKING WATER - ROOM T-2 RACK 1761 Received Temp: 34 F Iced (Y/N): Y	Samp. Date/Time/Temp 10/01/10 11:30am NA F	Sampled by Customer Sampled	
Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/01/10 06:52PM ARD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/01/10 05:15PM ARD
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL-FIELD	SM 4500CL G	0.87	mg/l	10/01/10 11:35AM JCN

L3503244-1:

Page 2 of 4

Serial Number: 1559896

Approved
11 OCT 2010
Thomas J. Hines, President

Exact copy
10/23/2010

QC Laboratories

Analytical Report



Account No: W05899, CHARLES RIVER LABORATORIES, INC.
Project No: W05899, CHARLES RIVER LABORATORIES, INC.

P.O. No: 6600061155
PWSID No:

Inv. No: 1249368

1. A water supply is considered bacteriologically "SAFE" if no Coliform bacteria are detected. To be considered "SAFE" your report should indicate "<1 col/100ml" or "NEG" for the Coliform Test. If your report indicates a positive result "POS" or a value of one (1) or greater then your supply is "UNSAFE FOR DRINKING" contact your local Health Dept. or QC for advice.

L3503244-2:

1. A water supply is considered bacteriologically "SAFE" if no Coliform bacteria are detected. To be considered "SAFE" your report should indicate "<1 col/100ml" or "NEG" for the Coliform Test. If your report indicates a positive result "POS" or a value of one (1) or greater then your supply is "UNSAFE FOR DRINKING" contact your local Health Dept. or QC for advice.

L3503244-3:

1. A water supply is considered bacteriologically "SAFE" if no Coliform bacteria are detected. To be considered "SAFE" your report should indicate "<1 col/100ml" or "NEG" for the Coliform Test. If your report indicates a positive result "POS" or a value of one (1) or greater then your supply is "UNSAFE FOR DRINKING" contact your local Health Dept. or QC for advice.

L3503244-4:

1. A water supply is considered bacteriologically "SAFE" if no Coliform bacteria are detected. To be considered "SAFE" your report should indicate "<1 col/100ml" or "NEG" for the Coliform Test. If your report indicates a positive result "POS" or a value of one (1) or greater then your supply is "UNSAFE FOR DRINKING" contact your local Health Dept. or QC for advice.

L3503244-5:

1. A water supply is considered bacteriologically "SAFE" if no Coliform bacteria are detected. To be considered "SAFE" your report should indicate "<1 col/100ml" or "NEG" for the Coliform Test. If your report indicates a positive result "POS" or a value of one (1) or greater then your supply is "UNSAFE FOR DRINKING" contact your local Health Dept. or QC for advice.

L3503244-6:

1. A water supply is considered bacteriologically "SAFE" if no Coliform bacteria are detected. To be considered "SAFE" your report should indicate "<1 col/100ml" or "NEG" for the Coliform Test. If your report indicates a positive result "POS" or a value of one (1) or greater then your supply is "UNSAFE FOR DRINKING" contact your local Health Dept. or QC for advice.

- A result of "ND" indicates the concentration of the analyte tested was either not detected or below the RLs.
- Definitions: ND=not detected; NEG=negative; POS=positive; COL=colonies; RLs=laboratory reporting limits; L/A=laboratory accident; TNTC=too numerous to count
- A result marked with "DRY" indicates that the result was calculated and reported on a dry weight basis.
- All analysis, except field tests are conducted in Southampton, PA unless otherwise identified.
- The test "pH lab" is analyzed upon receipt at the laboratory, the result will not be suitable for regulatory purposes.
- The reported results relate only to the samples.
- QC NELAP ID's: PA 09-00131, NJ PA166, FL E87954, NY 11223, CT PH-0768, DE PA-018, KY 90228, MD 206, EPA PA00018, Bioassay: PA 09-03574, NJ PA034, FL E87953, KS E10373, SC 89020001.
- QC STATE ID's: Wind Gap, NJ PA001, PA 48-01334; E RUTHERFORD NJ02015; Vineland NJ06005; Reading PA 06-03543.
- All samples are collected as "grab" samples unless otherwise identified.
- MCL= is the EPA recommended "maximum contaminant level" for a parameter. PLs=customer specific permit limits.
- The test results meet all requirements of NELAC unless otherwise specified.
- The report shall not be reproduced except in full without the written consent of the laboratory.

Exact copy
11-23-2010

Approved
11 OCT 2010
Thomas J. Hines, President

QC Laboratories**Analytical Report**

Account No: W05899, CHARLES RIVER LABORATORIES, INC.
Project No: W05899, CHARLES RIVER LABORATORIES, INC.

P.O. No: 6600061155
PWSID No:

Inv. No: 1249368

Regulatory authorities are assessing substantial fines for testing omissions. Please track your sample collections and results on a weekly, monthly, or quarterly basis to ensure compliance. QC's internet program 'LIVE ACCESS' will provide you with real-time access to collection dates and results. Please contact Customer Service for further information on acquiring LIVE ACCESS.

Approved
[Signature]
11 OCT 2010

*Exact copy
11/23/2010*

Thomas J. Hines
Thomas J. Hines, President



QC Laboratories

Analytical Report



Regarding:

MATTHEW VANEMAN
CHARLES RIVER LABORATORIES, INC.
905 SHEEHY DRIVE
HORSHAM, PA 19044

MATTHEW VANEMAN
CHARLES RIVER LABORATORIES, INC.
905 SHEEHY DRIVE
HORSHAM, PA 19044

Account No: W05899, CHARLES RIVER LABORATORIES, INC.
Project No: W05899, CHARLES RIVER LABORATORIES, INC.

P.O. No: 6600061155
PWSID No:

Inv. No: 1258935

Sample Number L3539696-1 Sample Description
DRINKING WATER - IN VITRO
Received Temp: 40 F Iced (Y/N): Y

Samp. Date/Time/Temp
11/05/10 12:45pm NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
-----------	--------	--------	-----	--------------------------

ENVIRONMENTAL MICROBIOLOGY

COLIFORM-MF SM 9222B
STANDARD PLATE COUNT SM 9215B

<1 col/100ml
14 col/ml

1. col/100ml
1. col/ml

11/06/10 01:12PM AMD
11/06/10 06:26AM CAS

FIELD SERVICES

CHLORINE RESIDUAL LOW LEVEL- SM 4500CL G
FIELD

< 0.02

mg/l

11/05/10 12:50PM JCN

Sample Number L3539696-2 Sample Description
DRINKING WATER - FORMULATION
Received Temp: 40 F Iced (Y/N): Y

Samp. Date/Time/Temp
11/05/10 12:58pm NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
-----------	--------	--------	-----	--------------------------

ENVIRONMENTAL MICROBIOLOGY

COLIFORM-MF SM 9222B
STANDARD PLATE COUNT SM 9215B

<1 col/100ml
<1 col/ml

1. col/100ml
1. col/ml

11/06/10 01:12PM AMD
11/06/10 06:26AM CAS

FIELD SERVICES

CHLORINE RESIDUAL LOW LEVEL- SM 4500CL G
FIELD

< 0.02

mg/l

11/05/10 01:03PM JCN

Sample Number L3539696-3 Sample Description
DRINKING WATER - FILL STATION
Received Temp: 40 F Iced (Y/N): Y

Samp. Date/Time/Temp
11/05/10 01:03pm NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
-----------	--------	--------	-----	--------------------------

ENVIRONMENTAL MICROBIOLOGY

COLIFORM-MF SM 9222B
STANDARD PLATE COUNT SM 9215B

<1 col/100ml
<1 col/ml

1. col/100ml
1. col/ml

11/06/10 01:12PM AMD
11/06/10 06:26AM CAS

FIELD SERVICES

CHLORINE RESIDUAL LOW LEVEL- SM 4500CL G
FIELD

0.84

mg/l

11/05/10 01:05PM JCN

Page 1 of 4

This report is a revision of report number 1583799
Serial Number: 1584209

Thomas J. Hines, President

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1205 Industrial Blvd., P.O. Box 514, Southampton, PA 18966-0514 Phone: 215-355-3900 Fax: 215-355-7231 www.qclaboratories.com

QC Laboratories

Analytical Report



Account No: W05899, CHARLES RIVER LABORATORIES, INC.
Project No: W05899, CHARLES RIVER LABORATORIES, INC.

P.O. No: 6600061155
PWSID No:

Inv. No: 1258935

Sample Number L3539696-4 Sample Description
DRINKING WATER - ANALYTICAL
Received Temp: 40 F Iced (Y/N): Y

Samp. Date/Time/Temp
11/05/10 01:07pm NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/06/10 01:12PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	11/06/10 06:26AM CAS
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL- FIELD	SM 4500CL G	< 0.02	mg/l	11/05/10 01:09PM JCN

Sample Number L3539696-5 Sample Description
DRINKING WATER - ROOM 36 RACK 289
Received Temp: 40 F Iced (Y/N): Y

Samp. Date/Time/Temp
11/05/10 01:11pm NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/06/10 01:12PM AMD
STANDARD PLATE COUNT	SM 9215B	1 col/ml	1. col/ml	11/06/10 06:26AM CAS
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL- FIELD	SM 4500CL G	0.76	mg/l	11/05/10 01:14PM JCN

Sample Number L3539696-6 Sample Description
DRINKING WATER - ROOM 47 RACK 666
Received Temp: 40 F Iced (Y/N): Y

Samp. Date/Time/Temp
11/05/10 01:15pm NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
ENVIRONMENTAL MICROBIOLOGY				
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/06/10 01:12PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	11/06/10 06:26AM CAS
FIELD SERVICES				
CHLORINE RESIDUAL LOW LEVEL- FIELD	SM 4500CL G	0.80	mg/l	11/05/10 01:17PM JCN

L3539696-1:

Page 2 of 4

This report is a revision of report number 1583799
Serial Number: 1584209

Thomas J. Hines
Thomas J. Hines, President

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AD 29/DEC/10

QC Laboratories

Analytical Report



Account No: W05899, CHARLES RIVER LABORATORIES, INC.
Project No: W05899, CHARLES RIVER LABORATORIES, INC.

P.O. No: 6600061155
PWSID No:

Inv. No: 1258935

1. A water supply is considered bacteriologically "SAFE" if no Coliform bacteria are detected. To be considered "SAFE" your report should indicate "<1 col/100ml" or "NEG" for the Coliform Test. If your report indicates a positive result "POS" or a value of one (1) or greater then your supply is "UNSAFE FOR DRINKING" contact your local Health Dept. or QC for advice.

L3539696-2:

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L3539696-6:

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- QC STATE ID's: Wind Gap, NJ PA001, PA 48-01334; E RUTHERFORD NJ02015; Vineland NJ06005; Reading PA 06-03543.
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Page 3 of 4

This report is a revision of report number 1583799
Serial Number: 1584209

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AS 29 DEC 10

Approved
Thomas J. Hines
17 Dec 2010
Thomas J. Hines, President

QC Laboratories

Analytical Report



Account No: W05899, CHARLES RIVER LABORATORIES, INC.
Project No: W05899, CHARLES RIVER LABORATORIES, INC.

P.O. No: 6600061155
PWSID No:

Inv. No: 1258935

Regulatory authorities are assessing substantial fines for testing omissions. Please track your sample collections and results on a weekly, monthly, or quarterly basis to ensure compliance. QC's internet program 'LIVE ACCESS' will provide you with real-time access to collection dates and results. Please contact Customer Service for further information on acquiring LIVE ACCESS.

Approved
[Signature]
17 Dec 2010

Page 4 of 4

This report is a revision of report number 1583799
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Thomas J. Hines
Thomas J. Hines, President

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PS 29 DEC 10



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Analysis Report

Page 1 of 3

Sample Description: #2 Formulation Lab (905) Grab Water Sample
Semi-Annual

LLI Sample # WW 6036579
LLI Group # 1203845
Account # 02423

Project Name: Semi-Annual

Collected: 07/20/2010 10:45 by EA

Charles River Laboratories

905 Sheehy Dr.

Horsham PA 19044-1297

Submitted: 07/20/2010 16:00

Reported: 07/29/2010 12:02

Discard: 08/13/2010

2FRM-

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Method Detection Limit*	As Received Limit of Quantitation	Dilution Factor
Herbicides		SW-846 8151A	ug/l	ug/l	ug/l	
01856	2,4-D	94-75-7	N.D.	0.15	0.48	1
01856	Dalapon	75-99-0	N.D.	0.24	1.2	1
01856	2,4-DB	94-82-6	N.D.	0.29	0.97	1
01856	Dicamba	1918-00-9	N.D.	0.077	0.29	1
01856	Dinoseb	88-85-7	N.D.	0.097	0.48	1
01856	2,4-DP (Dichlorprop)	120-36-5	N.D.	0.15	0.48	1
01856	MCPA	94-74-6	N.D.	290	970	1
01856	MCPP	93-65-2	N.D.	180	190	1
01856	Pentachlorophenol	87-86-5	N.D.	0.040	0.048	1
01856	2,4,5-T	93-76-5	N.D.	0.014	0.048	1
01856	2,4,5-TP	93-72-1	N.D.	0.030	0.048	1

Due to interfering peaks on the chromatogram, the values reported for various compounds represent the lowest reporting limits attainable.

Pesticides/PCBs		EPA 608	ug/l	ug/l	ug/l	
00178	Aldrin	309-00-2	N.D.	0.0041	0.020	1
00178	Alpha BHC	319-84-6	N.D.	0.0026	0.0098	1
00178	Beta BHC	319-85-7	N.D.	0.018	0.059	1
00178	Gamma BHC - Lindane	58-89-9	N.D.	0.0045	0.0098	1
00178	Chlordane	57-74-9	N.D.	0.068	0.49	1
00178	p,p-DDD	72-54-8	N.D.	0.0039	0.020	1
00178	p,p-DDE	72-55-9	N.D.	0.0049	0.020	1
00178	p,p-DDT	50-29-3	N.D.	0.011	0.029	1
00178	Delta BHC	319-86-8	N.D.	0.0041	0.0098	1
00178	Dieldrin	60-57-1	N.D.	0.0039	0.020	1
00178	Endosulfan I	959-98-8	N.D.	0.0029	0.0098	1
00178	Endosulfan II	33213-65-9	N.D.	0.0039	0.020	1
00178	Endosulfan Sulfate	1031-07-8	N.D.	0.0049	0.020	1
00178	Endrin	72-20-8	N.D.	0.0039	0.020	1
00178	Endrin Aldehyde	7421-93-4	N.D.	0.020	0.098	1
00178	Heptachlor	76-44-8	N.D.	0.0039	0.0098	1
00178	Heptachlor Epoxide	1024-57-3	N.D.	0.0029	0.0098	1
00178	PCB-1016	12674-11-2	N.D.	0.098	0.49	1
00178	PCB-1221	11104-28-2	N.D.	0.16	0.49	1
00178	PCB-1232	11141-16-5	N.D.	0.14	0.49	1
00178	PCB-1242	53469-21-9	N.D.	0.098	0.49	1
00178	PCB-1248	12672-29-6	N.D.	0.098	0.49	1
00178	PCB-1254	11097-69-1	N.D.	0.098	0.49	1
00178	PCB-1260	11096-82-5	N.D.	0.098	0.49	1
00178	Toxaphene	8001-35-2	N.D.	0.29	0.98	1

Metals		EPA 200.7 rev 4.4	mg/l	mg/l	mg/l	
07035	Arsenic	7440-38-2	N.D.	0.0098	0.0200	1
07046	Barium	7440-39-3	N.D.	0.00060	0.0050	1
07049	Cadmium	7440-43-9	N.D.	0.0020	0.0050	1
07051	Chromium	7440-47-3	N.D.	0.0034	0.0150	1
07055	Lead	7439-92-1	N.D.	0.0069	0.0150	1
07036	Selenium	7782-49-2	N.D.	0.0089	0.0200	1
07066	Silver	7440-22-4	N.D.	0.0023	0.0050	1

*=This limit was used in the evaluation of the final result

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TSN-40

Approved
06 Aug 2010



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Analysis Report

Page 2 of 3

Sample Description: #2 Formulation Lab (905) Grab Water Sample
Semi-Annual

LLI Sample # WW 6036579
LLI Group # 1203845
Account # 02423

Project Name: Semi-Annual

Collected: 07/20/2010 10:45 by EA

Charles River Laboratories

905 Sheehy Dr.

Horsham PA 19044-1297

Submitted: 07/20/2010 16:00

Reported: 07/29/2010 12:02

Discard: 08/13/2010

2FRM-

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Method Detection Limit*	As Received Limit of Quantitation	Dilution Factor
Metals						
07072	Zinc	EPA 200.7 rev 4.4 7440-66-6	mg/l N.D.	mg/l 0.0081	mg/l 0.0200	1
00259	Mercury	EPA 245.1 rev 3 7439-97-6	mg/l N.D.	mg/l 0.000056	mg/l 0.00020	1
Wet Chemistry						
01505	Bromide	EPA 300.0 24959-67-9	mg/l N.D.	mg/l 2.0	mg/l 2.5	5
00224	Chloride	16887-00-6	N.D.	1.0	2.0	5
01504	Fluoride	16984-48-8	N.D.	0.40	0.50	5
00368	Nitrate Nitrogen	14797-55-8	N.D.	0.25	0.50	5
01506	Nitrite Nitrogen	14797-65-0	N.D.	0.40	0.50	5
00228	Sulfate	14808-79-8	N.D.	1.5	5.0	5
00226	Ortho-Phosphate as P	EPA 365.3 7723-14-0	mg/l N.D.	mg/l 0.030	mg/l 0.090	1

General Sample Comments

PA DEP Lab Certification ID 36-00037, Expiration Date: 1/31/11

All QC is compliant unless otherwise noted. Please refer to the Quality Control Summary for overall QC performance data and associated samples.

Laboratory Sample Analysis Record

CAT No.	Analysis Name	Method	Trial#	Batch#	Analysis Date and Time	Analyst	Dilution Factor
01856	Herbicides in Water	SW-846 8151A	1	102040037A	07/26/2010 22:26	John W Perkins	1
00178	Pesticides/PCB's in Water	EPA 608	1	102030016A	07/23/2010 18:01	Lisa A Reinert	1
10241	Method 608 Water Extraction	EPA 608	1	102030016A	07/23/2010 02:40	Sherry L Morrow	1
00816	Water Sample Herbicide Extract	SW-846 8151A	1	102040037A	07/23/2010 02:30	Karen L Beyer	1
07035	Arsenic	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:42	Tara L Snyder	1
07046	Barium	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:42	Tara L Snyder	1
07049	Cadmium	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:42	Tara L Snyder	1
07051	Chromium	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:42	Tara L Snyder	1
07055	Lead	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:42	Tara L Snyder	1
07036	Selenium	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:42	Tara L Snyder	1
07066	Silver	EPA 200.7 rev 4.4	1	102025716002	07/24/2010 01:31	John W Yanzuk II	1
07072	Zinc	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:42	Tara L Snyder	1
00259	Mercury	EPA 245.1 rev 3	1	102025714001	07/22/2010 06:48	Damary Valentin	1
05716	EPA 600 ICP Digest (tot rec)	EPA 200.7 rev 4.4	1	102025716002	07/22/2010 09:05	Denise K Connors	1
05714	PW/WW Hg Digest	EPA 245.1 rev 3	1	102025714001	07/21/2010 15:15	Nelli S Markaryan	1
01505	Bromide	EPA 300.0	1	10202196601A	07/21/2010 18:38	Ashley M Adams	5
00224	Chloride	EPA 300.0	1	10202196601A	07/21/2010 18:38	Ashley M Adams	5

*This limit was used in the evaluation of the final result

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06 Aug 2010



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Analysis Report

Page 3 of 3

Sample Description: #2 Formulation Lab (905) Grab Water Sample
Semi-Annual

LLI Sample # WW 6036579
LLI Group # 1203845
Account # 02423

Project Name: Semi-Annual

Collected: 07/20/2010 10:45 by EA

Charles River Laboratories

905 Sheehy Dr.

Horsham PA 19044-1297

Submitted: 07/20/2010 16:00

Reported: 07/29/2010 12:02

Discard: 08/13/2010

2FRM-

Laboratory Sample Analysis Record

CAT No.	Analysis Name	Method	Trial#	Batch#	Analysis Date and Time	Analyst	Dilution Factor
01504	Fluoride	EPA 300.0	1	10202196601A	07/21/2010 18:38	Ashley M Adams	5
00368	Nitrate Nitrogen	EPA 300.0	1	10202196601A	07/21/2010 18:38	Ashley M Adams	5
01506	Nitrite Nitrogen	EPA 300.0	1	10202196601A	07/21/2010 18:38	Ashley M Adams	5
00228	Sulfate	EPA 300.0	1	10202196601A	07/21/2010 18:38	Ashley M Adams	5
00226	Ortho-Phosphate as P	EPA 365.3	1	10202022601A	07/21/2010 00:20	Daniel S Smith	1

Approved
[Signature]
06 Aug 2010

*This limit was used in the evaluation of the final result

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[Signature]



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Analysis Report

Page 1 of 3

Sample Description: #1 905 Analytical Lab Grab Water Sample
Semi-Annual

LLI Sample # WW 6036580
LLI Group # 1203845
Account # 02423

Project Name: Semi-Annual

Collected: 07/20/2010 10:55 by EA

Charles River Laboratories
905 Sheehy Dr.
Horsham PA 19044-1297

Submitted: 07/20/2010 16:00

Reported: 07/29/2010 12:02

Discard: 08/13/2010

1905-

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Method Detection Limit*	As Received Limit of Quantitation	Dilution Factor
Herbicides		SW-846 8151A	ug/l	ug/l	ug/l	
01856	2,4-D	94-75-7	N.D.	0.16	0.50	1
01856	Dalapon	75-99-0	N.D.	0.25	1.3	1
01856	2,4-DB	94-82-6	N.D.	0.30	1.0	1
01856	Dicamba	1918-00-9	N.D.	0.081	0.30	1
01856	Dinoseb	88-85-7	N.D.	0.10	0.50	1
01856	2,4-DP (Dichlorprop)	120-36-5	N.D.	0.20	0.50	1
01856	MCPA	94-74-6	N.D.	300	1,000	1
01856	MCPP	93-65-2	N.D.	50	200	1
01856	Pentachlorophenol	87-86-5	N.D.	0.060	0.060	1
01856	2,4,5-T	93-76-5	N.D.	0.015	0.050	1
01856	2,4,5-TP	93-72-1	N.D.	0.030	0.050	1

Due to interfering peaks on the chromatogram, the values reported for various compounds represent the lowest reporting limits attainable.

Pesticides/PCBs		EPA 608	ug/l	ug/l	ug/l	
00178	Aldrin	309-00-2	N.D.	0.0041	0.019	1
00178	Alpha BHC	319-84-6	N.D.	0.0026	0.0097	1
00178	Beta BHC	319-85-7	N.D.	0.018	0.058	1
00178	Gamma BHC - Lindane	58-99-9	N.D.	0.0044	0.0097	1
00178	Chlordane	57-74-9	N.D.	0.068	0.48	1
00178	p,p-DDD	72-54-8	N.D.	0.0039	0.019	1
00178	p,p-DDE	72-55-9	N.D.	0.0048	0.019	1
00178	p,p-DDT	50-29-3	N.D.	0.011	0.029	1
00178	Delta BHC	319-86-8	N.D.	0.0041	0.0097	1
00178	Dieldrin	60-57-1	N.D.	0.0039	0.019	1
00178	Endosulfan I	959-98-8	N.D.	0.0029	0.0097	1
00178	Endosulfan II	33213-65-9	N.D.	0.0039	0.019	1
00178	Endosulfan Sulfate	1031-07-8	N.D.	0.0048	0.019	1
00178	Endrin	72-20-8	N.D.	0.0039	0.019	1
00178	Endrin Aldehyde	7421-93-4	N.D.	0.019	0.097	1
00178	Heptachlor	76-44-8	N.D.	0.0039	0.0097	1
00178	Heptachlor Epoxide	1024-57-3	N.D.	0.0029	0.0097	1
00178	PCB-1016	12674-11-2	N.D.	0.097	0.48	1
00178	PCB-1221	11104-28-2	N.D.	0.15	0.48	1
00178	PCB-1232	11141-16-5	N.D.	0.14	0.48	1
00178	PCB-1242	53469-21-9	N.D.	0.097	0.48	1
00178	PCB-1248	12672-29-6	N.D.	0.097	0.48	1
00178	PCB-1254	11097-69-1	N.D.	0.097	0.48	1
00178	PCB-1260	11096-82-5	N.D.	0.097	0.48	1
00178	Toxaphene	8001-35-2	N.D.	0.29	0.97	1

Metals		EPA 200.7 rev 4.4	mg/l	mg/l	mg/l	
07035	Arsenic	7440-38-2	N.D.	0.0098	0.0200	1
07046	Barium	7440-39-3	N.D.	0.00060	0.0050	1
07049	Cadmium	7440-43-9	N.D.	0.0020	0.0050	1
07051	Chromium	7440-47-3	N.D.	0.0034	0.0150	1
07055	Lead	7439-92-1	N.D.	0.0069	0.0150	1
07036	Selenium	7782-49-2	N.D.	0.0089	0.0200	1
07066	Silver	7440-22-4	N.D.	0.0023	0.0050	1

*=This limit was used in the evaluation of the final result

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TT-23 Nov 10

Approved
06 Aug 2010



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Analysis Report

Page 2 of 3

Sample Description: #1 905 Analytical Lab Grab Water Sample
Semi-Annual

LLI Sample # WW 6036580
LLI Group # 1203845
Account # 02423

Project Name: Semi-Annual

Collected: 07/20/2010 10:55 by EA

Charles River Laboratories

905 Sheehy Dr.

Horsham PA 19044-1297

Submitted: 07/20/2010 16:00

Reported: 07/29/2010 12:02

Discard: 08/13/2010

1905-

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Method Detection Limit*	As Received Limit of Quantitation	Dilution Factor
Metals						
07072	Zinc	EPA 200.7 rev 4.4 7440-66-6	mg/l N.D.	mg/l 0.0081	mg/l 0.0200	1
00259	Mercury	EPA 245.1 rev 3 7439-97-6	mg/l N.D.	mg/l 0.000056	mg/l 0.00020	1
Wet Chemistry						
01505	Bromide	EPA 300.0 24959-67-9	mg/l N.D.	mg/l 2.0	mg/l 2.5	5
00224	Chloride	16887-00-6	N.D.	1.0	2.0	5
01504	Fluoride	16984-48-8	N.D.	0.40	0.50	5
00368	Nitrate Nitrogen	14797-55-8	N.D.	0.25	0.50	5
01506	Nitrite Nitrogen	14797-65-0	N.D.	0.40	0.50	5
00228	Sulfate	14808-79-8	N.D.	1.5	5.0	5
00226	Ortho-Phosphate as P	EPA 365.3 7723-14-0	mg/l N.D.	mg/l 0.030	mg/l 0.090	1

General Sample Comments

PA DEP Lab Certification ID 36-00037, Expiration Date: 1/31/11

All QC is compliant unless otherwise noted. Please refer to the Quality Control Summary for overall QC performance data and associated samples.

Approved
[Signature]
06 Aug 2010

Laboratory Sample Analysis Record

CAT No.	Analysis Name	Method	Trial#	Batch#	Analysis Date and Time	Analyst	Dilution Factor
01856	Herbicides in Water	SW-846 8151A	1	102040037A	07/26/2010 22:54	John W Perkins	1
00178	Pesticides/PCB's in Water	EPA 608	1	102030016A	07/23/2010 18:13	Lisa A Reinert	1
10241	Method 608 Water Extraction	EPA 608	1	102030016A	07/23/2010 02:40	Sherry L Morrow	1
00816	Water Sample Herbicide Extract	SW-846 8151A	1	102040037A	07/23/2010 02:30	Karen L Beyer	1
07035	Arsenic	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:52	Tara L Snyder	1
07046	Barium	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:52	Tara L Snyder	1
07049	Cadmium	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:52	Tara L Snyder	1
07051	Chromium	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:52	Tara L Snyder	1
07055	Lead	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:52	Tara L Snyder	1
07036	Selenium	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:52	Tara L Snyder	1
07066	Silver	EPA 200.7 rev 4.4	1	102025716002	07/24/2010 01:34	John W Yanzuk II	1
07072	Zinc	EPA 200.7 rev 4.4	1	102025716002	07/23/2010 03:52	Tara L Snyder	1
00259	Mercury	EPA 245.1 rev 3	1	102025714001	07/22/2010 06:52	Damary Valentin	1
05716	EPA 600 ICP Digest (tot rec)	EPA 200.7 rev 4.4	1	102025716002	07/22/2010 09:05	Denise K Connors	1
05714	PW/WW Hg Digest	EPA 245.1 rev 3	1	102025714001	07/21/2010 15:15	Nelli S Markaryan	1
01505	Bromide	EPA 300.0	1	10202196601A	07/21/2010 18:56	Ashley M Adams	5
00224	Chloride	EPA 300.0	1	10202196601A	07/21/2010 18:56	Ashley M Adams	5

*This limit was used in the evaluation of the final result

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**Analysis Report**

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Page 3 of 3

Sample Description: #1 905 Analytical Lab Grab Water Sample
Semi-Annual

LLI Sample # WW 6036580
LLI Group # 1203845
Account # 02423

Project Name: Semi-Annual

Collected: 07/20/2010 10:55 by EA

Charles River Laboratories

905 Sheehy Dr.

Horsham PA 19044-1297

Submitted: 07/20/2010 16:00

Reported: 07/29/2010 12:02

Discard: 08/13/2010

1905-

Laboratory Sample Analysis Record

CAT No.	Analysis Name	Method	Trial#	Batch#	Analysis Date and Time	Analyst	Dilution Factor
01504	Fluoride	EPA 300.0	1	10202196601A	07/21/2010 18:56	Ashley M Adams	5
00368	Nitrate Nitrogen	EPA 300.0	1	10202196601A	07/21/2010 18:56	Ashley M Adams	5
01506	Nitrite Nitrogen	EPA 300.0	1	10202196601A	07/21/2010 18:56	Ashley M Adams	5
00228	Sulfate	EPA 300.0	1	10202196601A	07/21/2010 18:56	Ashley M Adams	5
00226	Ortho-Phosphate as P	EPA 365.3	1	10202022601A	07/21/2010 00:20	Daniel S Smith	1

Approved
M. J. W.
06 Aug 2010

*This limit was used in the evaluation of the final result

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Explanation of Symbols and Abbreviations

The following defines common symbols and abbreviations used in reporting technical data:

N.D.	none detected	BMQL	Below Minimum Quantitation Level
TNTC	Too Numerous To Count	MPN	Most Probable Number
IU	International Units	CP Units	cobalt-chloroplatinate units
umhos/cm	micromhos/cm	NTU	nephelometric turbidity units
C	degrees Celsius	F	degrees Fahrenheit
meq	milliequivalents	lb.	pound(s)
g	gram(s)	kg	kilogram(s)
ug	microgram(s)	mg	milligram(s)
ml	milliliter(s)	l	liter(s)
m3	cubic meter(s)	ul	microliter(s)
<	less than - The number following the sign is the <u>limit of quantitation</u> , the smallest amount of analyte which can be reliably determined using this specific test.		
>	greater than		
J	estimated value - The result is \geq the Method Detection Limit (MDL) and $<$ the Limit of Quantitation (LOQ).		
ppm	parts per million - One ppm is equivalent to one milligram per kilogram (mg/kg), or one gram per million grams. For aqueous liquids, ppm is usually taken to be equivalent to milligrams per liter (mg/l), because one liter of water has a weight very close to a kilogram. For gases or vapors, one ppm is equivalent to one microliter of gas per liter of gas.		
ppb	parts per billion		
Dry weight basis	Results printed under this heading have been adjusted for moisture content. This increases the analyte weight concentration to approximate the value present in a similar sample without moisture. All other results are reported on an as-received basis.		

U.S. EPA CLP Data Qualifiers:

Organic Qualifiers		Inorganic Qualifiers	
A	TIC is a possible aldol-condensation product	B	Value is $<$ CRDL, but \geq IDL
B	Analyte was also detected in the blank	E	Estimated due to interference
C	Pesticide result confirmed by GC/MS	M	Duplicate injection precision not met
D	Compound quantitated on a diluted sample	N	Spike sample not within control limits
E	Concentration exceeds the calibration range of the instrument	S	Method of standard additions (MSA) used for calculation
N	Presumptive evidence of a compound (TICs only)	U	Compound was not detected
P	Concentration difference between primary and confirmation columns $>25\%$	W	Post digestion spike out of control limits
U	Compound was not detected	*	Duplicate analysis not within control limits
X,Y,Z	Defined in case narrative	+	Correlation coefficient for MSA <0.995

Analytical test results for methods listed on the laboratories' accreditation scope meet all requirements of NELAP unless otherwise noted under the individual analysis.

Measurement uncertainty values, as applicable, are available upon request.

Tests results relate only to the sample tested. Clients should be aware that a critical step in a chemical or microbiological analysis is the collection of the sample. Unless the sample analyzed is truly representative of the bulk of material involved, the test results will be meaningless. If you have questions regarding the proper techniques of collecting samples, please contact us. We cannot be held responsible for sample integrity, however, unless sampling has been performed by a member of our staff. This report shall not be reproduced except in full, without the written approval of the laboratory.

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ENRICHMENT ANALYSES



A Nestle' Purina PetCare Company
Checkerboard Square • St. Louis, MO 63164

ANALYSIS REPORT

To: JACKY JUDD (FS)
ANIMAL SPECIALTIES
2400 MILFORD SQUARE PIKE
QUAKERTOWN PA 18951

CC:

Page 1 of 2

DUPLICATE

Sample No.: L1015045-1 Receipt Date: 04/16/2010
Report Date: 04/28/2010

NYLABONE PETITE BONE, LOT 4/12/10

Test Code	Assay / Analyte	Result	Units
AS	Arsenic		
	Arsenic	< 0.20	ppm
CDF	Cadmium		
	Cadmium	< 0.0500	ppm
PB	Lead		
	Lead	< 0.0500	ppm
ORGP	Organophosphate pesticides		
	Diazinon	< 0.0200	ppm
	Disulfoton	< 0.0200	ppm
	Ethion	< 0.0200	ppm
	Malathion	< 0.0200	ppm
	Methyl Parathion	< 0.0200	ppm
	Parathion	< 0.0200	ppm
	Thimet	< 0.0200	ppm
	Thiodan	< 0.0200	ppm
	Trithion	< 0.0200	ppm
RSPB	Organochlorine pest.&PCB's		
	Heptachlor Epoxide	< 0.0200	ppm
	Heptachlor	< 0.0200	ppm
	DDE	< 0.0200	ppm
	Lindane	< 0.0200	ppm
	Endrin	< 0.0200	ppm

Approved
Joseph W. Jh
12-JAN-2011

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MEL 13 JAN 2011

Person responsible for report content: Lynn Loudermilk, Director.

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The symbol "<" or the words "less than" signifies that no analyte was measured at or above the stated lower limit of quantitation of the procedure under the conditions employed. The use of the symbol "<" or the words "less than" does not imply that traces of the analyte were present. The symbol ">" or the term "greater than" signifies that the analyte was determined to be present in an amount greater than the stated level. Samples submitted to NP Analytical Laboratories for testing are retained for a minimum of thirty (30) days after the analysis report is issued when sample stability permits. Requests for extended storage must be made to NP Analytical Laboratories prior to or at the time of sample submission.



A Nestle' Purina PetCare Company
Checkerboard Square • St. Louis, MO 63164

Sample No.: L1015045-1

Received: 04/16/2010

Page 2 of 2

Reported: 04/28/2010

DUPLICATE

NYLABONE PETTITE BONE, LOT 4/12/10

Test Code	Assay / Analyte	Result	Units
RSPB	Organochlorine pest.&PCB's	Mirex	< 0.0200 ppm
		Alpha-BHC	< 0.0200 ppm
		Delta-BHC	< 0.0200 ppm
		Aldrin	< 0.0200 ppm
		Dieldrin	< 0.0200 ppm
		DDT	< 0.0200 ppm
		Chlordane	< 0.0200 ppm
		Methoxychlor	< 0.0200 ppm
		Beta-BHC	< 0.0200 ppm
		HCB	< 0.0200 ppm
		PCB	< 0.150 ppm
AFTX	Aflatoxin screen, ELISA	Aflatoxins	< 5.0 ppb

Approved
Joseph W. Jh
12-Jan-2011

REVIEWED BY

Person responsible for report content: Lynn Loudermilk, Director.

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The symbol "<" or the words "less than" signifies that no analyte was measured at or above the stated lower limit of quantitation of the procedure under the conditions employed. The use of the symbol "<" or the words "less than" does not imply that traces of the analyte were present. The symbol ">" or the term "greater than" signifies that the analyte was determined to be present in an amount greater than the stated level. Samples submitted to NP Analytical Laboratories for testing are retained for a minimum of thirty (30) days after the analysis report is issued when sample stability permits. Requests for extended storage must be made to NP Analytical Laboratories prior to or at the time of sample submission.

APPENDIX 5 - HISTOPATHOLOGICAL REPORT

Note: The Quality Assurance Statement appearing on Page 5 of the Pathology Report includes a typographical error. The date currently appearing for findings submitted to the Study Director, Testing Facility Management, and Lead QAU states that the Draft Pathology Report and Supporting Documentation was submitted on 22-Feb-2011; however, the document was actually submitted on 23-Feb-2011. This typographical error did not impact the study in any way as this had no effect on the study data and the actual date was properly documented and can be verified by other methods.

The Summary and Individual Organ Weights (Absolute, Percent Body Weight, and Percent Brain Weight) (Day 29) tables (Table 2 of the attached Pathology Report; pages 14 through 29) were inadvertently identified with sequential table numbers (Tables 19, 20, 21, 22, 37, 38, 39, and 40) rather than all summary and individual tables being identified as “Table 2”. The incorrect numbering of the tables did not impact the study in any way because all of the appropriate data were presented and evaluated.



FINAL REPORT

Study Phase: Pathology

Test Site Phase Reference No. 0020004832

Testing Facility Study No. TQC00065

Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats

SPONSOR:

Cheminova A/S
P.O. Box 9
DK-7620 Lemvig
DENMARK

TESTING FACILITY:

Charles River Laboratories
Preclinical Services
905 Sheehy Drive, Building A
Horsham, PA 19044
USA

TEST SITE:

Charles River Laboratories
Pathology Associates - Illinois
2255 West Harrison Street
Chicago, IL 60612
USA

Page 1 of 95

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2. LIST OF APPENDICES

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3. COMPLIANCE STATEMENT

The portion of this study performed by Charles River Laboratories, Pathology Associates - Illinois was conducted in compliance with the following Good Laboratory Practice (GLP) regulations:

- Federal Insecticide, Fungicide and Rodenticide Act/Toxic Substances Control Act (FIFRA/TSCA); Good laboratory practice standards; Final Rule 40 C.F.R Part 160/792; August 17, 1989. U.S. Environmental Protection Agency.
- The Organisation for Economic Cooperation and Development (OECD) Principles on Good Laboratory Practice (C[97]186/Final)

This study was conducted in accordance with the procedures described herein. The report represents an accurate and complete record of the results obtained. There were no deviations from the above regulations that affected the overall integrity of the study or the interpretation of the study results and conclusions.

Date: 21-MAR-2012

Carol J. Detrisac, DVM, PhD, DACVP

Study Pathologist

Charles River Laboratories, Pathology Associates – Illinois


4. QUALITY ASSURANCE STATEMENT

This report has been inspected by the Pathology Associates' Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) regulations promulgated by the Environmental Protection Agency (EPA) and the Organisation for Economic Cooperation and Development (OECD). The report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU.

Dates Findings Submitted to:

<u>Dates of Inspection</u>	<u>Phase(s) Inspected</u>	<u>Study Pathologist and Pathology Associates Management</u>	<u>Study Director, Testing Facility Management, and Lead QAU</u>
21-Dec-2010	Tissue Trimming	22-Dec-2010	28-Dec-2010
14-Feb-2011	Draft Pathology Report and Supporting Documentation	15-Feb-2011	22-Feb-2011
20-Mar-2012	Final Pathology Report	20-Mar-2012	22-Mar-2012

In addition to the above-mentioned inspections, process-based and/or routine facility inspections were also conducted during the course of this study. Inspection findings, if any, specific to this study were reported by the QAU to the Study Director and Management and listed as a phase inspected on this QA Statement.


 Enosha Simmons
 Senior Quality Assurance Auditor
 Charles River Laboratories, Pathology Associates

23-MAR-2012
 Date

5. RESPONSIBLE PERSONNEL

Principal Investigator (Histopathology) and
Study Pathologist

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Charles River Pathology Associates
Phone: 312-567-4876
Fax: 312-567-4882
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Research Associate

J. Adam Caulk, BS, HT(ASCP)
Charles River Pathology Associates
Phone: 312-666-1505
Fax: 312-666-1764
Email: james.caulk@crl.com

6. INTRODUCTION

This report presents the pathology findings in rats assigned to the study entitled *Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats* (Study No. TQC00065). The objective of this study was to provide information on the possible adverse effects on CrI:CD (SD) rats resulting from repeated exposure to Malathion Technical over a 28-day exposure period. The study should provide information that can be used in the selection of dosage levels for subsequent studies.

The study was sponsored by Cheminova A/S, Lemvig, Denmark, where M. Jensen served as the Sponsor representative. John F. Barnett, Jr., B.S., Charles River Laboratories, Preclinical Services, Horsham, Pennsylvania, served as the Study Director.

7. MATERIALS AND METHODS

Experimental procedures applicable to pathology investigations are summarized in [Text Table 1](#) and [Text Table 2](#). Deviations to the pathology procedures performed by Charles River Laboratories, Pathology Associates - Illinois are listed in [Appendix 1](#).

Text Table 1
Experimental Design

Dosage Group	Number of Rats		Test Material	Concentration (ppm)	Batch Number
	M	F			
I	15	15	Carrier Control	0	B-TQC00065-A
II	15	15	Malathion Technical	100	B-TQC00065-B
III	15	15	Malathion Technical	500	B-TQC00065-C
IV	15	15	Malathion Technical	5000	B-TQC00065-D
V	15	15	Malathion Technical	10000	B-TQC00065-E

All animals were submitted for necropsy on Day 29. Necropsies were performed and organ weights were collected by Charles River Laboratories, Preclinical Services personnel. Except as noted in [Text Table 2](#) tissues were collected in 10% neutral buffered formalin.

Text Table 2
Tissue Collection and Examination

Provantis Tissue Term	Protocol Tissue Term	Collect	Weigh	Micro Eval	Comment
-	Animal identification	X	-	-	-
-	Gross lesions/masses	X	-	-	-
KIDNEY	Kidney	X	X	X	Paired weight and examination.
LIVER	Liver	X	X	X	-
NOSE, LEVELS 1-5	Nasal Cavity	X	-	X	Collect with sinuses.

Micro Eval = Microscopic Evaluation; X = procedure to be conducted; - = not required.

Tissues required for microscopic evaluation were trimmed, processed routinely, embedded in paraffin, and stained with hematoxylin and eosin (H&E) by Charles River Laboratories, Pathology Associates, Maryland. The nasal tissue was evaluated consistent with the procedure described by Young¹ (levels 2-5), with an additional rostral section to include the nares (level 1). Microscopic evaluation was conducted by the undersigned board-certified veterinary pathologist on nose, kidney and liver tissues from the 0 and 10000 ppm dosage groups. Tissues were evaluated by light microscopy, and the results were entered directly into a validated pathology computer program (Text Table 3) for preparation of data tables.

7.1. Computerized Systems

Critical computerized systems used in the study by the Test Site are listed below (See Text Table 3).

Text Table 3
Computerized Systems

System Name	Version Number	Description of Data Collected and/or Analyzed
Provantis NT 2000	V3.4	Histopathology (Test Site)
See Main Study Report	See Main Study Report	Necropsy and Organ Weight data were collected and tabulated by the Testing Facility

7.2. Disposition of Study Materials

Prior to finalization of the report, pathology materials were sent to Charles River Laboratories, Preclinical Services, Horsham, Pennsylvania, and the Final Report will be sent to the Study Director. The signed hard copy of the pathology report is considered raw data.

8. RESULTS AND DISCUSSIONS

8.1. Gross Pathology

8.1.1. Scheduled Euthanasia Animals (Day 29)

(Table 1, Appendix 2)

No test article-related gross findings were noted. The gross findings observed were considered incidental, of the nature commonly observed in this strain and age of rat, and/or were of similar incidence in control and treated animals and, therefore, were considered unrelated to administration of Malathion Technical.

8.2. Organ Weights

8.2.1. Scheduled Euthanasia Animals (Day 29)

(Table 2, Appendix 2)

Test article-related organ weight changes are summarized in Text Table 4.

Text Table 4
Summary Organ Weight Data – Scheduled Euthanasia (Day 29)

		Males				
Group	Dose (ppm)	I	II	III	IV	V
No. animals per group		0	100	500	5000	10000
		15	15	15	15	15
Liver						
	Absolute value (g)	15.95±1.34	16.12±1.26	16.54±1.80	19.68±2.20 ¹	20.84±2.16 ¹
	% of body weight (g)	4.026±0.164	4.111±0.241	4.167±0.215	5.225±0.228 ¹	5.947±0.326 ¹
	% of brain weight (g)	827.2±84.1	837.8±88.6	840.9±100.6	1008.2±96.1 ¹	1099.9±99.8 ¹
Kidney						
	Absolute value (g)	2.81±0.18	2.87±0.28	2.91±0.28	3.08±0.28	3.00±0.30
	% of body weight (g)	0.713±0.048	0.730±0.050	0.734±0.048	0.820±0.043 ¹	0.858±0.062 ¹
	% of brain weight (g)	145.9±11.7	149.0±17.8	147.9±14.3	158.1±12.9	158.6±16.6
		Females				
Group	Dose (ppm)	I	II	III	IV	V
No. animals per group		0	100	500	5000	10000
		15	15	15	15	15
Liver						
	Absolute value (g)	10.00±1.26	10.42±1.19	9.86±1.31	11.20±1.16 ²	12.06±2.20 ¹
	% of body weight (g)	4.003±0.307	4.089±0.219	4.003±0.265	4.386±0.295 ¹	5.070±0.301 ¹
	% of brain weight (g)	531.4±65.2	561.3±60.1	527.5±62.0	599.8±64.6 ²	650.7±108.2 ¹
Kidney						
	Absolute value (g)	1.87±0.13	1.97±0.21	1.94±0.16	2.03±0.14	2.04±0.21
	% of body weight (g)	0.753±0.042	0.777±0.082	0.791±0.043	0.802±0.088	0.868±0.071 ¹
	% of brain weight (g)	99.7±7.8	106.0±9.4	104.1±8.5	108.8±5.9 ¹	110.3±8.6 ¹

refer to data tables for actual significance levels and tests used

¹ significantly different from the carrier control group value (p≤0.01)

² significantly different from the carrier control group value (p≤0.05)

There was an effect of decrease in terminal body weights in Groups IV and V males and Group V females. The seemingly significant effect of dietary Malathion Technical on male kidney weights as a percentage of body weight is thus considered equivocal. Dietary Malathion Technical at either 5000 ppm or 10000 ppm had effect on the following organ weights: liver in males and liver and kidney in females. No other test article-related organ weight changes were noted.

8.3. Histopathology

8.3.1. Scheduled Euthanasia (Day 29)

(Table 3, Appendix 2)

Test article-related microscopic findings are summarized in Text Table 5.

Text Table 5
Summary Microscopic Findings – Scheduled Euthanasia (Day 29)

	Males		Females	
	I	V	I	V
	0	10000	0	10000
Group Dose (ppm) No. animals examined	15	15	15	15
Nose, Level 2 (No. Examined)	15	15	15	15
Depletion, Goblet Cell	(0) ^a	(15)	(0)	(14)
Minimal	0	1	0	4
Mild	0	3	0	6
Moderate	0	9	0	4
Marked	0	2	0	0
Nose, Level 3 (No. Examined)	15	15	15	15
Hyperplasia, Olfactory Epithelium	(0)	(15)	(0)	(15)
Minimal	0	3	0	6
Mild	0	12	0	9
Nose, Level 4 (No. Examined)	15	15	15	15
Hyperplasia, Olfactory Epithelium	(0)	(15)	(0)	(15)
Minimal	0	0	0	2
Mild	0	3	0	9
Moderate	0	12	0	4
Nose, Level 5 (No. Examined)	15	14	14	14
Hyperplasia, Olfactory Epithelium	(0)	(14)	(0)	(14)
Minimal	0	0	0	1
Mild	0	2	0	5
Moderate	0	12	0	8

^a Numbers in parentheses represent the number of animals with the finding.

Hyperplasia of olfactory epithelium consisted of increased numbers of nuclei. The hyperplasia was judged to be minimal when there was preservation of the nuclear free layer, mild when there was loss of the nuclear free layer and moderate when the olfactory epithelium had no nuclear free layer and the surface of the normally straight lining was undulating.

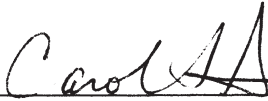
Hepatocellular degeneration, a combination of cellular hypertrophy and clumping of basophilic material in the cytoplasm, was present in two male livers. This finding may have been related to the increases in organ weight, but due to the small numbers of animals affected, this change was considered equivocal.

Other microscopic findings observed were considered incidental, of the nature commonly observed in this strain and age of rat, and/or were of similar incidence and severity in control and treated animals and, therefore, were considered unrelated to administration of Malathion Technical.

9. CONCLUSIONS

Oral (diet) administration of Malathion Technical to rats for 28 days at concentration of 10,000 ppm resulted in organ weight increases in the liver (males and females) and kidney (females only). There were no microscopic correlates for these organ weight changes. Microscopic findings related to the test article in rats provided diet at 10,000 ppm Malathion Technical were present in Nose, level 2 (goblet cell depletion) and Nose, levels 3, 4 and 5 (olfactory hyperplasia).

10. REPORT APPROVAL



Date: 21-MAR-2012

Carol J. Detrisac, DVM, PhD, DACVP

Study Pathologist

Charles River Laboratories, Pathology Associates – Illinois

11. REFERENCES

- ¹ Young, J.T., Histopathologic Examination of the Rat Nasal Cavity. *Fund. Appl. Toxicol.* 1:309-312, 1981.

Table 1
Pathology - Intergroup Comparison of Gross Pathology Observations (Day 29)

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PTA005-01/04

Pathology - Intergroup Comparison of Gross Pathology Observations
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:53

		--- MALES ---		--- FEMALES ---	
		0	10000	0	10000
		ppm	ppm	ppm	ppm
Removal Reason: SCHEDULE SACRIFICED		15	15	15	15
		(15)	(15)	(15)	(15)
KIDNEY;					
Submitted.....		(15)	(15)	(15)	(15)
No Visible Lesions.....		14	15	15	15
Tan Area; right		1	0	0	0
LIVER;					
Submitted.....		(15)	(15)	(15)	(15)
No Visible Lesions.....		15	15	15	15
NOSE, LEVEL 1;					
Submitted.....		(15)	(15)	(15)	(15)
No Visible Lesions.....		15	15	15	15
NOSE, LEVEL 2;					
Submitted.....		(15)	(15)	(15)	(15)
No Visible Lesions.....		15	15	15	15
NOSE, LEVEL 3;					
Submitted.....		(15)	(15)	(15)	(15)
No Visible Lesions.....		15	15	15	15
NOSE, LEVEL 4;					
Submitted.....		(15)	(15)	(15)	(15)
No Visible Lesions.....		15	15	15	15
NOSE, LEVEL 5;					
Submitted.....		(15)	(15)	(15)	(15)
No Visible Lesions.....		15	15	15	15
SKIN;					
Submitted.....		(1)	(1)	(0)	(0)
No Visible Lesions.....		0	0	0	0
Scab		1	0	0	0
Abrasion		0	1	0	0
EYE;					
Submitted.....		(0)	(0)	(1)	(0)
No Visible Lesions.....		0	0	0	0
Lesion		0	0	1	0

Table 2
Summary and Individual Organ Weights (Absolute, Percent Body Weight, and Percent
Brain Weight) (Day 29)

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 19 (PAGE 1): TERMINAL BODY WEIGHTS, ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM) ^a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
TERMINAL BODY WEIGHT	MEAN±S.D.	395.9 ± 27.3	392.1 ± 18.7	396.9 ± 38.1	376.1 ± 34.3	350.7 ± 33.5**
BRAIN	MEAN±S.D.	1.934 ± 0.107	1.931 ± 0.098	1.972 ± 0.092	1.950 ± 0.088	1.894 ± 0.082
BRAIN (%)	MEAN±S.D.	0.489 ± 0.036	0.495 ± 0.038	0.500 ± 0.049	0.521 ± 0.039	0.545 ± 0.043**
LIVER	MEAN±S.D.	15.95 ± 1.34	16.12 ± 1.26	16.54 ± 1.80	19.68 ± 2.20**	20.84 ± 2.16**
LIVER (%)	MEAN±S.D.	4.026 ± 0.164	4.111 ± 0.241	4.167 ± 0.215	5.225 ± 0.228**	5.947 ± 0.326**
KIDNEYS PAIRED	MEAN±S.D.	2.81 ± 0.18	2.87 ± 0.28	2.91 ± 0.28	3.08 ± 0.28	3.00 ± 0.30
KIDNEYS PAIRED (%)	MEAN±S.D.	0.713 ± 0.048	0.730 ± 0.050	0.734 ± 0.048	0.820 ± 0.043**	0.858 ± 0.062**

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

RATIOS (%) = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

a. Rats were given continual access to the carrier control or test substance in the diet.

** Significantly different from the carrier control group value (p≤0.01).

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 20 (PAGE 1): RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - SUMMARY - MALE RATS

DOSAGE GROUP CONCENTRATION (PPM)a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
BRAIN WEIGHT	MEAN±S.D.	1.934 ± 0.107	1.931 ± 0.098	1.972 ± 0.092	1.950 ± 0.088	1.894 ± 0.082
LIVER (%)	MEAN±S.D.	827.2 ± 84.1	837.8 ± 88.6	840.9 ± 100.6	1008.2 ± 96.1**	1099.9 ± 99.8**
KIDNEYS PAIRED (%)	MEAN±S.D.	145.9 ± 11.7	149.0 ± 17.8	147.9 ± 14.3	158.1 ± 12.9	158.6 ± 16.6

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % BRW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

a. Rats were given continual access to the carrier control or test substance in the diet.

** Significantly different from the carrier control group value ($p \leq 0.01$).

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 21 (PAGE 1): TERMINAL BODY WEIGHTS, ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM) ^a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
TERMINAL BODY WEIGHT	MEAN±S.D.	249.3 ± 21.2	254.8 ± 25.8	245.5 ± 19.5	255.8 ± 26.5	236.5 ± 30.5
BRAIN	MEAN±S.D.	1.882 ± 0.078	1.856 ± 0.072	1.868 ± 0.072	1.868 ± 0.056	1.850 ± 0.085
BRAIN (%)	MEAN±S.D.	0.758 ± 0.056	0.734 ± 0.066	0.766 ± 0.057	0.737 ± 0.071	0.791 ± 0.086
LIVER	MEAN±S.D.	10.00 ± 1.26	10.42 ± 1.19	9.86 ± 1.31	11.20 ± 1.16*	12.06 ± 2.20**
LIVER (%)	MEAN±S.D.	4.003 ± 0.307	4.089 ± 0.219	4.003 ± 0.265	4.386 ± 0.295**	5.070 ± 0.301**
KIDNEYS PAIRED	MEAN±S.D.	1.87 ± 0.13	1.97 ± 0.21	1.94 ± 0.16	2.03 ± 0.14	2.04 ± 0.21
KIDNEYS PAIRED (%)	MEAN±S.D.	0.753 ± 0.042	0.777 ± 0.082	0.791 ± 0.043	0.802 ± 0.088	0.868 ± 0.071**

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

a. Rats were given continual access to the carrier control or test substance in the diet.

* Significantly different from the carrier control group value ($p \leq 0.05$).** Significantly different from the carrier control group value ($p \leq 0.01$).

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 22 (PAGE 1): RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - SUMMARY - FEMALE RATS

DOSAGE GROUP CONCENTRATION (PPM)a		I 0 (CARRIER CONTROL)	II 100	III 500	IV 5000	V 10000
RATS TESTED	N	15	15	15	15	15
BRAIN WEIGHT	MEAN±S.D.	1.882 ± 0.078	1.856 ± 0.072	1.868 ± 0.072	1.868 ± 0.056	1.850 ± 0.085
LIVER (%)	MEAN±S.D.	531.4 ± 65.2	561.3 ± 60.1	527.5 ± 62.0	599.8 ± 64.6*	650.7 ± 108.2**
KIDNEYS PAIRED (%)	MEAN±S.D.	99.7 ± 7.8	106.0 ± 9.4	104.1 ± 8.5	108.8 ± 5.9**	110.3 ± 8.6**

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % BRW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.

a. Rats were given continual access to the carrier control or test substance in the diet.

* Significantly different from the carrier control group value ($p \leq 0.05$).** Significantly different from the carrier control group value ($p \leq 0.01$).

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 37 (PAGE 1): TERMINAL BODY WEIGHTS, ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT -
INDIVIDUAL DATA - MALE RATS

RAT NUMBER	TERMINAL BODY WEIGHT	BRAIN		LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW
DOSAGE	GROUP I	0 (CARRIER CONTROL) PPM					
216	360.	1.745	0.48	14.94	4.15	2.59	0.72
217	484.	1.923	0.40	20.08	4.15	2.94	0.61
218	389.	1.952	0.50	16.19	4.16	2.86	0.74
219	390.	2.044	0.52	15.84	4.06	2.84	0.73
220	400.	1.843	0.46	15.70	3.92	2.79	0.70
221	404.	1.864	0.46	15.99	3.96	2.99	0.74
222	397.	2.072	0.52	15.03	3.78	2.60	0.65
223	366.	1.950	0.53	14.45	3.95	2.50	0.68
224	398.	1.939	0.49	14.82	3.72	2.61	0.66
225	391.	1.823	0.47	15.89	4.06	3.08	0.79
226	382.	1.876	0.49	14.87	3.89	2.80	0.73
227	401.	2.036	0.51	16.03	4.00	2.80	0.70
228	389.	2.107	0.54	16.10	4.14	3.04	0.78
229	394.	2.025	0.51	16.12	4.09	2.96	0.75
230	394.	1.806	0.46	17.18	4.36	2.82	0.72
DOSAGE	GROUP II	100 PPM					
231	379.	1.775	0.47	17.06	4.50	2.72	0.72
232	394.	1.919	0.49	17.15	4.35	3.16	0.80
233	388.	1.873	0.48	15.88	4.09	2.84	0.73
234	419.	1.825	0.44	18.13	4.33	3.53	0.84
235	359.	1.849	0.52	15.16	4.22	2.45	0.68
236	397.	2.096	0.53	17.84	4.49	2.96	0.74
237	365.	2.036	0.56	13.82	3.79	2.54	0.70
238	389.	2.005	0.52	15.38	3.95	2.74	0.70
239	387.	1.967	0.51	15.35	3.97	2.58	0.67
240	412.	1.902	0.46	17.04	4.14	2.93	0.71
241	386.	2.068	0.54	16.35	4.24	2.84	0.74
242	431.	1.891	0.44	16.99	3.94	2.99	0.69
243	389.	1.959	0.50	14.78	3.80	2.64	0.68
244	385.	2.002	0.52	14.56	3.78	3.10	0.80
245	401.	1.804	0.45	16.37	4.08	3.01	0.75

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 37 (PAGE 2): TERMINAL BODY WEIGHTS, ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT -
INDIVIDUAL DATA - MALE RATS

RAT NUMBER	TERMINAL BODY WEIGHT	BRAIN		LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW
DOSAGE	GROUP III	500 PPM					
261	378.	1.814	0.48	17.36	4.59	2.84	0.75
262	408.	1.989	0.49	18.11	4.44	2.96	0.72
263	348.	1.914	0.55	14.80	4.25	2.68	0.77
264	411.	1.980	0.48	17.61	4.28	2.73	0.66
265	343.	1.872	0.54	14.00	4.08	2.68	0.78
266	445.	1.960	0.44	18.10	4.07	3.38	0.76
267	426.	1.918	0.45	18.43	4.33	2.69	0.63
268	377.	1.972	0.52	14.60	3.87	2.57	0.68
269	414.	2.013	0.49	17.88	4.32	3.25	0.78
270	384.	2.074	0.54	14.94	3.89	2.95	0.77
271	369.	2.212	0.60	14.55	3.94	2.72	0.74
272	415.	1.970	0.47	16.19	3.90	3.05	0.73
273	337.	1.899	0.56	14.42	4.28	2.61	0.77
274	456.	1.964	0.43	19.02	4.17	3.15	0.69
275	443.	2.026	0.46	18.14	4.09	3.44	0.78
DOSAGE	GROUP IV	5000 PPM					
201	373.	1.978	0.53	20.68	5.54	3.19	0.86
202	433.	2.028	0.47	23.17	5.35	3.69	0.85
203	343.	1.844	0.54	18.46	5.38	3.08	0.90
204	415.	2.023	0.49	22.52	5.43	3.30	0.80
205	371.	1.859	0.50	19.45	5.24	3.21	0.86
206	402.	2.083	0.52	21.39	5.32	3.34	0.83
207	398.	1.918	0.48	20.53	5.16	3.08	0.77
208	381.	2.071	0.54	20.14	5.29	2.87	0.75
209	363.	1.816	0.50	19.92	5.49	2.85	0.78
210	413.	2.011	0.49	20.74	5.02	3.27	0.79
211	340.	2.018	0.59	16.90	4.97	2.71	0.80
212	362.	1.864	0.51	17.18	4.74	2.86	0.79
213	399.	1.976	0.50	21.05	5.28	3.24	0.81
214	341.	1.909	0.56	17.98	5.27	3.01	0.88
215	308.	1.858	0.60	15.06	4.89	2.56	0.83

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 37 (PAGE 3): TERMINAL BODY WEIGHTS, ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT -
INDIVIDUAL DATA - MALE RATS

RAT NUMBER	TERMINAL BODY WEIGHT	BRAIN		LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW
DOSAGE	GROUP V	10000 PPM					
246	291.	1.683	0.58	17.65	6.06	2.77	0.95
247	374.	1.901	0.51	19.46	5.20	2.93	0.78
248	334.	1.958	0.59	21.64	6.48	3.04	0.91
249	365.	1.890	0.52	20.94	5.74	2.87	0.79
250	375.	1.866	0.50	23.19	6.18	3.23	0.86
251	392.	1.956	0.50	24.15	6.16	3.41	0.87
252	334.	1.870	0.56	20.31	6.08	3.02	0.90
253	389.	1.921	0.49	22.44	5.77	3.22	0.83
254	324.	1.942	0.60	18.20	5.62	2.62	0.81
255	388.	1.846	0.48	23.84	6.14	3.73	0.96
256	309.	1.879	0.61	19.66	6.36	2.89	0.94
257	304.	1.803	0.59	17.32	5.70	2.55	0.84
258	354.	1.966	0.56	21.59	6.10	2.76	0.78
259	383.	2.037	0.53	22.29	5.82	3.06	0.80
260	345.	1.896	0.55	19.97	5.79	2.92	0.85
ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.							

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 38 (PAGE 1): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - MALE RATS

RAT NUMBER	BRAIN WEIGHT	LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % BRW	ABS. WT.	REL. % BRW
DOSAGE	GROUP I	0 (CARRIER CONTROL) PPM			
216	1.745	14.94	856.16	2.59	148.42
217	1.923	20.08	1044.20	2.94	152.89
218	1.952	16.19	829.40	2.86	146.52
219	2.044	15.84	774.95	2.84	138.94
220	1.843	15.70	851.87	2.79	151.38
221	1.864	15.99	857.83	2.99	160.41
222	2.072	15.03	725.39	2.60	125.48
223	1.950	14.45	741.02	2.50	128.20
224	1.939	14.82	764.31	2.61	134.60
225	1.823	15.89	871.64	3.08	168.95
226	1.876	14.87	792.64	2.80	149.25
227	2.036	16.03	787.33	2.80	137.52
228	2.107	16.10	764.12	3.04	144.28
229	2.025	16.12	796.05	2.96	146.17
230	1.806	17.18	951.27	2.82	156.15
DOSAGE	GROUP II	100 PPM			
231	1.775	17.06	961.13	2.72	153.24
232	1.919	17.15	893.69	3.16	164.67
233	1.873	15.88	847.84	2.84	151.63
234	1.825	18.13	993.42	3.53	193.42
235	1.849	15.16	819.90	2.45	132.50
236	2.096	17.84	851.14	2.96	141.22
237	2.036	13.82	678.78	2.54	124.75
238	2.005	15.38	767.08	2.74	136.66
239	1.967	15.35	780.38	2.58	131.16
240	1.902	17.04	895.90	2.93	154.05
241	2.068	16.35	790.62	2.84	137.33
242	1.891	16.99	898.47	2.99	158.12
243	1.959	14.78	754.47	2.64	134.76
244	2.002	14.56	727.27	3.10	154.84
245	1.804	16.37	907.43	3.01	166.85
ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % BRW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.					

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TABLE 38 (PAGE 2): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - MALE RATS

RAT NUMBER	BRAIN WEIGHT	LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % BRW	ABS. WT.	REL. % BRW
DOSAGE	GROUP III	500 PPM			
261	1.814	17.36	957.00	2.84	156.56
262	1.989	18.11	910.51	2.96	148.82
263	1.914	14.80	773.25	2.68	140.02
264	1.980	17.61	889.39	2.73	137.88
265	1.872	14.00	747.86	2.68	143.16
266	1.960	18.10	923.47	3.38	172.45
267	1.918	18.43	960.90	2.69	140.25
268	1.972	14.60	740.36	2.57	130.32
269	2.013	17.88	888.23	3.25	161.45
270	2.074	14.94	720.35	2.95	142.24
271	2.212	14.55	657.78	2.72	122.96
272	1.970	16.19	821.83	3.05	154.82
273	1.899	14.42	759.35	2.61	137.44
274	1.964	19.02	968.43	3.15	160.39
275	2.026	18.14	895.36	3.44	169.79
DOSAGE	GROUP IV	5000 PPM			
201	1.978	20.68	1045.50	3.19	161.27
202	2.028	23.17	1142.50	3.69	181.95
203	1.844	18.46	1001.08	3.08	167.03
204	2.023	22.52	1113.20	3.30	163.12
205	1.859	19.45	1046.26	3.21	172.67
206	2.083	21.39	1026.88	3.34	160.34
207	1.918	20.53	1070.38	3.08	160.58
208	2.071	20.14	972.48	2.87	138.58
209	1.816	19.92	1096.92	2.85	156.94
210	2.011	20.74	1031.33	3.27	162.60
211	2.018	16.90	837.46	2.71	134.29
212	1.864	17.18	921.67	2.86	153.43
213	1.976	21.05	1065.28	3.24	163.97
214	1.909	17.98	941.85	3.01	157.67
215	1.858	15.06	810.55	2.56	137.78
ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % BRW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.					

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 38 (PAGE 3): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - MALE RATS

RAT NUMBER	BRAIN WEIGHT	LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % BRW	ABS. WT.	REL. % BRW
DOSAGE	GROUP V	10000 PPM			
246	1.683	17.65	1048.72	2.77	164.59
247	1.901	19.46	1023.67	2.93	154.13
248	1.958	21.64	1105.21	3.04	155.26
249	1.890	20.94	1107.94	2.87	151.85
250	1.866	23.19	1242.76	3.23	173.10
251	1.956	24.15	1234.66	3.41	174.34
252	1.870	20.31	1086.10	3.02	161.50
253	1.921	22.44	1168.14	3.22	167.62
254	1.942	18.20	937.18	2.62	134.91
255	1.846	23.84	1291.44	3.73	202.06
256	1.879	19.66	1046.30	2.89	153.80
257	1.803	17.32	960.62	2.55	141.43
258	1.966	21.59	1098.17	2.76	140.39
259	2.037	22.29	1094.26	3.06	150.22
260	1.896	19.97	1053.27	2.92	154.01
ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % BRW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.					

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 39 (PAGE 1): TERMINAL BODY WEIGHTS, ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT -
INDIVIDUAL DATA - FEMALE RATS

RAT NUMBER	TERMINAL BODY WEIGHT	BRAIN		LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW
DOSAGE	GROUP I	0 (CARRIER CONTROL) PPM					
316	237.	1.785	0.75	9.97	4.21	1.95	0.82
317	277.	1.873	0.68	12.00	4.33	2.18	0.79
318	250.	1.887	0.75	10.33	4.13	1.80	0.72
319	272.	1.933	0.71	10.75	3.95	1.91	0.70
320	250.	1.882	0.75	11.16	4.46	1.85	0.74
321	278.	1.990	0.72	10.98	3.95	2.03	0.73
322	236.	1.910	0.81	10.70	4.53	1.78	0.75
323	237.	1.993	0.84	9.34	3.94	1.83	0.77
324	223.	1.834	0.82	8.83	3.96	1.73	0.78
325	234.	1.854	0.79	8.97	3.83	1.86	0.79
326	293.	1.888	0.64	12.11	4.13	2.02	0.69
327	250.	1.901	0.76	8.98	3.59	1.75	0.70
328	224.	1.692	0.76	8.60	3.84	1.79	0.80
329	236.	1.964	0.83	8.02	3.40	1.71	0.72
330	243.	1.847	0.76	9.22	3.79	1.92	0.79
DOSAGE	GROUP II	100 PPM					
331	231.	1.845	0.80	10.19	4.41	2.03	0.88
332	280.	1.791	0.64	12.34	4.41	1.87	0.67
333	234.	1.736	0.74	8.56	3.66	1.73	0.74
334	250.	1.818	0.73	10.68	4.27	1.85	0.74
335	250.	1.837	0.73	9.87	3.95	2.05	0.82
336	290.	1.875	0.65	11.26	3.88	1.91	0.66
337	222.	1.775	0.80	8.83	3.98	1.59	0.72
338	260.	1.813	0.70	10.99	4.23	2.09	0.80
339	224.	1.934	0.86	9.05	4.04	1.94	0.87
340	248.	1.890	0.76	10.99	4.43	2.22	0.90
341	260.	1.795	0.69	10.56	4.06	1.87	0.72
342	279.	1.932	0.69	11.19	4.01	2.47	0.88
343	244.	1.923	0.79	9.58	3.93	1.83	0.75
344	312.	2.004	0.64	12.56	4.02	2.11	0.68
345	238.	1.877	0.79	9.66	4.06	1.98	0.83

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 39 (PAGE 2): TERMINAL BODY WEIGHTS, ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT -
INDIVIDUAL DATA - FEMALE RATS

RAT NUMBER	TERMINAL BODY WEIGHT	BRAIN		LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW
DOSAGE	GROUP III	500 PPM					
361	233.	1.837	0.79	9.24	3.96	1.91	0.82
362	261.	1.845	0.71	10.75	4.12	2.15	0.82
363	243.	1.971	0.81	10.35	4.26	2.05	0.84
364	290.	1.995	0.69	13.23	4.56	2.27	0.78
365	246.	1.887	0.77	10.19	4.14	1.79	0.73
366	264.	1.846	0.70	9.50	3.60	1.97	0.75
367	222.	1.727	0.78	8.76	3.94	1.93	0.87
368	253.	1.938	0.77	10.94	4.32	2.06	0.81
369	217.	1.864	0.86	8.05	3.71	1.66	0.76
370	240.	1.900	0.79	9.56	3.98	1.97	0.82
371	238.	1.813	0.76	9.26	3.89	2.01	0.84
372	258.	1.800	0.70	10.07	3.90	1.89	0.73
373	230.	1.819	0.79	9.03	3.93	1.72	0.75
374	262.	1.825	0.70	10.88	4.15	2.02	0.77
375	225.	1.950	0.87	8.07	3.59	1.75	0.78
DOSAGE	GROUP IV	5000 PPM					
301	225.	1.777	0.79	11.04	4.91	1.79	0.80
302	298.	1.919	0.64	13.73	4.61	2.15	0.72
303	250.	1.871	0.75	11.89	4.76	2.17	0.87
304	232.	1.846	0.80	9.89	4.26	1.98	0.85
305	216.	1.832	0.85	9.80	4.54	2.14	0.99
306	302.	1.843	0.61	12.54	4.15	2.04	0.68
307	251.	1.841	0.73	11.56	4.60	2.07	0.82
308	240.	1.928	0.80	9.70	4.04	2.09	0.87
309	263.	1.819	0.69	12.06	4.58	1.99	0.76
310	236.	1.962	0.83	10.40	4.41	2.16	0.92
311	256.	1.861	0.73	11.46	4.48	2.04	0.80
312	251.	1.919	0.76	9.74	3.88	1.98	0.79
313	244.	1.795	0.74	10.77	4.41	1.68	0.69
314	290.	1.953	0.67	11.68	4.03	2.21	0.76
315	283.	1.860	0.66	11.68	4.13	2.02	0.71

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 39 (PAGE 3): TERMINAL BODY WEIGHTS, ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO TERMINAL BODY WEIGHT -
INDIVIDUAL DATA - FEMALE RATS

RAT NUMBER	TERMINAL BODY WEIGHT	BRAIN		LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW	ABS. WT.	REL. % TBW
DOSAGE	GROUP V	10000 PPM					
346	203.	1.632	0.80	10.07	4.96	1.64	0.81
347	285.	1.919	0.67	16.02	5.62	2.41	0.84
348	265.	1.784	0.67	13.96	5.27	1.96	0.74
349	266.	1.964	0.74	14.22	5.34	2.25	0.84
350	202.	1.813	0.90	10.58	5.24	1.76	0.87
351	295.	1.890	0.64	16.48	5.59	2.33	0.79
352	213.	1.878	0.88	10.54	4.95	1.92	0.90
353	249.	1.934	0.78	12.86	5.16	2.04	0.82
354	241.	1.759	0.73	12.18	5.05	2.00	0.83
355	217.	1.821	0.84	9.89	4.56	1.99	0.92
356	233.	1.875	0.80	11.36	4.88	2.01	0.86
357	237.	1.901	0.80	11.20	4.72	2.29	0.97
358	194.	1.792	0.92	9.37	4.83	1.94	1.00
359	227.	1.885	0.83	11.04	4.86	2.18	0.96
360	221.	1.910	0.86	11.10	5.02	1.93	0.87

ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % TBW = (ORGAN WEIGHT/TERMINAL BODY WEIGHT) X 100.

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 40 (PAGE 1): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - FEMALE RATS

RAT NUMBER	BRAIN WEIGHT	LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % BRW	ABS. WT.	REL. % BRW
DOSAGE	GROUP I	0 (CARRIER CONTROL) PPM			
316	1.785	9.97	558.54	1.95	109.24
317	1.873	12.00	640.68	2.18	116.39
318	1.887	10.33	547.43	1.80	95.39
319	1.933	10.75	556.13	1.91	98.81
320	1.882	11.16	592.99	1.85	98.30
321	1.990	10.98	551.76	2.03	102.01
322	1.910	10.70	560.21	1.78	93.19
323	1.993	9.34	468.64	1.83	91.82
324	1.834	8.83	481.46	1.73	94.33
325	1.854	8.97	483.82	1.86	100.32
326	1.888	12.11	641.42	2.02	106.99
327	1.901	8.98	472.38	1.75	92.06
328	1.692	8.60	508.27	1.79	105.79
329	1.964	8.02	408.35	1.71	87.07
330	1.847	9.22	499.19	1.92	103.95
DOSAGE	GROUP II	100 PPM			
331	1.845	10.19	552.30	2.03	110.03
332	1.791	12.34	689.00	1.87	104.41
333	1.736	8.56	493.09	1.73	99.65
334	1.818	10.68	587.46	1.85	101.76
335	1.837	9.87	537.29	2.05	111.59
336	1.875	11.26	600.53	1.91	101.87
337	1.775	8.83	497.46	1.59	89.58
338	1.813	10.99	606.18	2.09	115.28
339	1.934	9.05	467.94	1.94	100.31
340	1.890	10.99	581.48	2.22	117.46
341	1.795	10.56	588.30	1.87	104.18
342	1.932	11.19	579.19	2.47	127.85
343	1.923	9.58	498.18	1.83	95.16
344	2.004	12.56	626.75	2.11	105.29
345	1.877	9.66	514.65	1.98	105.49
ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % BRW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.					

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 40 (PAGE 2): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - FEMALE RATS

RAT NUMBER	BRAIN WEIGHT	LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % BRW	ABS. WT.	REL. % BRW
DOSAGE	GROUP III	500 PPM			
361	1.837	9.24	502.99	1.91	103.97
362	1.845	10.75	582.66	2.15	116.53
363	1.971	10.35	525.11	2.05	104.01
364	1.995	13.23	663.16	2.27	113.78
365	1.887	10.19	540.01	1.79	94.86
366	1.846	9.50	514.63	1.97	106.72
367	1.727	8.76	507.24	1.93	111.75
368	1.938	10.94	564.50	2.06	106.30
369	1.864	8.05	431.87	1.66	89.06
370	1.900	9.56	503.16	1.97	103.68
371	1.813	9.26	510.76	2.01	110.86
372	1.800	10.07	559.44	1.89	105.00
373	1.819	9.03	496.43	1.72	94.56
374	1.825	10.88	596.16	2.02	110.68
375	1.950	8.07	413.85	1.75	89.74
DOSAGE	GROUP IV	5000 PPM			
301	1.777	11.04	621.27	1.79	100.73
302	1.919	13.73	715.48	2.15	112.04
303	1.871	11.89	635.49	2.17	115.98
304	1.846	9.89	535.75	1.98	107.26
305	1.832	9.80	534.93	2.14	116.81
306	1.843	12.54	680.41	2.04	110.69
307	1.841	11.56	627.92	2.07	112.44
308	1.928	9.70	503.11	2.09	108.40
309	1.819	12.06	663.00	1.99	109.40
310	1.962	10.40	530.07	2.16	110.09
311	1.861	11.46	615.80	2.04	109.62
312	1.919	9.74	507.56	1.98	103.18
313	1.795	10.77	600.00	1.68	93.59
314	1.953	11.68	598.05	2.21	113.16
315	1.860	11.68	627.96	2.02	108.60
ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % BRW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.					

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PROTOCOL TQC00065: ORAL (DIET) REPEATED DOSE 28-DAY TOXICITY STUDY OF MALATHION TECHNICAL IN RATS

TABLE 40 (PAGE 3): ORGAN WEIGHTS AND RATIOS (%) OF ORGAN WEIGHT TO BRAIN WEIGHT - INDIVIDUAL DATA - FEMALE RATS

RAT NUMBER	BRAIN WEIGHT	LIVER		KIDNEYS PAIRED	
		ABS. WT.	REL. % BRW	ABS. WT.	REL. % BRW
DOSAGE	GROUP V	10000 PPM			
346	1.632	10.07	617.03	1.64	100.49
347	1.919	16.02	834.81	2.41	125.59
348	1.784	13.96	782.51	1.96	109.86
349	1.964	14.22	724.03	2.25	114.56
350	1.813	10.58	583.56	1.76	97.08
351	1.890	16.48	871.96	2.33	123.28
352	1.878	10.54	561.24	1.92	102.24
353	1.934	12.86	664.94	2.04	105.48
354	1.759	12.18	692.44	2.00	113.70
355	1.821	9.89	543.11	1.99	109.28
356	1.875	11.36	605.87	2.01	107.20
357	1.901	11.20	589.16	2.29	120.46
358	1.792	9.37	522.88	1.94	108.26
359	1.885	11.04	585.68	2.18	115.65
360	1.910	11.10	581.15	1.93	101.05
ALL WEIGHTS WERE RECORDED IN GRAMS (G). ABS. WT. = ORGAN WEIGHT. REL. % BRW = (ORGAN WEIGHT/BRAIN WEIGHT) X 100.					

Table 3
Pathology - Intergroup Comparison of Histopathology Observations (Day 29)

No microscopic evaluation of the brain was performed because the brain was used for cholinesterase evaluation.

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PTA005-01/04

Pathology - Intergroup Comparison of Histopathology Observations
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:55

Observations: Neo-Plastic and Non Neo-Plastic

Removal Reason: SCHEDULE SACRIFICED

	MALES		FEMALES	
	0	10000	0	10000
	ppm	ppm	ppm	ppm
Number of Animals on Study :	15	15	15	15
Number of Animals Completed:	(15)	(15)	(15)	(15)

KIDNEY;				
Examined.....	(15)	(15)	(15)	(15)
Within Normal Limits.....	11	13	14	14
Fibrosis; focal	(0)	(1)	(1)	(0)
minimal	0	1	1	0
Hydronephrosis	(2)	(0)	(0)	(0)
minimal	2	0	0	0
Mineralization; focal	(1)	(0)	(0)	(0)
minimal	1	0	0	0
Basophilia; tubular	(3)	(0)	(0)	(0)
minimal	2	0	0	0
mild	1	0	0	0
Cyst; tubular	1	1	0	1
Infiltration, Mixed Cell	(0)	(0)	(0)	(1)
minimal	0	0	0	1
LIVER;				
Examined.....	(15)	(15)	(15)	(15)
Within Normal Limits.....	15	11	7	7
Degeneration; hepatocellular	(0)	(2)	(0)	(0)
minimal	0	1	0	0
mild	0	1	0	0
Necrosis	(0)	(1)	(0)	(0)
minimal	0	1	0	0
Apoptosis	(0)	(1)	(0)	(0)
minimal	0	1	0	0
Vacuolation; hepatocellular; Periportal	(0)	(0)	(8)	(8)
minimal	0	0	5	8
mild	0	0	3	0
NOSE, LEVEL 1;				
Examined.....	(15)	(15)	(15)	(15)
Within Normal Limits.....	15	15	15	15
NOSE, LEVEL 2;				
Examined.....	(15)	(15)	(15)	(15)
Within Normal Limits.....	13	0	15	1
Hyperplasia; Transitional Epithelium	(1)	(1)	(0)	(0)
minimal	1	1	0	0
Depletion; Goblet Cell	(0)	(15)	(0)	(14)

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PTA005-01/04

Pathology - Intergroup Comparison of Histopathology Observations
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:55

Observations: Neo-Plastic and Non Neo-Plastic

Removal Reason: SCHEDULE SACRIFICED

	MALES		FEMALES	
	0	10000	0	10000
	ppm	ppm	ppm	ppm
Number of Animals on Study :	15	15	15	15
Number of Animals Completed:	(15)	(15)	(15)	(15)
NOSE, LEVEL 2; (continued)				
minimal	0	1	0	4
mild	0	3	0	6
moderate	0	9	0	4
marked	0	2	0	0
Infiltration, Mixed Cell	(1)	(0)	(0)	(0)
minimal	1	0	0	0
NOSE, LEVEL 3;				
Examined.....	(15)	(15)	(15)	(15)
Within Normal Limits.....	15	0	15	0
Hyperplasia; Olfactory Epithelium	(0)	(15)	(0)	(15)
minimal	0	3	0	6
mild	0	12	0	9
Infiltration, Mixed Cell	(0)	(1)	(0)	(0)
minimal	0	1	0	0
NOSE, LEVEL 4;				
Examined.....	(15)	(15)	(15)	(15)
Within Normal Limits.....	15	0	15	0
Hyperplasia; Olfactory Epithelium	(0)	(15)	(0)	(15)
minimal	0	0	0	2
mild	0	3	0	9
moderate	0	12	0	4
Hyperplasia; Mucosa-Associated Lymphoid Tissue	(0)	(1)	(0)	(0)
mild	0	1	0	0
NOSE, LEVEL 5;				
Examined.....	(15)	(14)	(14)	(14)
Within Normal Limits.....	14	0	14	0
Not Examined: NOT FOUND AT TRIMMING	0	1	1	1
Hemorrhage; peracute; Lumen	(1)	(0)	(0)	(0)
minimal	1	0	0	0
Hyperplasia; Olfactory Epithelium	(0)	(14)	(0)	(14)
minimal	0	0	0	1
mild	0	2	0	5
moderate	0	12	0	8

Appendix 1
Deviations

DEVIATIONS

All deviations that occurred during the portion of the study performed by the Charles River Laboratories, Pathology Associates - Illinois have been authorized/acknowledged by the Study Director, assessed for impact, and documented in the study records. All protocol deviations are listed below.

None of the deviations were considered to have impacted the overall integrity of the study or the interpretation of the study results and conclusions.

Histopathology

- Some of the tissues listed in the protocol and subsequent amendments for histopathologic evaluation were not recovered on the slide for microscopic evaluation. Nose, level 5 from 3 animals were not found at trimming. This had no impact on the study.

Appendix 2
Pathology - Individual Animal Data (Concise Edition)

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 216 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used: TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 217 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Hyperplasia; Transitional Epithelium; minimal

NOSE, LEVEL 5;
Hemorrhage; Lumen; peracute; minimal

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 3 NOSE, LEVEL 4

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 218 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 219 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 220 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations:

SKIN;
Scab

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 221 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 222 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations:

Correlated with:

KIDNEY;

Tan Area; right (TGL): One, measuring 0.4 x 0.2 cm KIDNEY; Basophilia; tubular; mild (H)

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEY;

Mineralization; focal; minimal

Basophilia; tubular; mild KIDNEY; Tan Area; right (G)

The following tissues were within normal limits:

LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date: 09-Feb-2011 07:56

Animal No.: 223 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEY;
 Hydronephrosis; minimal

The following tissues were within normal limits:

LIVER	NOSE, LEVEL 1	NOSE, LEVEL 2	NOSE, LEVEL 3	NOSE, LEVEL 4	NOSE, LEVEL 5
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Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 224 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 225 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 226 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEY;
 Hydronephrosis; minimal
 Basophilia; tubular; minimal

The following tissues were within normal limits:

LIVER	NOSE, LEVEL 1	NOSE, LEVEL 2	NOSE, LEVEL 3	NOSE, LEVEL 4	NOSE, LEVEL 5
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Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 227 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Infiltration, Mixed Cell; minimal

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 228 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 229 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 230 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEY;
 Basophilia; tubular; minimal
 Cyst; tubular

The following tissues were within normal limits:

LIVER	NOSE, LEVEL 1	NOSE, LEVEL 2	NOSE, LEVEL 3	NOSE, LEVEL 4	NOSE, LEVEL 5
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Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 316 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEY;
Fibrosis; focal; minimal

The following tissues were within normal limits:

LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4

The following tissues have not been examined:

NOSE, LEVEL 5; NOT FOUND AT TRIMMING

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 317 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
 Vacuolation; Periportal; hepatocellular; mild

The following tissues were within normal limits:

KIDNEY	NOSE, LEVEL 1	NOSE, LEVEL 2	NOSE, LEVEL 3	NOSE, LEVEL 4	NOSE, LEVEL 5
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Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 318 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 319 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 320 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
 Vacuolation; Periportal; hepatocellular; minimal

The following tissues were within normal limits:

KIDNEY NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 321 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 322 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations:

EYE;
Lesion: Displaced pupil and microphthalmia

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
Vacuolation; Periportal; hepatocellular; minimal

The following tissues were within normal limits:

KIDNEY NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 323 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 324 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used: TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 325 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
 Vacuolation; Periportal; hepatocellular; minimal

The following tissues were within normal limits:

KIDNEY	NOSE, LEVEL 1	NOSE, LEVEL 2	NOSE, LEVEL 3	NOSE, LEVEL 4	NOSE, LEVEL 5
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Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 326 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
 Vacuolation; Periportal; hepatocellular; mild

The following tissues were within normal limits:

KIDNEY NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 327 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
 Vacuolation; Periportal; hepatocellular; minimal

The following tissues were within normal limits:

KIDNEY NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
 Vacuolation; Periportal; hepatocellular; minimal

The following tissues were within normal limits:

KIDNEY NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 329 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 330 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Certified Rodent Diet 5002 Dose: 0 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;
 Vacuolation; Periportal; hepatocellular; mild

The following tissues were within normal limits:

KIDNEY NOSE, LEVEL 1 NOSE, LEVEL 2 NOSE, LEVEL 3 NOSE, LEVEL 4 NOSE, LEVEL 5

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 246 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 247 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEY;

Fibrosis; focal; minimal

LIVER;

Apoptosis; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 248 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Degeneration; hepatocellular; mild

NOSE, LEVEL 2;

Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 249 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 250 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild
Infiltration, Mixed Cell; minimal

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate
Hyperplasia; Mucosa-Associated Lymphoid Tissue; mild

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

The following tissues have not been examined:

NOSE, LEVEL 5; NOT FOUND AT TRIMMING

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 251 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations:

SKIN;
Abrasion

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 252 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Degeneration; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 253 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Hyperplasia; Transitional Epithelium; minimal
Depletion; Goblet Cell; marked

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 254 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Necrosis; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 255 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEY;

Cyst; tubular

NOSE, LEVEL 2;

Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

LIVER

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 256 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; marked

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 257 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; mild

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; mild

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 258 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; mild

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 259 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; mild

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 260 Group: 5 Sex: Male Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 16NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 16NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; minimal

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; mild

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
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Date: 09-Feb-2011 07:56

Animal No.: 346 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Vacuolation; Periportal; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date: 09-Feb-2011 07:56

Animal No.: 347 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; mild

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date: 09-Feb-2011 07:56

Animal No.: 348 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Vacuolation; Periportal; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; mild

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; mild

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date: 09-Feb-2011 07:56

Animal No.: 349 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Vacuolation; Periportal; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; mild

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 350 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; minimal

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 351 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

KIDNEY;

Cyst; tubular
Infiltration, Mixed Cell; minimal

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; minimal

The following tissues were within normal limits:

LIVER NOSE, LEVEL 1 NOSE, LEVEL 2

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 352 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Vacuolation; Periportal; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 353 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Vacuolation; Periportal; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; mild

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; mild

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date: 09-Feb-2011 07:56

Animal No.: 354 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Vacuolation; Periportal; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; mild

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; mild

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date: 09-Feb-2011 07:56

Animal No.: 355 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Vacuolation; Periportal; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; mild

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; minimal

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

The following tissues have not been examined:

NOSE, LEVEL 5; NOT FOUND AT TRIMMING

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 356 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; minimal

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; mild

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date: 09-Feb-2011 07:56

Animal No.: 357 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; mild

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Date: 09-Feb-2011 07:56

Animal No.: 358 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; minimal

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; minimal

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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PTA019-01/00

Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

Animal No.: 359 Group: 5 Sex: Female Species: Rat Strain: Sprague Dawley

Test Material: Malathion Technical (CHA 300) Dose: 10000 ppm Route: Oral Diet Study Type: Toxicity
Date of Death : 17NOV2010 Study Day No. (Week): 29 (5) Mode of Death: SCHEDULE SACRIFICED
Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

NOSE, LEVEL 2;
Depletion; Goblet Cell; moderate

NOSE, LEVEL 3;
Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;
Hyperplasia; Olfactory Epithelium; moderate

NOSE, LEVEL 5;
Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY LIVER NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

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Final Pathology Report

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PTA019-01/00

Pathology - Individual Animal Data (Concise Edition)
Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats
Charles River Laboratories Study No. TQC00065

Date: 09-Feb-2011 07:56

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Date of Necropsy: 17NOV2010 ** NECROPSY COMPLETE **

Pathologist: Carol J. Detrisac ** EXAMINATION COMPLETE **

Terminal Body Weight: None

Gross Pathology Observations: None

Any remaining protocol required tissues, which have been examined, have no visible lesions

Histo Pathology Observations:

LIVER;

Vacuolation; Periportal; hepatocellular; minimal

NOSE, LEVEL 2;

Depletion; Goblet Cell; minimal

NOSE, LEVEL 3;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 4;

Hyperplasia; Olfactory Epithelium; mild

NOSE, LEVEL 5;

Hyperplasia; Olfactory Epithelium; moderate

The following tissues were within normal limits:

KIDNEY

NOSE, LEVEL 1

Codes Used:TGL = Trackable Gross Lesion, G = Gross Finding, H = Histo Finding.

APPENDIX 6 - ANALYTICAL REPORT



FINAL REPORT

Study Phase: Dose Analysis

Project No. TQC00065AA
Testing Facility Study No. TQC00065

Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats

AUTHOR:

Jason Sarsoza, BSc
(Principal Investigator)

TESTING FACILITY:

Charles River Laboratories
Preclinical Services
905 Sheehy Drive, Building A
Horsham, PA 19044
USA

SPONSOR:

Cheminova A/S
P.O. Box 9
DK-7620 Lemvig
Denmark

December 9, 2011

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1. REPORT REVIEW AND APPROVAL SIGNATURE

This project was performed under my overall scientific guidance and management. The report provides a full and accurate record of the raw data.



Jason Sarsoza, BSc
Principal Investigator
Research Scientist I, Laboratory Sciences
Charles River Laboratories Preclinical Services

09 DEC 2011

Date


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2. COMPLIANCE STATEMENT

This project was conducted in compliance with provisions of EPA Good laboratory practice (GLP) standards (40 CFR 160/792) and The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final] that are applicable to GLP compliant testing. This report was issued and approved by a Principal Investigator who had responsibility for the technical conduct of the analytical work performed as well as for the interpretation, analysis, documentation and reporting of deviations and results and is intended for use by the nonclinical laboratory Study Director relying on this testing.

Principal Investigator:

 09DEC2011

Jason Sarsoza, BSc/Date
Research Scientist I, Laboratory Sciences
Charles River Laboratories Preclinical Services

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3. QUALITY ASSURANCE STATEMENT

This study has been inspected by the QAU to assure conformance with the GLP regulations US Environmental Protection Agency, Good Laboratory Practice Regulations, Chapter I Protection of Environment, 40 C.F.R. 160/792 and Organisation for Economic Co-operation and Development (1998), The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final. Reports were submitted in accordance with SOPs as follows.

QAU INSPECTION DATES

Dates of Inspection	Phase(s) Inspected	<u>Dates Findings Submitted to:</u>	
		Study Director	Study Director Management
19 OCT 2010	Sample Preparation	25 OCT 2010	25 OCT 2010
04, 06 DEC 2010	Analytical Data	06 DEC 2010	06 DEC 2010
04, 06 DEC 2010	Analytical Report	06 DEC 2010	06 DEC 2010
09 DEC 2011	Final Report	09 DEC 2011	09 DEC 2011

The Final Report has been reviewed to assure that it accurately describes the materials and methods, and that the reported results accurately reflect the raw data.



Brandon Tobias, BS
Quality Assurance Auditor I
Charles River Laboratories
Preclinical Services, Pennsylvania



Date

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4. RESPONSIBLE PERSONNEL

Principal Investigator Jason Sarsoza, BSc
Research Scientist I, Laboratory Sciences

Research Assistant III Phinh Xu Ngo
Laboratory Sciences

Research Assistant I Kelly Pool, BS
Laboratory Sciences

Senior Manager Julian Gulbinski, III, BS, MBA
Laboratory Sciences

Vice President Alan Bartlett, CChem, FRSC
Laboratory Sciences

5. DATES OF TECHNICAL PERFORMANCE

Experimental Start Date 19 October 2010
Experimental Completion Date 11 November 2010

6. MAINTENANCE OF RAW DATA AND RECORDS

The original Final Report and raw data will be maintained in the Charles River Laboratories Preclinical Services Archives Department located in Pennsylvania. Archival material will be indexed by Study Number TQC00065.

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7. SUMMARY

The purpose of this project was to determine the concentration and homogeneity of Malathion Technical in dose formulations from Study No. TQC00065 titled “Oral (Diet) Repeated Dose 28-Day Toxicity Study of Malathion Technical in Rats.”

Samples of dose formulations were analyzed for Malathion by high-performance liquid chromatography with ultraviolet detection (HPLC-UV). The method was validated for the analysis of dose formulations at concentrations ranging from 40 ppm to 20000 ppm of Malathion Technical in meal form of Certified Rodent Diet® #5002 containing 5% corn oil.

Results for all dose formulations met the acceptance criteria for concentration (within $\pm 10\%$ of nominal concentration) and homogeneity ($\leq 5\%$ relative standard deviation).

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8. MATERIALS AND METHODS

8.1. Analytical Reference Standards

Identity:	Malathion Technical
Manufacturer:	Cheminova
Lot number:	D2014-OSJ-MLT-01-S
Purity:	95.8% w/w (96% applied)
Expiration date:	28 September 2013
Storage conditions:	5 ± 3°C, protected from light
Testing Facility Material ID:	CSA-10758

Identity:	Malathion (Analytical Standard)
Manufacturer:	Cheminova
Lot number:	650-OSJ-36E
Purity:	99.6% w/w
Expiration date:	1 March 2018
Storage conditions:	-15°C to -30°C, protected from light
Testing Facility Material ID:	CSA-10744

The characterization of the analytical reference standards is the responsibility of the Sponsor, as are the method of synthesis, fabrication or derivation, and stability determinations. Certificates of Analysis are contained in [Appendix 1](#).

8.2. Sample Receipt and Storage

Three sets of samples were received from PCS-PA Formulation Laboratory. The first set was received on 19 October 2010 and the last set was received on 08 November 2010. The samples were received packaged with cold packs, protected from light and in satisfactory condition. Samples were either analyzed upon receipt or were stored at 2°C to 8°C, protected from light. All samples were analyzed within the established stability period (22 days).

8.3. Sample Analysis

Samples of dose formulations were analyzed for Malathion Technical according to the validated method described in Charles River Laboratories Preclinical Services Analytical Procedure MALA02 for the “Analysis of Malathion in Meal Form of Certified Rodent Diet #5002 Containing 5% Corn Oil Dose Formulations by HPLC-UV.” A copy of the most recent version of the Analytical Procedure is contained in [Appendix 2](#).

9. DATA COLLECTION AND STATISTICAL METHODS

TotalChrom[®], Version 6.2.1 (PerkinElmer[®]) software was used for acquisition of HPLC data, assessment of system suitability, and integration of the peak area of the analyte. After integration of the peak areas, data were exported to a verified Excel[®] (Microsoft[®]) spreadsheet. The Excel spreadsheet was used for regression analysis and calculation of Malathion Technical concentrations and descriptive statistics.

10. RESULTS

Concentration and homogeneity results are summarized in [Table 1](#). Results and conclusions for each analytical run are provided in the Dose Formulation Analysis Reports, which are contained in [Appendix 3](#).

10.1. Concentration

Mean measured Malathion Technical concentrations for all dose formulations were within the acceptable limits ($\pm 10\%$ of nominal concentration).

10.2. Homogeneity

The relative standard deviation (RSD) of the mean of the average concentration values for the top, middle, and bottom of each dose formulation was calculated to assess homogeneity. Homogeneity was acceptable ($\leq 5\%$ RSD) for all dose formulations.

TABLES

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Table 1 Summary of Concentration and Homogeneity Results

Sample Occasion (Preparation Date)	Group	Nominal Concentration (ppm)	Mean Measured Concentration (ppm)	Mean Bias (%)	Homogeneity (%RSD)
Start of Study (18 October 2010)	I	0	ND	NA	NA
	II	100	100.5	0.5	2.1
	III	500	496.7	-0.7	1.9
	IV	5000	4882	-2.4	0.4
	V	10000	9962	-0.4	1.2
Week 2 (25 October 2010)	I	0	ND	NA	-
	II	100	100.2	0.2	-
	III	500	490.7	-1.9	-
	IV	5000	5077	1.5	-
	V	10000	10350	3.5	-
End of Study (09 November 2010)	I	0	ND	NA	-
	II	100	105.2	5.2	-
	III	500	502.6	0.5	-
	IV	5000	5046	0.9	-
	V	10000	9510	-4.9	-
RSD	Relative standard deviation				
ND	None detected				
NA	Not applicable				
-	Not required				

APPENDICES

APPENDIX 1
CERTIFICATE OF ANALYSIS

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Denmark

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CVR-No. DK 12 76 00 43

Certificate of Analysis

TEM 010-08

Test substance certified:

Test substance:	Malathion Technical fortified
CHA Code No.:	-
Batch No.:	D2014-OSJ-MLT-01-S
Origin of test substance:	<input checked="" type="checkbox"/> Laboratory <input type="checkbox"/> Pilot plant <input type="checkbox"/> Commercial

Analysis:

Content of Malathion:	95.8% w/w
Identified by:	¹ H-NMR and ¹³ C-NMR Spectroscopy, Mass Spectrometry and IR Spectroscopy
Quantified by:	GC (Method VAM 001-02)
Date of analysis:	September 28, 2010

Information of the test substance:

Appearance:	Pale yellowish liquid
Storage:	Refrigerator
Tap density:	Not determined
Expiry date:	September 28, 2013

Information of analyte(s):

Common name:	Malathion
CAS name:	Butanedioic acid ((dimethoxyphosphino-thioyl) thio)-, diethyl ester
CAS No.:	121-75-5
Molecular formula:	C ₁₀ H ₁₉ O ₆ PS ₂
Molecular mass:	330.36 g/mol
Structure formula:	

Statement of GLP Compliance

The identification and quantification were performed at Cheminova A/S and conducted according to FIFRA Good Laboratory Practice Standards, 40 CFR Part 160 and the OECD Principles of Good Laboratory Practices.

Date

November 9, 2010

Barbara Hinz

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Certificate of Analysis

REF 019-03

Test substance certified:

Test substance:	Analytical standard of Malathion		
Batch No.:	650-OSJ-36E		
Origin of test substance:	<input checked="" type="checkbox"/> Laboratory	<input type="checkbox"/> Pilot plant	<input type="checkbox"/> Commercial

Analysis:

Content of Malathion:	99.6 % w/w
Identified by:	¹ H-NMR and ¹³ C-NMR Spectroscopy, IR Spectroscopy, UV spectroscopy and Mass Spectrometry
Determination of purity by:	Quantitative ³¹ P-NMR
Date of analysis:	March 1, 2010

Information of the test substance:

Appearance:	Colourless liquid
Storage:	< -20°C
Expiry date:	March 1, 2018

Information of analyte(s):

Common name:	-
CAS name:	Butanedioic acid [(dimethoxy-phosphinothioyl)thio]-, diethyl ester
CAS No.:	121-75-5
Molecular formula:	C ₁₀ H ₁₈ O ₆ PS ₂
Molecular mass:	330.36 g/mol
Structure formula:	

Statement of GLP Compliance

The identification and determination of purity were performed at Cheminova A/S and conducted according to FIFRA Good Laboratory Practice Standards, 40 CFR Part 160 and the OECD Principles of Good Laboratory Practices.

Date

March 2, 2010

APPENDIX 2 ANALYTICAL PROCEDURE

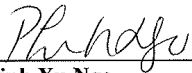
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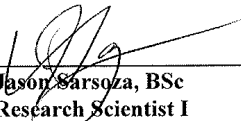
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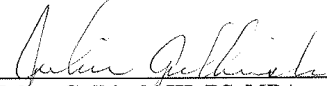


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**Analytical Procedure for the
Analysis of Malathion in Meal Form of Certified Rodent Diet® #5002
Containing 5% Corn Oil Dose Formulations by HPLC-UV**

Prepared By:  05 DEC 2011
Phinh Xu Ngo
Research Assistant III
Date

Reviewed By:  05 DEC 2011
Jason Sarsoza, BSc
Research Scientist I
Date

Authorized By:  05 Dec 2011
Julian Gulbinski III, BS, MBA
Senior Manager, Laboratory Sciences
Date

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1 Purpose

The purpose of this analytical procedure is to accurately determine the concentration of Malathion in Meal form of Certified Rodent Diet® #5002 containing 5% corn oil dose formulations. This analytical procedure is suitable for GLP sample analysis.

2 Scope

Analysis of Malathion in dose formulation samples with limitations as stated below.

Vehicle: Meal form of Certified Rodent Diet® #5002 containing 5% Corn Oil

Sample Volume (or Amount): 1 g

Volumetric Samples [] Gravimetric Samples [x] Both []

Concentrations Covered by Analytical Procedure:

NOTE: Concentrations have been corrected for purity of 99.6% (Calibration Range) and 96% (Valid Sample Range).

Final Injected Concentration

LOD	NA
Calibration Standard Range	1.5 – 27 µg/mL
Valid Sample Range	40 – 20 000 ppm

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3 Stability

Description	Concentration Range	Storage Conditions	Time Period
Process Stability (Standards)	1.5 - 27 µg/mL	15°C	39 hours
Process Stability (Spiked Samples)	2 -20 µg/mL	15°C	58 hours
Stability Period 1	40 – 20 000 ppm	20°C to 25°C	22 Days
Stability Period 2	40 – 20 000 ppm	2 to 8°C	22 Days
Standard Stability (Standards)	1.5 - 27 µg/mL	2 to 8°C	6 Days
Standard Stability (Spiked Samples)	2 – 20 µg/mL	2 to 8°C	18 Days

Note: all storage conditions are unprotected from light unless specified otherwise.

4 Definitions/Abbreviations

HPLC:	High Performance Liquid Chromatography
ND:	None detected
N/A:	Not applicable
MPA:	Mobile Phase A
MPB:	Mobile Phase B
LOD:	Limit of Detection
LLOQ:	Lower Limit of Quantitation

5 Correction Factors

Purity/Salt Factor:	Refer to Protocol (for spiked samples) and Certificate of Analysis (for calibration standards).
Density:	None – no correction

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6 Materials

6.1 Chemicals

Water, HPLC grade or equivalent
Acetonitrile (ACN), HPLC grade or equivalent

6.2 Supplies

Volumetric flasks
Volumetric pipettes
Eppendorf repeater and Combi tips
Centrifuge
Tumbler Glas Col Cat # 099A RD44512 or equivalent
50 mL polypropylene conical tubes
Polypropylene screw top bottle
20 mL glass scintillation vials
Autosampler Vial Caps Snap-It Teflon Split Septa caps or equivalent
Millipore, 0.22 μ , 13 mm diameter, GV PVDF filter

7 Procedure

7.1 Preparation of Reagents

Other volumes may be prepared using the same proportions. Store all reagents at room temperature and use within 1 month unless noted otherwise.

7.1.1 Mobile Phase A, Acetonitrile

Transfer approximately 1000 mL ACN into a suitable container.

7.1.2 Mobile Phase B, Water

Transfer approximately 1000 mL water into a suitable container. Use within 1 week of opening bottle ("Use by" date).

7.1.3 Needle Rinse, ACN:Water, 90:10, v:v

Transfer 450 mL ACN into a suitable container and add 50 mL water. Mix well.

7.1.4 Diluent or Extraction Solution, 100% Acetonitrile

Use as supplied.

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7.2 Preparation of Stocks, Working Stocks, Standards and Blanks

Different volumes may be prepared with Project Scientist approval as long as concentrations remain the same.

Stocks, working stocks, standards and blanks should be stored at $5^{\circ}\text{C} \pm 3^{\circ}\text{C}$.

7.2.1 Preparation of Stocks

	Malathion Analytical Standard (CSA-10744) weight (mg)*	Volumetric Flask (mL)	Diluent
Stock A	60.24 ± 1.2	100	Diluent
Stock B	60.24 ± 1.2	100	Diluent

* Record weights to the nearest 0.01 mg. Weights are corrected for a purity of 99.6%.

7.2.2 Preparation of Working Stocks

	Aliquot from Stock A (mL)	Aliquot from Stock B (mL)	Volumetric Flask (mL)	Diluent
Working Stock A	10	N/A	100	Diluent
Working Stock B	N/A	10	100	Diluent

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7.2.3 Preparation of Standards and Diluent Blank

Calibration Standards	Aliquot from Working Stock A (mL)	Aliquot from Working Stock B (mL)	Volumetric Flask (mL)	Diluent
A1	0.5	N/A	20	Diluent
A2	2	N/A	20	Diluent
A3	6	N/A	20	Diluent
B1	N/A	1	20	Diluent
B2	N/A	4	20	Diluent
B3	N/A	9	20	Diluent
Diluent Blank	N/A	N/A	*	Diluent

* Transfer approximately 1mL Diluent into an injection vial.

7.3 Preparation of Spiked Samples and Vehicle Blanks

Different volumes may be prepared with Project Scientist approval as long as concentrations remain the same.

Spike stocks, spiked samples and vehicle blanks should be stored at $5^{\circ}\text{C} \pm 3^{\circ}\text{C}$.

7.3.1 Preparation of Spike Stock B

	Malathion Technical (CSA-10758) weight (mg)*	Volumetric Flask (mL)	Diluent
Spike Stock B	208.3 ± 4.0	5	Diluent

* Material with different CSA number may be used as long as the material has the same lot/batch no. used to prepare the dose formulations. Record weights to the nearest 0.01 mg; weights are corrected for a purity of 96%.

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7.3.2 Preparation of Spike Stock A

Spiked Samples	Aliquot from Spike Stock B (mL)	Volumetric Flask (mL)	Diluent
Spike Stock A	0.5	250	Diluent

7.4 Preparation of Spiked Samples and Vehicle Blanks

Prepare spiked samples and vehicle blank in duplicate at each level.

Spiked Samples	Aliquot from Spike Stock A (mL)	Aliquot from Spike Stock B (mL)	Feed (g)*	Corn Oil (mg)**	Extraction Solution Added (mL)***
Spike A	0.5	NA	1.0	50 ± 2.0	20
Spike B	NA	0.5	1.0	50 ± 2.0	20
Vehicle Blank	NA	NA	1.0	50 ± 2.0	20

* Record weights to the nearest 0.001 g.

** Record weights to the nearest 0.01 mg.

*** Use a verified repeater pipette or volumetric pipette

7.4.1 Weigh blank rodent diet directly into tared 50 mL polypropylene conical tubes.

7.4.2 For Spike A and Spike B, add Spike Stock A and Spike Stock B, respectively, to the diet and dry spiked diets for at least 75 minutes at ambient temperature, under a fume hood.

7.4.3 Add corn oil to the dried spiked diets (spiked samples) and blank diet (vehicle blanks). Mix to coat the diet with corn oil.

7.4.4 Add the required amount of extraction solution.

7.4.5 Tightly cap the tubes, tumble in a rotary tumbler for at least 75 minutes at a speed set at 50%.

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7.4.6 Centrifuge for 10 minutes at a speed set at 2500 rpm.

7.4.7 Filter extracts into individual 20 mL glass scintillation vials, discarding the first 1 mL of filtrate to waste.

7.4.8 Dilute Spike B extracts as indicated in the dilution table below. Mix well and transfer an aliquot of each final dilution into individual autosampler vials.

Spiked Sample	Aliquot of Spike B (mL)	Volumetric Flask (mL)	Diluent
Spike B	0.5	25	Diluent

7.4.9 Transfer aliquots of each spike A and vehicle blank filtrate into individual autosampler vials.

7.5 Sample Preparation

Dilution schemes other than those listed in the tables below may be utilized with Project Scientist approval. The sample concentrations for all dilutions must be within the validated range of the method.

If samples are provided in single, extract each sample in duplicate. If samples are provided in duplicate, extract each sample in single.

Diluted samples should be stored at $5^{\circ}\text{C} \pm 3^{\circ}\text{C}$.

7.5.1 Weigh 1.0 g of sample directly into a tarred 50 mL polypropylene conical tube using a balance capable of reading at least 0.001 g.

7.5.2 Using a verified repeater pipette or volumetric pipette, add 20 mL Extraction Solution.

7.5.3 Tightly cap the tubes, tumble in a rotary tumbler for at least 75 minutes at a speed set at 50%.

7.5.4 Centrifuge for 10 minutes at a speed set at 2500 rpm.

7.5.5 Filter extracts into individual 20 mL glass scintillation vials, discarding the first 1 mL of filtrate to waste.

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7.5.6 The initial sample extracts may be diluted further as indicated in the Dilution table below. Mix well and transfer an aliquot of each final dilution into individual auto sampler vials.

Extraction		
Sample Concentration Range (ppm)	Sample Size (g)*	Extraction Solution Added (mL)**
0 and from 40 to 20 000	1.0	20

* Record weights to the nearest 0.001 g.

** Use a verified repeater pipette or volumetric pipette

Dilution			
Sample Concentration Ranges (ppm)	Aliquot from Extract (mL)	Final Dilution Volumetric Flask Size (mL)	Diluent
0 and from 40 to 359	N/A	N/A	N/A
From 360 to 599	5	10	Diluent
From 600 to 3599	1	10	Diluent
From 3600 to 8999	1	25	Diluent
From 9000 to 20 000	0.5	25	Diluent

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7.6 Analytical Run Sequence and Composition

7.6.1 The typical run list should follow this order

≥ 3 system checks	test injections
5 replicate injections	system suitability (B3 standard)
1 injection each	six point calibration curve
1 injection	diluent blank
1 injection each	vehicle blank and spiked samples
1 injection	check standard (A3)
≤ 10 injections	unknown samples
1 injection	check standard (A3)

7.6.2 Repeat last two lines as necessary if more than 10 samples are analyzed. A single replicate of the check standard is analyzed after the last unknown sample in the entire analysis batch.

7.7 Analytical Conditions

Use the HPLC system described below, adjusting the solvent ratio if necessary, to approximate the retention time listed below. Refer to the SOP for Chromatographic System Suitability.

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7.7.1 Instrumental

Pump: PerkinElmer Series 200 or equivalent
 Autosampler: PerkinElmer Series 200 or equivalent
 Detector: PerkinElmer Series 200 or equivalent
 Column Heater: PerkinElmer, Peltier Column Oven Series 200 or equivalent
 Peltier Tray: PerkinElmer Series 200 or equivalent
 Degasser: PerkinElmer Series 200 or equivalent
 Analytical Column: Phenomenex, Luna C18(2), 250 x 4.6 mm, 5µm
 Column Temperature: 30°C
 Autosampler Temp: 15°C
 Detection: Ultraviolet @ 210nm
 Sampling rate: 2 points/second
 Injection Volume: 25 µL
 Mobile Phase A: 100% Acetonitrile
 Mobile Phase B: 100% Water
 Needle Rinse: Acetonitrile:Water, 90:10, v:v
 Flow Rate: 1.4 mL/min
 Run Time: 60 minutes
 Typical Retention Time for Malathion*: 26.8 ± 1.3 minutes

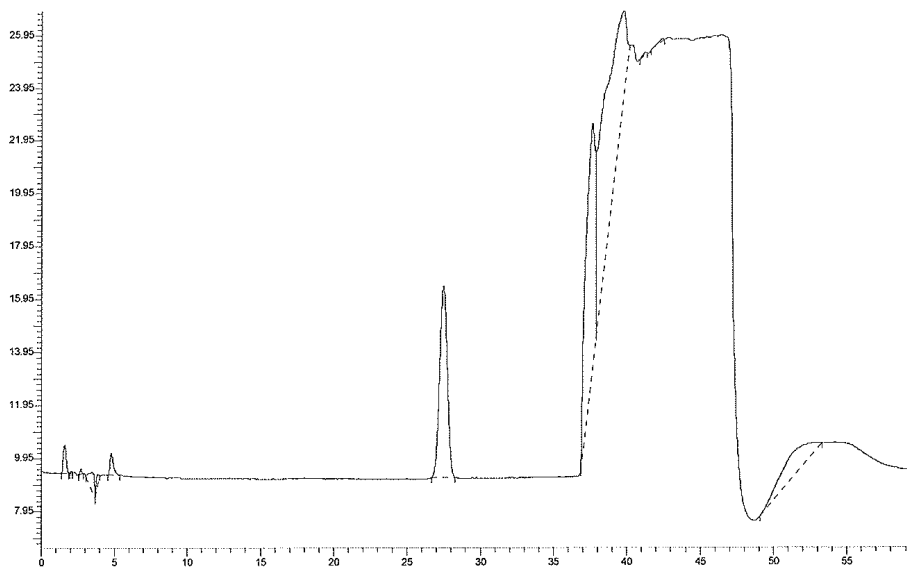
Run Type:	Gradient			
	<u>Time (min)</u>	<u>MPA%</u>	<u>MPB%</u>	<u>Curve**</u>
	0.5	45	55	0
	34.0	45	55	0
	0.1	90	10	1
	10.0	90	10	0
	0.1	45	55	1
	15.8	45	55	0

* Retention times outside of this window may be accepted with Project Scientist approval as long as there are no significant peaks interfering with the Malathion.

** Gradient (1 denotes a linear Curve).

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7.7.2 Example Chromatogram for B3 Standard



7.8 Calculations

- 7.8.1 Chromatograms will be automatically integrated and visually inspected for an acceptable integration.
- 7.8.2 Calculate the relative standard deviation (%) of the peak areas, the relative standard deviation (%) of the retention time and the mean tailing factor for five system suitability injections.
- 7.8.3 Calculate the reference standard concentration of the calibration standards, in terms of microgram of Malathion per milliliter.
- 7.8.4 Compute the unweighted linear regression relating the peak areas of the standards to their respective Malathion concentrations, without blank correction.
- 7.8.5 Compute the correlation coefficient for the standard curve.

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7.8.6 Using the peak area of the spiked samples and samples, and the regression equation, determine the concentration in ppm of Malathion. Correct for the dilution factor if necessary.

7.8.7 Concentrations found to be less than the lowest calibration standard will be reported as <LLOQ. In cases, such as blank samples, where no peak is observed, the results will be reported as none detected (ND).

7.8.8 Calculate mean concentrations for replicate samples. Calculate the percent error from theoretical as: (mean concentration found – theoretical concentration) / theoretical concentration x 100.

7.9 Acceptance Criteria

7.9.1 System Suitability

The Malathion peaks in the five system suitability injections must meet the following acceptable limits: The mean tailing factor ≤ 2 , the relative standard deviation (%) of the peak areas $\leq 2\%$, and the relative standard deviation (%) of the retention time $\leq 2\%$. If the criteria are out of the acceptable limits, make corrections to the HPLC system and repeat the suitability injections.

7.9.2 Correlation Coefficient

The correlation coefficient for the standard curve must not be less than 0.995. If the value is not greater than or equal to 0.995, repeat the preparation of the standard curve.

7.9.3 Calibration Standards

The back-calculated concentrations for calibration standards must be within $\pm 5\%$ of their nominal theoretical concentrations. Standards not meeting criteria can be dropped as long as no more than 20% of standards are dropped. The LLOQ or ULOQ will be redefined to the remaining lowest or highest standards if necessary.

7.9.4 Check Standards

The back-calculated concentration for the A3 check standards must be within 5% of nominal theoretical concentration.

7.9.5 Spiked Samples

The back-calculated concentrations for the spiked samples must be within $\pm 15\%$ of their nominal theoretical concentration.

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7.9.6 Replication of Results

Replicate concentrations found for diet formulations must not vary by more than 15%. Acceptance is defined as: $(\text{low value} / \text{high value}) \geq 0.85$. Results that do not meet this criterion will be reviewed by the Project Scientist. Reason for acceptance will be documented in the raw data.

8 Revision History

- 8.1 Initial Analytical Procedure: Method validation performed at Charles River Laboratories Preclinical Services, Pennsylvania under project TQC00067DX.
- 8.2 Revision 00 to 01:
 - 8.2.1 Section 3: Added Stability Period 1 and 2, and Standard Stability data.
 - 8.2.2 Preparation of Spiked Samples and Vehicle Blanks form: Added space to document corn oil details.
- 8.3 Revision 01 to 02:
 - 8.3.1 Section 3: Changed the storage condition.
- 8.4 Revision 02 to 03:
 - 8.4.1 Section 8.3: Corrected typographical error.
- 8.5 Revision 03 to 04:
 - 8.5.1 Section 2: Correct vehicle identification.
 - 8.5.2 Section 7.7.2: Updated chromatogram.

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APPENDIX I BATCH AND REAGENT PAPERWORK

'Preparation of Reagents', 'Calibration Standard Preparation', 'Preparation of Spike Stocks', 'Preparation of Spiked Samples and Vehicle Blanks', 'Preparation of Samples' and 'Instrument Parameters' sheets in the AP appendix will be copied from the current signed AP revision, filled out recording raw data, and placed into batch folders to be stored with the study materials.

Paperwork not included in the AP appendix may also be utilized if reviewed, approved, and initialed/dated by a Project Scientist or management, and documented/filled-out properly.

Approval for batch paperwork not included in the AP should occur the day of and/or prior to the batch if possible, but this may not always be possible, in which case posterior approval will be acceptable.

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Preparation of Reagents Prepared by: _____ Date: _____

Batch ID: _____

NA ☐ Mobile Phase A (Acetonitrile) ID: _____ - _____ - _____ -MPA

Transfer approximately _____ mL ACN into a suitable container.

Storage Temperature: Room Temperature (22±5°C)

Expiration Date: _____

NA ☐ Mobile Phase B (Water) ID: _____ - _____ - _____ -MPB

Transfer approximately _____ mL water into a suitable container.

Storage Temperature: Room Temperature (22±5°C)

Expiration Date: _____

NA ☐ Needle Rinse (Acetonitrile:Water, 90:10, v:v)

ID: _____ - _____ - _____ -NR

Transfer _____ mL ACN into a suitable container and add _____ mL water. Mix well.

Storage Temperature: Room Temperature (22±5°C)

Expiration Date: _____

Materials Used:

Water:	Vendor: _____	Grade: _____	Use by: _____	Lot #: _____	Exp: _____
Acetonitrile:	Vendor: _____	Grade: _____	Strength / Purity: _____	Lot #: _____	Exp: _____

Approved by:  Date: 05 DEC 2011

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Calibration Standard Preparation

Batch ID:

Analyst Initials: _____ Date: _____				
Stock Solutions				
Compound Name		Weight (mg)	Final Vol. (mL)	ID
	Stock A			Project Number-Notebook Number-Batch Number- -STKA
	Stock B			-STKB
Balance ID: _____ Standard Used: CSA- _____				
Diluting Solution ID: _____ Supplier: _____ Lot: _____ Expiry Date: _____				
Working Stock Solutions				
	mL of STKA	mL of STKB	Final Vol. (mL)	ID
Working Stock A				Project Number-Notebook Number-Batch Number- -WSTKA
Working Stock B				-WSTKB
Pipette ID: _____				
Diluting Solution ID: _____ Supplier: _____ Lot: _____ Expiry Date: _____				
Calibration Standards				
Standard	mL of WSTKA	mL of WSTKB	Final Vol. (mL)	ID
A1				Project Number-Notebook Number-Batch Number- -A1 -B1 -A2 -B2 -A3 -B3 -DBlk
B1				
A2				
B2				
A3				
B3				
Diluent Blank			<input type="checkbox"/> ¹	
Pipette ID: _____				
Diluting Solution ID: _____ Supplier: _____ Lot: _____ Expiry Date: _____				
¹ Transfer ~ 1 mL of Diluent into an injection vial Dilutions stored in unit _____				

Approved by:  Date: 05 DEC 2011

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Preparation of Spiked Stocks

Batch ID:

Analyst Initials: _____ Date: _____					
Spike Stock B Solution					
Compound Name		Weight (mg)	Final Vol. (mL)	ID	
	Spike Stock B			Project Number-Notebook Number-Batch Number- _____	-SPK STKB
Balance ID: _____ Standard Used: CSA- _____					
Diluting Solution ID: _____ Supplier: _____ Lot: _____ Expiry Date: _____					
Spike Stock A Solution					
	mL of SPK STK B	Final Vol. (mL)	ID		
Spike Stock A			Project Number-Notebook Number-Batch Number- _____	-SPK STKA	
Pipette ID: _____					
Diluting Solution ID: _____ Supplier: _____ Lot: _____ Expiry Date: _____					
Dilutions stored in unit _____					

Approved by: 197 Date: 05DEC2011

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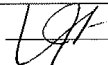
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Preparation of Spiked Samples and Vehicle Blanks

Batch ID: _____

Analyst Initials: _____ Date: _____									
Spiked Samples and Vehicle Blanks									
	Extraction					Dilution		ID	
	mL of SPK STK A ^A	mL of SPK STK B ^A	Feed (g) ^C	Corn Oil (mg) ^D	Extraction Solution Added (mL) ^B	mL of Super-natant ^A	Final Vol. (mL)		
A1								Project Number-Notebook Number-Batch Number- _____	-SPK A1
A2									-SPK A2
B1									-SPK B1
B2									-SPK B2
VBLK a									-VBLK a
VBLK b									-VBLK b
Pipette ID: ^A _____ ^B _____ Balance ID: ^C _____ <input type="checkbox"/> (weigh into 50 mL polypropylene tubes) ^D _____ Feed: Meal Form Certified Rodent Diet @ #5002 ID: _____ Supplier: _____ Lot: _____ Exp: _____ Diluting Solution ID: _____ Supplier: _____ Lot: _____ Expiry Date: _____ <u>Extraction Procedure</u> 1. Allow spiked feed to dry at ambient temperature, under a fume hood. Start Time: _____ End Time: _____ 2. Add corn oil to diet and mix <input type="checkbox"/> ; Corn Oil: Supplier: _____ Lot #: _____ Expiration Date: _____ 3. After adding extraction solution, tightly cap tubes and mix on a rotary tumbler Start Time: _____ End Time: _____ Speed: _____ Tumbler ID: _____ 4. Centrifuge tubes: _____ rpm _____ minutes. Centrifuge ID: _____ 5. Filter extracts, discard first 1 mL to waste Filter – Supplier: _____ Type: _____ Pore Size: _____ Diameter: _____ Lot: _____ Storage unit _____									

Approved by:  Date: 05 DEC 2011


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Instrument Parameters

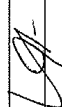
Batch ID:				
Analyst Initials:		Date:		
Data System:		TotalChrom 6.2.1		
PALC#:				
Column:	Brand			
	Type			
	Size (LxW, particle size)			
	S/N			
Pressure:		psi		
Sampling Rate:		pts/sec		
Column Temperature:		deg C		
Autosampler Temperature:		deg C		
Wavelength:		nm		
Injection Volume:		µL		
Run Time:		min		
Flow Rate:		mL/min		
Sequence:				
Mobile Phase A:				
Mobile Phase B:				
Needle Rinse:				
Run Type:		Gradient Program		
	Time (min)	%MPA	%MPB	Curve

Approved by:  Date: 05 DEC 2011

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Sample Preparation

Analyst Initials:		Batch ID:		Date:			
Samples Received:		General ID:		Prep Date(s):			
Group No.	Sample ID	Conc. (ppm)	Sample Weights(g) ^A	Vol. of Extraction Solution Added (mL) ^B	mL of Extract ^C	Vol. of Dilution (mL)	Final Dilution ID
							Project Number-Notebook Number-Batch Number
Balance ID: ^A <input type="checkbox"/> (weigh into 50 mL polypropylene tubes) Pipette ID: ^B _____ C _____							
Diluting Solution ID: _____ Supplier: _____ Lot: _____ Expiry Date: _____							
1. Tightly cap the tubes and mix on a rotary tumbler Start Time: _____ End Time: _____ Speed _____ % Tumbler ID: _____							
2. Centrifuge tubes at _____ rpm for _____ minutes Centrifuge ID: _____							
3 Filter extracts, discard first 1 mL to waste; Filter— Supplier: _____ Type: _____ Pore Size: _____							
Diameter: _____ Lot: _____ Storage Unit: _____							

Approved by:  Date: 05 DEC 2011

APPENDIX 3
DOSE FORMULATION ANALYSIS REPORTS

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DOSE FORMULATION ANALYSIS REPORT

Sponsor: Cheminova A/S
Study Facility: Charles River Laboratories Preclinical Services, Pennsylvania
Protocol Number: TQC00065
Analyte: Malathion
Analytical Facility: Charles River Laboratories Preclinical Services, Pennsylvania
Batch ID: TQC00065AA-1-001-1
Sampling Criteria: Start of Study Concentration and Homogeneity Analysis
Vehicle: Meal Form of Certified Rodent Diet #5002 with 5% Corn Oil
Storage Conditions: 5±3°C, Protect From Light
Analytical Procedure: MALA02 Revision 00
Analysis Date: October 18, 2010
Notes: Standards were corrected for a purity of 99.6%.

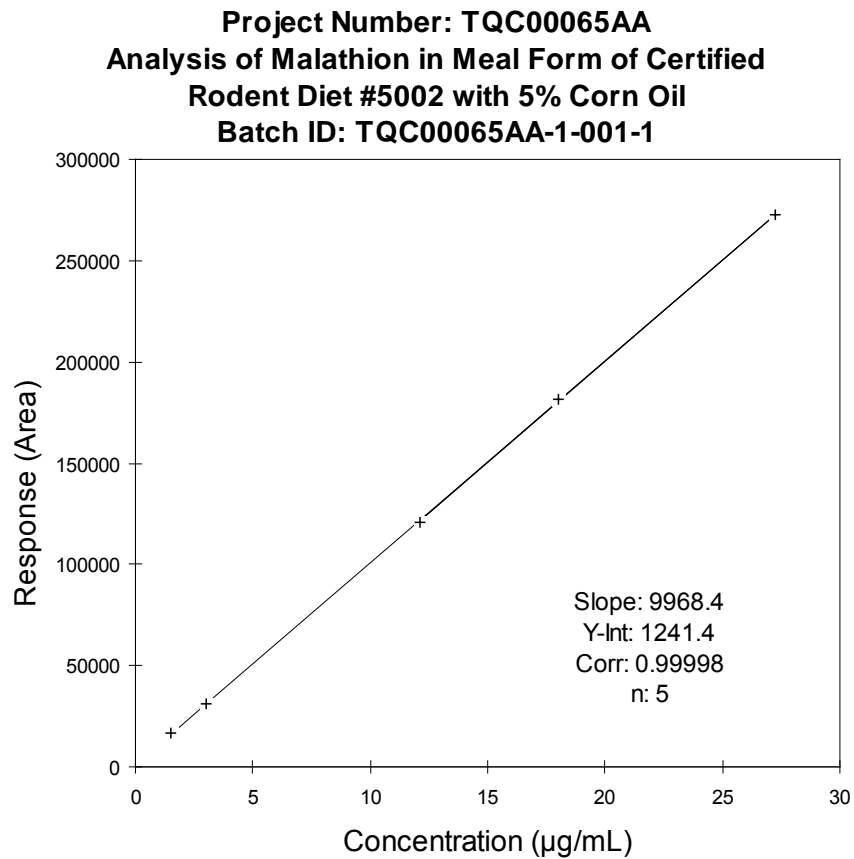
RESULTS: (Concentrations in µg/mL (Standards), ppm (Samples); ND = none detected)

CALIBRATION STANDARDS

Standard <u>Description</u>	Nominal <u>Conc.</u>	Response <u>Area</u>	Calculated <u>Conc.</u>	% <u>Bias</u>	"X" = <u>Exclude</u>	Criteria <u>Limit</u>	Standard <u>Pass/Fail</u>
Cal Std A1	1.502	16828	1.564	+4.1		5%	PASS
Cal Std B1	3.024	30921	2.977	-1.6		5%	PASS
Cal Std A2	6.010	59802	5.875	-2.2	X	5%	PASS
Cal Std B2	12.10	121067	12.02	-0.7		5%	PASS
Cal Std A3	18.03	181779	18.11	+0.4		5%	PASS
Cal Std B3	27.22	272415	27.2	-0.1		5%	PASS

CHECK STANDARDS

Standard <u>Description</u>	Nominal <u>Conc.</u>	Response <u>Area</u>	Dilution <u>Factor</u>	Conc. <u>Found</u>	% <u>Bias</u>	Criteria <u>Limit</u>	Standard <u>Pass/Fail</u>
Check Std A3	18.03	180734	1	18.01	-0.1	5%	PASS
Check Std A3	18.03	182528	1	18.19	+0.9	5%	PASS
Check Std A3	18.03	182072	1	18.14	+0.6	5%	PASS
Check Std A3	18.03	183596	1	18.29	+1.4	5%	PASS



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SAMPLES

<u>Sample Description</u>	<u>Prep Date</u>	<u>Nominal Sample Conc.</u>	<u>Replicate</u>	<u>Response Area</u>	<u>Total Dilution Factor</u>	<u>Density Corrected ppm</u>	<u>Mean ppm Found</u>	<u>% Bias</u>
Group I Top	10/18/10	0	A	0	19.92	ND		
			B	0	19.69	ND		
Group I Middle	10/18/10	0	A	0	19.59	ND		
			B	0	19.90	ND		
Group I Bottom	10/18/10	0	A	0	20.00	ND		
			B	0	19.67	ND		
Group II Top	10/18/10	100	A	53776	19.88	104.8	102.8	+2.8
			B	51893	19.84	100.8		
Group II Middle	10/18/10	100	A	51623	19.69	99.49	99.69	-0.3
			B	51719	19.72	99.88		
Group II Bottom	10/18/10	100	A	51548	19.84	100.1	98.89	-1.1
			B	50020	19.96	97.67		
Group III Top	10/18/10	500	A	128572	39.33	502.4	507.0	+1.4
			B	130782	39.37	511.6		
Group III Middle	10/18/10	500	A	123719	39.88	490.0	495.0	-1.0
			B	126196	39.88	499.9		
Group III Bottom	10/18/10	500	A	122681	39.72	483.9	488.1	-2.4
			B	126345	39.22	492.2		
Group IV Top	10/18/10	5000	A	98974	496.5	4868	4904	-1.9
			B	100012	498.5	4939		
Group IV Middle	10/18/10	5000	A	101203	494.1	4954	4880	-2.4
			B	99263	488.8	4806		
Group IV Bottom	10/18/10	5000	A	100373	491.2	4884	4862	-2.8
			B	98692	495.0	4840		
Group V Top	10/18/10	10000	A	101622	998.0	10050	10070	+0.7
			B	104001	977.5	10080		
Group V Middle	10/18/10	10000	A	100087	1000	9916	9978	-0.2
			B	102021	993.0	10040		
Group V Bottom	10/18/10	10000	A	100137	983.3	9755	9838	-1.6
			B	101327	988.1	9921		

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HOMOGENEITY

Sample	Nominal	Grand		
<u>Description</u>	<u>Sample</u>	<u>Mean</u>	<u>%</u>	<u>%</u>
	<u>Conc.</u>	<u>Conc.</u>	<u>RSD</u>	<u>Error</u>
Group II	100	100.5	2.1	0.5
Group III	500	496.7	1.9	-0.7
Group IV	5000	4882	0.4	-2.4
Group V	10000	9962	1.2	-0.4

CONCLUSIONS: Results indicate that the formulations are within the acceptable limits of $\pm 10\%$ of the nominal concentrations. The formulations are also within the acceptable limits of $\leq 5\%$ RSD for homogeneity.

ACTIONS TAKEN: None

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DOSE FORMULATION ANALYSIS REPORT

Sponsor: Cheminova A/S
Study Facility: Charles River Laboratories Preclinical Services, Pennsylvania
Protocol Number: TQC00065
Analyte: Malathion
Analytical Facility: Charles River Laboratories Preclinical Services, Pennsylvania
Batch ID: TQC00065AA-1-002-1
Sampling Criteria: Week Two Concentration Analysis
Vehicle: Meal From of Certified Rodent Diet #5002 with 5% Corn Oil
Storage Conditions: NA
Analytical Procedure: MALA02 Revision 00
Analysis Date: October 25, 2010
Notes: Standards were corrected for a purity of 99.6%

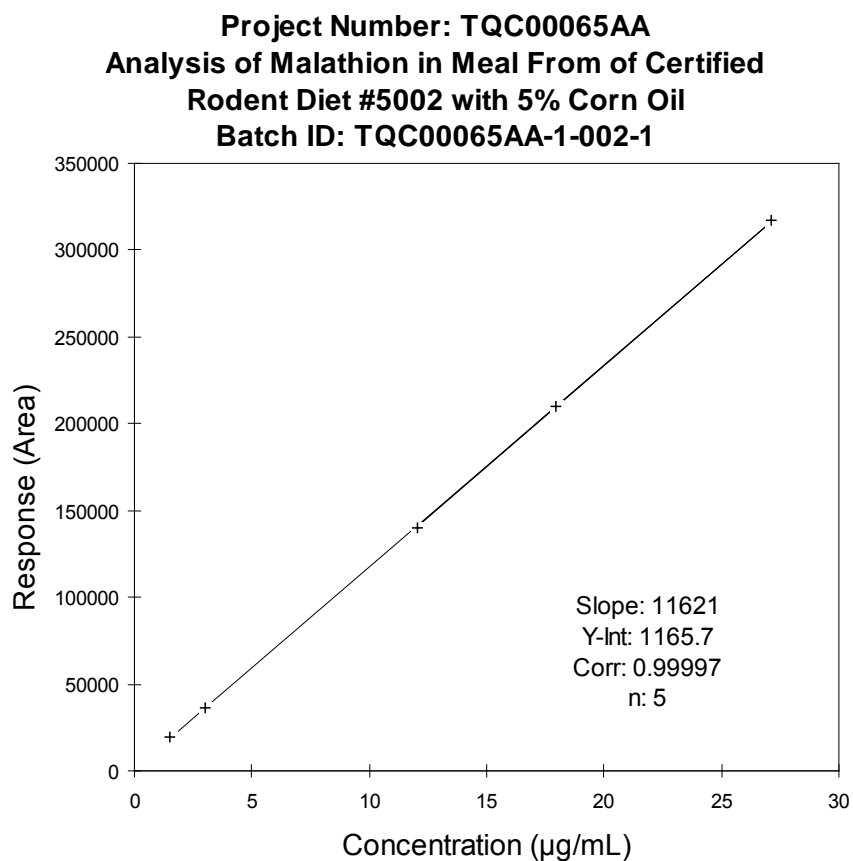
RESULTS: (Concentrations in µg/mL (Standards), ppm (Samples); ND = none detected)

CALIBRATION STANDARDS

Standard <u>Description</u>	Nominal <u>Conc.</u>	Response <u>Area</u>	Calculated <u>Conc.</u>	% <u>Bias</u>	"X" = <u>Exclude</u>	Criteria <u>Limit</u>	Standard <u>Pass/Fail</u>
Cal Std A1	1.497	19142	1.547	+3.3		5%	PASS
Cal Std B1	3.014	36514	3.042	+0.9		5%	PASS
Cal Std A2	5.990	69083	5.844	-2.4	X	5%	PASS
Cal Std B2	12.06	139778	11.93	-1.1		5%	PASS
Cal Std A3	17.97	210070	17.98	+0.1		5%	PASS
Cal Std B3	27.13	317025	27.18	+0.2		5%	PASS

CHECK STANDARDS

Standard <u>Description</u>	Nominal <u>Conc.</u>	Response <u>Area</u>	Dilution <u>Factor</u>	Conc. <u>Found</u>	% <u>Bias</u>	Criteria <u>Limit</u>	Standard <u>Pass/Fail</u>
Check Std A3	17.97	211959	1	18.14	+0.9	5%	PASS
Check Std A3	17.97	213132	1	18.24	+1.5	5%	PASS



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SAMPLES

<u>Sample Description</u>	<u>Prep Date</u>	<u>Nominal Sample Conc.</u>	<u>Replicate</u>	<u>Response Area</u>	<u>Total Dilution Factor</u>	<u>Density Corrected ppm</u>	<u>Mean ppm Found</u>	<u>% Bias</u>
Group I	10/25/10	0	A	0	19.92	ND		
			B	0	19.96	ND		
Group II	10/25/10	100	A	60966	19.98	102.8	100.2	+0.2
			B	57877	20.00	97.60		
Group III	10/25/10	500	A	145146	39.80	493.1	490.7	-1.9
			B	144122	39.68	488.2		
Group IV	10/25/10	5000	A	120805	496.5	5112	5077	+1.5
			B	118695	498.5	5042		
Group V	10/25/10	10000	A	118589	997.0	10070	10350	+3.5
			B	125526	992.1	10620		

CONCLUSIONS: Results indicate that the formulations are within the acceptable limits of $\pm 10\%$ of nominal concentrations.

ACTIONS TAKEN: None

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DOSE FORMULATION ANALYSIS REPORT

Sponsor: Cheminova A/S
Study Facility: Charles River Laboratories Preclinical Services, Pennsylvania
Protocol Number: TQC00065
Analyte: Malathion
Analytical Facility: Charles River Laboratories Preclinical Services, Pennsylvania
Batch ID: TQC00065AA-1-003-1
Sampling Criteria: Week Four (End of Study) Concentration Analysis
Vehicle: The Meal Form of Certified Rodent Diet #5002 with 5% Corn Oil
Storage Conditions: 5±3°C, Protected From Light
Analytical Procedure: MALA02 Revision 00
Analysis Date: November 09, 2010
Notes: Standards were corrected for a purity of 99.6%.

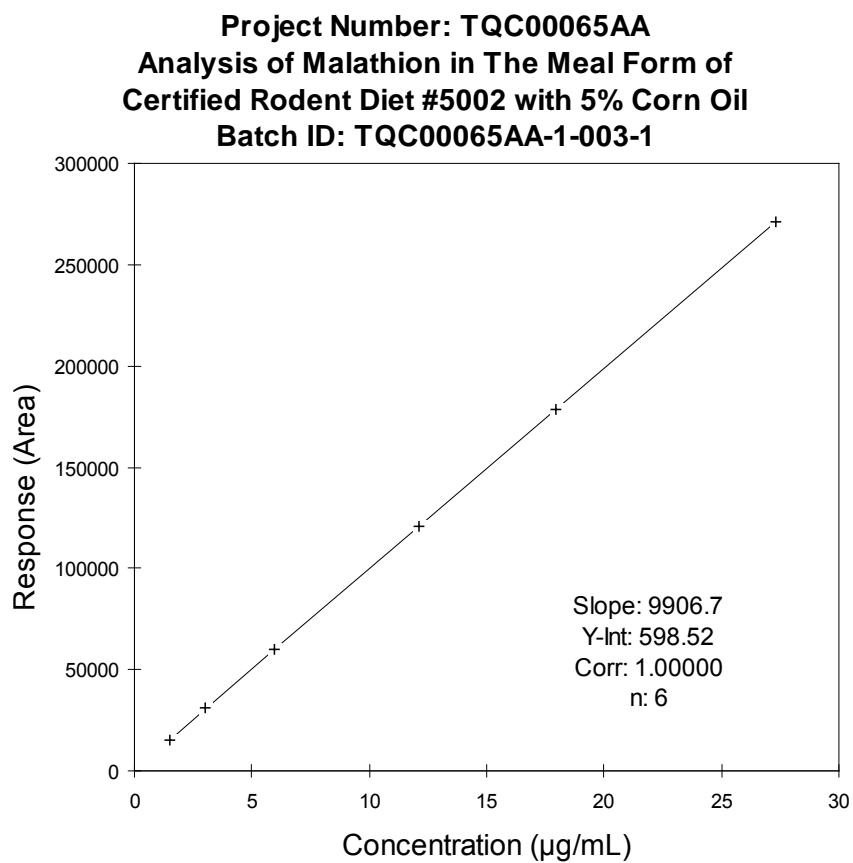
RESULTS: (Concentrations in µg/mL (Standards), ppm (Samples); ND = none detected)

CALIBRATION STANDARDS

Standard <u>Description</u>	Nominal <u>Conc.</u>	Response <u>Area</u>	Calculated <u>Conc.</u>	% <u>Bias</u>	"X" = <u>Exclude</u>	Criteria <u>Limit</u>	Standard <u>Pass/Fail</u>
Cal Std A1	1.498	15260	1.480	-1.2		5%	PASS
Cal Std B1	3.033	31094	3.078	+1.5		5%	PASS
Cal Std A2	5.991	59632	5.959	-0.5		5%	PASS
Cal Std B2	12.13	120759	12.13	0.0		5%	PASS
Cal Std A3	17.97	178685	17.98	+0.1		5%	PASS
Cal Std B3	27.3	271041	27.30	0.0		5%	PASS

CHECK STANDARDS

Standard <u>Description</u>	Nominal <u>Conc.</u>	Response <u>Area</u>	Dilution <u>Factor</u>	Conc. <u>Found</u>	% <u>Bias</u>	Criteria <u>Limit</u>	Standard <u>Pass/Fail</u>
Check Std A3	17.97	178603	1	17.97	0.0	5%	PASS
Check Std A3	17.97	179450	1	18.05	+0.4	5%	PASS



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SAMPLES

<u>Sample Description</u>	<u>Prep Date</u>	<u>Nominal Sample Conc.</u>	<u>Replicate</u>	<u>Response Area</u>	<u>Total Dilution Factor</u>	<u>Density Corrected ppm</u>	<u>Mean ppm Found</u>	<u>% Bias</u>
Group I	11/08/10	0	A	0	19.98	ND		
			B	0	19.84	ND		
Group II	11/08/10	100	A	53606	19.86	106.3	105.2	+5.2
			B	52372	19.90	104.0		
Group III	11/08/10	500	A	123877	40.00	497.8	502.6	+0.5
			B	127743	39.53	507.3		
Group IV	11/08/10	5000	A	99418	498.0	4968	5046	+0.9
			B	104032	490.7	5123		
Group V	11/08/10	10000	A	94031	995.0	9384	9510	-4.9
			B	97491	985.2	9636		

CONCLUSIONS: Results indicate that the formulations are within the acceptable limits of $\pm 10\%$ of nominal concentrations.

ACTIONS TAKEN: None

APPENDIX 7 - BENCHMARK DOSE MODELING REPORT



**Benchmark Dose Modeling for
Cholinesterase Inhibition for
Malathion in TQC65**

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December 7, 2011

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QMS QA ID no. V10532.000 A0T0 1211 RR07

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This report contains confidential and proprietary information of Cheminova A/S, which must not be disclosed to anyone except the employees of this company or to persons authorized by law or juridical judgment, without the expressed and written approval of Cheminova A/S.

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This report provides a statistical evaluation of certain data from the following study:

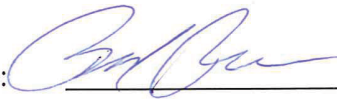
“Benchmark dose modeling for cholinesterase inhibition for malathion in TQC65”

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Author:

Rick Reiss, Sc.D.
Exponent

Signature: _____



Date: _____

12/7/11

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Executive Summary

Cheminova conducted a 28-day repeated dose dietary toxicity study of malathion technical in rats (Barnett, 2012).

This report presents a benchmark dose (BMD) analysis of the data for red blood cell (RBC) and brain cholinesterase inhibition. BMD analysis provides a statistical estimate of the dose that causes a given level of inhibition. BMD estimates are generally more accurate than No Observed Effect Levels (NOELs) because (1) they are not as sensitive to sample size, (2) not as sensitive to the dose levels tested, and (3) they model the shape of the dose-response curve.

BMD estimates were calculated corresponding to plausible values of interest for risk assessment, including BMDs corresponding to 20% (BMD₂₀) inhibition of RBC cholinesterase and 10% inhibition (BMD₁₀) of brain cholinesterase.

An exponential model recommended by the U.S. Environmental Protection Agency (EPA) was used and provided an adequate fit to the data. The BMD estimates are summarized in the table below.

Compartment	BMD	BMD Estimate (mg/kg-bw/day) [BMDL in parentheses]	
		Males	Females
RBC	BMD ₂₀	45.6 (37.7)	42.9 (34.6)
Brain	BMD ₁₀	215.8 (145.1)	159.2 (135.3)

Introduction

This report provides an analysis of cholinesterase data from a 28-day repeated dose dietary toxicity study of malathion technical in rats (Barnett, 2012).

The basis for the analysis in this report is the estimation of benchmark doses (BMDs). BMD modeling is an alternative to No Observed Effect Levels (NOELs) in dose-response analysis. A NOEL is typically defined based on statistical comparisons of the response at each dose level with the control group. In comparison, a BMD is estimated by defining a response level of interest (e.g., a 20 percent difference from controls [BMD₂₀]) and estimating the dose that results in that level of change based on a regression analysis of the response against dose. The U.S. Environmental Protection Agency (EPA) policy mandates the statistical lower limit of the estimate be used as the point-of-departure for risk assessment (e.g., EPA 2000, EPA 2006). The 95 percent lower confidence limit on the BMD estimate is abbreviated as BMDL.

The BMD approach provides significant advantages in dose-response analysis (e.g., EPA, 2000), particularly in comparing responses across different assays or across time points within the same assay. The advantages of the BMD approach include:

- **Not as sensitive to sample size.** The NOEL is highly dependent on the sample size of the study. With large sample sizes, lower NOELs can be estimated (unless there is a clear biological threshold) because smaller differences in response can be detected. In contrast, there is no difference in the estimated BMD as a function of sample size, but the estimate is improved with larger sample sizes because the error bounds around the BMD usually are reduced (i.e., only the BMDL changes with sample size).
- **Not as sensitive to dose levels tested.** The NOEL is highly dependent on the study dose selection and the final estimate must be one of the dose levels tested, whereas the BMD can be a dose in between the dosage levels tested. Poor dose selection can result in higher or lower NOELs than justified, or sometimes a NOEL cannot be established. The BMD approach requires only

that the doses tested in the study achieve a range of responses to characterize the dose-response curve, and the BMD value can be any level across the dosage spectrum in the experiment.

- **Models the shape of the dose-response curve.** The BMD approach explicitly accounts for the shape of the dose-response curve, while the NOEL approach does not take into account the shape of the dose-response relationship.

Methodology

BMDs were estimated using EPA's methodology for cholinesterase inhibition as outlined in EPA (2006). The general dose-response model of an exponential declining curve has the following form:

$$Che = A \left[P_B + (1 - P_B) * \exp \left(\frac{\log \left(\frac{1 - P_B - BMR}{1 - P_B} \right)}{BMD} * Dose \right) \right] \quad (1)$$

where:

- Che = cholinesterase activity
- A = level of cholinesterase activity in the absence of exposure to the organophosphate
- P_B = fraction of cholinesterase activity remaining at a very high dose of the organophosphate.
- BMR = level of inhibition at which to estimate the benchmark dose (e.g., 0.20 for a 20 percent inhibition).
- BMD = benchmark dose.
- $Dose$ = dose of the chemical.

Due to difficulties simultaneously fitting A , BMD , and P_B , the P_B parameters were estimated by testing various combinations of P_B for males and females and choosing the model with the highest maximum likelihood. A power function accounted for heteroscedasticity (i.e., differences in the variance across groups).

The models were implemented in the R programming language (R Core Development Team 2011).

Available Data

The 28-day toxicity study included measurements of red blood cell (RBC) and brain cholinesterase levels. Fifteen rats were assigned to each of four dose groups (100, 500, 5000, and 10000 ppm in feed) plus a control. The actual doses were tabulated in the study report and are summarized in Table 1.

Table 1. Doses by group for cholinesterase study

Feed Level (ppm)	Male Dose (mg/kg/day)	Female Dose (mg/kg/day)
100	9.2	9.4
500	46.1	47.4
5000	457.5	461.3
10,000	947.8	910.1

RBC Cholinesterase Inhibition

Table 2 summarizes the RBC cholinesterase data used in the BMD analysis. RBC cholinesterase levels were statistically significantly reduced in the 500, 5000, and 10,000 ppm dose groups for males and the 100, 500, 5000, and 10,000 ppm dose groups for females.

Table 2. Summary of RBC cholinesterase data used in analysis

Sex	Dose (ppm) / Response (Mean \pm SD) (Units/mL)				
	0	100	500	5000	10,000
Male	1.447 \pm 0.190 (15)	1.389 \pm 0.169 (15)	1.124 \pm 0.199** (15)	0.254 \pm 0.070** (13)	0.165 \pm 0.088** (12)
Female	1.518 \pm 0.189 (15)	1.324 \pm 0.119** (15)	1.078 \pm 0.182** (15)	0.259 \pm 0.110** (11)	0.128 \pm 0.058** (10)

Note: Number of animals is presented in the parentheses.

*Statistically significant, $p < 0.05$

**Statistically significant, $p < 0.01$

Brain Cholinesterase Inhibition

Table 3 summarizes the brain cholinesterase data used in the BMD analysis. Brain cholinesterase levels were significantly reduced in the 5000, and 10,000 ppm dose groups for males and females, and also for the 500 ppm dose group for males.

Table 3. Summary of brain cholinesterase data used in analysis

Sex	Dose (ppm) / Response (Mean \pm SD) (Units/g)				
	0	100	500	5000	10,000
Male	13.314 \pm 0.981 (15)	12.959 \pm 0.881 (15)	12.355 \pm 0.793* (15)	10.458 \pm 1.026** (15)	10.494 \pm 1.381** (15)
Female	13.642 \pm 0.962 (15)	13.437 \pm 1.151 (15)	13.007 \pm 0.683 (15)	10.226 \pm 0.466** (15)	7.119 \pm 2.186** (15)

Note: Number of animals is presented in the parentheses.

*Statistically significant, $p < 0.05$

**Statistically significant, $p < 0.01$

Benchmark Dose Analysis

RBC Cholinesterase Inhibition

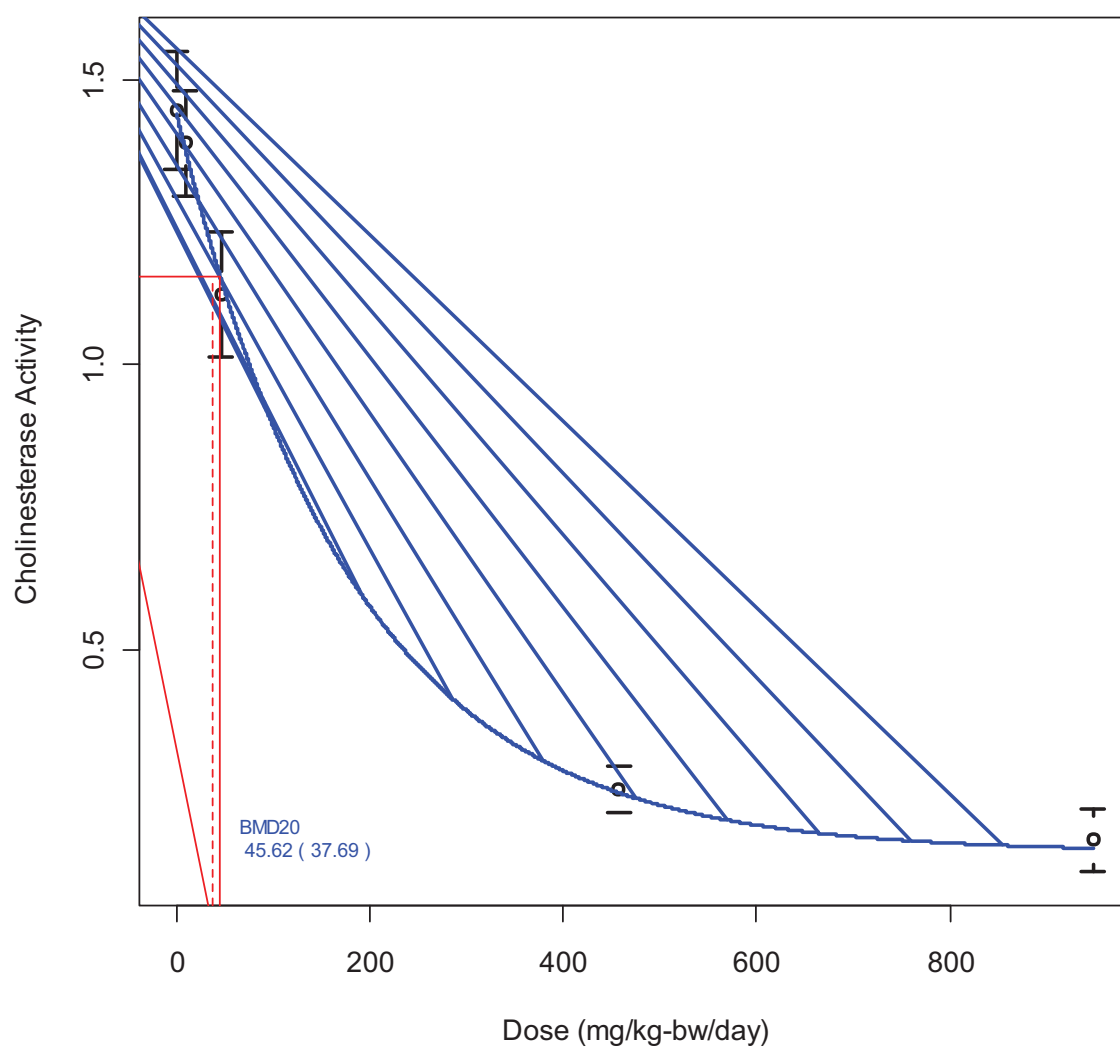
The exponential model described above was used to fit the RBC cholinesterase data and estimate BMDs for 20% inhibition. Table 4 summarizes the BMD results and the values of the other fitted parameters in the dose-response model. The RBC BMD₂₀s were 45.6 mg/kg-bw/day (BMDL₂₀=37.7 mg/kg-bw/day) for males and 42.9 mg/kg-bw/day (BMDL₂₀=34.6 mg/kg-bw/day) for females. Figures 1 and 2 show the dose-response fits to the data. The fits closely match the observations.

Table 4. Benchmark dose results for RBC cholinesterase

Sex	A (unit/mL)	P_B	BMD ₂₀ (BMDL ₂₀) (mg/kg-bw/day)
Male	1.442	0.1	45.6 (37.7)
Female	1.437	0.1	42.9 (34.6)

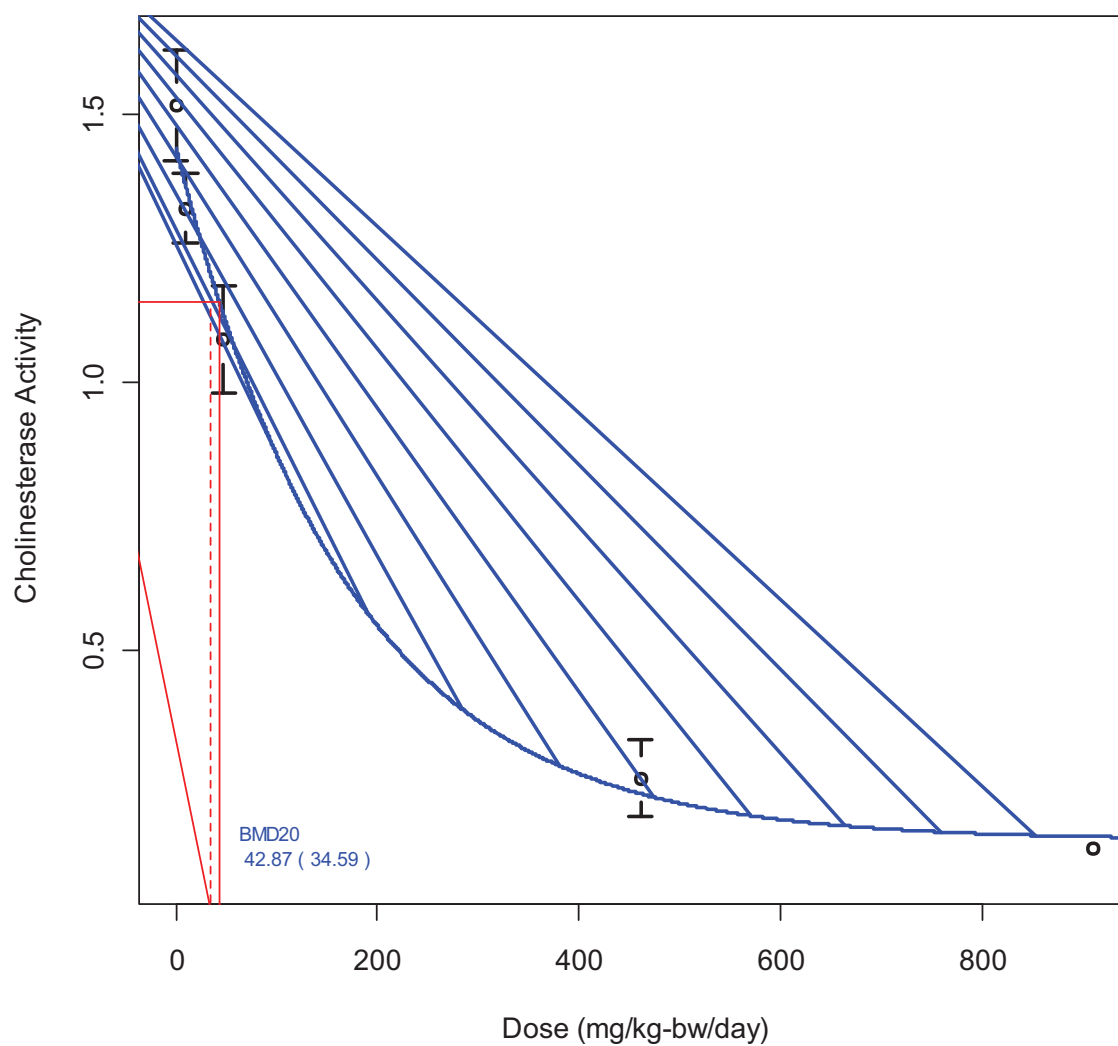
Note: A defines the cholinesterase inhibition without exposure and P_B defines the asymptotic limit for cholinesterase inhibition at a high dose.

Figure 1. Dose-response fit for RBC cholinesterase inhibition for males



Note: The BMD is shown with the solid red line and the BMDL is shown with the dashed red line.

Figure 2. Dose-response fit for RBC cholinesterase inhibition for females



Note: The BMD is shown with the solid red line and the BMDL is shown with the dashed red line.

Brain Cholinesterase Inhibition

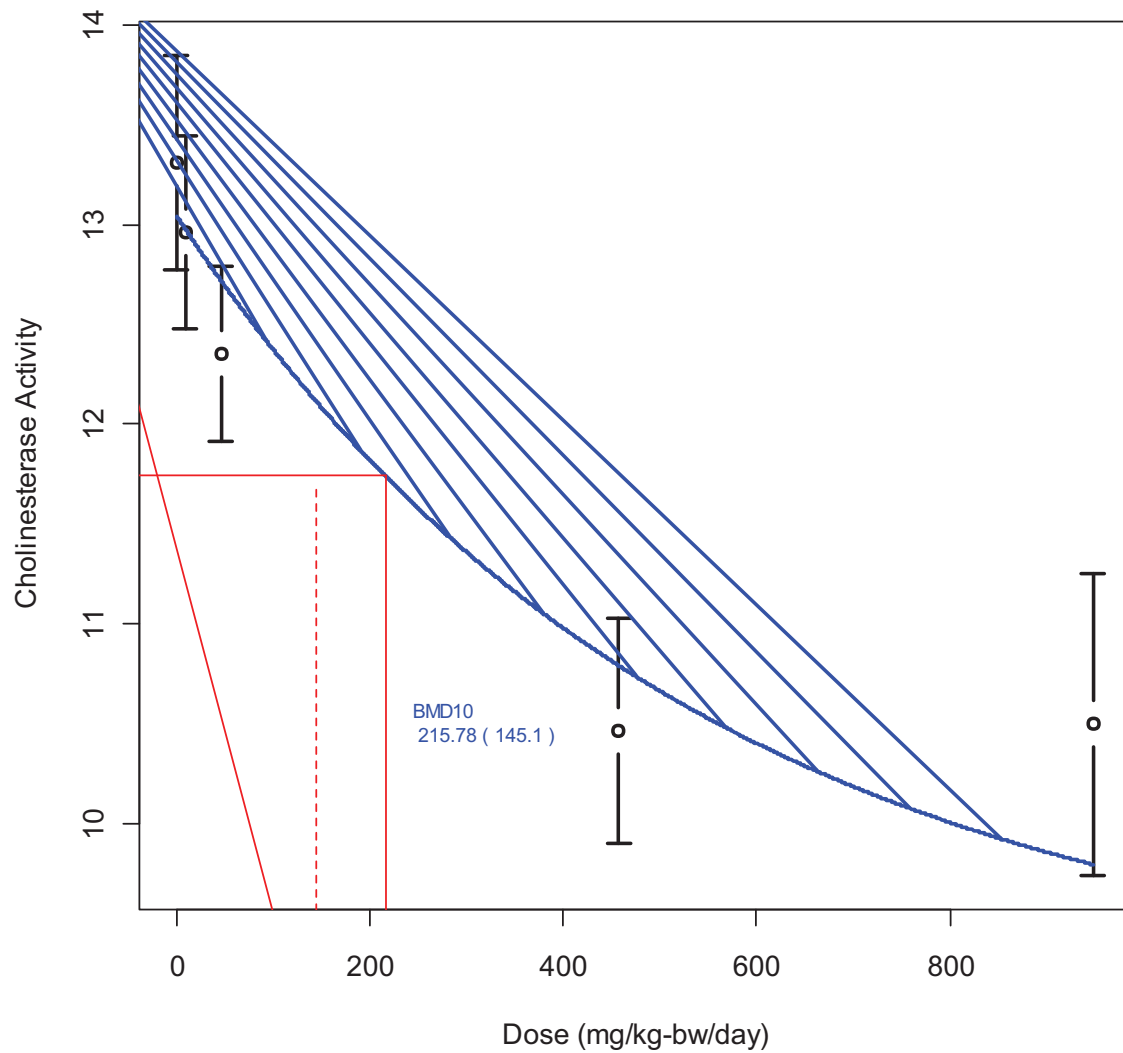
The exponential model described above was used to fit the brain cholinesterase data and estimate BMDs for 10% inhibition. The brain BMD₁₀s were 215.8 mg/kg-bw/day (BMDL₁₀=145.1 mg/kg-bw/day) for males and 159.2 mg/kg-bw/day (BMDL₁₀=135.3 mg/kg/day) for females. Table 5 summarizes the BMD results. Figures 3 and 4 show the dose-response fits to the data. The fits match the observations within the 95th percentile uncertainty bounds of the dose group means.

Table 5. Benchmark dose results for brain cholinesterase

Sex	A (units/g)	P_B	BMD ₁₀ (BMDL ₁₀) (mg/kg-bw/day)
Male	13.045	0	215.8 (145.1)
Female	13.549	0.7	159.2 (135.3)

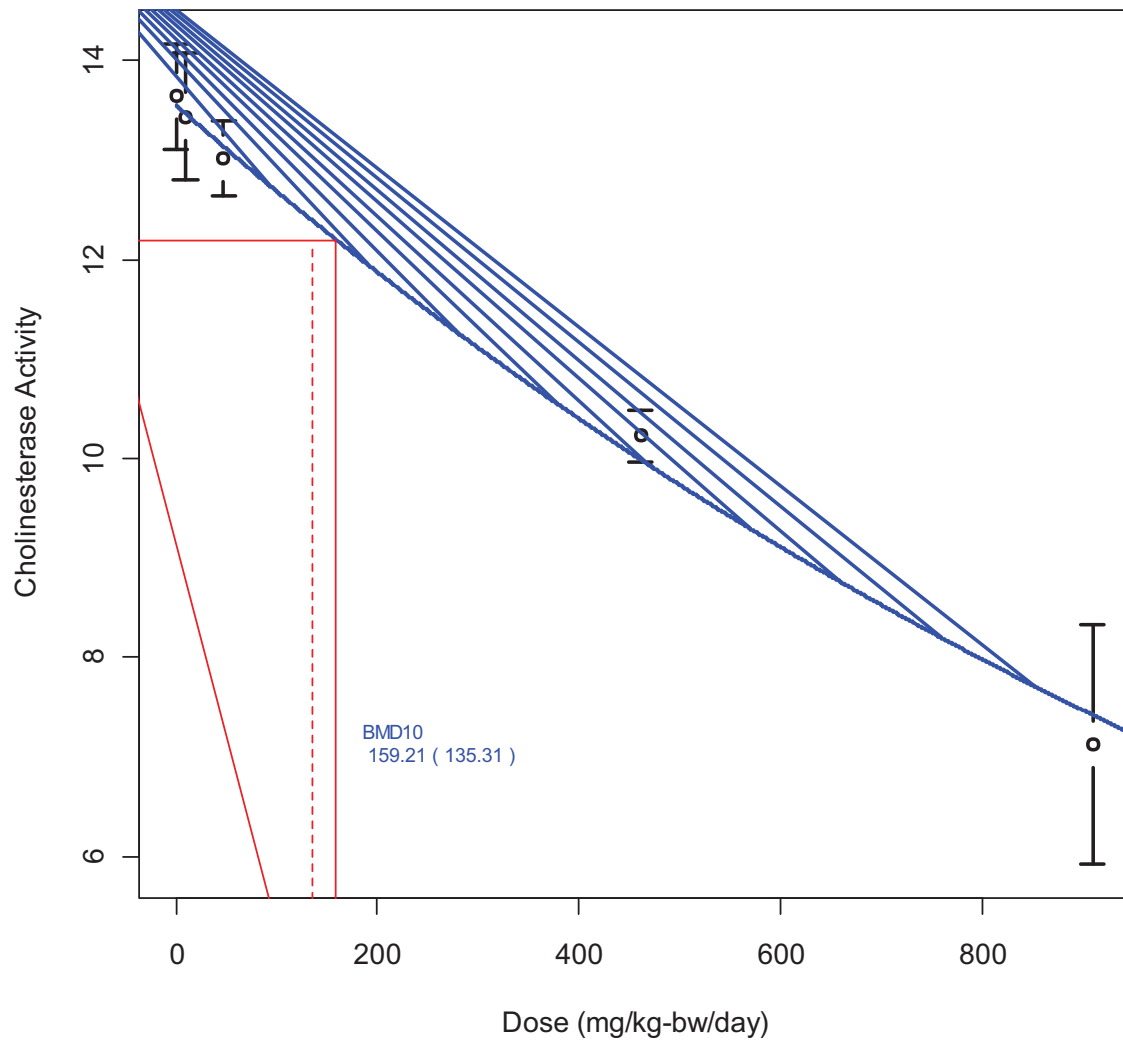
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Figure 3. Dose-response fit for brain cholinesterase inhibition for males



Note: The BMD is shown with the solid red line and the BMDL is shown with the dashed red line.

Figure 4. Dose-response fit for brain cholinesterase inhibition for females



Note: The BMD is shown with the solid red line and the BMDL is shown with the dashed red line.

Conclusions

This report provides BMD estimates for a 28-day toxicity dietary study of malathion technical in rats.

BMDs were estimated with an exponential model recommended by the U.S. EPA, which provided an adequate fit to the data. The RBC BMD₂₀ estimates were 45.6 mg/kg-bw/day (BMDL₂₀=37.7 mg/kg-bw/day) for males and 42.9 mg/kg-bw/day (BMDL₂₀=34.6 mg/kg-bw/day) for females. The brain BMD₁₀ estimates were 215.8 mg/kg-bw/day (BMDL₁₀=145.1 mg/kg-bw/day) for males and 159.2 mg/kg-bw/day (BMDL₁₀=135.3 mg/kg-bw/day) for females.

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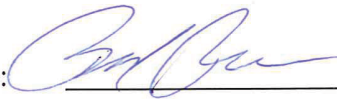
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that the doses tested in the study achieve a range of responses to characterize the dose-response curve, and the BMD value can be any level across the dosage spectrum in the experiment.

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BMDs were estimated using EPA's methodology for cholinesterase inhibition as outlined in EPA (2006). The general dose-response model of an exponential declining curve has the following form:

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where:

- Che = cholinesterase activity
- A = level of cholinesterase activity in the absence of exposure to the organophosphate
- P_B = fraction of cholinesterase activity remaining at a very high dose of the organophosphate.
- BMR = level of inhibition at which to estimate the benchmark dose (e.g., 0.20 for a 20 percent inhibition).
- BMD = benchmark dose.
- $Dose$ = dose of the chemical.

Due to difficulties simultaneously fitting A , BMD , and P_B , the P_B parameters were estimated by testing various combinations of P_B for males and females and choosing the model with the highest maximum likelihood. A power function accounted for heteroscedasticity (i.e., differences in the variance across groups).

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The 28-day toxicity study included measurements of red blood cell (RBC) and brain cholinesterase levels. Fifteen rats were assigned to each of four dose groups (100, 500, 5000, and 10000 ppm in feed) plus a control. The actual doses were tabulated in the study report and are summarized in Table 1.

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RBC Cholinesterase Inhibition

Table 2 summarizes the RBC cholinesterase data used in the BMD analysis. RBC cholinesterase levels were statistically significantly reduced in the 500, 5000, and 10,000 ppm dose groups for males and the 100, 500, 5000, and 10,000 ppm dose groups for females.

Table 2. Summary of RBC cholinesterase data used in analysis

Sex	Dose (ppm) / Response (Mean \pm SD) (Units/mL)				
	0	100	500	5000	10,000
Male	1.447 \pm 0.190 (15)	1.389 \pm 0.169 (15)	1.124 \pm 0.199** (15)	0.254 \pm 0.070** (13)	0.165 \pm 0.088** (12)
Female	1.518 \pm 0.189 (15)	1.324 \pm 0.119** (15)	1.078 \pm 0.182** (15)	0.259 \pm 0.110** (11)	0.128 \pm 0.058** (10)

Note: Number of animals is presented in the parentheses.

*Statistically significant, $p < 0.05$

**Statistically significant, $p < 0.01$

Brain Cholinesterase Inhibition

Table 3 summarizes the brain cholinesterase data used in the BMD analysis. Brain cholinesterase levels were significantly reduced in the 5000, and 10,000 ppm dose groups for males and females, and also for the 500 ppm dose group for males.

Table 3. Summary of brain cholinesterase data used in analysis

Sex	Dose (ppm) / Response (Mean \pm SD) (Units/g)				
	0	100	500	5000	10,000
Male	13.314 \pm 0.981 (15)	12.959 \pm 0.881 (15)	12.355 \pm 0.793* (15)	10.458 \pm 1.026** (15)	10.494 \pm 1.381** (15)
Female	13.642 \pm 0.962 (15)	13.437 \pm 1.151 (15)	13.007 \pm 0.683 (15)	10.226 \pm 0.466** (15)	7.119 \pm 2.186** (15)

Note: Number of animals is presented in the parentheses.

*Statistically significant, $p < 0.05$

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Benchmark Dose Analysis

RBC Cholinesterase Inhibition

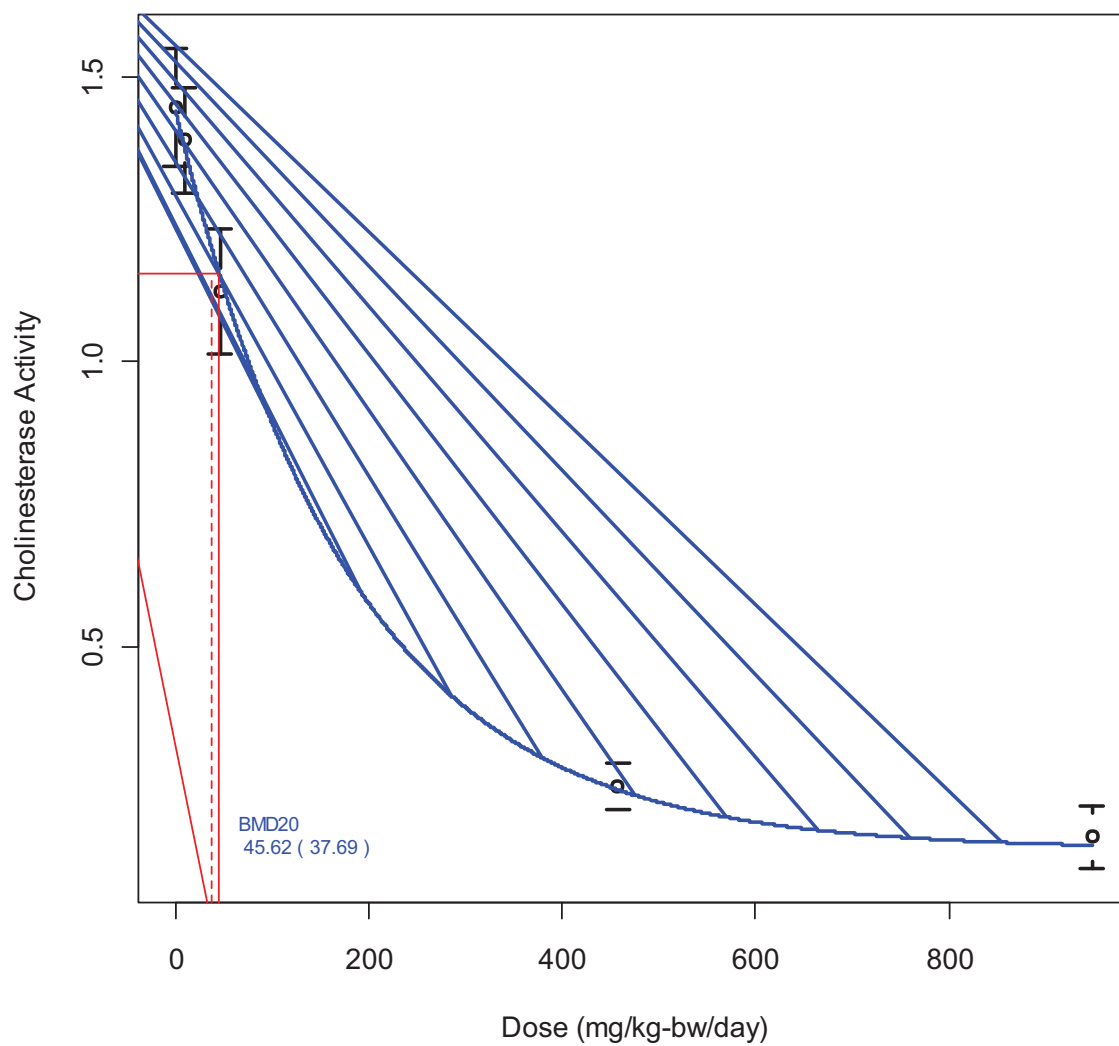
The exponential model described above was used to fit the RBC cholinesterase data and estimate BMDs for 20% inhibition. Table 4 summarizes the BMD results and the values of the other fitted parameters in the dose-response model. The RBC BMD₂₀s were 45.6 mg/kg-bw/day (BMDL₂₀=37.7 mg/kg-bw/day) for males and 42.9 mg/kg-bw/day (BMDL₂₀=34.6 mg/kg-bw/day) for females. Figures 1 and 2 show the dose-response fits to the data. The fits closely match the observations.

Table 4. Benchmark dose results for RBC cholinesterase

Sex	A (unit/mL)	P_B	BMD ₂₀ (BMDL ₂₀) (mg/kg-bw/day)
Male	1.442	0.1	45.6 (37.7)
Female	1.437	0.1	42.9 (34.6)

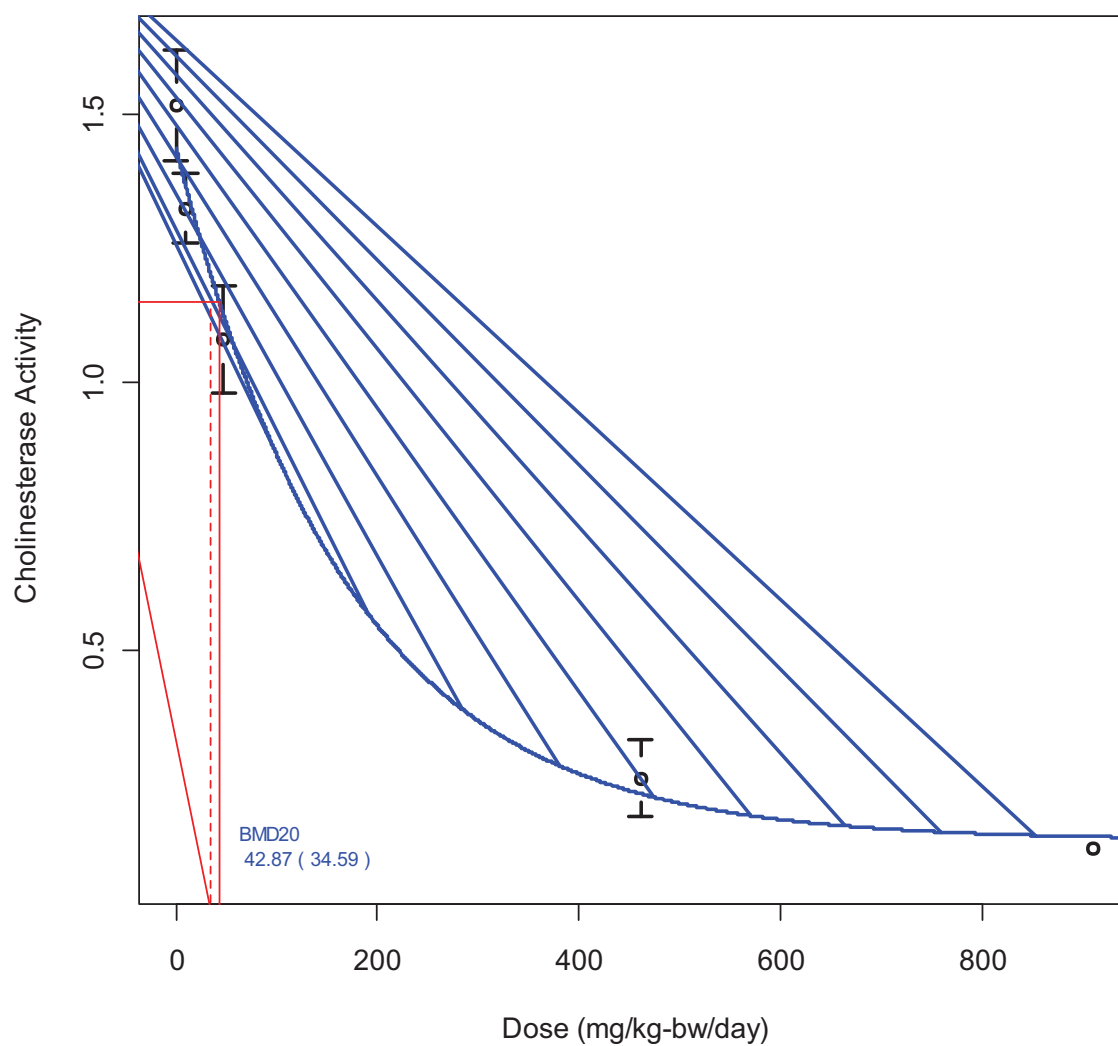
Note: A defines the cholinesterase inhibition without exposure and P_B defines the asymptotic limit for cholinesterase inhibition at a high dose.

Figure 1. Dose-response fit for RBC cholinesterase inhibition for males



Note: The BMD is shown with the solid red line and the BMDL is shown with the dashed red line.

Figure 2. Dose-response fit for RBC cholinesterase inhibition for females



Note: The BMD is shown with the solid red line and the BMDL is shown with the dashed red line.

Brain Cholinesterase Inhibition

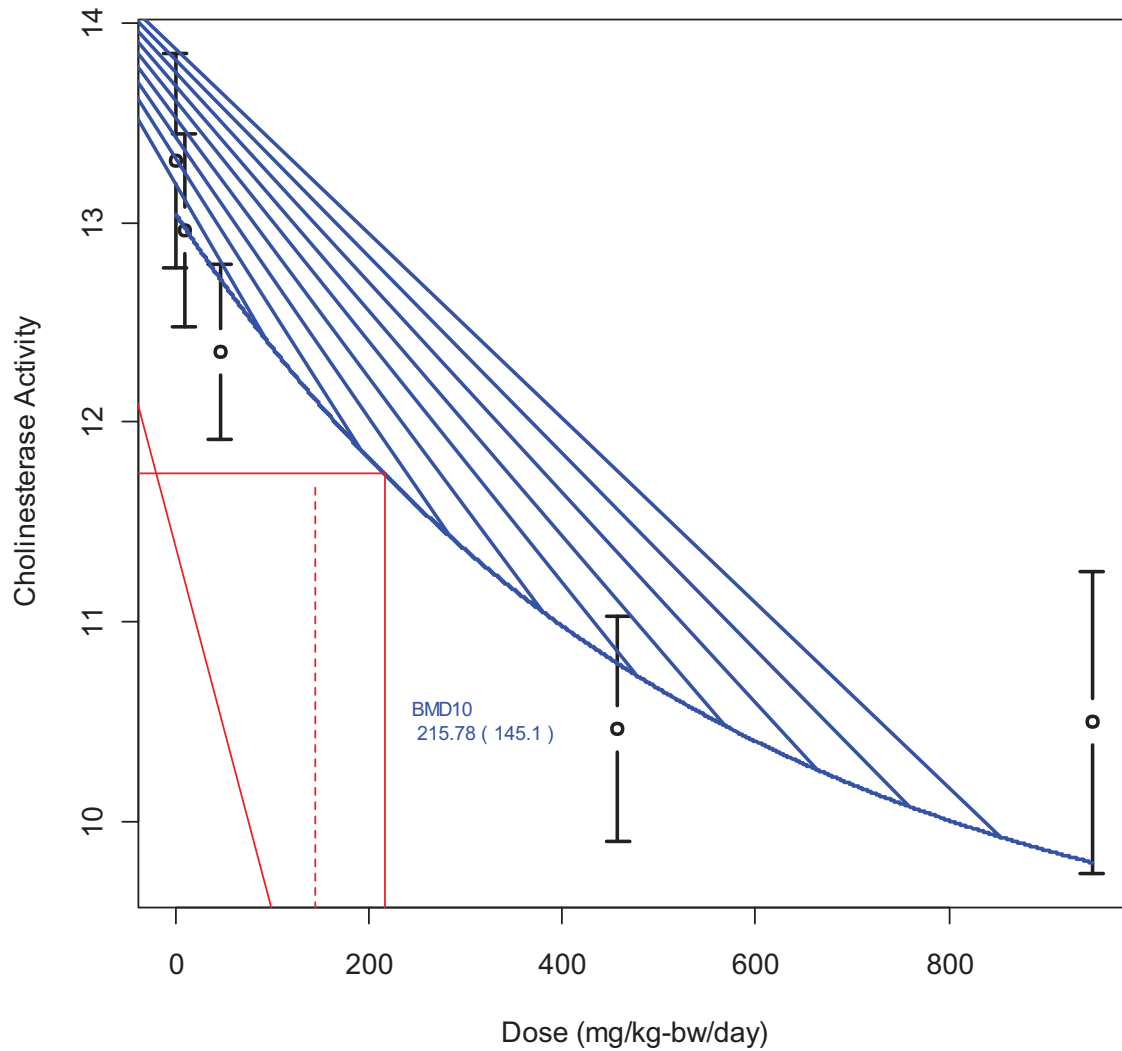
The exponential model described above was used to fit the brain cholinesterase data and estimate BMDs for 10% inhibition. The brain BMD₁₀s were 215.8 mg/kg-bw/day (BMDL₁₀=145.1 mg/kg-bw/day) for males and 159.2 mg/kg-bw/day (BMDL₁₀=135.3 mg/kg/day) for females. Table 5 summarizes the BMD results. Figures 3 and 4 show the dose-response fits to the data. The fits match the observations within the 95th percentile uncertainty bounds of the dose group means.

Table 5. Benchmark dose results for brain cholinesterase

Sex	A (units/g)	P_B	BMD ₁₀ (BMDL ₁₀) (mg/kg-bw/day)
Male	13.045	0	215.8 (145.1)
Female	13.549	0.7	159.2 (135.3)

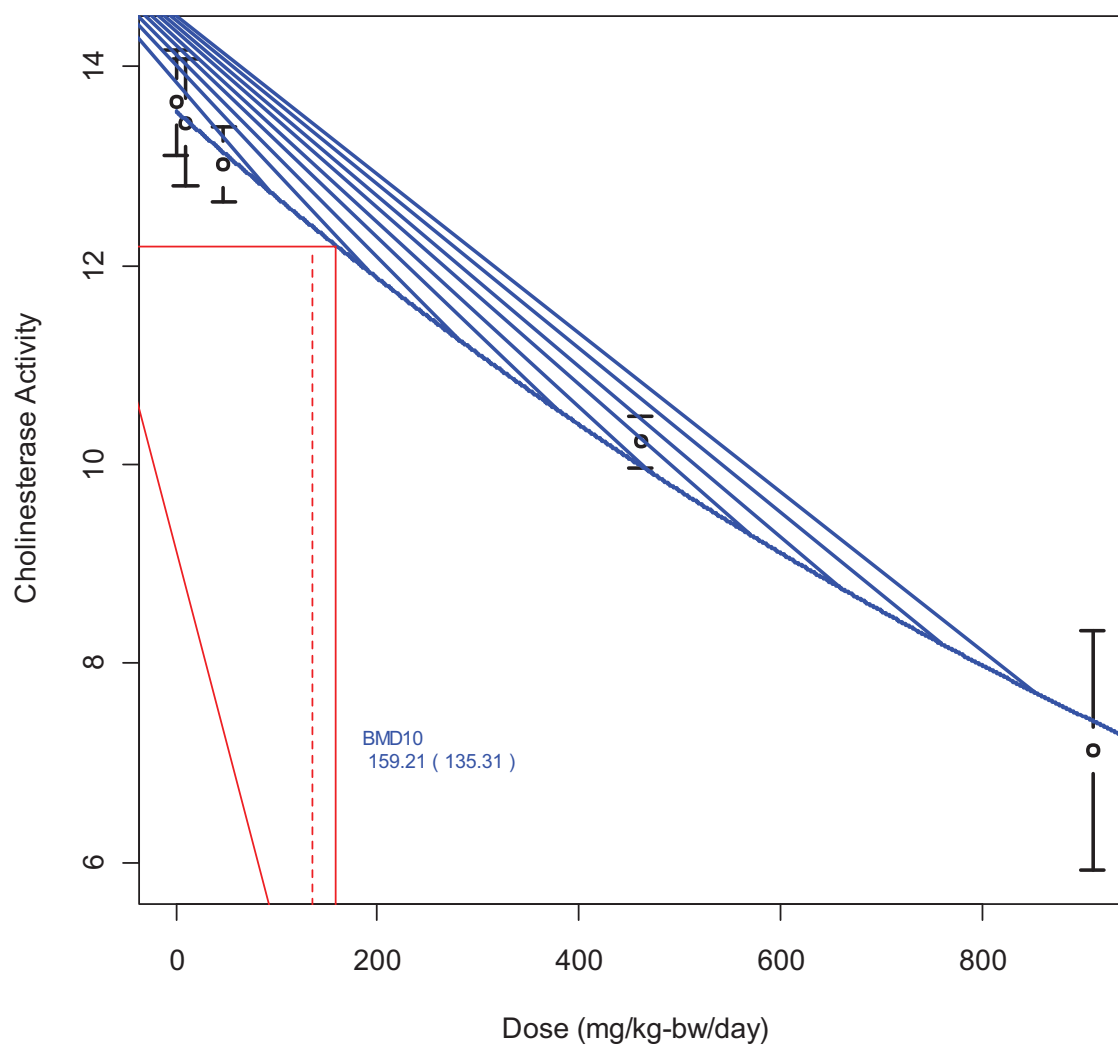
Note: A defines the cholinesterase inhibition without exposure and P_B defines the asymptotic limit for cholinesterase inhibition at a high dose.

Figure 3. Dose-response fit for brain cholinesterase inhibition for males



Note: The BMD is shown with the solid red line and the BMDL is shown with the dashed red line.

Figure 4. Dose-response fit for brain cholinesterase inhibition for females



Note: The BMD is shown with the solid red line and the BMDL is shown with the dashed red line.

Conclusions

This report provides BMD estimates for a 28-day toxicity dietary study of malathion technical in rats.

BMDs were estimated with an exponential model recommended by the U.S. EPA, which provided an adequate fit to the data. The RBC BMD₂₀ estimates were 45.6 mg/kg-bw/day (BMDL₂₀=37.7 mg/kg-bw/day) for males and 42.9 mg/kg-bw/day (BMDL₂₀=34.6 mg/kg-bw/day) for females. The brain BMD₁₀ estimates were 215.8 mg/kg-bw/day (BMDL₁₀=145.1 mg/kg-bw/day) for males and 159.2 mg/kg-bw/day (BMDL₁₀=135.3 mg/kg-bw/day) for females.

References

Barnett, J.F. 2012. Oral (diet) repeated dose 28-day toxicity study of malathion technical in rats. Charles River Laboratories, Preclinical Services, Study No. TQC00065.

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