

FINAL REPORT

Study Title

Oral (Gavage) Repeat Dose Comparative Cholinesterase Study
of Malathion and Malaoxon in Juvenile Rats

Data Requirement

U.S. Environmental Protection Agency (1998). Health Effects Test Guidelines. OPPTS
870.6300: Developmental Neurotoxicity Study, August, 1998.

U.S. Environmental Protection Agency (2001). Guidance on Cholinesterase Measures in DNT
and Related Studies, October 29, 2001.

Organisation for Economic Co-operation and Development (1997). OECD Guideline for Testing
of Chemicals. No. 424: Neurotoxicity Study in Rodents, adopted 21 July 1997.

Author

John F. Barnett, Jr., B.S.
(Study Director)

Study Completed On

21 April 2006
(Audited Final Report)

Performing Laboratory

Charles River Laboratories
Preclinical Services
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Horsham, PA, USA 19044

Subcontracting Facilities

Charles River Laboratories Preclinical Services
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Laboratory Project ID

Charles River Laboratories Preclinical Services Protocol Number: TQC00013

STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

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

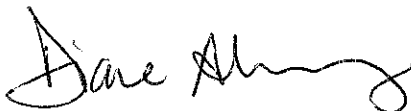
This statement supersedes any other claims of confidentiality that may appear in this report.

Company: Cheminova A/S

Company Agent: Diane Allemang

Title: Vice President, Regulatory Affairs
Cheminova, Inc.
EPA Agent of Cheminova A/S

Date:



Signature:

April 24, 2006

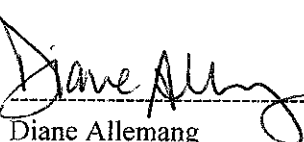
These data are the property of Cheminova A/S and as such, are considered to be confidential for all purposes other than compliance with FIFRA Section 10. Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality, which may exist under any other statute or in any other country.

GOOD LABORATORY PRACTICE STATEMENT

This study was conducted in accordance with the Good Laboratory Practice regulations of the U.S. Environmental Protection Agency (EPA FIFRA)^a, Japanese Ministry of Agriculture, Forestry and Fisheries^b, and Organisation for Economic Co-operation and Development (OECD)^c with this exception: the analyses for the Batch Analytical Certificates performed by Cheminova A/S were conducted in accordance with the EPA FIFRA and OECD Good Laboratory Practice Standards only. A Quality Assurance Statement for the Batch Analytical Certificates detailing the critical phase inspections and the routing of these inspections to the Study Director and Management as well as audit findings were not provided to the Study Director.

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.

Sponsor/Submitter:

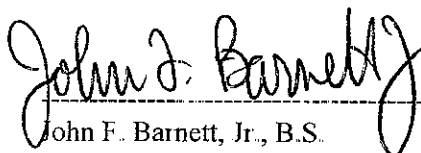


Diane Allemang
Vice President, Regulatory Affairs
Cheminova, Inc.
EPA Agent of Cheminova A/S

4-24-06

Date

Study Director:



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

21 Apr 2006

Date

-
- a. U.S. Environmental Protection Agency. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); Good Laboratory Practice Standards; Final Rule. 40 CFR Part 160.
 - b. Japanese Ministry of Agriculture, Forestry and Fisheries (1999). Good Laboratory Practice Standards. 11 Nousan No. 6283.
 - c. Organisation for Economic Co-operation and Development (1998). The Revised OECD Principles of Good Laboratory Practice [C(97)186/Final].

FLAGGING STATEMENT

I have applied the criteria of 40 CFR 158.34 for flagging studies for potential adverse effects to the results of the attached study. This study neither meets nor exceeds any of the applicable criteria.

Company: Cheminova A/S

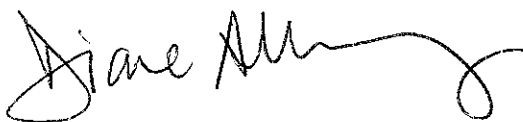
Company Agent: Diane Allemang

Title: Vice President, Regulatory Affairs
Cheminova, Inc.
EPA Agent of Cheminova A/S

Date:

April 24, 2006

Signature:

A handwritten signature in black ink, appearing to read "Diane Allemang", with a long horizontal flourish extending to the right.

**TITLE: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE
CHOLINESTERASE STUDY OF MALATHION AND
MALAOXON IN JUVENILE RATS**

**CHARLES RIVER LABORATORIES
PRECLINICAL SERVICES, PENNSYLVANIA
PROTOCOL NUMBER: TQC00013**

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**TITLE: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE
CHOLINESTERASE STUDY OF MALATHION AND
MALAOXON IN JUVENILE RATS**

**CHARLES RIVER LABORATORIES
PRECLINICAL SERVICES, PENNSYLVANIA
PROTOCOL NUMBER: TQC00013**

1. SUMMARY AND CONCLUSION

The objective of this study was to determine the effect of repeated daily dosing of young pre-weaning rats with Malathion and Malaoxon on erythrocyte and brain acetylcholinesterase activity.

1.1. Summary

Twenty-four litters with five male and five female pups per litter were randomly assigned to nine dosage groups (Groups I through IX). The pups from twelve of these litters were assigned to the vehicle control and malathion dosage groups: 0 (Vehicle), 5, 25, 50 and 150 mg/kg/day corresponding to Groups I through V. The pups from the other twelve litters were assigned to the vehicle control and malaoxon dosage groups: 0 (Vehicle), 0.1, 1, 2.5 and 4 mg/kg/day corresponding to Group I and Groups VI through IX. Suspensions of the test substances in the vehicle, corn oil, or the vehicle alone were administered via oral gavage once daily to the pups on postnatal days 11 through 21 (PNDs 11^a through 21). The dosage volume was 5 mL/kg for both test substances and the vehicle.

Checks for viability were made twice daily. Clinical observations were recorded daily before dosage administration and 60 ± 10 minutes after administration. Body weights were recorded the day after arrival, on the day of randomization and daily during the dosage period.

-
- a. The day of birth is designated postnatal day 0 (day 0 of lactation) in Addendum 10 to the Pesticide Assessment Guidelines of the U.S. Environmental Protection Agency (EPA). This same day is designated day 1 postpartum (day 1 of lactation) in the Standard Operating Procedures of the Testing Facility. Throughout the protocol and the raw data, the day of birth was designated day 1 postpartum (day 1 of lactation) and all subsequent ages of the F1 generation rats and days of the lactation period were determined and cited accordingly. In the text of this report, as well as the summary and individual tables, the day of birth has been adjusted so that the day of birth and all subsequent postpartum days match the EPA guideline.

At the end of the dosage period (PND 21), whole blood samples were collected from each of the pups following decapitation, and the brains were removed. The samples were collected at 2 hours postdosage for the pups assigned to the malathion dosage groups and 30 minutes postdosage for the pups assigned to the malaoxon dosage groups. These blood and brain samples were analyzed for cholinesterase levels. All pups were then discarded without further evaluation.

At 150 mg/kg/day, both male and female pups administered malathion were observed with adverse clinical signs (tremors in the head or whole body in both the male and female pups; decreased motor activity, impaired righting reflex and splayed forelimbs (both) in the male pups; and pale extremities in the female pups).

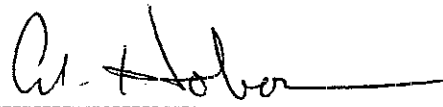
No test substance-related mortality, effects on body weights or body weight gains were observed in either the malathion or malaoxon dosage groups.

Statistically significant reductions in red blood cell (RBC) cholinesterase levels were observed in the 25, 50 and 150 mg/kg/day dosage groups for both the male and female pups administered malathion, and the 1, 2.5 and 4 mg/kg/day dosage groups for both male and female pups administered malaoxon. Brain cholinesterase levels were statistically significantly reduced only in the 150 mg/kg/day dosage group for both male and female pups administered malathion. There were no statistically significant or biologically important differences in brain cholinesterase levels in the male or female pups administered malaoxon.

1.2. Conclusion

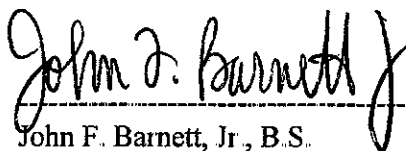
Repeated oral (gavage) administration of malathion to male and female pups during PNDs 11 to 21 resulted in clinical signs (tremors, decreased motor activity, impaired righting reflex, splayed forelimbs and pale extremities) in the 150 mg/kg/day dosage group for male and/or female pups during the first few days of administration. There was also a treatment-related statistically significant reduction in RBC cholinesterase activity observed in the 25, 50 and 150 mg/kg/day dosage groups for both male and female pups compared with controls. Brain cholinesterase activity was also statistically significantly reduced in the 150 mg/kg/day dosage group male and female pups compared with controls. The NOAEL for cholinesterase inhibition was considered to be 5 mg/kg/day for both the male and female pups administered malathion.

Repeated oral (gavage) administration of malaoxon to male and female pups during PNDs 11 to 21 resulted in no treatment-related effects other than a statistically significant decrease in RBC cholinesterase levels in the 1, 2.5 and 4 mg/kg/day dosage group male and female pups compared with controls. The NOAEL for cholinesterase inhibition was considered to be 0.1 mg/kg/day for both the male and female pups administered malaoxon.

 21-Apr-06

Alan M. Hoberman, Ph.D., DABT
Director of Research

Date

 21-Apr-2006

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

Date

2. DESCRIPTION OF TEST PROCEDURES

2.1. Conduct of Study

2.1.1. Sponsor

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

2.1.2. Testing Facility

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

2.1.3. Study Number

TQC00013

2.1.4. Objective of the Study

The objective of this study was to determine the effect of repeated daily dosing of young pre-weaning rats with malathion and malaoxon on erythrocyte and brain acetylcholinesterase activity, and to fulfill the data requirements of a Data-Call-In notice issued by the EPA on October 7, 2004 (I.D. GDCI-057701-24675).

2.1.5. Study Design

The requirements of the U.S. Environmental Protection Agency (EPA)^(1,2) and Organisation for Economic Co-operation and Development (OECD)⁽³⁾ were used as the basis for study design.

2.1.6. Regulatory Compliance

This study was conducted in compliance with the Good Laboratory Practice (GLP) regulations of the EPA⁽⁴⁾, the JMAFF⁽⁵⁾ and the OECD⁽⁶⁾. Quality Assurance Unit findings derived from the inspections during the conduct of this study are documented and have been provided to the Study Director and the Testing Facility Management.

2.1.7. Ownership of the Study

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

2.1.8. Study Monitor

Judith Hauswirth, Ph.D. (Toxicology Consultant)

2.1.9. Sponsor's Representative

Terri Spanogle (Senior Scientist, Cheminova, Inc., 1620 Eye Street NW, Suite 615, Washington, DC 20006 USA)

2.1.10. Study Director

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

2.1.11. Technical Performance

2.1.12. Charles River Laboratories Preclinical Services

2.1.12.1. Pennsylvania

John F. Barnett Sr., B.S. (Director of Operations)
Christopher J. Rivera, B.S. (Study Supervisor)
Adria R. Kling, B.A. (Laboratory Technician)
Brian M. McCullough, B.S. (Necropsy Laboratory Technician)
Anastasia R. Orloski, B.S. (Formulation Laboratory Technician)
Julian Gulbinski III, B.S., M.B.A. (Scientist)

2.1.12.2. Massachusetts

Dorothy Savage, B.S. (Principal Investigator) - Concentration and homogeneity analyses

2.1.13. Report Preparation

John F. Barnett, Jr., B.S.
Benjamin J. Kosko, B.A. (Study Coordinator)
Tina M. Glemser, B.S. (Data Management Specialist)
Emily J. Wash, B.A. (Report Administrator)

2.1.14. Report Review

John A. Foss, Ph.D., (Director of Neurobehavioral Toxicology)

2.1.15. Date Protocol Signed

27 January 2006

2.1.16. Dates of Technical Performance**2.1.16.1. Key Study Dates**

Experimental Start	30 JAN 06
Experimental Completion	14 FEB 06

2.1.16.2. Malathion

Dam and Pup Arrival	24 JAN 06
Dosage Administration - Pups (PND ^a s 11 to 21)	30 JAN 06 - 10 FEB 06
Dams Sacrificed (PND 21)	09 FEB 06 - 10 FEB 06
Blood Collection and Pup Sacrifice (PND 21)	09 FEB 06 - 10 FEB 06

2.1.16.3. Malaoxon

Dam and Pup Arrival	31 JAN 06
Dosage Administration - Pups (PNDs 11 to 21)	03 FEB 06 - 14 FEB 06
Dams Sacrificed (PND 21)	13 FEB 06 - 14 FEB 06
Blood Collection and Pup Sacrifice (PND 21)	13 FEB 06 - 14 FEB 06

2.1.17. Records Maintained

The original report, raw data and reserve samples of the bulk test substance and bulk vehicle are retained in the archives of the Testing Facility. Any preserved tissues are retained in the archives of the Testing Facility for two years after the mailing of the draft final report, after which time the Sponsor will decide their final disposition. All unused test substance formulations were discarded at the Testing Facility. Disposition of the remaining bulk test substances is documented in the raw data. Back-up samples will be discarded at the Testing Facility following consultation with Sponsor's Representative.

2.2. Test Substances Information**2.2.1. Descriptions**

Malathion (synonymous with Fyfanon Technical) - a clear pale yellowish liquid
Purity: 96.0%
CAS No.: 121-75-5

Malaoxon - a clear, colorless liquid
Purity: 97.7%
CAS No.: 1634-78-2

a. PND is an abbreviation for postnatal day.

2.2.2. Lot Numbers

Malathion - 9010501

Malaoxon - 849-BSe-42C

2.2.3. Dates Received and Storage Conditions

The test substance Malaoxon was received on 19 October 2005 and 22 December 2005 and the test substance Malathion was received on 5 December 2005. Malaoxon was stored frozen (approximately -20°C), protected from light upon receipt. Malathion was stored refrigerated (2°C to 8°C), protected from light upon receipt. Beginning on 13 January 2006, malathion was stored frozen (approximately -20°C), protected from light at the request of the Study Director and Sponsor's Representative.

2.2.4. 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. Bulk test substances were 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 activities, standard safety precautions were followed.

2.2.5. Analysis of Purity

Information to document or certify the identity, composition, strength, purity and stability of the test substances was provided by the Sponsor to the Testing Facility. Certificates of Analysis for both malathion and malaoxon are attached to the protocol (ATTACHMENT 2) and are available in APPENDIX D. The Sponsor Representative's signature and approval of the protocol indicates that appropriate documentation of the method of synthesis, fabrication or derivation of the test substances are on file and that it is available to the appropriate regulatory agencies should it be requested. The expiration dates for malathion and malaoxon are 03 November 2006 and 04 March 2009, respectively.

2.3. Vehicle Information**2.3.1. Description**

Corn oil - a viscous yellow liquid

2.3.2. Lot Number

065K0077

2.3.3. Date Received and Storage Conditions

The vehicle was received from Sigma-Aldrich, St. Louis, MO, USA, on 11 January 2006 and stored at room temperature.

2.3.4. Special Handling Instructions

Standard safety precautions (use of protective clothing, gloves, dust-mist/HEPA-filtered mask, safety goggles or safety glasses with side shields) were taken when handling the vehicle.

2.3.5. Analysis of Activity

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the vehicle that would have interfered with the results of this study.

Documentation or certification of the identity, composition, strength, purity and stability of the corn oil were limited to that supplied by the manufacturer. This documentation is available in APPENDIX F.

2.4. Test Substance Preparation and Storage Conditions

Suspensions of each test substance were prepared once at the Testing Facility. Prepared suspensions were stored refrigerated (2°C to 8°C) protected from light.

2.4.1. Adjustment for Purity

The test substances were considered 100% pure for the purposes of dosage calculations.

2.4.2. Sample Information

Sampling				
Bulk Test Substance Reserve				
Sample Size: 1 g				
Test Substance	Lot Number	Date Sampled	Storage Condition	Date Archived ^a
Malathion	9010501	07 FEB 06	F	24 FEB 06
Malaoxon	849-BSe-42C	07 FEB 06	F	24 FEB 06
Vehicle Reserve				
Sample Size: 5 mL				
Name	Date Sampled	Storage Conditions	Date Archived ^a	
Corn oil	07 FEB 06	RT	24 FEB 06	
Concentration and Homogeneity ^b				
Sample Size: 1 mL				
Malathion				
Date Sampled	Date Shipped	Recipient	Shipping Conditions	Purpose
30 JAN 06	30 JAN 06	Charles River Laboratories Preclinical Services Massachusetts	R	C, H
Malaoxon				
Date Sampled	Date Shipped	Recipient	Shipping Conditions	Purpose
02 FEB 06	02 FEB 06	Charles River Laboratories Preclinical Services Massachusetts	R	C, H

- a. Reserve samples were transferred to the Testing Facility archives.
- b. Quadruplicate samples were taken from the top, middle and bottom of each concentration on the day of preparation. Two samples from each quadruplicate set were shipped for analysis to the Charles River Laboratories Preclinical Services, Massachusetts, USA, analytical laboratory; the remaining samples were retained at the Testing Facility as backup samples and stored refrigerated (2°C to 8°C).

RT - Room temperature

F - Frozen, protected from light (-20°C)

R - Refrigerated, protected from light (2°C to 8°C)

C - Concentration

H - Homogeneity

2.4.3. Analytical Results

Information to document the stability of the prepared formulations bracketing the range of concentrations used in this study was provided by the Sponsor to the Study Director. Results of concentration and homogeneity analyses are available in APPENDIX G.

2.4.3.1. Stability

Stability data for the prepared formulations in the corn oil vehicle bracketing the concentrations in this study are on file with the Sponsor (Huntingdon Life Sciences (HLS) Study No. CHV 0121/053810 [MRID 46756705] and HLS Report CHV 066/013331 [MRID 45646401]) and was not determined during the conduct of this study.

2.5. Test System**2.5.1. Species**

Rat

2.5.2. Strain

Crl:CD(SD)

2.5.3. Supplier (Source)

Charles River Laboratories, Inc., Raleigh, NC, USA.

2.5.4. Sex

Male and female (Note: F0 generation dams were provided by the Supplier to maintain the F1 generation pups and were not considered part of the Test System.)

2.5.5. Rationale for Test System

The Crl:CD(SD) rat was selected as the Test System because this strain of rat has been widely used throughout the industry for nonclinical studies.

2.5.6. Test System Data - F1 Generation Pups**Shipment 1**

Number of Dams	14
Number of Pups	120
Date of Birth	19 JAN 06 - 20 JAN 06
Age at Arrival	4 - 5 days
Weight (g) the Day after Arrival	7.8 - 16.5
Weight (g) at Study Assignment	14.3 - 29.8

Shipment 2

Number of Dams	14
Number of Pups	120
Date of Birth	23 JAN 06 - 24 JAN 06
Age at Arrival	7 - 8 days
Weight (g) the Day after Arrival	11.0 - 20.7
Weight (g) at Study Assignment	15.8 - 24.1

2.5.7. Method of Randomization**2.5.7.1. Dams**

The female rats were naturally bred at the Supplier's facility by breeder male rats of the same source and strain. The day of pup delivery was designated day 0 of lactation (postpartum). The female rats were allowed to deliver their litters at the Supplier and shipped to arrive at the Testing Facility on PNDs 4, 5, 7 and 8.

2.5.7.2. F1 Generation Pups

On PNDs 9 or 10, twenty-four litters of approximately ten pups per litter (five males and five females) were randomly assigned to study. The pups from twelve of these litters were assigned to the Malathion dosage groups, and the other twelve litters were assigned to the Malaoxon dosage groups. One male and one female pup from each of the litters were assigned to each of five respective dosage groups. The pups were of good general health (no adverse clinical signs) following physical examination of the pups and adequate body weights. Cross-fostering was performed due to an insufficient number of male and/or female pups within the litter.

The pups in the Malathion groups were assigned to the following dosage group:

Paw Tattoo	Dosage Group Assignment
Male Paw Tattoo 1	0 (Vehicle) mg/kg/day
Male Paw Tattoo 2	5 mg/kg/day
Male Paw Tattoo 3	25 mg/kg/day
Male Paw Tattoo 4	50 mg/kg/day
Male Paw Tattoo 5	150 mg/kg/day
Female Paw Tattoo 6	0 (Vehicle) mg/kg/day
Female Paw Tattoo 7	5 mg/kg/day
Female Paw Tattoo 8	25 mg/kg/day
Female Paw Tattoo 9	50 mg/kg/day
Female Paw Tattoo 10	150 mg/kg/day

The pups in the Malaoxon groups were assigned to the following dosage group:

Paw Tattoo	Dosage Group Assignment
Male Paw Tattoo 1	0 (Vehicle) mg/kg/day
Male Paw Tattoo 2	0.1 mg/kg/day
Male Paw Tattoo 3	1 mg/kg/day
Male Paw Tattoo 4	2.5 mg/kg/day
Male Paw Tattoo 5	4 mg/kg/day
Female Paw Tattoo 6	0 (Vehicle) mg/kg/day
Female Paw Tattoo 7	0.1 mg/kg/day
Female Paw Tattoo 8	1 mg/kg/day
Female Paw Tattoo 9	2.5 mg/kg/day
Female Paw Tattoo 10	4 mg/kg/day

2.5.8. System of Identification

2.5.8.1. Dams

Female rats were assigned temporary animal numbers at receipt. The rats were permanently identified using Monel[®] self-piercing ear tags (No. MSPT 20101 Gey Band and Tag Co., Inc., Norristown, PA, USA) upon litter assignment to study. Cage tags were marked with the study number, permanent rat number, sex, generation, test substance identification, group number and dosage level.

2.5.8.2. F1 Generation Pups

On PNDs 9 or 10, pups selected for study were individually identified by tattoo according to the Standard Operating Procedures of the Testing Facility. Ink was injected under the skin of the paws to identify individual pups. Cage tags were marked with the study number, permanent rat number, sex, generation, test substance identification, group number and dosage level.

2.6. Husbandry

2.6.1. Research Facility Registration

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

2.6.2. 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 64°F to 79°F (18°C to 26°C); relative humidity was targeted at 30% to 70%^a.

a. See APPENDIX H (ENVIRONMENTAL AND HUSBANDRY REPORTS).

2.6.3. Housing

Each dam with a litter of male and female pups was housed in a common nesting box during the postpartum period. All cage sizes and housing conditions were in compliance with the *Guide for the Care and Use of Laboratory Animals*⁽⁷⁾.

2.6.4. Light

An automatically controlled 12-hours light:12-hours dark fluorescent light cycle was maintained. Each dark period began at 1900 hours.

2.6.5. Sanitization

Cages were changed approximately every other week. Bedding was changed as often as necessary to keep the rats dry and clean.

2.6.6. Diet

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

2.6.7. Diet Analysis

Analyses were routinely performed by the feed supplier. No contaminants at levels exceeding the maximum concentration 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 H.

Neither the Sponsor nor the Study Director are aware of any potential contaminants likely to have been present in the feed that would have interfered with the results of this study.

2.6.8. 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 individual water bottles attached to the cages. Chlorine was added to the processed water as a bacteriostat.

2.6.9. 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 H.

Neither the Sponsor nor the Study Director are aware of any potential contaminants likely to have been present in the water that would have interfered with the results of this study.

2.6.10. Nesting Material

Bed-o'cobs[®] bedding (The Andersons Industrial Products Group, Maumee, OH, USA) was used as the nesting material.

2.6.11. Nesting Analysis

Each lot of bedding is analyzed for possible contamination (Lancaster Laboratories, Lancaster, PA, USA). Copies of the results of the bedding analyses are available in the raw data and in APPENDIX H.

Neither the Sponsor nor the Study Director are aware of any potential contaminants likely to have been present in the bedding that would have interfered with the results of this study.

2.7. Methods

2.7.1. Dosage Administration

Dosage Group	Number of pups per sex	Test Substance	Dosage* (mg/kg/day)	Concentration	Dose Volume (mL/kg)	Assigned F1 Generation Numbers	
						Male Rats	Female Rats
I	24 ^b	Corn oil	0 (Vehicle)	0	5	5101, 5201, 5301, 5401, 5501, 5601, 5701 5801, 5901, 6001, 6101, 6201 6301, 6401, 6501, 6601, 6701, 6801, 6901, 7001, 7101, 7201, 7301, 7401	5106, 5206, 5306, 5406, 5506, 5606, 5706, 5806, 5906, 6006, 6106, 6206, 6306, 6406, 6506, 6606, 6706, 6806 6906, 7006, 7106, 7206, 7306, 7406
II	12	Malathion	5	1	5	6302, 6402, 6502, 6602, 6702, 6802, 6902, 7002, 7102, 7202, 7302, 7402	6307, 6407, 6507, 6607, 6707, 6807, 6907, 7007, 7107, 7207, 7307, 7407
III	12	Malathion	25	5	5	6303, 6403, 6503, 6603, 6703, 6803, 6903, 7003, 7103, 7203, 7303, 7403	6308, 6408, 6508, 6608, 6708, 6808, 6908, 7008, 7108, 7208, 7308, 7408
IV	12	Malathion	50	10	5	6304, 6404, 6504, 6604, 6704, 6804, 6904, 7004, 7104, 7204, 7304, 7404	6309, 6409, 6509, 6609, 6709, 6809, 6909, 7009, 7109, 7209, 7309, 7409
V	12	Malathion	150	30	5	6305, 6405, 6505, 6605, 6705, 6805, 6905, 7005, 7105, 7205, 7305, 7405	6310, 6410, 6510, 6610, 6710, 6810, 6910, 7010, 7110, 7210, 7310, 7410
VI	12	Malaoxon	0.1	0.02	5	5102, 5202, 5302, 5402, 5502, 5602, 5702, 5802, 5902, 6002, 6102, 6202	5107, 5207, 5307, 5407, 5507, 5607, 5707, 5807, 5907, 6007, 6107, 6207
VII	12	Malaoxon	1	0.2	5	5103, 5203, 5303, 5403, 5503, 5603, 5703, 5803, 5903, 6003, 6103, 6203	5108, 5208, 5308, 5408, 5508, 5608, 5708, 5808, 5908, 6008, 6108, 6208
VIII	12	Malaoxon	2.5	0.5	5	5104, 5204, 5304, 5404, 5504, 5604, 5704, 5804, 5904, 6004, 6104, 6204	5109, 5209, 5309, 5409, 5509, 5609, 5709, 5809, 5909, 6009, 6109, 6209
IX	12	Malaoxon	4	0.8	5	5105, 5205, 5305, 5405, 5505, 5605, 5714 ^c , 5805, 5905, 6005, 6105, 6205	5110, 5210, 5310, 5410, 5510, 5610, 5710, 5810, 5910, 6010, 6110, 6210

- a. The test substances were considered 100% pure for the purpose of dosage calculation
- b. Twelve of these pups were dosed and sacrificed with the Malathion pups and the other twelve with the Malaoxon pups.
- c. Two male pups in litter 12757 were tattooed as pup number four. Prior to dosage administration one of the pups was picked to be 5705 and tattooed as pup number 14. This pup's permanent number was changed from 5705 to 5714.

2.7.2. Rationale for Dosage Selection and for Time-of-Peak Effect for Cholinesterase Inhibition

Dosages for the pups were selected based on data collected in a repeat dose range-finding cholinesterase study with Malaoxon and Malathion (TQC00011) conducted at Charles River Laboratories Preclinical Services Pennsylvania. The doses used during the conduct of the TQC00011 study were 5, 15 and 50 mg/kg/day for Malathion and 0.05, 0.1 and 1 mg/kg/day for Malaoxon. During this study, there were no test substance-related adverse clinical observations apparent, and minimal cholinesterase inhibition was observed.

Blood and brain cholinesterase sampling was performed at 2 hours post-dose for malathion and at 30 minutes post-dose for malaoxon. The timing for sample collection

for each compound was selected based upon time-of-peak effect data obtained from a preliminary repeated dose study (TQC00012) conducted by Charles River Preclinical Services and after consultation with the US EPA (e-mail message from Thomas Moriarity of the EPA to Paul Whatling of Cheminova, Inc., dated February 2, 2006).

2.7.3. Route and Rationale for Route of Administration

The oral (gavage) route was selected for use because: 1) the exact dosage can be accurately administered via gavage; and 2) the oral route is a potential route of exposure.

2.7.4. Frequency of Administration

The pups were administered the test substance and/or the vehicle once daily from PNDs 11 through 21. Dosages were adjusted daily for body weights recorded prior to administration and dosage administration occurred at approximately the same time each day.

2.7.5. Method of Study Performance

2.7.5.1. Dams

Viability observations were recorded at least twice daily. Maternal behavior, clinical observations and body weights were recorded the day after arrival. Feed consumption was monitored as feed was replenished on an as-needed basis. This information was recorded to monitor the general health and well-being of the dams.

2.7.5.2. F1 Generation Pups

Litters were observed for dead pups at least twice daily. The pups in each litter were counted on the day after arrival and on the day of randomization. Clinical observations were recorded once daily the day after arrival during the predosage period by litter and prior to and 60 ± 10 minutes after dosage administration except on the day of sacrifice when clinical observations were performed just prior to sacrifice^a. Body weights were recorded the day after arrival, on the day of randomization and daily during the dosage period.

2.7.6. Gross Necropsy

2.7.6.1. Dams

On day 21 postpartum, all dams were sacrificed by carbon dioxide asphyxiation and discarded without further evaluation.

a SEE APPENDIX E (DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY), items 1 through 4.

2.7.6.2. F1 Generation Pups

All surviving pups were sacrificed by decapitation without anesthesia on PND 21. Sacrifice was immediately followed by blood collection and brain dissection.

Pups that died were necropsied for the cause of death or condition on the day the observation was made. The lungs, trachea and esophagus were perfused and saved in neutral buffered 10% formalin for possible future evaluation.

2.7.7. Cholinesterase Assay

At the end of the dosage period (PND 21), whole blood samples (approximately 0.40 to 0.60 mLs each) were collected from each of the pups assigned for cholinesterase assay⁽⁸⁻⁹⁾. The whole blood samples were collected within 10 seconds from each pup following decapitation. The whole blood samples were collected at 2 hours postdosage from the male and female pups assigned to the malathion dosage groups and 30 minutes postdosage for the pups assigned to the malaoxon dosage groups (timing began with the gavage of the pup and ended with decapitation for blood collection). The time of each blood collection was recorded in the raw data. All samples were labeled with study number, date of collection, pup number, dosage level, day of study, species, generation, group, sex, storage conditions and timepoint.

Approximately 0.40 to 0.60 mLs of whole blood were collected into 1.3 mL EDTA-coated (lavender-top) tubes. Blood samples were stored on cold packs until being processed for RBC cholinesterase levels according to the Testing Facility's Standard Operating Procedure. Cholinesterase assays were conducted on the day of blood collection. Results of these analyses are available in APPENDIX B and C.

After blood sample collection, the brain was excised, and the weight was recorded to three decimal places. The brains were stored on ice until being assayed for cholinesterase levels according to the Testing Facility's Standard Operating Procedure. Cholinesterase assays were conducted on the day of pup sacrifice. Results of these analyses are available in APPENDIX B and C.

2.7.8. Data Collection and Statistical Analyses

2.7.8.1. Data Collection

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* and *SoftMax[®] Pro* (version 4.0). All data were tabulated, summarized and/or statistically analyzed using the *Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System*, *Microsoft[®] Excel* (part of *Microsoft[®] Office 97/2000/XP*), *Quattro Pro 8*, *The SAS System* (version 6.12) and/or *Softmax[®] Pro* (version 4.0).

2.7.8.2. Statistical Analyses

Cholinesterase values for red blood cells and brains were evaluated as separate dependent variables in a one-way analyses of variance (ANOVA) at each combination of sex (male and female). Sample collection intervals were used as the independent variable in the ANOVA. In the event that the ANOVA was significant ($p \geq 0.05$), the interval with the largest value was compared with the values at each of the other intervals using Dunnett's test.

3. RESULTS - MALATHION

3.1. Analytical Results (APPENDIX G)

Dosing solutions of malathion prepared in corn oil were analyzed and were found to be acceptable and homogeneous under the conditions of the study. All dosing solutions used for dose administration were analyzed and were found to be 2.3%, 1.5%, 1.7% and -0.2% of the targeted concentrations for the 1 mg/mL, 5 mg/mL, 10 mg/mL and 30 mg/mL formulations, respectively. The homogeneity values obtained were 1.0%, 1.5%, 1.0% and 1.3% RSD for the 1 mg/mL, 5 mg/mL, 10 mg/mL and 30 mg/mL formulations, respectively. All analytical reports can be found in APPENDIX G.

3.2. Mortality, Clinical and Necropsy Observations (Summaries - Tables B1 and B2; Individual Data - Tables B9 and B10)

3.2.1. Mortality

Female pup 6807 in the 5 mg/kg/day dosage group was found dead on PND 19, the ninth day after the initiation of dosage administration. This pup was gaining weight prior to being found dead. This pup was partially cannibalized; however, the tissues that were remaining appeared normal at necropsy. This death was not considered to be test substance-related because it was not dosage-dependent. No deaths occurred at the three higher dosages.

All other pups survived until scheduled sacrifice.

3.2.2. Clinical Observations

Clinical signs related to administration of the test substance were observed in both the male and the female pups in the 150 mg/kg/day dosage group during the first few days of dosage administration (between PNDs 11 and 14). These clinical signs included tremors in the head or whole body in both the male and female pups; decreased motor activity, impaired righting reflex and splayed forelimbs (both) in the male pups; and pale extremities in the female pups.

The remaining clinical observation (an absent left eye in one of the 25 mg/kg/day female pups) was considered unrelated to the test substance because the incidence was not dosage dependent.

3.3. Body Weights and Body Weight Changes
(Figures 1 and 2: Summaries - Tables B3 and B4; Individual Data - Tables B11 and B12)

There were no biologically important differences among the dosage groups in body weights or body weight changes during the dosage period. On PND 21, the body weight averages for all dosage groups administered malathion were within 7% of the vehicle control group value.

3.4. Red Blood Cell (RBC) Cholinesterase Levels
(Summaries - Tables B5 and B6; Individual Data - Tables B13 and B14)

As summarized in Text Table 1, both the male and female pups administered malathion at dosages of 25 mg/kg/day and higher had statistically significantly reduced ($p \leq 0.05$ to $p \leq 0.01$) RBC cholinesterase levels as compared with the vehicle control group. The values in the 5 mg/kg/day dosage groups were comparable to the vehicle control values.

Text Table 1: Malathion RBC Cholinesterase Levels			
Group	Dosage (mg/kg/day)	Mean ChE ChE U/mL \pm S.D. (n)	Percent Decrease Compared with Controls
Male Pups			
I	0 (Vehicle)	2.316 \pm 0.373 (12)	--
II	5	2.067 \pm 0.384 (12)	10.8%
III	25	1.967 \pm 0.383 (12)*	15.1%
IV	50	1.527 \pm 0.276 (12)**	34.1%
V	150	1.063 \pm 0.274 (11)**	54.1%
Female Pups			
I	0 (Vehicle)	2.119 \pm 0.272 (12)	--
II	5	2.022 \pm 0.338 (11)	4.6%
III	25	1.746 \pm 0.213 (12)**	17.6%
IV	50	1.482 \pm 0.192 (12)**	30.1%
V	150	1.024 \pm 0.163 (12)**	51.7%

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

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

3.5. Brain Cholinesterase Levels (Summaries - Tables B7 and B8; Individual Data - Tables B15 and B16)

As summarized in Text Table 2, both the male and female pups administered the 150 mg/kg/day dosage of malathion had statistically significantly reduced ($p \leq 0.01$) brain cholinesterase levels as compared with the vehicle control group. The values in the 50 mg/kg/day dosage and lower were comparable to the vehicle control values.

Text Table 2: Malathion Brain Cholinesterase Levels			
Group	Dosage (mg/kg/day)	Mean ChE ChE U/G \pm S.D. (n)	Percent Decrease Compared with Controls
Male Pups			
I	0 (Vehicle)	12.104 \pm 1.706 (10)	--
II	5	12.063 \pm 1.038 (12)	0.3%
III	25	12.292 \pm 0.725 (12)	a
IV	50	12.093 \pm 1.070 (12)	0.1%
V	150	10.354 \pm 1.605 (12)**	14.5%
Female Pups			
I	0 (Vehicle)	11.880 \pm 1.791 (12)	--
II	5	12.448 \pm 0.856 (11)	b
III	25	11.745 \pm 0.702 (12)	1.1%
IV	50	12.170 \pm 0.884 (12)	c
V	150	9.886 \pm 1.643 (12)**	16.8%

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

- a. No inhibition occurred; value was 1.6% greater than the control value.
- b. No inhibition occurred; value was 4.8% greater than the control value.
- c. No inhibition occurred; value was 2.4% greater than the control value.

4. CONCLUSION - MALATHION

Repeated oral (gavage) administration of malathion to male and female pups during PNDs 11 to 21 resulted in clinical signs (tremors, decreased motor activity, impaired righting reflex, splayed forelimbs and pale extremities) in the 150 mg/kg/day dosage group for male and/or female pups during the first few days of administration. There was also a treatment-related statistically significant reduction in RBC cholinesterase activity observed in the 25, 50 and 150 mg/kg/day dosage groups for both male and female pups compared with controls. Brain cholinesterase activity was also statistically significantly reduced in the 150 mg/kg/day dosage group male and female pups compared with controls. The NOAEL for cholinesterase inhibition was considered to be 5 mg/kg/day for both the male and female pups administered malathion.

5. RESULTS - MALAOXON

5.1. Analytical Results (APPENDIX G)

Dosing solutions of malaoxon prepared in corn oil were analyzed and were found to be acceptable and homogeneous under the conditions of the study. All dosing solutions used for dose administration were analyzed and were found to be -5.1%, -6.8%, -1.4% and -8.1% of the targeted concentrations for the 0.02 mg/mL, 0.2 mg/mL, 0.5 mg/mL and 0.8 mg/mL formulations, respectively. The homogeneity values obtained were 1.1%, 2.0%, 0.9% and 0.4% RSD for the 0.02 mg/mL, 0.2 mg/mL, 0.5 mg/mL and 0.8 mg/mL formulations, respectively. All analytical reports can be found in APPENDIX G.

5.2. Mortality, Clinical and Necropsy Observations (Summaries - Tables C1 and C2; Individual Data - Tables C9 and C10)

5.2.1. Mortality

All pups survived until scheduled sacrifice with the exception of one male pup at 1 mg/kg/day found dead on PND 11 and one female pup at 2.5 mg/kg/day found dead on PND 16. These deaths were not considered to be test substance-related because at necropsy it became apparent that they were the result of intubation errors. Clinical and necropsy observations and body weights are summarized below. All other male and female pups survived to scheduled sacrifice.

Male pup 5403 in the 1 mg/kg/day dosage group was found dead on PND 11, the first day of dosage administration. At necropsy, all lobes of the lungs were pale and spongy and a white frothy material was present in the trachea; all other tissues appeared normal. This death was the result of an intubation error.

Female pup 5609 in the 2.5 mg/kg/day dosage group was found dead on PND 16, the sixth day after the initiation of dosage administration. This pup was gaining weight prior to being found dead. At necropsy, all lobes of the lungs were pale and spongy; all other tissues appeared normal. This death was the result of an intubation error.

5.2.2. Clinical Observations

All clinical observations were considered unrelated to the administration of the test substance because: 1) the incidences were not dosage dependent; or 2) the observation occurred in only one pup in the dosage groups. These clinical observations included a scab on the neck and urine stained abdominal fur.

5.3. Body Weights and Body Weight Changes (Figures 3 and 4: Summaries - Tables C3 and C4; Individual Data - Tables C11 and C12)

There were no biologically important differences among the dosage groups in body weights or body weight changes during the dosage period. On PND 21, the body weight averages for all dosage groups administered malaoxon were within 5% of the vehicle control group value.

5.4. Red Blood Cell (RBC) Cholinesterase Levels (Summaries - Tables C5 and C6; Individual Data - Tables C13 and C14)

As summarized in Text Table 3, RBC cholinesterase levels were statistically significantly reduced ($p \leq 0.05$ to $p \leq 0.01$) in both the male and female pups administered malaoxon at dosages of 1 mg/kg/day and higher as compared with the vehicle controls. The values in the 0.1 mg/kg/day dosage groups were comparable to the vehicle control values.

Text Table 3: Malaoxon RBC Cholinesterase Levels			
Group	Dosage (mg/kg/day)	Mean ChE ChE U/mL \pm S.D. (n)	Percent Decrease Compared with Controls
Male Pups			
I	0 (Vehicle)	1.930 \pm 0.285 (12)	--
VI	0.1	1.895 \pm 0.331 (12)	1.8%
VII	1	1.657 \pm 0.188 (10)*	14.1%
VIII	2.5	1.047 \pm 0.109 (12)**	45.8%
IX	4	0.943 \pm 0.275 (12)**	51.1%
Female Pups			
I	0 (Vehicle)	1.788 \pm 0.148 (12)	--
VI	0.1	1.926 \pm 0.316 (12)	a
VII	1	1.546 \pm 0.145 (12)*	13.5%
VIII	2.5	1.167 \pm 0.151 (11)**	34.7%
IX	4	0.978 \pm 0.362 (12)**	45.3%

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

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

a. No inhibition occurred; value was 7.7% greater than the control value.

5.5. Brain Cholinesterase Levels (Summaries - Tables C7 and C8; Individual Data - Tables C15 and C16)

As summarized in Text Table 4, the brain cholinesterase levels were comparable with the vehicle control group values for both the male and female pups after repeated administration of malaoxon at dosages up to 4 mg/kg/day.

Text Table 4: Malaoxon Brain Cholinesterase Levels			
Group	Dosage (mg/kg/day)	Mean ChE ChE U/G \pm S.D. (n)	Percent Decrease Compared with Controls
Male Pups			
I	0 (Vehicle)	11.867 \pm 0.393 (12)	--
VI	0.1	11.897 \pm 0.893 (12)	a
VII	1	12.131 \pm 0.867 (11)	b
VIII	2.5	11.746 \pm 0.864 (12)	1.0%
IX	4	11.890 \pm 0.857 (12)	c
Female Pups			
I	0 (Vehicle)	12.311 \pm 0.954 (12)	--
VI	0.1	12.065 \pm 0.763 (12)	2.0%
VII	1	12.664 \pm 1.939 (12)	d
VIII	2.5	12.065 \pm 0.938 (11)	2.0%
IX	4	12.529 \pm 0.439 (12)	e

- a. No inhibition occurred; value was 0.3% greater than the control value.
- b. No inhibition occurred; value was 2.2% greater than the control value.
- c. No inhibition occurred; value was 0.2% greater than the control value.
- d. No inhibition occurred; value was 2.9% greater than the control value.
- e. No inhibition occurred; value was 1.8% greater than the control value.

6. CONCLUSION - MALAOXON

Repeated oral (gavage) administration of malaoxon to male and female pups during PNDs 11 to 21 resulted in no treatment-related effects other than a statistically significant decrease in RBC cholinesterase levels in the 1, 2.5 and 4 mg/kg/day dosage group male and female pups compared with controls. The NOAEL for cholinesterase inhibition was considered to be 0.1 mg/kg/day for both the male and female pups administered malaoxon.

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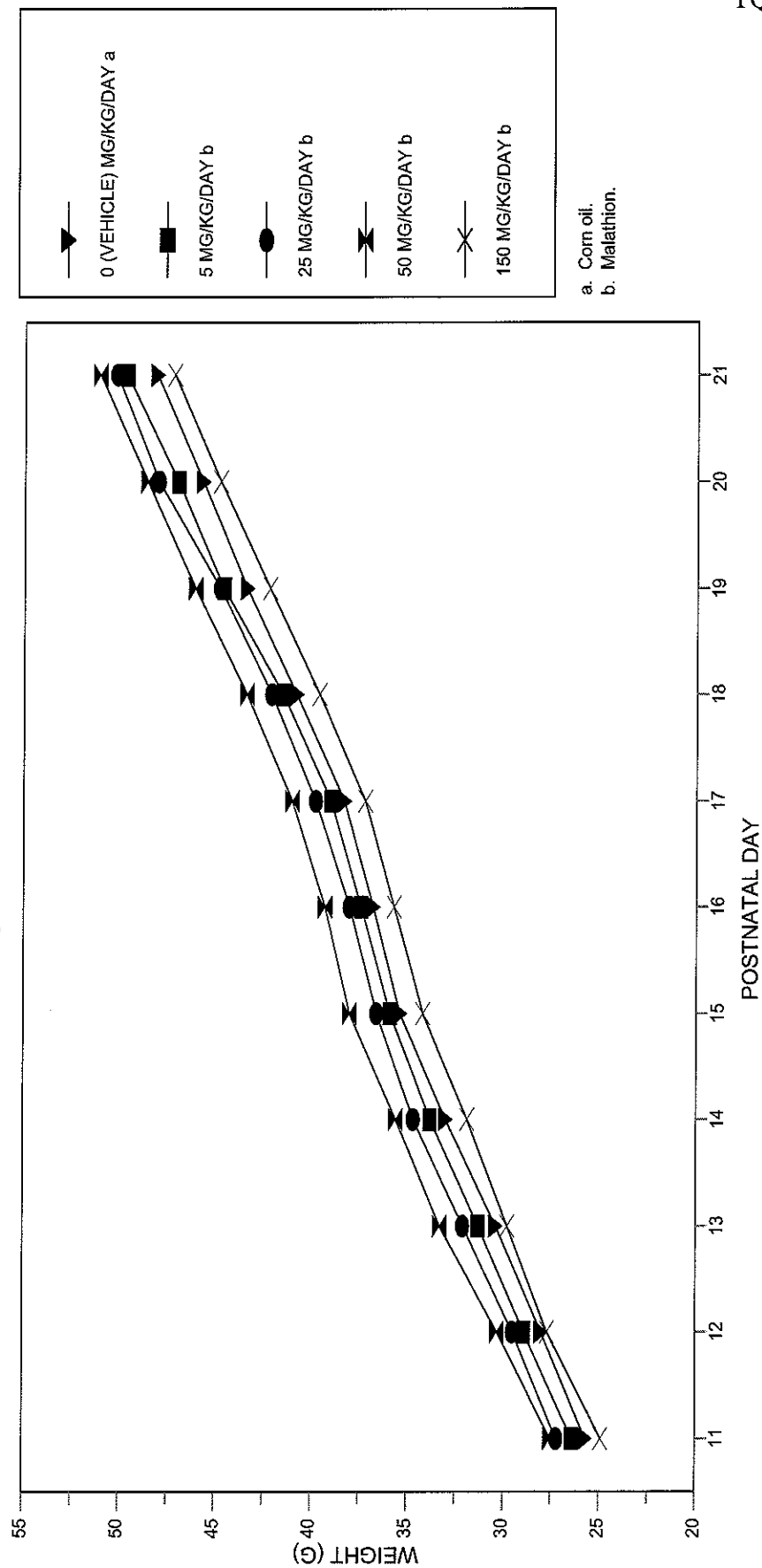
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APPENDIX A
REPORT FIGURES

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

BODY WEIGHTS MALE PUPS - MALATHION

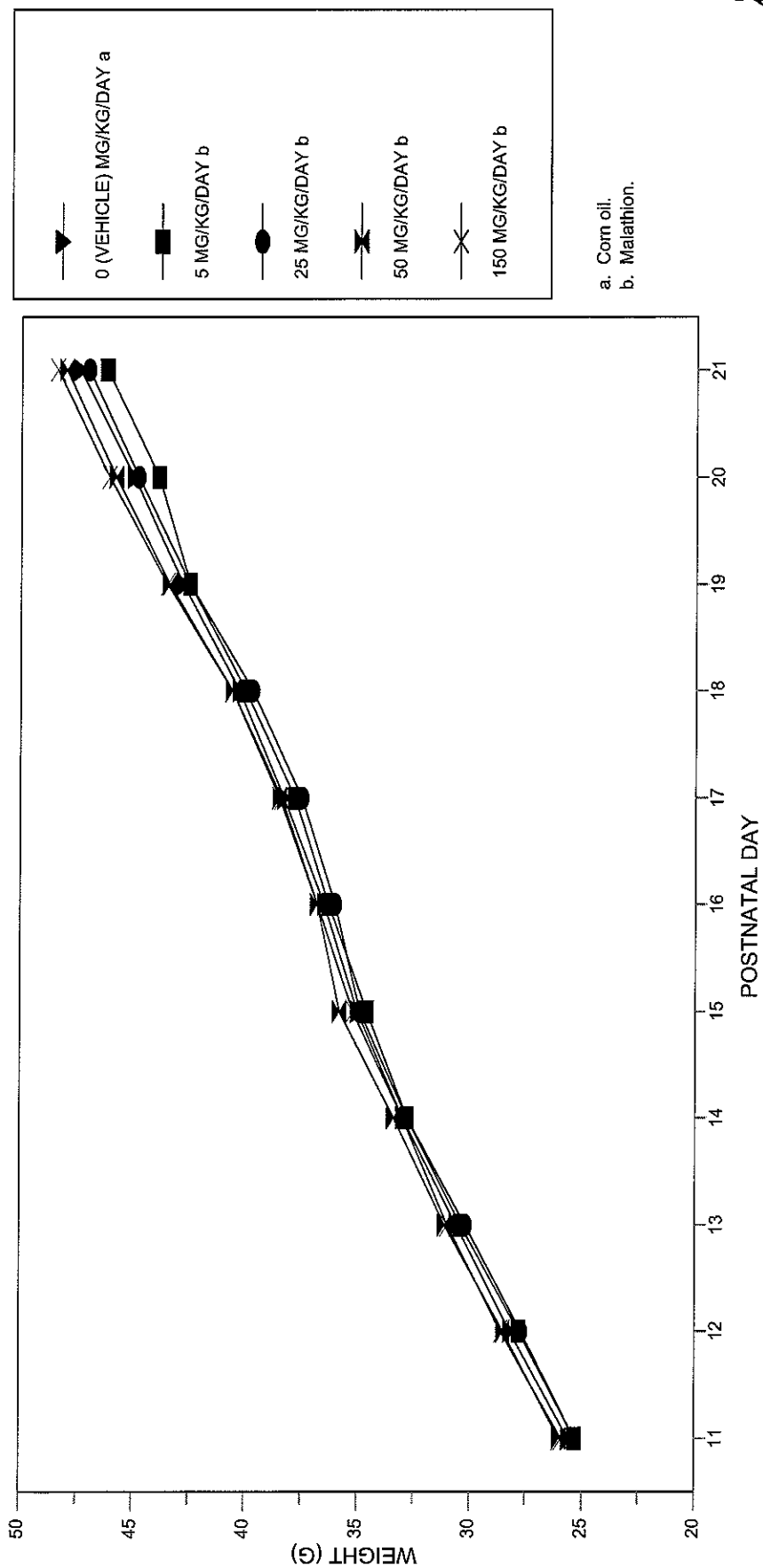
Figure 1



PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

BODY WEIGHTS FEMALE PUPS - MALATHION

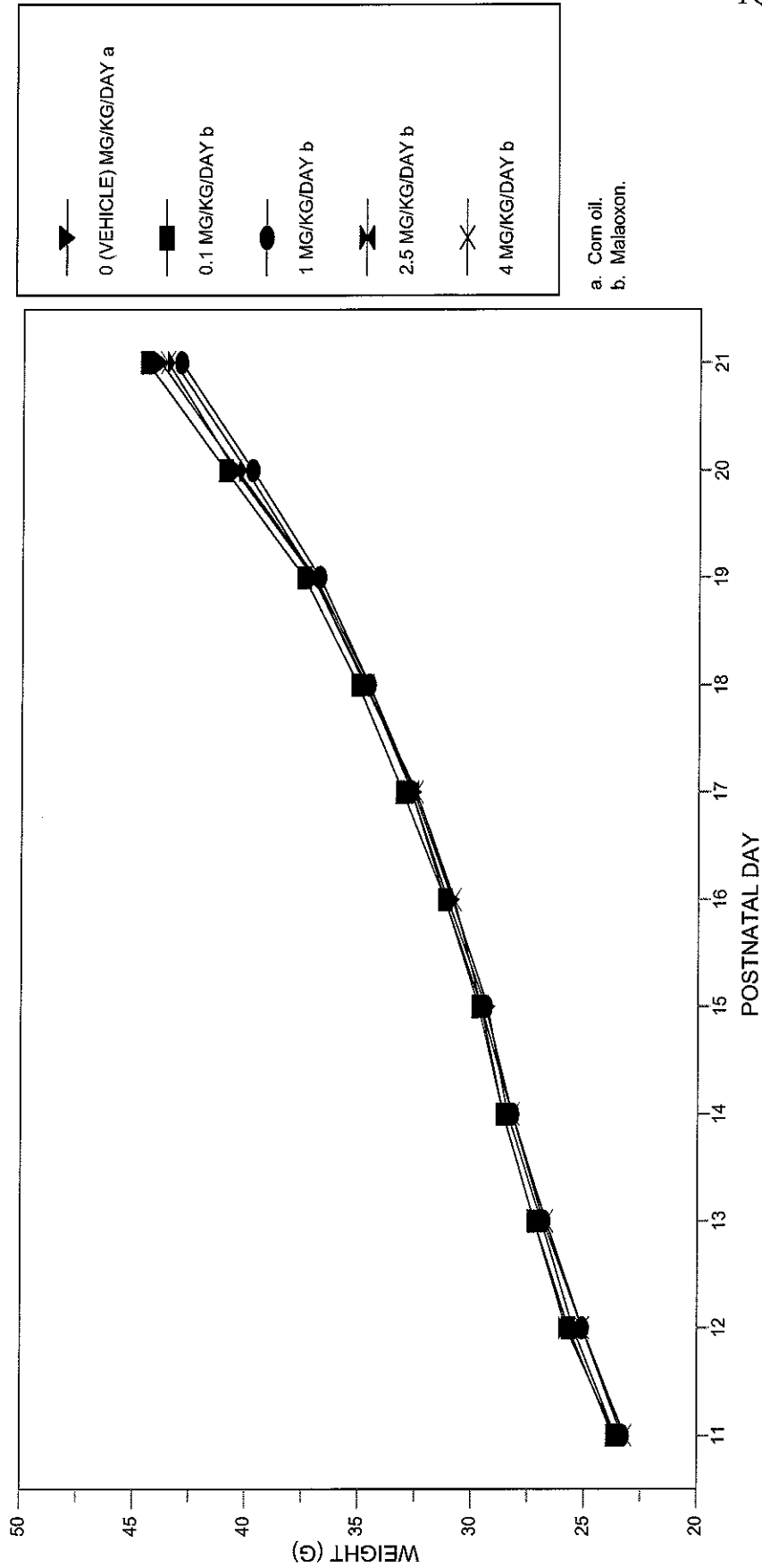
Figure 2



PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

BODY WEIGHTS MALE PUPS - MALAOXON

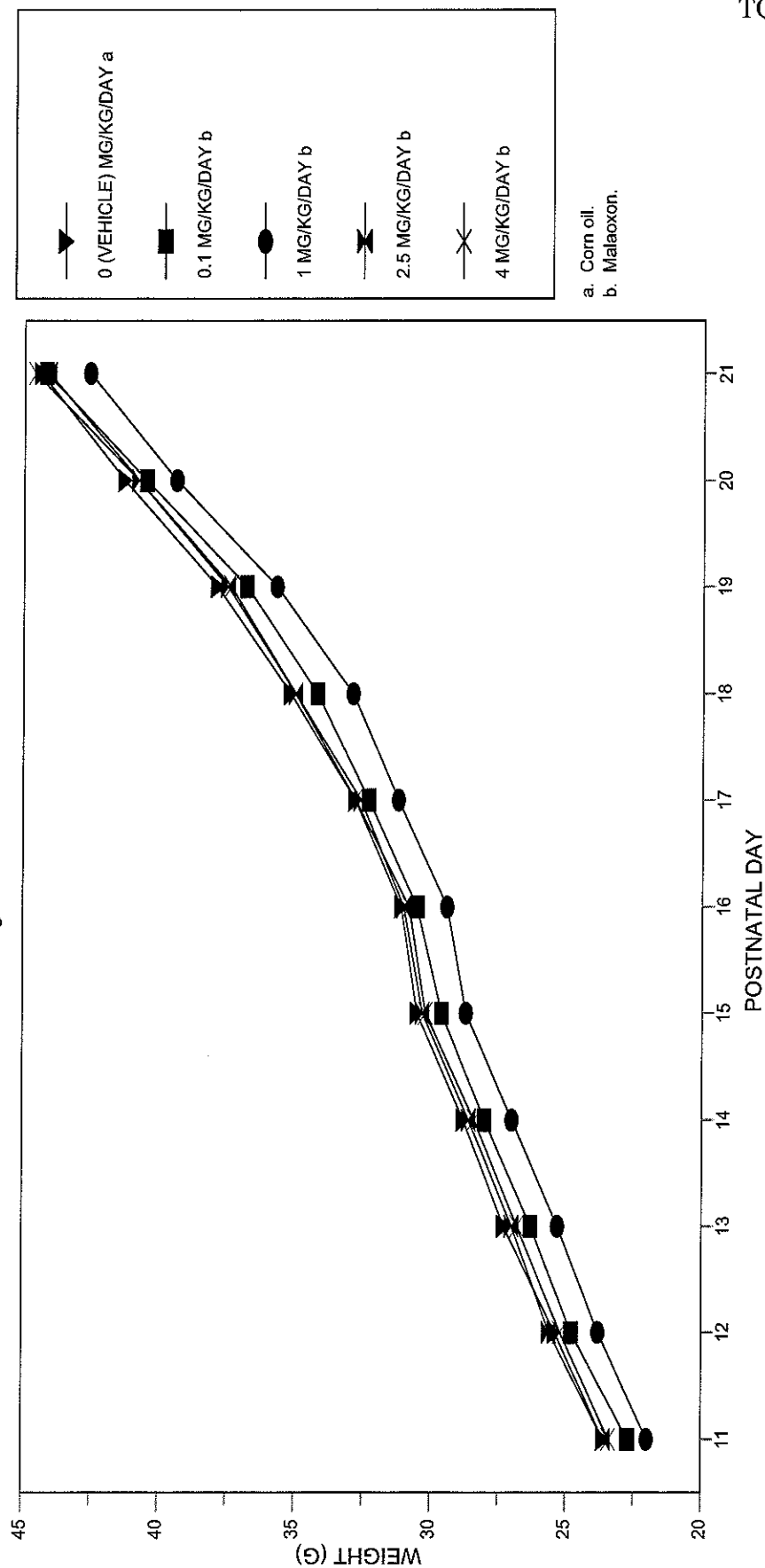
Figure 3



PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

BODY WEIGHTS FEMALE PUPS - MALAOXON

Figure 4



APPENDIX B
REPORT MALATHION TABLES

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B1 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - MALE PUPS - MALATHION

DOSAGE GROUP	I	II	III	IV	V
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	5	25	50	150
TEST SUBSTANCE	CORN OIL	MALATHION	MALATHION	MALATHION	MALATHION
MAXIMUM POSSIBLE INCIDENCE	132/ 12	132/ 12	132/ 12	132/ 12	132/ 12
MORTALITY	0	0	0	0	0
HEAD OR WHOLE BODY: TREMORS, INTERMITTENT	0/ 0	0/ 0	0/ 0	0/ 0	11/ 7
DECREASED MOTOR ACTIVITY	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
IMPAIRED RIGHTING REFLEX	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
BOTH FORELIMBS: SPLAYED	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1

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

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF PUPS WITH OBSERVATION.

a. Dosing occurred on postnatal days 11 through 21.

PROTOCOL TOC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B2 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - FEMALE PUPS - MALATHION

DOSAGE GROUP	I	II	III	IV	V
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	5	25	50	150
TEST SUBSTANCE	CORN OIL	MALATHION	MALATHION	MALATHION	MALATHION
MAXIMUM POSSIBLE INCIDENCE	132/ 12	130/ 12	132/ 12	132/ 12	132/ 12
FOUND DEAD	0	1b	0	0	0
HEAD OR WHOLE BODY: TREMORS, CONTINUOUS 1-10 MINUTES AND/OR INTERMITTENT	0/ 0	0/ 0	0/ 0	0/ 0	8/ 5
PALE EXTREMITIES	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
LEFT EYE: ABSENT	0/ 0	0/ 0	3/ 1	0/ 0	0/ 0

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

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF PUPS WITH OBSERVATION.

a. Dosing occurred on postnatal days 11 through 21.

b. Pup 6807 was found dead on postnatal day 19.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B3 (PAGE 1): BODY WEIGHTS AND BODY WEIGHT CHANGES - SUMMARY - MALE PUPS - MALATHION

DOSAGE GROUP DOSAGE (MG/KG/DAY) ^a TEST SUBSTANCE	N	I 0 (VEHICLE) CORN OIL		II 5 MALATHION		III 25 MALATHION		IV 50 MALATHION		V 150 MALATHION	
		12	12	12	12	12	12	12	12	12	12
PUPS TESTED											
BODY WEIGHT (G)											
DAY 11	MEAN±S.D.	25.7 ± 2.6	26.4 ± 2.9	27.2 ± 2.1	27.5 ± 2.2	24.9 ± 2.0					
DAY 12	MEAN±S.D.	28.0 ± 2.9	28.9 ± 3.1	29.5 ± 1.7	30.3 ± 2.6	27.7 ± 2.6					
DAY 13	MEAN±S.D.	30.4 ± 2.9	31.3 ± 3.4	32.1 ± 1.5	33.3 ± 3.0	29.8 ± 2.6					
DAY 14	MEAN±S.D.	33.0 ± 2.8	33.8 ± 3.6	34.7 ± 1.9	35.6 ± 2.6	31.9 ± 2.7					
DAY 15	MEAN±S.D.	35.4 ± 3.2	35.9 ± 4.0	36.6 ± 2.1	38.0 ± 3.3	34.2 ± 2.8					
DAY 16	MEAN±S.D.	36.8 ± 4.1	37.4 ± 4.5	38.0 ± 2.4	39.3 ± 4.1	35.7 ± 3.2					
DAY 17	MEAN±S.D.	38.3 ± 5.0	39.0 ± 5.4	39.8 ± 3.3	41.0 ± 5.1	37.2 ± 4.0					
DAY 18	MEAN±S.D.	40.8 ± 5.4	41.5 ± 6.6	42.1 ± 4.2	43.4 ± 5.9	39.6 ± 4.6					
DAY 19	MEAN±S.D.	43.4 ± 6.6	44.6 ± 7.4	44.8 ± 5.1	46.1 ± 6.8	42.2 ± 5.4					
DAY 20	MEAN±S.D.	45.7 ± 6.8	47.0 ± 7.4	48.0 ± 5.6	48.6 ± 7.5	44.8 ± 6.0					
DAY 21	MEAN±S.D.	48.1 ± 7.0	49.7 ± 7.7	50.2 ± 4.6	51.1 ± 6.9	47.2 ± 5.7					
BODY WEIGHT CHANGE (G)											
DAYS 11 - 14	MEAN±S.D.	+7.4 ± 1.2	+7.3 ± 1.2	+7.5 ± 1.2	+8.1 ± 1.3	+7.0 ± 1.2					
DAYS 14 - 17	MEAN±S.D.	+5.3 ± 3.0	+5.2 ± 2.8	+5.0 ± 2.8	+5.4 ± 2.9	+5.3 ± 2.4					
DAYS 17 - 21	MEAN±S.D.	+9.8 ± 2.6	+10.7 ± 2.7	+10.5 ± 1.9	+10.0 ± 2.4	+9.9 ± 2.2					
DAYS 11 - 21	MEAN±S.D.	+22.4 ± 5.3	+23.2 ± 5.5	+23.0 ± 4.2	+23.5 ± 5.3	+22.2 ± 5.1					

DAY(S) = POSTNATAL DAY(S)

a. Dosing occurred on postnatal days 11 through 21.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B4 (PAGE 1): BODY WEIGHTS AND BODY WEIGHT CHANGES - SUMMARY - FEMALE PUPS - MALATHION

DOSAGE GROUP DOSAGE (MG/KG/DAY)a TEST SUBSTANCE	N	I 0 (VEHICLE) CORN OIL		II 5 MALATHION		III 25 MALATHION		IV 50 MALATHION		V 150 MALATHION	
		12	12	12	12	12	12	12	12	12	12
PUPS TESTED											
BODY WEIGHT (G)											
DAY 11	MEAN±S.D.	25.6 ± 1.7	25.3 ± 1.8	25.3 ± 1.8	25.3 ± 2.2	25.3 ± 2.2	25.3 ± 2.2	26.0 ± 1.6	25.9 ± 1.8		
DAY 12	MEAN±S.D.	28.2 ± 1.8	27.8 ± 2.0	27.8 ± 2.0	27.7 ± 2.5	27.7 ± 2.5	27.7 ± 2.5	28.5 ± 1.7	28.6 ± 1.9		
DAY 13	MEAN±S.D.	30.6 ± 2.1	30.4 ± 2.2	30.4 ± 2.2	30.2 ± 2.7	30.2 ± 2.7	30.2 ± 2.7	31.1 ± 1.8	31.0 ± 2.2		
DAY 14	MEAN±S.D.	33.0 ± 1.9	32.8 ± 2.4	32.8 ± 2.4	32.8 ± 3.1	32.8 ± 3.1	32.8 ± 3.1	33.4 ± 1.9	33.0 ± 1.8		
DAY 15	MEAN±S.D.	35.0 ± 2.4	34.6 ± 2.3	34.6 ± 2.3	34.9 ± 3.4	34.9 ± 3.4	34.9 ± 3.4	35.8 ± 2.0	35.2 ± 2.1		
DAY 16	MEAN±S.D.	36.5 ± 3.0	36.3 ± 2.9	36.3 ± 2.9	36.0 ± 4.0	36.0 ± 4.0	36.0 ± 4.0	36.8 ± 2.8	36.8 ± 2.5		
DAY 17	MEAN±S.D.	38.3 ± 4.2	37.8 ± 3.6	37.8 ± 3.6	37.5 ± 4.3	37.5 ± 4.3	37.5 ± 4.3	38.5 ± 3.5	38.4 ± 3.6		
DAY 18	MEAN±S.D.	40.3 ± 4.7	40.0 ± 4.0	40.0 ± 4.0	39.7 ± 4.5	39.7 ± 4.5	39.7 ± 4.5	40.6 ± 4.3	40.6 ± 3.9		
DAY 19	MEAN±S.D.	42.8 ± 5.6	42.5 ± 5.0	42.5 ± 5.0	42.5 ± 5.2	42.5 ± 5.2	42.5 ± 5.2	43.4 ± 5.0	43.5 ± 5.0		
DAY 20	MEAN±S.D.	45.0 ± 5.5	43.9 ± 5.0	43.9 ± 5.0	44.8 ± 5.3	44.8 ± 5.3	44.8 ± 5.3	45.8 ± 5.2	46.1 ± 5.5		
DAY 21	MEAN±S.D.	47.4 ± 5.1	46.2 ± 4.9	46.2 ± 4.9	47.0 ± 4.8	47.0 ± 4.8	47.0 ± 4.8	48.0 ± 4.6	48.4 ± 5.1		
BODY WEIGHT CHANGE (G)											
DAYS 11 - 14	MEAN±S.D.	+7.4 ± 1.1	+7.5 ± 1.1	+7.5 ± 1.1	+7.5 ± 1.2	+7.5 ± 1.2	+7.5 ± 1.2	+7.4 ± 1.0	+7.2 ± 1.0		
DAYS 14 - 17	MEAN±S.D.	+5.3 ± 2.7	+5.0 ± 2.6	+5.0 ± 2.6	+4.7 ± 2.4	+4.7 ± 2.4	+4.7 ± 2.4	+5.1 ± 2.2	+5.4 ± 2.8		
DAYS 17 - 21	MEAN±S.D.	+9.1 ± 1.4	+8.8 ± 1.9	+8.8 ± 1.9	+9.5 ± 1.2	+9.5 ± 1.2	+9.5 ± 1.2	+9.5 ± 1.5	+9.9 ± 2.6		
DAYS 11 - 21	MEAN±S.D.	+21.8 ± 4.2	+21.0 ± 3.9	+21.0 ± 3.9	+21.7 ± 3.6	+21.7 ± 3.6	+21.7 ± 3.6	+22.0 ± 3.8	+22.5 ± 4.9		

DAY (S) = POSTNATAL DAY (S)

1 = NUMBER OF VALUES AVERAGED

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes values for pup 6807, which was found dead on postnatal day 19.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B5 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - MALE PUPS - MALATHION

DOSAGE GROUP	I	II	III	IV	V
DOSAGE (MG/KG/DAY)a	0 (VEHICLE)	5	25	50	150
TEST SUBSTANCE	CORN OIL	MALATHION	MALATHION	MALATHION	MALATHION
PUPS TESTED	12	12	12	12	11b

CHOLINESTERASE LEVELS (UNITS/ML) MEAN±S.D. 2.316 ± 0.373 2.067 ± 0.384 1.967 ± 0.383 * 1.527 ± 0.276 ** 1.063 ± 0.274 **

% INHIBITION

a. Dosing occurred on postnatal days 11 through 21. 10.8 15.1 34.1 54.1

b. Excludes values for pup 6905, which did not have a sample analyzed.

* Significantly different from the vehicle control group value (p<0.05).

** Significantly different from the vehicle control group value (p<0.01).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B6 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - FEMALE PUPS - MALATHION

DOSAGE GROUP	I	II	III	IV	V
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	5	25	50	150
TEST SUBSTANCE	CORN OIL	MALATHION	MALATHION	MALATHION	MALATHION
PUPS TESTED	12	11b	12	12	12
N					
CHOLINESTERASE LEVELS (UNITS/ML) MEAN±S.D.	2.119 ± 0.272	2.022 ± 0.338	1.746 ± 0.213 **	1.482 ± 0.192 **	1.024 ± 0.163 **
% INHIBITION		4.6	17.6	30.1	51.7

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes values for pup 6807, which was found dead on postnatal day 19.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B7 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALE PUPS - MALATHION

DOSAGE GROUP	I	II	III	IV	V
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	5	25	50	150
TEST SUBSTANCE	CORN OIL	MALATHION	MALATHION	MALATHION	MALATHION
PUPS TESTED	105	12	12	12	12
	N				
BRAIN WEIGHT (G)	MEAN±S.D. 1.436 ± 0.087	1.464 ± 0.093	1.488 ± 0.074	1.467 ± 0.088	1.405 ± 0.109
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D. 12.104 ± 1.706	12.063 ± 1.038	12.292 ± 0.725	12.093 ± 1.070	10.354 ± 1.605 **
% INHIBITION		0.3	-1.6	0.1	14.5

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes values for pups that did not have samples analyzed.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B8 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - FEMALE PUPS - MALATHION

DOSAGE GROUP	I	II	III	IV	V
DOSAGE (MG/KG/DAY) ^a	0 (VEHICLE)	5	25	50	150
TEST SUBSTANCE	CORN OIL	MALATHION	MALATHION	MALATHION	MALATHION
PUPS TESTED	12	11b	12	12	12
	N				
BRAIN WEIGHT (G)	MEAN±S.D. 1.418 ± 0.061	1.403 ± 0.061	1.435 ± 0.046	1.424 ± 0.065	1.410 ± 0.100
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D. 11.880 ± 1.791	12.448 ± 0.856	11.745 ± 0.702	12.170 ± 0.884	9.886 ± 1.643 **
% INHIBITION		-4.8	1.1	-2.4	16.8

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes values for pup 6807, which was found dead on postnatal day 19.

** Significantly different from the vehicle control group value (p<0.01).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B9 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	DESCRIPTION	
DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY	CORN OIL
6301	NO ADVERSE FINDINGS	
6401	NO ADVERSE FINDINGS	
6501	NO ADVERSE FINDINGS	
6601	NO ADVERSE FINDINGS	
6701	NO ADVERSE FINDINGS	
6801	NO ADVERSE FINDINGS	
6901	NO ADVERSE FINDINGS	
7001	NO ADVERSE FINDINGS	
7101	NO ADVERSE FINDINGS	
7201	NO ADVERSE FINDINGS	
7301	NO ADVERSE FINDINGS	
7401	NO ADVERSE FINDINGS	
DOSAGE GROUP II	5 MG/KG/DAY	MALATHION
6302	NO ADVERSE FINDINGS	
6402	NO ADVERSE FINDINGS	
6502	NO ADVERSE FINDINGS	
6602	NO ADVERSE FINDINGS	
6702	NO ADVERSE FINDINGS	
6802	NO ADVERSE FINDINGS	
6902	NO ADVERSE FINDINGS	
7002	NO ADVERSE FINDINGS	
7102	NO ADVERSE FINDINGS	
7202	NO ADVERSE FINDINGS	
7302	NO ADVERSE FINDINGS	
7402	NO ADVERSE FINDINGS	
PND = POSTNATAL DAY		

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B9 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	DESCRIPTION
DOSAGE GROUP III	25 MG/KG/DAY
MALATHION	
6303	NO ADVERSE FINDINGS
6403	NO ADVERSE FINDINGS
6503	NO ADVERSE FINDINGS
6603	NO ADVERSE FINDINGS
6703	NO ADVERSE FINDINGS
6803	NO ADVERSE FINDINGS
6903	NO ADVERSE FINDINGS
7003	NO ADVERSE FINDINGS
7103	NO ADVERSE FINDINGS
7203	NO ADVERSE FINDINGS
7303	NO ADVERSE FINDINGS
7403	NO ADVERSE FINDINGS
DOSAGE GROUP IV	50 MG/KG/DAY
MALATHION	
6304	NO ADVERSE FINDINGS
6404	NO ADVERSE FINDINGS
6504	NO ADVERSE FINDINGS
6604	NO ADVERSE FINDINGS
6704	NO ADVERSE FINDINGS
6804	NO ADVERSE FINDINGS
6904	NO ADVERSE FINDINGS
7004	NO ADVERSE FINDINGS
7104	NO ADVERSE FINDINGS
7204	NO ADVERSE FINDINGS
7304	NO ADVERSE FINDINGS
7404	NO ADVERSE FINDINGS

PND = POSTNATAL DAY

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B9 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	DESCRIPTION
DOSAGE GROUP V	150 MG/KG/DAY
	MALATHION
6305	PND (12) HEAD: TREMORS - INTERMITTENT
	PND (14) WHOLE BODY: TREMORS - INTERMITTENT
6405	PND (12) WHOLE BODY: TREMORS - INTERMITTENT
6505	PND (12) IMPAIRED RIGHTING REFLEX
	PND (12) DECREASED MOTOR ACTIVITY
	PND (12-14) WHOLE BODY: TREMORS - INTERMITTENT
6605	PND (11) HEAD: TREMORS - INTERMITTENT
6705	NO ADVERSE FINDINGS
6805	NO ADVERSE FINDINGS
6905	PND (12) WHOLE BODY: TREMORS - INTERMITTENT
7005	NO ADVERSE FINDINGS
7105	NO ADVERSE FINDINGS
7205	PND (12) DECREASED MOTOR ACTIVITY
	PND (12) HEAD: TREMORS - INTERMITTENT
	PND (12) BOTH FORELIMBS: SPLAYED
7305	PND (11-12) WHOLE BODY: TREMORS - INTERMITTENT
7405	NO ADVERSE FINDINGS

PND = POSTNATAL DAY

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B10 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	DESCRIPTION
DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY
	CORN OIL
6306	NO ADVERSE FINDINGS
6406	NO ADVERSE FINDINGS
6506	NO ADVERSE FINDINGS
6606	NO ADVERSE FINDINGS
6706	NO ADVERSE FINDINGS
6806	NO ADVERSE FINDINGS
6906	NO ADVERSE FINDINGS
7006	NO ADVERSE FINDINGS
7106	NO ADVERSE FINDINGS
7206	NO ADVERSE FINDINGS
7306	NO ADVERSE FINDINGS
7406	NO ADVERSE FINDINGS
DOSAGE GROUP II	5 MG/KG/DAY
	MALATHION
6307	NO ADVERSE FINDINGS
6407	NO ADVERSE FINDINGS
6507	NO ADVERSE FINDINGS
6607	NO ADVERSE FINDINGS
6707	NO ADVERSE FINDINGS
6807	FOUND DEAD (DEATH OCCURRED 6 HOURS AND 47 MINUTES AFTER DOSAGE ADMINISTRATION) a
6907	NO ADVERSE FINDINGS
7007	NO ADVERSE FINDINGS
7107	NO ADVERSE FINDINGS
7207	NO ADVERSE FINDINGS
7307	NO ADVERSE FINDINGS
7407	NO ADVERSE FINDINGS
PND = POSTNATAL DAY	
a. At necropsy, pup was partially cannibalized. All other tissues appeared normal.	

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B10 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	DESCRIPTION	
DOSAGE GROUP III	25 MG/KG/DAY	MALATHION
6308	NO ADVERSE FINDINGS	
6408	NO ADVERSE FINDINGS	
6508	NO ADVERSE FINDINGS	
6608	NO ADVERSE FINDINGS	
6708	NO ADVERSE FINDINGS	
6808	NO ADVERSE FINDINGS	
6908	NO ADVERSE FINDINGS	
7008	LEFT EYE: ABSENT	
7108	NO ADVERSE FINDINGS	
7208	NO ADVERSE FINDINGS	
7308	NO ADVERSE FINDINGS	
7408	NO ADVERSE FINDINGS	
DOSAGE GROUP IV	50 MG/KG/DAY	MALATHION
6309	NO ADVERSE FINDINGS	
6409	NO ADVERSE FINDINGS	
6509	NO ADVERSE FINDINGS	
6609	NO ADVERSE FINDINGS	
6709	NO ADVERSE FINDINGS	
6809	NO ADVERSE FINDINGS	
6909	NO ADVERSE FINDINGS	
7009	NO ADVERSE FINDINGS	
7109	NO ADVERSE FINDINGS	
7209	NO ADVERSE FINDINGS	
7309	NO ADVERSE FINDINGS	
7409	NO ADVERSE FINDINGS	
PND = POSTNATAL DAY		

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B10 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	DESCRIPTION	
	DOSAGE GROUP V	150 MG/KG/DAY
MALATHION		
6310	PND (11)	PALE EXTREMITIES
	PND (11)	WHOLE BODY: TREMORS - CONTINUOUS 10 MINUTES
	PND (11)	HEAD: TREMORS - CONTINUOUS 1 MINUTE
	PND (12)	HEAD: TREMORS - INTERMITTENT
	PND (12)	WHOLE BODY: TREMORS - INTERMITTENT
6410		NO ADVERSE FINDINGS
6510		NO ADVERSE FINDINGS
6610		NO ADVERSE FINDINGS
6710	PND (11)	HEAD: TREMORS - INTERMITTENT
	PND (13)	WHOLE BODY: TREMORS - INTERMITTENT
6810		NO ADVERSE FINDINGS
6910		NO ADVERSE FINDINGS
7010	PND (12- 13)	HEAD: TREMORS - INTERMITTENT
7110		NO ADVERSE FINDINGS
7210		NO ADVERSE FINDINGS
7310		NO ADVERSE FINDINGS
7410	PND (12)	HEAD: TREMORS - INTERMITTENT

PND = POSTNATAL DAY

TABLE B11 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	DAY 11	12	13	14	15	16	17	18	19	20	21
	DOSAGE GROUP I			O (VEHICLE)	MG/KG/DAY			CORN OIL			
6301	26.7	30.1	32.5	35.3	39.1	41.2	43.2	45.7	50.4	50.7	51.6
6401	27.9	30.1	32.4	35.0	37.7	40.0	42.3	44.7	45.7	48.9	51.5
6501	27.0	28.5	31.3	33.9	37.4	39.5	42.6	45.9	51.9	53.8	57.1
6601	25.0	27.1	29.7	32.8	34.9	36.3	38.7	42.0	44.0	48.5	51.2
6701	28.6	31.1	34.5	36.5	39.2	42.0	44.2	47.4	52.2	55.4	57.8
6801	22.9	25.0	26.8	29.6	32.7	34.8	37.6	39.3	42.2	45.4	47.9
6901	27.0	29.6	31.0	33.3	36.8	39.1	40.5	43.1	45.5	47.3	50.3
7001	29.0	31.7	33.4	33.9	34.6	35.6	36.1	39.2	42.0	44.3	45.8
7101	21.8	23.0	26.8	29.5	29.9	30.3	31.2	33.0	34.5	35.7	37.6
7201	23.2	25.9	28.2	30.6	32.5	33.5	33.2	35.0	35.7	37.6	40.4
7301	22.0	23.9	25.9	29.2	31.1	29.5	29.2	30.9	32.2	33.8	36.2
7401	27.3	29.8	33.0	37.0	38.4	39.3	41.3	43.1	44.4	46.6	50.0
	DOSAGE GROUP II			5 MG/KG/DAY				MALATHION			
6302	29.2	32.3	35.1	37.4	39.9	43.3	45.1	48.7	53.7	55.5	57.5
6402	27.5	29.6	32.3	35.2	38.7	41.1	43.6	46.0	47.6	50.9	54.3
6502	26.4	29.5	32.7	35.3	37.3	40.4	42.9	47.4	53.4	54.9	56.6
6602	26.3	28.5	30.7	33.5	36.7	38.1	40.8	43.6	47.1	50.3	53.6
6702	28.0	31.1	34.5	38.0	40.0	41.6	44.1	47.4	50.1	52.5	54.0
6802	24.4	26.7	29.1	31.3	34.4	36.9	39.2	41.5	45.5	48.2	49.6
6902	29.5	31.4	33.4	36.7	40.0	40.9	42.9	47.6	50.1	51.3	56.6
7002	29.5	32.5	34.2	35.6	35.2	36.5	37.5	40.0	43.5	46.5	51.3
7102	19.0	21.1	22.4	24.7	25.9	27.4	27.1	27.5	28.6	30.4	31.9
7202	25.3	27.6	29.6	31.8	33.2	33.6	34.0	36.0	38.6	40.3	42.7
7302	25.1	27.3	29.7	32.3	33.7	33.4	33.2	34.4	36.3	39.6	41.8
7402	27.3	29.6	32.2	33.8	35.4	35.8	37.8	38.2	41.2	43.7	46.7

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B11 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	DAY 11										MALATHION									
	DOSAGE GROUP III																			
	11	12	13	14	15	16	17	18	19	20	21									
	25 MG/KG/DAY																			
6303	27.1	29.8	32.3	35.1	38.3	41.0	43.6	47.1	50.9	54.3	56.5									
6403	25.6	28.1	31.2	34.1	37.2	40.1	42.9	45.3	46.7	49.7	52.3									
6503	25.2	27.3	29.8	31.9	36.3	37.1	40.3	44.6	48.8	53.7	54.2									
6603	28.7	31.6	34.4	37.5	39.2	40.3	42.4	45.6	49.3	53.4	53.3									
6703	32.1	31.6	33.3	37.5	38.4	40.0	42.5	44.9	49.3	53.0	54.1									
6803	27.2	29.7	33.0	34.4	36.4	39.2	42.1	44.5	48.0	50.4	53.0									
6903	28.2	30.3	32.5	35.3	37.2	39.4	41.1	44.9	47.1	50.3	51.6									
7003	27.4	30.1	32.3	33.4	34.0	35.8	36.7	38.5	40.7	43.8	46.7									
7103	24.2	26.9	30.1	33.9	33.2	34.7	34.5	34.9	36.6	40.2	45.4									
7203	24.8	27.3	29.8	31.6	33.6	33.3	33.9	35.3	36.2	38.3	41.3									
7303	28.2	30.8	32.9	36.8	39.3	37.7	38.4	39.1	41.6	44.0	46.2									
7403	28.0	30.2	33.3	35.1	36.6	37.4	38.8	40.2	42.2	44.4	48.4									
PUP #	DOSAGE GROUP IV										MALATHION									
	50 MG/KG/DAY																			
6304	30.1	33.9	37.5	40.3	43.4	44.5	48.2	51.9	56.0	59.9	61.8									
6404	28.2	30.4	35.3	36.3	39.3	43.0	44.6	46.5	48.8	50.5	53.3									
6504	29.0	31.4	33.8	36.3	39.4	42.8	45.5	48.4	50.6	51.8	54.0									
6604	26.3	28.9	32.1	34.6	37.4	38.7	40.6	43.3	45.0	47.8	49.8									
6704	30.3	34.8	38.8	40.1	44.2	45.3	48.5	51.9	57.2	62.2	62.6									
6804	26.5	29.0	32.4	34.8	37.6	39.8	41.5	44.5	48.8	52.3	55.5									
6904	29.5	31.9	34.9	36.7	39.8	41.0	43.3	46.7	49.1	51.7	53.1									
7004	29.7	32.5	34.5	35.2	35.7	37.1	38.1	40.0	42.3	44.2	47.8									
7104	25.4	27.9	31.7	34.1	35.6	34.4	34.8	36.5	37.8	40.5	42.7									
7204	23.8	26.5	29.0	31.8	34.6	34.4	34.3	35.6	38.2	39.6	42.5									
7304	26.1	28.2	29.6	32.7	34.1	33.6	34.8	36.1	38.1	40.1	43.9									
7404	25.4	27.9	30.5	34.6	35.6	36.7	38.2	39.3	41.0	42.8	45.8									

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B11 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	DOSAGE GROUP V										MALATHION				
	DAY 11	12	13	14	15	16	17	18	19	20	21				
												150 MG/KG/DAY			
6305	24.0	26.7	29.0	31.5	34.4	36.5	39.2	42.4	45.0	48.2	49.5				
6405	23.2	25.3	27.7	30.0	34.2	35.9	38.9	42.0	44.1	46.8	49.2				
6505	21.9	23.6	25.2	27.9	29.5	32.4	33.6	36.6	40.1	42.5	45.0				
6605	26.9	30.0	32.2	35.5	38.1	40.6	43.1	46.0	49.7	54.3	57.1				
6705	28.2	31.8	33.9	37.1	39.7	42.3	44.2	46.9	51.5	53.8	55.4				
6805	24.5	27.0	30.2	31.9	33.5	36.3	38.8	42.3	45.6	49.3	51.2				
6905	26.1	28.6	30.3	33.1	34.9	36.7	39.1	42.8	45.5	47.0	48.7				
7005	26.5	30.0	32.3	31.4	32.6	33.8	35.0	37.1	38.8	41.2	45.0				
7105	27.1	31.3	32.9	33.9	35.1	35.8	35.3	36.1	37.3	40.0	42.4				
7205	24.5	26.9	29.1	32.0	35.2	34.2	34.5	35.4	37.5	39.2	42.3				
7305	23.3	25.6	27.0	28.5	31.7	31.0	31.1	32.7	34.4	35.7	38.0				
7405	23.1	25.2	28.1	30.1	31.6	33.1	34.2	35.3	36.9	39.3	42.2				

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL IQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B12 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

	DAY 11	12	13	14	15	16	17	18	19	20	21
PUP #	DOSAGE GROUP I										
	0 (VEHICLE) MG/KG/DAY										
	CORN OIL										
6306	27.5	30.3	33.1	35.2	38.4	40.6	44.1	47.1	51.0	51.9	53.5
6406	25.1	27.8	30.5	32.8	36.1	39.7	41.2	42.4	44.3	46.3	49.3
6506	25.3	27.5	30.4	33.2	35.9	37.5	40.4	42.5	45.7	47.0	49.9
6606	26.3	28.5	31.4	34.1	36.2	38.0	41.2	43.1	47.8	51.4	53.6
6706	25.3	28.7	31.4	34.3	36.5	38.0	40.7	42.7	46.0	49.0	49.5
6806	25.5	28.3	30.9	33.4	35.3	37.4	40.8	43.4	46.7	48.0	50.7
6906	28.0	31.2	33.8	36.3	38.4	39.3	41.8	45.1	48.0	49.4	52.0
7006	28.0	30.2	32.6	32.8	33.1	34.7	36.0	38.2	39.5	41.9	45.3
7106	24.9	27.1	28.4	31.0	31.1	32.6	31.9	34.2	35.2	39.4	41.0
7206	25.1	27.5	29.8	31.5	33.2	33.4	34.1	35.4	37.1	38.5	41.7
7306	22.3	24.8	26.6	29.4	31.4	31.3	31.2	32.2	34.1	35.3	38.7
7406	23.9	26.1	28.7	31.9	34.5	35.5	36.2	37.4	38.9	41.3	44.0
PUP #	DOSAGE GROUP II										
	5 MG/KG/DAY										
	MALATHION										
6307	27.4	30.7	33.0	35.5	38.3	40.4	42.5	44.6	46.9	48.8	51.6
6407	23.0	25.5	28.6	31.1	34.0	36.4	38.5	39.5	41.8	42.9	44.7
6507	23.4	24.8	27.2	29.9	32.0	34.2	38.2	39.8	42.8	44.2	45.8
6607	25.3	27.5	30.4	32.9	34.8	37.2	39.4	42.8	47.2	49.1	51.4
6707	26.0	28.2	30.7	34.8	36.6	39.6	41.7	44.2	47.7	51.0	52.3
6807	25.9	28.7	32.2	34.9	36.7	39.4	41.6	45.0	49.0	a	
6907	27.8	30.6	32.9	35.1	37.4	39.5	41.0	43.5	46.3	48.2	51.2
7007	25.3	27.7	30.6	30.4	30.8	32.3	32.7	35.0	37.3	39.2	40.7
7107	27.5	29.8	32.5	36.1	35.1	35.8	36.6	38.5	40.3	43.7	47.4
7207	22.8	25.4	27.9	30.3	32.9	33.2	32.8	35.0	35.4	36.5	40.4
7307	23.4	25.9	27.5	30.2	32.8	32.5	32.7	34.0	35.0	37.2	39.3
7407	26.3	28.5	31.8	32.7	34.4	35.4	36.4	38.1	40.2	42.0	44.0

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

a. Pup 6807 was found dead on postnatal day 19.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B12 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

DAY 11												12	13	14	15	16	17	18	19	20	21
PUP #	DOSAGE GROUP III											MALATHION									
	25 MG/KG/DAY																				
6308	25.0	27.4	31.0	33.4	36.0	37.8	39.4	42.6	45.8	47.9	48.2										
6408	28.2	31.0	33.5	37.3	39.5	42.0	43.5	45.3	47.7	47.8	52.1										
6508	21.2	23.0	24.9	26.6	28.0	30.7	33.5	35.9	39.0	42.0	42.9										
6608	24.5	26.2	29.4	32.2	34.9	35.5	38.0	40.7	44.6	48.7	50.2										
6708	28.5	30.9	34.4	37.6	40.7	42.8	44.7	46.7	51.0	54.4	56.0										
6808	26.2	28.8	31.2	34.1	37.9	40.3	42.3	45.0	49.0	50.7	51.5										
6908	25.1	27.7	29.7	31.8	34.1	35.1	36.9	39.4	41.8	44.3	46.3										
7008	27.7	30.4	32.3	33.9	33.4	34.8	35.9	38.3	40.9	43.2	44.9										
7108	25.2	27.7	29.3	32.2	33.0	32.8	32.8	34.8	36.8	39.2	42.7										
7208	22.6	25.2	28.1	30.6	33.3	33.2	34.2	35.6	37.7	39.4	42.8										
7308	23.2	25.3	26.9	29.5	32.4	31.5	31.6	32.8	34.6	36.2	39.7										
7408	26.3	28.7	31.7	34.8	35.6	36.4	37.6	39.4	41.2	43.5	46.7										
PUP #	DOSAGE GROUP IV											MALATHION									
	50 MG/KG/DAY																				
6309	25.2	27.9	30.2	33.0	36.1	37.2	39.2	42.1	45.9	46.4	47.5										
6409	28.1	30.2	32.8	34.9	38.6	40.1	42.7	44.0	46.7	49.1	52.0										
6509	26.9	29.4	32.5	34.4	36.8	38.5	41.6	45.6	49.6	52.6	53.4										
6609	25.1	27.5	30.2	32.4	34.7	36.4	38.0	41.9	44.5	47.9	49.8										
6709	26.2	29.1	31.8	34.6	37.4	39.2	41.7	43.7	47.8	51.6	52.5										
6809	26.3	28.5	31.2	33.9	36.9	39.3	41.7	44.4	48.0	51.0	52.5										
6909	26.4	28.9	31.6	34.7	36.6	37.6	39.7	43.3	46.5	47.9	50.3										
7009	27.6	30.3	32.5	32.8	33.4	34.6	35.5	37.9	40.3	41.9	43.4										
7109	25.5	28.8	31.8	34.7	35.7	34.5	35.9	36.9	38.9	40.8	43.9										
7209	22.0	24.4	26.7	28.7	31.5	31.1	31.4	31.2	33.1	35.9	39.7										
7309	25.2	27.2	29.0	31.5	34.1	33.6	34.4	35.7	37.8	39.9	42.8										
7409	27.7	30.3	33.1	35.3	37.3	39.4	40.3	41.0	42.4	44.6	48.4										

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B12 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	DOSAGE GROUP V										MALATHION				
	DAY 11	12	13	14	15	16	17	18	19	20	21				
					150 MG/KG/DAY										
6310	26.4	28.8	30.7	33.5	37.2	39.2	41.6	44.9	49.1	51.9	53.3				
6410	26.4	28.7	30.5	33.2	36.5	38.6	40.9	43.1	44.3	46.2	47.5				
6510	23.4	26.4	28.8	30.9	33.7	36.5	38.1	40.9	45.4	48.5	50.0				
6610	26.1	29.1	31.0	33.3	35.8	37.0	40.2	43.9	48.3	53.1	55.5				
6710	27.7	31.1	34.6	36.7	38.8	40.6	43.3	45.0	48.8	51.9	54.1				
6810	25.3	28.3	30.7	33.4	34.9	37.4	39.1	42.3	47.0	49.4	51.2				
6910	25.6	28.0	30.8	33.0	37.1	38.7	43.3	43.7	47.5	49.2	51.7				
7010	28.2	31.4	33.6	33.6	33.4	34.9	36.0	38.6	40.6	43.9	46.5				
7110	28.1	30.6	33.6	34.9	35.0	36.4	36.7	38.5	41.1	42.8	45.8				
7210	22.2	24.6	26.5	29.4	30.8	31.3	31.7	33.3	35.2	36.9	40.6				
7310	25.2	28.5	30.2	32.4	34.4	34.1	33.9	34.9	35.7	37.6	40.0				
7410	26.1	28.2	30.7	33.3	35.4	36.3	36.7	38.0	39.0	42.2	44.3				

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B13 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY	DOSAGE GROUP II	MALATHION
6301	2.773			
6401	2.074			
6501	2.110			
6601	2.623			
6701	1.983			
6801	1.837			
6901	1.641a			
	2.194			
7001	3.151			
7101	3.330a			
	2.205			
7201	X			DNR
	2.161			
7301	2.470			
7401	2.206			
PUP #	DOSAGE GROUP I		DOSAGE GROUP II	
	2.213	5 MG/KG/DAY		MALATHION
6302	2.213			
6402	1.742			
6502	1.622			
6602	1.786			
6702	2.807			
6802	1.704			
6902	2.638			
7002	2.034			
7102	2.247			
7202	2.212			
7302	X			DNR
	2.129			
7402	X			DNR
	1.673			

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSE

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B13 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
	DOSAGE GROUP III	25 MG/KG/DAY	
6303	2.316		MALATHION
6403	1.693		
6503	2.376		
6603	2.103		
6703	2.089		
6803	1.566		
6903	2.389		
7003	2.189		
7103	X		DNR
	1.584		
7203	X		DNR
	1.351		
7303	2.363		
7403	X		DNR
	1.587		
PUP #	DOSAGE GROUP IV		MALATHION
	50 MG/KG/DAY		
6304	1.569		
6404	1.697		
6504	1.379		
6604	1.501		
6704	1.468		
6804	1.839		
6904	1.083		
7004	1.778		
7104	X		DNR
	1.074		
7204	1.696		
7304	1.913		
7404	X		DNR
	1.325		

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSE
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.
 HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.
 DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B13 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	DOSAGE GROUP V	FINAL CHOLINESTERASE (UNITS/ML)	FOOTNOTE	MALATHION
6305	1.263			
6405	1.575			
6505	1.014			
6605	1.212			
6705	0.798			
6805	1.147			
6905	a			
7005	X		DNR	
	1.184			
7105	X		DNR	
	0.858			
7205	1.021			
7305	0.528			
7405	1.098			

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSIS
LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample was not analyzed.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAXON IN JUVENILE RATS

TABLE B14 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	0 (VEHICLE) MG/KG/DAY	CORN OIL
	DOSAGE GROUP I	DOSAGE GROUP II			
6306	2.108				
6406	2.346				
6506	2.535				
6606	1.548				
6706	2.049				
6806	1.951				
6906	2.207				
7006	X		DNR		
	2.174				
7106	2.256				
7206	2.355				
7306	X		DNR		
	1.743				
7406	2.152				
MALATHION					
PUP #	DOSAGE GROUP I	DOSAGE GROUP II	5 MG/KG/DAY		
6307	X		DNR		
	1.534				
6407	1.684				
6507	2.618				
6607	1.659				
6707	2.324				
6807	FOUND DEAD ON POSTNATAL DAY 19				
6907	1.729				
7007	2.108				
7107	2.039				
7207	2.348				
7307	2.074				
7407	2.120				

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSES.
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B14 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
	DOSAGE GROUP III	DOSAGE GROUP IV	
6308	1.853		25 MG/KG/DAY MALATHION
6408	1.887		
6508	1.681		
6608	1.785		
6708	2.026		
6808	2.073		
6908	1.377		
7008	1.912		
7108	1.502		
7208	1.647		
7308	1.606		
7408	1.597		
6309	1.362		50 MG/KG/DAY MALATHION
6409	1.456		
6509	1.402		
6609	1.586		
6709	1.587		
6809	1.647		
6909	1.314		
7009	1.559		
7109	X		DNR
	1.042		
7209	1.797		
7309	1.574		
7409	1.462		

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSES.
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B14 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	DOSAGE GROUP V	FINAL CHOLINESTERASE (UNITS/ML)	FOOTNOTE
6310	1.097		150 MG/KG/DAY MALATHION
6410	1.017		
6510	0.929		
6610	0.967		
6710	0.961		
6810	1.169		
6910	1.406		
7010	X		DNR
	0.878		
7110	0.837		
7210	X		DNR
	0.916		
7310	1.181		
7410	0.926		

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSES.
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B15 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA -- MALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY	
6301	1.548		12.775	CORN OIL
6401	1.515		13.001	
6501	1.456		13.099	
6601	a			
6701	a			
6801	1.390		10.848b	
	1.390		11.942	
6901	1.571		11.695	
7001	1.409		12.288	
7101	1.415		11.860	
7201	1.420		7.720	
7301	1.336		12.483	
7401	1.304		14.181	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSES.
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample was not analyzed.

b. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B15 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP II	5 MG/KG/DAY	
6302	1.568		12.516	MALATHION
6402	1.403		12.394	
6502	1.468		12.401	
6602	1.344		12.750	
6702	1.631		10.820	
6802	1.459		10.241	
6902	1.577		11.534	
7002	1.472		7.163a	
	1.472		X	DNR
	1.472		11.034	
7102	1.318		11.605	
7202	1.476		12.361	
7302	1.429		13.462	
7402	1.419		13.638	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSES.
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HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B15 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP III	25 MG/KG/DAY	
6303	1.602		13.008	MALATHION
6403	1.479		13.462	
6503	1.457		13.466	
6603	1.515		11.983	
6703	1.496		11.698	
6803	1.518		11.699	
6903	1.601		11.548	
7003	1.394		12.560	
7103	1.401		11.295	
7203	1.372		12.005	
7303	1.529	X		DNR
	1.529		12.332	
7403	1.496		12.452	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSES.

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B15 (PAGE 4): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP IV	50 MG/KG/DAY	
6304	1.573		13.397	
6404	1.502		12.369	
6504	1.519		12.130	
6604	1.419		11.455	
6704	1.608		X	DNR
	1.608		10.574	
6804	1.517		10.800	
6904	1.381		10.994	
7004	1.304		14.281	
7104	1.374		11.963	
7204	1.436		12.216	
7304	1.511		X	DNR
	1.511		12.715	
7404	1.464		12.216	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSES.
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HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B15 (PAGE 5): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP V	150 MG/KG/DAY	
6305	1.475		11.921	
6405	1.430		12.712	
6505	1.312		X	DNR
	1.312		8.780a	
	1.312		9.779	
	1.567		9.886	
6605	1.485		9.238	
6705	1.449		10.578	
6805	1.322		6.732	
6905	1.412		11.542	
7005	1.477		10.537	
7205	1.457		9.361	
7305	1.310		X	DNR
	1.310		9.948	
7405	1.164		12.017	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSES.
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HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B16 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY	
6306	1.379		12.649	CORN OIL
6406	1.411		12.648	
6506	1.478		12.563	
6606	1.385		6.330a	
	1.385		11.315	
6706	1.409		10.915a	
	1.409		11.566	
6806	1.487		10.712a	
	1.487		11.303	
6906	1.560		7.883a	
	1.560		11.764	
7006	1.428		6.032a	
	1.428		15.150	
7106	1.367		11.731	
7206	1.356		7.282	
7306	1.376		12.866	
7406	1.384		11.717	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALY
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B16 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP II	5 MG/KG/DAY	
6307	1.373		11.857	MALATHION
6407	1.411		12.230	
6507	1.394		13.878	
6607	1.451		7.230a	
	1.451		11.587	
6707	1.462		11.868	
6807	FOUND DEAD ON POSTNATAL DAY 19			
6907	1.516		12.188	
7007	1.388		12.422	
7107	1.426		11.209	
7207	1.293		13.316	
7307	1.380		12.757	
7407	1.338		13.611	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSIS
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HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B16 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP III	25 MG/KG/DAY	
6308	1.463		11.820	
6408	1.488		11.793	
6508	1.384		12.517	
6608	1.398		6.644a	
	1.398		12.249	
6708	1.521		11.515	
6808	1.429		10.221	
6908	1.476		11.666	
7008	1.406		12.334	
7108	1.371		10.749	
7208	1.454		11.978	
7308	1.424		11.499	
7408	1.405		X	DNR
	1.405		12.600	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALY
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HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B16 (PAGE 4): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		50 MG/KG/DAY	MALATHION	
6309	1.454	12.426		
6409	1.362	13.096		
6509	1.455	12.755		
6609	1.383	6.643a		
	1.383	12.584		
6709	1.445	11.128		
6809	1.484	11.193		
6909	1.504	11.598		
7009	1.440	13.195		
7109	1.271	10.410		
7209	1.422	12.212		
7309	1.485	12.605		
7409	1.386	12.836		

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALY
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HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B16 (PAGE 5): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALATHION

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP V	150 MG/KG/DAY	
6310	1.504		10.563	
6410	1.343		11.988	
6510	1.405		8.708a	
	1.405		8.831	
6610	1.404		4.003a	
	1.404		7.987	
6710	1.574		10.137	
6810	1.494		10.175	
6910	1.458		6.241	
7010	1.477		12.771a	
	1.477		10.812	
7110	1.202		8.773	
7210	1.305		11.269	
7310	1.381		11.423	
7410	1.374		10.435	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSIS
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

APPENDIX C
REPORT MALAOXON TABLES

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C1 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - MALE PUPS - MALAOXON

DOSAGE GROUP	I	VI	VII	VIII	IX
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	0.1	1	2.5	4
TEST SUBSTANCE	CORN OIL	MALAOXON	MALAOXON	MALAOXON	MALAOXON
MAXIMUM POSSIBLE INCIDENCE	132/ 12	132/ 12	122/ 12	132/ 12	132/ 12
FOUND DEAD	0	0	1b	0	0
NECK: SCAB	0/ 0	0/ 0	0/ 0	6/ 1	0/ 0

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

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF PUPS WITH OBSERVATION.

a. Dosing occurred on postnatal days 11 through 21.

b. Pup 5403 was found dead on postnatal day 11.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C2 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - FEMALE PUPS - MALAOXON

DOSAGE GROUP	I	VI	VII	VIII	IX
DOSAGE (MG/KG/DAY) ^a	0 (VEHICLE)	0.1	1	2.5	4
TEST SUBSTANCE	CORN OIL	MALAOXON	MALAOXON	MALAOXON	MALAOXON
MAXIMUM POSSIBLE INCIDENCE	132/ 12	132/ 12	132/ 12	127/ 12	132/ 12
FOUND DEAD	0	0	0	1b	0
URINE-STAINED ABDOMINAL FUR	0/ 0	3/ 1	0/ 0	0/ 0	0/ 0

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

N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF PUPS WITH OBSERVATION.

a. Dosing occurred on postnatal days 11 through 21.

b. Pup 5609 was found dead on postnatal day 16.

PROTOCOL IQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C3 (PAGE 1): BODY WEIGHTS AND BODY WEIGHT CHANGES - SUMMARY - MALE PUPS - MALAOXON

DOSAGE GROUP	I	VI	VII	VIII	IX
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	0.1	1	2.5	4
TEST SUBSTANCE	CORN OIL	MALAOXON	MALAOXON	MALAOXON	MALAOXON
PUPS TESTED	N	12	12	12	12
DAY 11	MEAN±S.D.	23.6 ± 2.7	23.7 ± 2.6	23.6 ± 2.2	23.2 ± 2.1
DAY 12	MEAN±S.D.	25.5 ± 2.6	25.7 ± 2.6	25.8 ± 2.6	25.1 ± 2.1
DAY 13	MEAN±S.D.	26.9 ± 2.8	27.2 ± 3.0	27.2 ± 2.9	26.7 ± 2.2
DAY 14	MEAN±S.D.	28.4 ± 2.8	28.6 ± 2.9	28.6 ± 3.0	28.2 ± 2.0
DAY 15	MEAN±S.D.	29.3 ± 2.8	29.7 ± 2.7	29.6 ± 2.9	29.6 ± 2.4
DAY 16	MEAN±S.D.	30.9 ± 2.6	31.2 ± 2.6	31.2 ± 2.8	30.8 ± 2.1
DAY 17	MEAN±S.D.	32.6 ± 2.6	33.1 ± 2.8	32.7 ± 2.8	32.5 ± 2.5
DAY 18	MEAN±S.D.	34.6 ± 2.9	35.1 ± 3.0	34.7 ± 2.6	34.8 ± 2.9
DAY 19	MEAN±S.D.	37.0 ± 2.9	37.5 ± 3.2	37.1 ± 2.5	37.1 ± 2.8
DAY 20	MEAN±S.D.	40.5 ± 3.7	41.0 ± 3.0	40.1 ± 3.0	40.6 ± 3.6
DAY 21	MEAN±S.D.	43.9 ± 4.2	44.5 ± 3.1	43.3 ± 2.9	43.6 ± 4.0
BODY WEIGHT CHANGE (G)					
DAYS 11 - 14	MEAN±S.D.	+4.8 ± 1.4	+4.8 ± 1.5	+5.0 ± 1.4	+5.0 ± 1.5
DAYS 14 - 17	MEAN±S.D.	+4.2 ± 1.3	+4.5 ± 1.7	+4.1 ± 1.4	+4.3 ± 1.6
DAYS 17 - 21	MEAN±S.D.	+11.3 ± 2.4	+11.4 ± 2.3	+10.6 ± 1.4	+11.2 ± 2.9
DAYS 11 - 21	MEAN±S.D.	+20.4 ± 2.6	+20.8 ± 2.0	+19.7 ± 2.1	+20.5 ± 3.1

DAY(S) = POSTNATAL DAY(S)

I | = NUMBER OF VALUES AVERAGED

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes values for pup 5403, which was found dead on postnatal day 11.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C4 (PAGE 1): BODY WEIGHTS AND BODY WEIGHT CHANGES - SUMMARY - FEMALE PUPS - MALAOXON

DOSAGE GROUP		I 0 (VEHICLE) CORN OIL	VI 0.1 MALAOXON		VII 1 MALAOXON		VIII 2.5 MALAOXON		IX 4 MALAOXON	
TEST SUBSTANCE			MALAOXON		MALAOXON		MALAOXON		MALAOXON	
PUPS TESTED		12	12	12	12	12	12	12	12	12
BODY WEIGHT (G)										
DAY 11	MEAN±S.D.	23.6 ± 1.4	22.7 ± 2.0	22.0 ± 2.2	23.6 ± 2.1				23.4 ± 1.8	
DAY 12	MEAN±S.D.	25.4 ± 1.6	24.8 ± 2.5	23.8 ± 2.3	25.6 ± 2.6				25.2 ± 2.3	
DAY 13	MEAN±S.D.	27.3 ± 1.9	26.3 ± 2.7	25.3 ± 2.2	27.0 ± 2.8				26.8 ± 2.5	
DAY 14	MEAN±S.D.	28.8 ± 1.9	28.0 ± 2.7	27.0 ± 2.4	28.6 ± 3.2				28.4 ± 2.4	
DAY 15	MEAN±S.D.	30.5 ± 1.8	29.6 ± 2.3	28.7 ± 1.8	30.3 ± 2.9				30.2 ± 2.6	
DAY 16	MEAN±S.D.	31.1 ± 2.4	30.5 ± 2.4	29.4 ± 1.9	31.0 ± 2.9				30.8 ± 2.6	
DAY 17	MEAN±S.D.	32.8 ± 2.3	32.3 ± 2.4	31.2 ± 2.3	32.6 ± 3.1 1 111b				32.8 ± 2.7	
DAY 18	MEAN±S.D.	35.2 ± 2.1	34.2 ± 2.4	32.9 ± 2.1	35.0 ± 3.3 1 111b				35.0 ± 2.6	
DAY 19	MEAN±S.D.	37.9 ± 2.2	36.8 ± 2.6	35.7 ± 2.2	37.5 ± 3.0 1 111b				37.4 ± 2.8	
DAY 20	MEAN±S.D.	41.3 ± 3.1	40.5 ± 2.9	39.4 ± 2.5	40.8 ± 3.7 1 111b				40.8 ± 3.3	
DAY 21	MEAN±S.D.	44.4 ± 3.8	44.2 ± 3.3	42.6 ± 2.9	44.1 ± 4.0 1 111b				44.6 ± 3.8	
BODY WEIGHT CHANGE (G)										
DAYS 11 - 14	MEAN±S.D.	+5.2 ± 1.1	+5.3 ± 1.1	+5.0 ± 0.9	+5.0 ± 1.3				+5.0 ± 0.9	
DAYS 14 - 17	MEAN±S.D.	+4.0 ± 1.8	+4.2 ± 1.1	+4.2 ± 1.3	+3.8 ± 1.0 1 111b				+4.4 ± 1.4	
DAYS 17 - 21	MEAN±S.D.	+11.7 ± 3.0	+12.0 ± 1.8	+11.4 ± 1.8	+11.5 ± 2.4 1 111b				+11.8 ± 2.5	
DAYS 11 - 21	MEAN±S.D.	+20.8 ± 3.4	+21.5 ± 2.4	+20.6 ± 1.9	+20.4 ± 2.7 1 111b				+21.2 ± 3.3	

DAY(S) = POSTNATAL DAY(S)

1 1 = NUMBER OF VALUES AVERAGED

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes values for pup 5609, which was found dead on postnatal day 16.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C5 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - MALE PUPS - MALAOXON

DOSAGE GROUP	I	VI	VII	VIII	IX
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	0.1	1	2.5	4
TEST SUBSTANCE	CORN OIL	MALAOXON	MALAOXON	MALAOXON	MALAOXON
PUPS TESTED	12	12	10b	12	12
N					

CHOLINESTERASE LEVELS (UNITS/ML) MEAN±S.D. 1.930 ± 0.285 1.895 ± 0.331 1.657 ± 0.188 * 1.047 ± 0.109 ** 0.943 ± 0.275 **

% INHIBITION

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes pups that were found dead or had samples that were not analyzed.

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

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

PROTOCOL TOC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C6 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - FEMALE PUPS - MALAOXON

DOSAGE GROUP	I	VI	VII	VIII	IX
DOSAGE (MG/KG/DAY)a	0 (VEHICLE)	0.1	1	2.5	4
TEST SUBSTANCE	CORN OIL	MALAOXON	MALAOXON	MALAOXON	MALAOXON
PUPS TESTED	12	12	12	11b	12
N					
CHOLINESTERASE LEVELS (UNITS/ML) MEAN±S.D.	1.788 ± 0.148	1.926 ± 0.316	1.546 ± 0.145 *	1.167 ± 0.151 **	0.978 ± 0.362 **
% INHIBITION		-7.7	13.5	34.7	45.3

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes values for pup 5609, which was found dead on postnatal day 16.

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

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C7 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALE PUPS - MALAOXON

DOSAGE GROUP	I	VI	VII	VIII	IX
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	0.1	1	2.5	4
TEST SUBSTANCE	CORN OIL	MALAOXON	MALAOXON	MALAOXON	MALAOXON
PUPS TESTED	12	12	11b	12	12
N					
BRAIN WEIGHT (G)	MEAN±S.D. 1.431 ± 0.060	1.412 ± 0.059	1.384 ± 0.071	1.410 ± 0.069	1.419 ± 0.075
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D. 11.867 ± 0.393	11.897 ± 0.893	12.131 ± 0.867	11.746 ± 0.864	11.890 ± 0.857
% INHIBITION		-0.3	-2.2	1.0	-0.2
a. Dosing occurred on postnatal days 11 through 21.					
b. Excludes values for pup 5403, which was found dead on postnatal day 11.					

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C8 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - FEMALE PUPS - MALAOXON

DOSAGE GROUP	I	VI	VII	VIII	IX
DOSAGE (MG/KG/DAY) a	0 (VEHICLE)	0.1	1	2.5	4
TEST SUBSTANCE	CORN OIL	MALAOXON	MALAOXON	MALAOXON	MALAOXON
PUPS TESTED	12	12	12	11b	12
N					
BRAIN WEIGHT (G)	MEAN±S.D. 1.360 ± 0.045	1.325 ± 0.080	1.265 ± 0.156	1.342 ± 0.076	1.330 ± 0.072
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D. 12.311 ± 0.954	12.065 ± 0.763	12.664 ± 1.939	12.065 ± 0.938	12.529 ± 0.439
% INHIBITION		2.0	-2.9	2.0	-1.8

a. Dosing occurred on postnatal days 11 through 21.

b. Excludes values for pup 5609, which was found dead on postnatal day 16.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C9 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	DESCRIPTION	
DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY	CORN OIL
5101	NO ADVERSE FINDINGS	
5201	NO ADVERSE FINDINGS	
5301	NO ADVERSE FINDINGS	
5401	NO ADVERSE FINDINGS	
5501	NO ADVERSE FINDINGS	
5601	NO ADVERSE FINDINGS	
5701	NO ADVERSE FINDINGS	
5801	NO ADVERSE FINDINGS	
5901	NO ADVERSE FINDINGS	
6001	NO ADVERSE FINDINGS	
6101	NO ADVERSE FINDINGS	
6201	NO ADVERSE FINDINGS	
DOSAGE GROUP VI	0.1 MG/KG/DAY	MALAOXON
5102	NO ADVERSE FINDINGS	
5202	NO ADVERSE FINDINGS	
5302	NO ADVERSE FINDINGS	
5402	NO ADVERSE FINDINGS	
5502	NO ADVERSE FINDINGS	
5602	NO ADVERSE FINDINGS	
5702	NO ADVERSE FINDINGS	
5802	NO ADVERSE FINDINGS	
5902	NO ADVERSE FINDINGS	
6002	NO ADVERSE FINDINGS	
6102	NO ADVERSE FINDINGS	
6202	NO ADVERSE FINDINGS	

PND = POSTNATAL DAY

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C9 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	DESCRIPTION
DOSAGE GROUP VII	1 MG/KG/DAY
5103	NO ADVERSE FINDINGS
5203	NO ADVERSE FINDINGS
5303	NO ADVERSE FINDINGS
5403	FOUND DEAD (DEATH OCCURRED 50 MINUTES AFTER DOSAGE ADMINISTRATION) a
5503	NO ADVERSE FINDINGS
5603	NO ADVERSE FINDINGS
5703	NO ADVERSE FINDINGS
5803	NO ADVERSE FINDINGS
5903	NO ADVERSE FINDINGS
6003	NO ADVERSE FINDINGS
6103	NO ADVERSE FINDINGS
6203	NO ADVERSE FINDINGS
DOSAGE GROUP VIII	2.5 MG/KG/DAY
5104	NO ADVERSE FINDINGS
5204	NO ADVERSE FINDINGS
5304	NO ADVERSE FINDINGS
5404	NECK: SCAB (0.3 CM IN DIAMETER)
5504	NO ADVERSE FINDINGS
5604	NO ADVERSE FINDINGS
5704	NO ADVERSE FINDINGS
5804	NO ADVERSE FINDINGS
5904	NO ADVERSE FINDINGS
6004	NO ADVERSE FINDINGS
6104	NO ADVERSE FINDINGS
6204	NO ADVERSE FINDINGS

PND = POSTNATAL DAY

a. At necropsy, all lobes of the lungs were pale and spongy and a white frothy material was present in the trachea. All other tissues appeared normal.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C9 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	DESCRIPTION
DOSAGE GROUP IX	4 MG/KG/DAY
	MALAOXON
5105	NO ADVERSE FINDINGS
5205	NO ADVERSE FINDINGS
5305	NO ADVERSE FINDINGS
5405	NO ADVERSE FINDINGS
5505	NO ADVERSE FINDINGS
5605	NO ADVERSE FINDINGS
5714	NO ADVERSE FINDINGS
5805	NO ADVERSE FINDINGS
5905	NO ADVERSE FINDINGS
6005	NO ADVERSE FINDINGS
6105	NO ADVERSE FINDINGS
6205	NO ADVERSE FINDINGS

PND = POSTNATAL DAY

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C10 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	DESCRIPTION
DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY
5106	CORN OIL
5206	NO ADVERSE FINDINGS
5306	NO ADVERSE FINDINGS
5406	NO ADVERSE FINDINGS
5506	NO ADVERSE FINDINGS
5606	NO ADVERSE FINDINGS
5706	NO ADVERSE FINDINGS
5806	NO ADVERSE FINDINGS
5906	NO ADVERSE FINDINGS
6006	NO ADVERSE FINDINGS
6106	NO ADVERSE FINDINGS
6206	NO ADVERSE FINDINGS
DOSAGE GROUP VI	0.1 MG/KG/DAY
5107	MALAOXON
5207	NO ADVERSE FINDINGS
5307	NO ADVERSE FINDINGS
5407	NO ADVERSE FINDINGS
5507	NO ADVERSE FINDINGS
5607	NO ADVERSE FINDINGS
5707	NO ADVERSE FINDINGS
5807	NO ADVERSE FINDINGS
5907	NO ADVERSE FINDINGS
6007	URINE-STAINED ABDOMINAL FUR
6107	NO ADVERSE FINDINGS
6207	NO ADVERSE FINDINGS

PND = POSTNATAL DAY

PROTOCOL TOC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C10 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	DESCRIPTION	
DOSAGE GROUP VII	1 MG/KG/DAY	MALAOXON
5108	NO ADVERSE FINDINGS	
5208	NO ADVERSE FINDINGS	
5308	NO ADVERSE FINDINGS	
5408	NO ADVERSE FINDINGS	
5508	NO ADVERSE FINDINGS	
5608	NO ADVERSE FINDINGS	
5708	NO ADVERSE FINDINGS	
5808	NO ADVERSE FINDINGS	
5908	NO ADVERSE FINDINGS	
6008	NO ADVERSE FINDINGS	
6108	NO ADVERSE FINDINGS	
6208	NO ADVERSE FINDINGS	
DOSAGE GROUP VIII	2.5 MG/KG/DAY	MALAOXON
5109	NO ADVERSE FINDINGS	
5209	NO ADVERSE FINDINGS	
5309	NO ADVERSE FINDINGS	
5409	NO ADVERSE FINDINGS	
5509	NO ADVERSE FINDINGS	
5609	FOUND DEAD (DEATH OCCURRED 1 HOUR AND 1 MINUTE AFTER DOSAGE ADMINISTRATION) a	
5709	NO ADVERSE FINDINGS	
5809	NO ADVERSE FINDINGS	
5909	NO ADVERSE FINDINGS	
6009	NO ADVERSE FINDINGS	
6109	NO ADVERSE FINDINGS	
6209	NO ADVERSE FINDINGS	
PND = POSTNATAL DAY		
a. At necropsy, all lobes of the lungs were pale and spongy. All other tissues appeared normal.		

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C10 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	DESCRIPTION
DOSAGE GROUP IX	4 MG/KG/DAY
	MALAOXON
5110	NO ADVERSE FINDINGS
5210	NO ADVERSE FINDINGS
5310	NO ADVERSE FINDINGS
5410	NO ADVERSE FINDINGS
5510	NO ADVERSE FINDINGS
5610	NO ADVERSE FINDINGS
5710	NO ADVERSE FINDINGS
5810	NO ADVERSE FINDINGS
5910	NO ADVERSE FINDINGS
6010	NO ADVERSE FINDINGS
6110	NO ADVERSE FINDINGS
6210	NO ADVERSE FINDINGS
PND = POSTNATAL DAY	

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C11 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

DAY 11		DAY 12		DAY 13		DAY 14		DAY 15		DAY 16		DAY 17		DAY 18		DAY 19		DAY 20		DAY 21	
PUP #	DOSAGE GROUP I										CORN OIL										
	0 (VEHICLE) MG/KG/DAY																				
5101	20.8	24.2	26.4	28.1	28.5	30.3	31.2	33.4	34.0	37.0	38.5										
5201	25.1	28.2	30.3	32.4	33.7	35.1	37.0	40.0	43.1	47.1	51.4										
5301	20.6	21.8	23.2	24.3	25.8	27.6	29.2	31.5	34.4	38.2	42.9										
5401	24.3	27.0	29.1	29.3	30.1	31.7	34.4	36.7	39.2	42.4	45.4										
5501	19.7	22.7	23.6	24.9	25.7	27.1	28.8	29.8	32.6	34.2	37.7										
5601	21.2	22.8	23.4	25.6	27.9	29.7	33.1	35.6	38.0	41.0	42.5										
5701	23.6	24.5	27.3	29.2	29.5	30.6	32.3	32.8	35.9	38.5	42.1										
5801	28.5	30.9	32.0	33.5	34.1	35.8	36.6	38.6	40.0	45.0	49.0										
5901	23.6	25.0	25.1	27.0	26.8	29.8	31.7	33.3	36.9	41.7	46.1										
6001	27.6	27.7	29.4	30.5	31.8	32.6	34.0	36.0	37.9	43.3	48.0										
6101	24.7	26.6	27.2	29.0	30.0	31.3	32.6	35.2	37.3	43.9	43.9										
6201	23.1	24.4	26.1	26.9	28.2	29.1	30.2	32.8	34.6	37.0	39.6										

DAY 11		DAY 12		DAY 13		DAY 14		DAY 15		DAY 16		DAY 17		DAY 18		DAY 19		DAY 20		DAY 21	
PUP #	DOSAGE GROUP VI										MALAOXON										
	0.1 MG/KG/DAY																				
5102	26.8	29.4	32.6	33.3	34.5	35.8	37.6	39.2	41.3	44.3	46.7										
5202	25.4	27.8	29.6	31.5	33.0	34.7	36.4	38.1	40.5	42.6	46.1										
5302	22.9	24.2	25.3	26.5	28.0	29.5	31.8	34.6	39.0	43.0	47.2										
5402	22.2	25.2	26.4	27.4	27.7	29.0	30.9	34.0	37.3	42.0	46.3										
5502	18.5	20.5	22.2	23.3	24.7	26.7	27.8	28.7	29.9	33.6	36.5										
5602	22.0	24.6	25.3	26.2	28.9	30.7	35.0	36.2	38.5	41.4	44.2										
5702	21.0	23.6	25.8	28.6	29.1	30.2	30.9	31.9	34.0	36.9	41.5										
5802	27.5	29.9	31.9	32.5	32.5	34.0	35.5	38.8	40.4	43.0	45.7										
5902	25.8	26.1	27.8	28.8	30.8	33.3	33.3	33.4	37.2	41.3	45.1										
6002	25.3	26.7	28.2	30.6	31.1	32.5	34.0	36.4	37.6	42.7	47.0										
6102	24.6	25.6	26.4	28.3	29.9	31.3	33.2	36.5	38.9	42.2	45.5										
6202	22.9	24.5	25.7	26.9	28.5	29.8	30.6	33.8	35.8	39.2	42.2										

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C11 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

	DAY 11	12	13	14	15	16	17	18	19	20	21
PUP #	MALAOXON										
	1 MG/KG/DAY										
DOSAGE GROUP VII	MALAOXON										
5103	24.1	26.1	29.1	30.2	32.1	33.2	34.8	35.6	36.9	39.8	44.1
5203	23.5	26.2	27.9	29.8	30.9	33.0	34.1	36.8	39.6	42.0	43.4
5303	21.6	22.9	23.5	24.8	26.1	28.1	30.3	33.1	35.8	38.2	41.5
5403	21.7	FOUND DEAD ON POSTNATAL DAY 11									
5503	18.7	20.1	21.9	22.8	23.4	26.6	26.8	27.6	30.0	32.2	34.8
5603	22.0	23.6	24.6	26.6	28.3	30.2	34.0	37.3	39.5	41.7	44.8
5703	22.1	24.2	27.1	30.0	30.0	31.8	32.4	32.9	35.0	38.6	42.1
5803	25.7	28.3	30.4	31.3	32.2	32.9	34.6	37.4	38.3	41.0	43.6
5903	23.7	24.7	26.1	27.3	28.4	30.8	33.4	34.4	37.1	41.0	46.1
6003	28.4	28.8	30.8	31.3	33.1	33.3	35.1	36.9	39.5	45.0	48.6
6103	23.2	25.0	26.3	27.8	29.6	31.1	32.2	34.4	36.9	39.8	42.5
6203	24.5	26.4	27.7	28.7	29.8	31.0	31.8	34.5	36.1	38.8	41.7
PUP #	MALAOXON										
	2.5 MG/KG/DAY										
DOSAGE GROUP VIII	MALAOXON										
5104	26.8	29.7	32.9	34.6	35.3	36.9	38.2	40.1	41.5	44.3	47.0
5204	22.9	25.8	27.4	29.1	31.7	33.2	34.7	36.1	40.0	42.2	44.6
5304	20.2	21.4	22.4	23.5	24.9	26.9	28.6	30.7	35.0	36.5	40.9
5404	24.5	27.5	29.8	30.4	30.9	32.5	34.2	36.2	38.7	42.4	45.3
5504	20.7	23.6	25.6	26.6	27.8	29.9	30.5	31.8	33.5	37.4	41.1
5604	21.5	23.0	24.1	25.8	27.2	29.3	32.8	35.5	37.5	40.0	43.7
5704	23.6	25.3	27.3	30.1	29.8	31.8	32.2	33.9	36.3	39.2	41.0
5804	26.2	29.0	30.0	30.6	31.3	32.2	33.3	34.7	37.1	39.9	42.8
5904	23.3	24.4	25.8	26.5	27.0	28.7	30.6	33.4	35.2	37.6	40.9
6004	26.4	29.0	28.2	30.4	31.4	32.3	34.7	36.9	37.7	44.2	48.7
6104	25.1	26.5	28.4	29.6	31.0	32.5	34.3	35.7	39.2	42.0	45.2
6204	21.9	23.8	24.8	25.6	26.5	27.9	28.3	31.9	33.6	35.5	38.8

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C11 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	MALAOXON										
	4 MG/KG/DAY										
	DAY 11	12	13	14	15	16	17	18	19	20	21
DOSAGE GROUP IX											
5105	21.6	24.0	26.9	28.6	29.9	31.1	32.2	33.5	35.6	39.3	41.7
5205	21.5	24.0	26.3	28.2	30.9	32.1	32.7	34.3	36.4	38.0	39.3
5305	21.8	23.0	24.0	25.1	26.5	28.6	30.4	32.8	37.2	42.3	46.7
5405	23.9	27.6	29.7	31.0	31.4	33.0	34.8	37.6	40.6	45.8	49.5
5505	18.6	20.6	21.9	24.3	24.1	26.2	27.5	28.8	31.3	32.9	35.1
5605	23.1	25.3	26.5	27.9	32.4	32.8	36.9	40.3	42.4	43.9	46.9
5714	23.5	24.8	27.5	29.4	29.8	30.8	32.0	33.6	36.1	38.2	40.9
5805	26.6	28.4	29.8	30.5	31.7	33.0	34.7	36.4	39.6	42.3	44.5
5905	24.2	25.6	25.6	26.9	27.4	29.1	31.1	33.1	35.1	38.9	42.9
6005	25.0	26.7	28.8	30.4	31.7	32.6	34.6	37.2	37.4	44.8	48.2
6105	23.6	25.1	26.0	27.8	29.5	30.3	30.9	34.7	36.7	41.4	44.3
6205	24.7	26.2	27.1	28.2	29.9	30.4	31.9	35.4	36.9	39.3	43.7

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C12 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

DAY 11		12	13	14	15	16	17	18	19	20	21				
PUP #	DOSAGE GROUP I			0 (VEHICLE) MG/KG/DAY								CORN OIL			
	25.2	27.6	30.5	31.5	33.1	34.8	35.0	36.8	38.6	41.0	43.6				
5106	25.2	27.6	30.5	31.5	33.1	34.8	35.0	36.8	38.6	41.0	43.6				
5206	23.8	25.8	28.2	30.1	32.4	33.5	35.1	37.2	39.5	41.7	43.7				
5306	24.0	25.0	25.7	27.0	30.1	31.2	33.0	36.5	40.2	45.8	51.7				
5406	24.7	28.2	29.8	30.5	32.9	32.9	35.4	37.7	39.5	44.1	48.0				
5506	20.6	23.7	25.3	26.6	29.0	29.0	30.4	32.6	34.9	37.0	39.5				
5606	21.4	22.9	24.4	26.2	29.7	30.9	32.8	36.3	39.3	42.7	44.4				
5706	23.5	25.4	28.3	29.9	32.3	32.8	34.2	36.0	38.9	42.9	45.1				
5806	25.4	27.0	28.6	30.9	30.3	30.3	31.7	34.0	37.0	40.0	43.0				
5906	24.2	25.8	26.6	28.7	28.9	29.7	32.3	34.9	39.6	44.4	48.3				
6006	23.7	24.7	27.8	29.5	30.0	30.7	32.7	34.2	35.3	40.1	43.5				
6106	24.1	25.7	27.3	28.4	30.2	31.6	33.6	35.8	39.0	41.3	45.0				
6206	22.4	23.6	25.1	26.3	27.1	25.5	27.1	30.3	33.5	34.8	37.5				

DAY 11		12	13	14	15	16	17	18	19	20	21				
PUP #	DOSAGE GROUP VI			0.1 MG/KG/DAY								MALAOXON			
	26.0	29.3	31.8	32.9	34.3	35.7	37.6	39.7	42.4	45.3	49.8				
5107	26.0	29.3	31.8	32.9	34.3	35.7	37.6	39.7	42.4	45.3	49.8				
5207	23.4	27.1	27.9	30.3	32.1	32.5	34.6	36.3	38.5	42.5	46.5				
5307	19.8	21.1	21.6	23.1	25.9	26.7	27.9	30.5	32.6	35.3	40.6				
5407	22.0	24.3	26.3	27.5	29.7	30.2	32.3	33.9	37.4	42.2	46.6				
5507	23.6	25.9	27.7	28.4	30.6	31.8	32.2	33.9	37.0	42.3	46.1				
5607	19.2	21.4	22.4	24.8	27.8	29.3	31.4	33.9	36.4	40.3	43.7				
5707	20.6	22.4	24.7	26.0	27.9	28.4	30.0	30.9	33.0	36.1	38.3				
5807	24.3	26.8	27.9	30.7	30.3	31.1	32.9	34.9	37.4	39.4	42.4				
5907	23.2	23.8	25.1	27.6	27.4	28.6	32.0	33.5	36.8	39.9	42.5				
6007	24.3	26.8	27.5	29.9	30.1	31.2	33.2	34.5	36.1	42.2	46.9				
6107	24.1	25.1	26.4	28.2	30.8	32.0	33.1	35.6	39.0	42.4	45.9				
6207	22.4	24.2	25.9	26.9	28.2	28.3	30.0	32.5	35.0	37.9	41.6				

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C12 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

DOSAGE GROUP VII											
PUP #	DAY 11	12	13	14	15	16	17	18	19	20	21
MALAOXON											
1 MG/KG/DAY											
5108	22.2	25.2	27.6	28.9	31.2	32.0	33.6	34.6	37.2	40.0	42.8
5208	24.6	26.1	27.6	29.2	30.6	31.1	32.5	34.4	36.9	39.4	42.2
5308	21.5	23.0	23.4	24.7	27.7	27.6	29.0	31.9	35.1	40.0	44.6
5408	22.3	24.9	26.8	27.7	30.4	30.3	32.3	34.0	37.1	40.9	42.7
5508	19.6	21.8	23.3	24.4	27.6	27.9	28.8	29.6	32.8	37.4	41.2
5608	19.7	21.2	22.6	24.9	27.3	28.8	32.0	34.3	36.0	39.9	43.1
5708	19.3	20.7	23.3	25.1	26.5	27.0	28.0	29.2	31.2	35.3	38.3
5808	24.4	26.4	27.9	30.1	30.2	30.4	31.8	34.0	37.7	40.2	44.2
5908	24.2	25.5	25.8	28.4	28.0	29.6	32.8	34.2	37.7	41.8	45.6
6008	25.1	26.8	28.4	30.9	31.4	32.8	35.4	35.9	38.3	44.0	48.2
6108	20.2	21.4	22.8	24.5	26.7	27.9	29.5	31.3	34.2	36.9	39.1
6208	20.5	22.2	24.1	25.0	27.3	27.9	29.0	31.6	34.1	36.4	39.4
DOSAGE GROUP VIII											
PUP #	2.5 MG/KG/DAY										
MALAOXON											
5109	24.2	26.9	29.1	30.9	32.2	32.9	34.2	36.8	38.2	40.8	42.9
5209	25.4	28.5	29.6	31.2	33.0	34.0	35.8	38.6	41.0	43.6	46.6
5309	20.8	22.3	22.5	23.6	26.8	27.7	29.3	32.0	35.7	39.3	43.8
5409	25.3	27.7	29.3	30.1	32.5	33.1	34.3	37.7	40.1	45.4	48.8
5509	21.0	23.8	25.5	26.3	28.5	29.0	30.6	32.2	34.4	36.5	39.4
5609	21.6	23.4	25.1	26.0	30.2	31.2	FOUND DEAD ON POSTNATAL DAY 16				
5709	26.2	28.3	31.0	33.3	35.6	36.0	36.9	38.9	40.7	43.4	46.5
5809	25.1	27.5	28.3	29.8	30.1	30.5	31.9	34.0	36.8	38.9	41.9
5909	24.0	25.4	25.9	28.3	28.5	29.0	31.6	33.7	37.7	42.7	46.4
6009	25.5	27.6	29.3	31.9	32.2	33.1	36.4	38.4	40.1	45.2	50.0
6109	23.6	24.7	26.0	28.0	29.0	29.6	30.6	33.4	36.8	39.2	42.6
6209	20.0	20.7	22.5	23.4	25.4	26.0	27.4	28.8	31.0	33.4	36.6

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C12 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	DAY 11 12 13 14 15 16 17 18 19 20 21										
	DOSAGE GROUP IX										
	4 MG/KG/DAY										
	MALAOXON										
5110	25.9	29.2	31.6	32.3	35.1	35.6	37.3	39.3	40.9	43.1	45.7
5210	25.6	28.0	29.9	31.6	34.7	35.0	37.6	38.7	41.1	45.3	49.1
5310	22.1	23.2	24.4	25.3	28.0	29.1	31.2	34.3	35.9	38.9	44.8
5410	24.6	27.5	29.7	30.1	33.0	32.9	34.8	37.1	40.1	46.3	51.4
5510	23.4	25.4	26.9	28.2	30.7	31.7	33.0	33.8	37.3	40.7	44.3
5610	20.8	22.2	23.5	25.6	28.7	29.6	32.1	36.1	38.8	43.0	48.0
5710	21.8	23.7	26.2	27.6	29.0	29.2	30.7	31.8	33.5	37.4	41.8
5810	24.1	26.3	27.1	29.4	29.0	29.6	31.0	32.9	36.5	39.8	42.4
5910	25.2	25.6	26.4	29.6	29.3	30.1	33.3	35.2	37.4	40.7	45.9
6010	23.7	25.5	27.0	28.9	29.6	29.7	32.2	34.1	35.8	38.6	41.9
6110	22.5	24.0	25.5	27.2	29.0	30.2	32.4	35.5	38.8	40.8	42.8
6210	21.0	22.1	23.8	25.0	26.8	26.4	28.1	30.6	32.3	34.8	37.2

DAY = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C13 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY	CORN OIL	
5101	2.183			
5201	1.720			
5301	1.629			
5401	1.731			
5501	2.624			
5601	1.836			
5701	1.906			
5801	1.955			
5901	2.096			
6001	1.871			
6101	4.255a			
	1.580			
6201	2.030			
PUP #	DOSAGE GROUP VI		MALAOXON	
	0.1 MG/KG/DAY			
5102	2.256			
5202	2.647			
5302	1.663			
5402	1.868			
5502	2.188			
5602	1.647			
5702	1.855			
5802	1.814			
5902	1.699			
6002	1.583			
6102	2.008			
6202	1.509			

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSE
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C13 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP VII	1 MG/KG/DAY
5103	1.639	
5203	a	
5303	1.231	
5403	FOUND DEAD ON POSTNATAL DAY 11	
5503	1.961	
5603	1.675	
5703	1.560	
5803	1.740	
5903	1.632	
6003	1.685	
6103	1.817	
6203	1.628	
PUP #	DOSAGE GROUP VIII	2.5 MG/KG/DAY
5104	1.315	
5204	0.850	
5304	1.021	
5404	1.002	
5504	1.035	
5604	1.071	
5704	1.125	
5804	1.021	
5904	1.022	
6004	1.036	
6104	0.967	
6204	1.099	

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HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

a. Sample was not analyzed.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C13 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
	DOSAGE GROUP IX	4 MG/KG/DAY	
5105	0.744		
5205	0.549		
5305	0.656		
5405	X		DNR
	0.894		
5505	0.688		
5605	X		DNR
	1.037		
5714	0.770		
5805	1.203		
5905	1.101		
6005	1.481		
6105	1.195		
6205	X		DNR
	0.993		

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PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C14 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY	CORN OIL	
5106	1.734			
5206	1.797			
5306	1.949			
5406	1.942			
5506	1.844			
5606	1.870			
5706	1.728			
5806	1.966			
5906	1.818			
6006	X		DNR	
	1.507			
6106	X		HIGH	
	1.541			
6206	1.754			
PUP #	DOSAGE GROUP VI		MALAOXON	
	0.1 MG/KG/DAY			
5107	1.740			
5207	2.556			
5307	1.788			
5407	2.362			
5507	2.080			
5607	2.120			
5707	X		DNR	
	2.004			
5807	1.991			
5907	1.603			
6007	1.564			
6107	1.646			
6207	1.655			

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HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C14 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
	DOSAGE GROUP VII	1 MG/KG/DAY	
5108	1.343		
5208	1.439		
5308	1.410		
5408	1.645		
5508	1.326		
5608	1.641		
5708	1.450		
5808	2.173a		
	1.652		
5908	1.739		
6008	1.565		
6108	1.644		
6208	1.700		
PUP #	DOSAGE GROUP VIII		MALAOXON
	DOSAGE GROUP VIII	2.5 MG/KG/DAY	
5109	1.475		
5209	1.200		
5309	1.087		
5409	1.139		
5509	1.273		
5609	FOUND DEAD ON POSTNATAL DAY 16		
5709	X		DNR
	1.229		
5809	1.145		
5909	1.147		
6009	0.848		
6109	1.084		
6209	1.206		

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSE
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 HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.
 DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.
 a. Sample reanalyzed after an initial acceptable value was obtained; the initial acceptable value was excluded from summarization and statistical analyses.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C14 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	FINAL CHOLINESTERASE (UNITS/ML)	FOOTNOTE
DOSAGE GROUP IX		4 MG/KG/DAY
5110	0.850	MALAOXON
5210	0.816	
5310	0.786	
5410	0.836	
5510	0.884	
5610	0.832	
5710	0.567	
5810	1.437	
5910	1.546	
6010	0.766	
6110	0.729	
6210	1.686	

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C15 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY	
5101	1.410		11.631	CORN OIL
5201	1.494		12.335	
5301	1.387		11.385	
5401	1.493		12.179	
5501	1.427		11.464	
5601	1.459		11.709	
5701	1.455		12.646	
5801	1.494		11.913	
5901	1.303		11.582	
6001	1.385		11.499	
6101	1.487		11.902	
6201	1.376		12.153	
PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP VI	0.1 MG/KG/DAY	
5102	1.480		13.260	MALAOXON
5202	1.429		11.342	
5302	1.408		12.151	
5402	1.492		11.723	
5502	1.320		11.511	
5602	1.435		13.118	
5702	1.308		12.146	
5802	1.359		11.972	
5902	1.442		11.796	
6002	1.407		11.639	
6102	1.472		9.767	
6202	1.391		12.340	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALY
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.
 HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.
 DNR = DUPLICATE ANALYSIS OF THE SAME SAMPLE DOES NOT MEET REPRODUCIBILITY CRITERIA.

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C15 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
	DOSAGE GROUP VII		1 MG/KG/DAY	MALAOXON	
5103	1.328		14.146		
5203	1.225		11.085		
5303	1.389		12.391		
5403	FOUND DEAD ON POSTNATAL DAY 11				
5503	1.332		11.664		
5603	1.374		12.422		
5703	1.472		11.270		
5803	1.443		12.307		
5903	1.398		12.472		
6003	1.416		11.470		
6103	1.462		11.534		
6203	1.380		12.682		

PUP #	BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
	DOSAGE GROUP VIII		2.5 MG/KG/DAY	MALAOXON	
5104	1.521		12.498		
5204	1.318		11.892		
5304	1.415		11.435		
5404	1.502		10.892		
5504	1.347		11.978		
5604	1.385		12.090		
5704	1.401		11.058		
5804	1.316		10.797		
5904	1.454		12.097		
6004	1.440		10.283		
6104	1.466		12.982		
6204	1.352		12.951		

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSIS

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C15 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALE PUPS - MALAOXON

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP IX	4 MG/KG/DAY	
5105	1.335		12.334	MALAOXON
5205	1.360		11.693	
5305	1.385		12.178	
5405	1.424		12.081	
5505	1.306		9.771	
5605	1.507		11.893	
5714	1.511		12.260	
5805	1.539		12.592	
5905	1.391		12.944	
6005	1.368		12.278	
6105	1.481		11.928	
6205	1.421		10.732	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSIS

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C16 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	BRAIN (G)	DOSAGE GROUP I	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
			0 (VEHICLE)	MALAOXON	
5106	1.389		12.970		CORN OIL
5206	1.359		11.596		
5306	1.422		11.307		
5406	1.352		11.970		
5506	1.315		12.877		
5606	1.330		12.455		
5706	1.356		13.607		
5806	1.363		11.874		
5906	1.363		10.958		
6006	1.313		14.215		
6106	1.453	X			DNR
	1.453		11.844		
6206	1.302		12.054		
PUP #	DOSAGE GROUP VI		0.1 MG/KG/DAY		MALAOXON
5107	1.320		12.839		
5207	1.361		12.484		
5307	1.192		12.514		
5407	1.440		11.566		
5507	1.344		12.054		
5607	1.361		12.833		
5707	1.287		12.794		
5807	1.172		12.471		
5907	1.381		11.609		
6007	1.282		11.411		
6107	1.388		10.266		
6207	1.368		11.943		

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSIS
 LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C16 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
	DOSAGE GROUP VII	1 MG/KG/DAY	2.5 MG/KG/DAY	MALAOXON	
5108	1.217	13.927			
5208	0.852	17.474			
5308	1.165	12.068			
5408	1.367	10.182			
5508	1.154	13.364			
5608	1.367	11.762			
5708	1.331	11.292			
5808	1.428	10.439			
5908	1.271	12.003			
6008	1.311	12.867			
6108	1.377	12.698			
6208	1.336	13.895			

PUP #	DOSAGE GROUP VIII	2.5 MG/KG/DAY		MALAOXON	
5109	1.206	12.432			
5209	1.412	13.890			
5309	1.327	11.190			
5409	1.402	11.259			
5509	1.367	12.371			
5609	FOUND DEAD ON POSTNATAL DAY 16				
5709	1.457	12.230			
5809	1.303	13.353			
5909	1.269	10.827			
6009	1.372	11.370			
6109	1.385	11.712			
6209	1.259	12.077			

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSIS

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

PROTOCOL TQC00013: ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE C16 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - FEMALE PUPS - MALAOXON

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)		FOOTNOTE
		DOSAGE GROUP IX	4 MG/KG/DAY	
5110	1.263		12.313	MALAOXON
5210	1.342		12.253	
5310	1.224		12.286	
5410	1.417		12.399	
5510	1.365		12.529	
5610	1.360		12.761	
5710	1.343		12.458	
5810	1.263		13.066	
5910	1.423		11.736	
6010	1.229		13.360	
6110	1.416		12.243	
6210	1.311		12.943	

X = SAMPLE RESULTS DO NOT MEET ACCEPTABILITY CRITERIA; VALUES WERE NOT REPORTED OR INCLUDED IN SUMMARIZATION AND STATISTICAL ANALYSIS

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

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

APPENDIX D
PROTOCOL



PROTOCOL TQC00013

STUDY TITLE

Oral (Gavage) Repeat Dose Comparative Cholinesterase Study of Malathion and Malaoxon in Juvenile Rats

OBJECTIVE

The objective of this study is to determine the effect of repeated daily dosing of young pre-weaning rats with Malathion and Malaoxon on erythrocyte and brain acetyl cholinesterase activity.

TESTING FACILITY

Charles River Laboratories
Preclinical Services
905 Sheehy Drive, Building A
Horsham, PA 19044
USA
Tel: 215 443 8710
Fax: 215 443 8587

STUDY DIRECTOR

John F. Barnett, Jr., B.S.
Senior Scientist
Address as cited above for Testing Facility.
E-Mail: john.barnettjr@us.crl.com

SPONSOR

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

STUDY MONITOR

Terri Spanogle
Senior Scientist
Cheminova, Inc.
1620 Eye Street NW, Suite 615
Washington, DC 20006
USA
Tel: 202.463.0489
Fax: 202.463.1493
Email: tls.us@cheminova.com

**SPONSOR'S
REPRESENTATIVE**

Judith Hauswirth, Ph.D.
Toxicology Consultant

REGULATORY CITATIONS

U.S. Environmental Protection Agency (1998). *Health Effects Test Guidelines*.
OPPTS 870.6300: Developmental Neurotoxicity Study, August, 1998.

U.S. Environmental Protection Agency (2001). *Guidance on Cholinesterase Measures in
DNT and Related Studies*, October 29, 2001.

Organisation for Economic Co-operation and Development (1997). *OECD Guideline for
Testing of Chemicals*. No. 424: Neurotoxicity Study in Rodents, adopted 21 July 1997.

U.S. Environmental Protection Agency. Federal Insecticide, Fungicide and Rodenticide
Act (FIFRA); Good Laboratory Practice Standards; Final Rule. 40 CFR Part 160.

Japanese Ministry of Agriculture, Forestry and Fisheries (1999). *Good Laboratory
Practice Standards*. 11 Nousan No. 6283.

Organisation for Economic Co-operation and Development (1998). *The Revised OECD
Principles of Good Laboratory Practice* [C(97)186/Final].

REGULATORY COMPLIANCE

This study will be conducted in compliance with the Good Laboratory Practice (GLP)
regulations cited above.

All changes or revisions of this protocol shall be documented, signed by the Study
Director and the Sponsor's Representative, 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 significant 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 facility conducting that portion of the study. The QAU for this facility will conduct critical phase inspections and audit respective results and reports for that study portion according to the SOPs of that facility. Such critical phase inspection reports and report audits will be submitted by the facility 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 facility and provided to the Testing Facility for inclusion in the final report. In addition, this facility will provide a statement of GLP compliance, as described above, signed by the Principal Investigator for inclusion in the final report.

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

STUDY SCHEDULE

See ATTACHMENT 1 to the protocol.

TEST SUBSTANCES AND VEHICLE**Identification****Test Substances**

Malathion (synonymous with Fyfanon Technical which may appear in study records and on labels for the test substance) (lot identification: 9010501)

Lot Number:	9010501
Purity:	96.0%
CAS Number:	121-75-5
Expiration:	November 3, 2006

Malaoxon (lot identification: 849-BSe-42C)

Lot Number:	849-BSe-42C
Purity:	97.7%
CAS Number:	1634-78-2
Expiration:	March 4, 2009

The Sponsor provided to the Testing Facility documentation or certification of the identity, composition, strength, purity and stability of the test substance (Certificate of Analysis). This documentation will be included in the final report. Certificates of Analysis for both Malathion (lot number 9010501) and the Malaoxon (lot number 849 BSe-42C) are attached to this protocol (ATTACHMENT 2). The Sponsor Representative's signature and approval of the protocol indicates that appropriate documentation of the method of synthesis, fabrication or derivation of the test substance is on file and that it is available to the appropriate regulatory agencies should it be requested.

Vehicle

Corn Oil (lot identification and Supplier will be documented in the raw data).

Documentation or certification of the identity, composition, strength, purity and stability of the corn oil will be limited to that supplied by the manufacturer. This documentation will be included in the final report.

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the vehicle that would interfere with the results of this study. Therefore, no analyses other than those mentioned in this protocol will be conducted.

Safety Precautions

Double nitrile gloves, full faced positive pressure hood, appropriate eye protection and Tyvek[®] suit are to be worn during formulation preparation and dosage administration. Bulk test substances 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 Sheets (MSDS) are attached to the protocol (ATTACHMENT 3).

Storage

Bulk Test Substances: Malathion - frozen (approximately -20°C), protected from light.
Malaaxon - frozen (approximately -20°C), protected from light.
Bulk Vehicle: Room temperature
Prepared Formulations: Refrigerated (2°C - 8°C), protected from light.

All test substance shipments should be addressed to the attention of Mark Coker, Manager of Formulations, at the previously cited Testing Facility address and telephone number.

Shipments should include information concerning storage conditions and shipping cartons should be labeled appropriately. The recipient should be notified in advance of shipment.

FORMULATION**Frequency of Preparation**

Formulations (suspensions) will be prepared once for each test substance at the Testing Facility.

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

Adjustment for Purity

The test substances will be considered 100% pure for the purpose of dosage calculations.

Testing Facility Reserve Samples

The Testing Facility will reserve a sample of approximately 1 g of each lot of bulk test substances and approximately 5 mLs of the vehicle used during the course of the study. Samples will be stored under the previously cited conditions.

ANALYSES

Analyses of dosing suspensions will be performed by the Charles River Laboratories' facility in Worcester, MA. 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.

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 $\leq 15\%$; 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 $\leq 5\%$.

Analyses of Prepared Formulations

Concentration and Homogeneity

Concentration and homogeneity of the prepared suspensions will be verified during the course of this study. Quadruplicate samples (1.0 mL each) will be taken from the top, middle and bottom of each concentration on the day of preparation. Two samples from each quadruplicate set will be shipped for analysis to the Charles River Laboratories Preclinical Services, Massachusetts analytical laboratory; the remaining samples will be retained at the Testing Facility as backup samples and stored refrigerated (2°C to 8°C). Backup samples will be discarded at the Testing Facility following consultation with the Sponsor's Representative.

Stability

Stability data for prepared formulations in the corn oil vehicle bracketing the concentrations in this study are on file with the Sponsor and will not be determined during the conduct of this study. This information will be provided to the Study Director.

Shipping Instructions

Samples to be analyzed will be shipped overnight (on cold packs) to:

Principal Investigator: Dorothy Savage, B.S.
Charles River Laboratories
Preclinical Services
57 Union Street
Worcester, MA 01608
Telephone: 508.890.0100
Telefax: 508.791.9713
E-mail: dorothy.savage@us.crl.com

The recipient will be notified in advance of sample shipment.

DISPOSITION

Prepared formulations will be discarded at the Testing Facility. Backup samples will be discarded at the Testing Facility upon approval of the Sponsor's Representative. Disposition of the remaining bulk test substance will be documented in the raw data.

TEST SYSTEM

Species/Strain and Reason for Selection

The Crl:CD(SD) rat was selected as the Test System because this strain of rat has been widely used throughout the industry for nonclinical studies.

Number**Neonatal Rats:**

Fo generation population
acclimated:

Twenty-eight female rats with litters of ten pups
(five male pups and five female pups).

F1 generation population
selected for study:

Twenty-four litters of ten pups per litter (five males
and five females) will be evaluated. Twelve of
these litters will be administered malathion (with
vehicle) and twelve will be administered malaoxon
(with vehicle).

Body Weight and Age

Seven dams and pups will be ordered to arrive at the Testing Facility on days 5, 6, 8
and 9 postpartum, respectively. Actual body weights will be recorded the day after
receipt and will be documented in the raw data. The weight range will be included in the
final report.

Sex

Dams will be used only as breeders to produce the pups and are not considered part of the
Test System.

Male and female pups will be given one of the test substances and/or the vehicle. Equal
numbers of male and female pups from each litter will be used (when possible).

Source

Charles River Laboratories, Inc.

Fo generation female rats and F1 generation pups will be shipped in filtered cartons by
air freight and/or truck from Charles River Laboratories, Inc., to the Testing Facility.

Identification**Adult Rats:**

Female rats are assigned temporary animal numbers at receipt. The rats will be permanently identified using Monel[®] self-piercing ear tags (Gey Band and Tag Co., Inc., No. MSPT 20101).

Neonatal Rats:

On days 10 or 11 postpartum, pups selected for study will be individually identified by tattoo according to the Standard Operating Procedures of the Testing Facility. Ink will be injected under the skin of the paws to identify individual pups.

ANIMAL HUSBANDRY

All cage sizes and housing conditions are in compliance with the *Guide for the Care and Use of Laboratory Animals*⁽¹⁾.

Housing

Each dam with a litter of male and female pups will be housed in a common nesting box during the postpartum period.

Nesting Material

Nesting material (bed-o'cobs[®]) will be provided.

Bedding will be changed as often as necessary to keep the animals dry and clean. Bedding changes will be documented in the raw data. Analyses for possible contamination are conducted on each lot of bedding and documented in the raw data.

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 64°F to 79°F (18°C to 26°C) and monitored constantly. Room humidity will also be monitored constantly and maintained at 30% to 70%.

Light

An automatically controlled 12-hour light:12-hour dark fluorescent light cycle will be maintained. Each dark period will begin at 1900 hours. 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.

Diet

Rats will be given Certified Rodent Diet® #5002 (PMI® Nutrition International, Inc.) available *ad libitum* from individual feeders.

Water

Water will be available *ad libitum* from individual bottles attached to the cages 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.

Contaminants

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the certified diet, the drinking water or the nesting material at levels that would 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.

DAY NUMBERING SYSTEM

The day of birth is designated postnatal day 0 (day 0 of lactation) in Addendum 10 to the Pesticide Assessment Guidelines of the U.S. Environmental Protection Agency (EPA). This same day is designated day 1 postpartum (day 1 of lactation) in the Standard Operating Procedures of the Testing Facility. Throughout this protocol, the day of birth will be designated day 1 postpartum (day 1 of lactation) and all subsequent ages of the F1 generation rats and days of the lactation period will be determined and cited accordingly. Therefore, the day of sacrifice for the day 12 postpartum male and female pups is actually day 11 postpartum using the EPA designation. Also, throughout the study observation day (OD) will be equivalent to day of postpartum.

RANDOMIZATION**Dams:**

The female rats will be naturally bred at the Supplier's facility by breeder male rats of the same source and strain. The day of delivery will be designated day 1 of lactation (postpartum). The female rats will be allowed to deliver their litters at the Supplier and shipped to arrive at the Testing Facility on days 5, 6, 8 or 9 postpartum.

Pups:

On days 10 or 11 postpartum, twenty-four litters of approximately ten pups per litter (five males and five females) will be assigned to study. The pups from twelve of these litters will be assigned to the malathion dosage groups, and the other twelve litters will be assigned to the malaoxon dosage groups. One male and one female pup from each of the litters will be assigned to each of five respective dosage groups. The pups will be of good general health (no adverse clinical signs) following physical examination of the pups and adequate body weights.

The pups in the Malathion will be assigned to the following dosage group:

Paw Tattoo	Dosage Group Assignment
Male Paw Tattoo 1	0 (Vehicle) mg/kg/day
Male Paw Tattoo 2	5 mg/kg/day
Male Paw Tattoo 3	25 mg/kg/day
Male Paw Tattoo 4	50 mg/kg/day
Male Paw Tattoo 5	150 mg/kg/day
Female Paw Tattoo 6	0 (Vehicle) mg/kg/day
Female Paw Tattoo 7	5 mg/kg/day
Female Paw Tattoo 8	25 mg/kg/day
Female Paw Tattoo 9	50 mg/kg/day
Female Paw Tattoo 10	150 mg/kg/day

The pups in the Malaoxon will be assigned to the following dosage group:

Paw Tattoo	Dosage Group Assignment
Male Paw Tattoo 1	0 (Vehicle) mg/kg/day
Male Paw Tattoo 2	0.1 mg/kg/day
Male Paw Tattoo 3	1 mg/kg/day
Male Paw Tattoo 4	2.5 mg/kg/day
Male Paw Tattoo 5	4 mg/kg/day
Female Paw Tattoo 6	0 (Vehicle) mg/kg/day
Female Paw Tattoo 7	0.1 mg/kg/day
Female Paw Tattoo 8	1 mg/kg/day
Female Paw Tattoo 9	2.5 mg/kg/day
Female Paw Tattoo 10	4 mg/kg/day

ADMINISTRATION

Route and Reason for Choice

The oral (gavage) route was selected for use because: 1) the exact dosage can be accurately administered via gavage; and 2) the oral route is a potential route of exposure.

Method and Frequency

Dams:

Dams will not be administered the test substance or the vehicle.

Pups:

The pups will be administered the test substance and/or the vehicle once daily from day 12 through day 22 postpartum.

Rationale for Dosage Selection

Dosages for the pups were selected based on data collected in a repeat dose range-finding cholinesterase study with Malaoxon and Malathion (TQC00011) conducted at Charles River Laboratories Preclinical Services Pennsylvania. The doses used during the conduct of the TQC00011 study were 5, 15 and 50 mg/kg/day for Malathion and 0.05, 0.1 and 1 mg/kg/day for Malaoxon. During this study, there were no test substance-related adverse clinical observations apparent and minimal cholinesterase inhibition observed. The time postdosage that cholinesterase levels are being evaluated was determined based on the time-of-peak effect established in the TQC00012 study. The doses used during the conduct of the TQC00012 study were 150 mg/kg/day for Malathion and 4 mg/kg/day for Malaoxon. During this study, there were no test substance-related adverse clinical

observations apparent; however, cholinesterase inhibition was observed as a result of administration of both test substances.

The test substance, under the conditions of use in this study, should cause no or no more than momentary pain and/or distress. Should unanticipated clinical effects occur that do or may result in pain and/or distress, the Study Director will consult the veterinary staff and appropriate animal care measures will be taken to alleviate the pain and/or distress while ensuring the scientific integrity of the study, including dosing holidays, reduction in administered dose or euthanasia. The Sponsor's Representative will be informed as soon as possible about these unanticipated effects and the response to those effects.

Dosage Levels, Concentrations and Volumes

Dosage Group	Number of Pups per Sex	Test Substance	Dosage (mg/kg/day) ^a	Concentration (mg/mL)	Dosage Volume (mL/kg)	Batch Number
I	24 ^b	Corn Oil	0 (Vehicle)	0	5	B-TQC00013-A(Day.Month.Year)
II	12	Malathion	5	1	5	B-TQC00013-B(Day.Month.Year)
III	12	Malathion	25	5	5	B-TQC00013-C(Day.Month.Year)
IV	12	Malathion	50	10	5	B-TQC00013-D(Day.Month.Year)
V	12	Malathion	150	30	5	B-TQC00013-E(Day.Month.Year)
VI	12	Malaoxon	0.1	0.02	5	B-TQC00013-F(Day.Month.Year)
VII	12	Malaoxon	1	0.2	5	B-TQC00013-G(Day.Month.Year)
VIII	12	Malaoxon	2.5	0.5	5	B-TQC00013-H(Day.Month.Year)
IX	12	Malaoxon	4	0.8	5	B-TQC00013-I(Day.Month.Year)

a The test substances will be considered 100% pure for the purpose of dosage calculations

b Twelve of these pups will be dosed and sacrificed with the Malathion pups and the other twelve with the Malaoxon pups

TESTS, ANALYSES AND MEASUREMENTS - DAMS

Viability observations will be recorded at least twice daily. Maternal behavior, clinical observations and body weights will be recorded the day after arrival. Clinical observations may be recorded more frequently than cited above. Feed consumption will be monitored as feed is replenished on an as-needed basis. This information will be recorded to monitor the general health and well-being of the dams; these data will not be tabulated or summarized in the final report.

METHOD OF SACRIFICE - DAMS

The dams will be sacrificed by carbon dioxide asphyxiation.

NECROPSY - DAMS**Scheduled Sacrifice of Dams with Litters Assigned to Study**

On day 22 postpartum, dams will be sacrificed by carbon dioxide asphyxiation and discarded without further evaluation.

Scheduled Sacrifice of Dams with Litters Not Assigned to Study

Dams with litters not assigned to the study will be sacrificed by carbon dioxide asphyxiation after dosage administration of pups assigned to the study. Carcasses will be discarded without further evaluation.

Dams with No Surviving Pups

Dams with no surviving pups will be sacrificed by carbon dioxide asphyxiation after the last pup is found dead or missing (presumed cannibalized). Carcasses will be discarded without further evaluation.

Dams Found Dead or Moribund

Dams that die or are sacrificed because of moribund condition will be discarded without further evaluation. Litters from these dams will be excluded from the study.

TESTS, ANALYSES AND MEASUREMENTS - PUPS**Viability**

All Periods:

Litters will be observed for dead pups at least twice daily. The pups in each litter will be counted on the day after arrival and on the day of randomization.

Clinical Observations and/or General Appearance

Predosage Period: Once daily after the day of arrival (by litter).

Dosage Period: Prior to and 60 ± 10 minutes after dosage administration, except on the day of sacrifice when clinical observations will be performed just prior to sacrifice.

Clinical observations may be recorded more frequently than cited above.

Body Weights

Predosage Period: Day after arrival.

Dosage Period: Daily.

CHOLINESTERASE ASSAY**Blood and Brain Sample Collection**

At the end of the dosage period (day 22 postpartum), whole blood samples (approximately 0.40 to 0.60 mLs each) will be collected from each of the pups assigned for cholinesterase assay⁽²⁻³⁾. The whole blood samples will be collected within 10 seconds from each pup following decapitation. The whole blood samples will be collected at 2 hours postdosage from the male and female pups assigned to the Malathion dosage groups and 1 hour postdosage for the pups assigned to the Malaoxon dosage groups (timing begins with the gavage of the animal and ends with decapitation for blood collection). The time of each blood collection will be recorded in the raw data. (If necessary, blood may be collected from an alternate site; if so, the alternate site will be documented in the raw data). All samples will be labeled with study number, date of collection, animal number, dosage level, day of study, species, generation, group, sex, storage conditions and timepoint.

RBC

Approximately 0.40 to 0.60 mLs of whole blood will be collected into 1.2 mL EDTA-coated (lavender-top) tubes. Blood samples will be stored on ice until being processed for RBC cholinesterase levels according to the Testing Facility's Standard Operating Procedure. Cholinesterase assays will be conducted on the day of blood collection.

Brains

After blood sample collection, the brain will be excised, and the weight will be recorded to three decimal places. The brains will be stored on ice until being assayed for cholinesterase levels according to the Testing Facility's Standard Operating Procedure. Cholinesterase assays will be conducted on the day of pup sacrifice.

METHOD OF SACRIFICE - PUPS

Pups assigned to study that survive to scheduled termination will be sacrificed by decapitation without anesthesia. All other pups will be sacrificed by an intraperitoneal injection of sodium pentobarbital (pups \leq 14 days of age) or by carbon dioxide asphyxiation (pups \geq 15 days of age).

NECROPSY - PUPS

Scheduled Sacrifice

Pups assigned to the study will be sacrificed by decapitation on day 22 postpartum. Sacrifice will be immediately followed by blood collection and brain dissection, and the pups will then be discarded without further evaluation.

Pups Found Dead Before Dosage Administration on Day 12 Postpartum or Unscheduled Sacrifice

Pups that die before dosage administration or are sacrificed because of moribund condition will be discarded without further evaluation.

Pups Not Selected for Study

All pups not selected for study will be sacrificed by an intraperitoneal injection of sodium pentobarbital and discarded without further evaluation.

Pups Found Dead or Unscheduled Sacrifice After Initiation of Dosage Administration

Pups that die or are sacrificed before scheduled termination will be necropsied for the cause of death or condition on the day the observation is made. The lungs, trachea and esophagus will be perfused and saved in neutral buffered 10% formalin for possible future evaluation. Additional tissues may be retained at the discretion of the Study Director.

STATISTICAL EVALUATION

Cholinesterase values for red blood cells and brains will be evaluated as separate dependent variables in one-way analyses of variance (ANOVA) at each combination of sex (male and female). Sample collection interval will be used as the independent variable in the ANOVA. In the event that the ANOVA is significant ($p \geq 0.05$), the interval with the largest value will be compared with values at each of the other intervals using Dunnett's test.

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* and the *Vivarium Temperature and Relative Humidity Monitoring System*. 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*, *Microsoft® Excel* (part of *Microsoft® Office 97/2000/XP*), *Quattro Pro 8* and/or *The SAS System* (version 6.12) and/or *Softmax® Pro* (version 4.0).

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 as 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 two years after mailing of the draft final report, after which time the Sponsor will be contacted to determine the disposition of these materials.

RECORDS TO BE MAINTAINED

Protocol, Amendments and Deviations.
Study Schedules
Test Substance, Vehicle and/or Reagent Receipt, Preparation and Use.
Animal Acquisition.
Randomization Schedules.
Treatment (if prescribed by Staff Veterinarian).
General Comments.
Clinical Observations and/or General Appearance.
Body Weights.
Litter Observations.
Blood and Brain Sample Collection and Processing.
Cholinesterase Data.
Photographs (if required).
Study Maintenance (room and environmental records).
Feed, Water and Bedding Analyses.
Packing and/or Shipment Lists.

KEY PERSONNEL

Director of Research: Alan M. Hoberman, Ph.D., DABT
Senior Scientist and Study Director: John F. Barnett Jr., B.S.
Director of Operations: John F. Barnett, Sr., B.S.
Senior Manager, Study Management: Jo Anne Vico, B.S.
Senior Manager, Regulatory Compliance: Nancy A. Catricks, M.S.
Attending Veterinarian: Dena C. Lebo, V.M.D., Division Veterinarian
Chair, Institutional Animal Care and Use Committee: Douglas B. Learn, Ph.D.
Consultant, Veterinary Pathology: W. Ray Brown, D.V.M., Ph.D., Diplomate, ACVP

FINAL REPORT

The day of birth is designated postnatal day 0 (day 0 of lactation) in Addendum 10 to the Pesticide Assessment Guidelines of the U.S. Environmental Protection Agency (EPA). This same day is designated day 1 postpartum (day 1 of lactation) in the Standard Operating Procedures of the Testing Facility. In the report text, as well as summary and individual tables, the day of birth will be adjusted so that the day of birth and all subsequent lactation/postpartum days match the EPA guideline.

The Study Director may provide periodic updates of study progress to the Sponsor's Representative. Draft summary tables of unaudited computer-recorded data may accompany these updates. Statistical analyses will not be performed on these interim data. The report will be formatted to comply with EPA's PR Notice 86-5 report formatting requirements.

An audited report will be prepared including: all applicable items listed in 40 CFR Part 160, abstract, summaries of the methods, results and conclusion; table of contents; Study Director's GLP compliance statement; copy of the protocol; amendments; QAU statement; summary and individual tables; and reports of supporting data.

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.

The Sponsor's Representative will receive one copy of the draft report. A copy of the final report will be provided 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. A hard copy printed from the electronic file will accompany the final report on CD-ROM. The hard copy of the report with original signatures retained at the Testing Facility will be considered the original.

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 Care and Use of Laboratory Animals⁽¹⁾, the relevant SOPs of the Testing Facility, and the protocol. Anticipated or suspected clinical signs and a course of action agreed upon by the Study Director, veterinary staff and Sponsor should these clinical signs be observed are documented in this protocol.

Adverse observations will be promptly reported to the Study Director and veterinary staff. The veterinarian may make recommendations regarding treatment 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.

Treatment of the animal(s) may occur without notification of the Sponsor when such treatment, 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.

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.

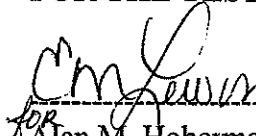
The signature of the Sponsor's representative below is assurance that the study is not an unnecessary duplication of previous work. Documentation for the necessity of this study may be obtained from the Sponsor. No alternative procedures were available to meet the stated purposes of the study.

REFERENCES

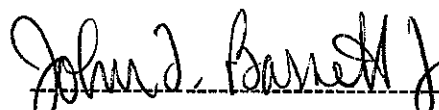
1. Institute of Laboratory Animal Resources (1996). *Guide for the Care and Use of Laboratory Animals*. National Academy Press, Washington, D.C.
2. U.S. Environmental Protection Agency (1997). A set of scientific issues being considered by the agency concerning the office of pesticide programs (OPP) cholinesterase inhibition policy. Scientific Advisory Panel (SAP) June, 1997, Meeting.
3. Lassiter.TL., Barone.S Jr., and Padilla.S. Ontogenetic differences in the regional and cellular acetylcholinesterase and butyrylcholinesterase activity in the rat brain. Dev Brain Res 1998; 105 :109-123

PROTOCOL APPROVAL

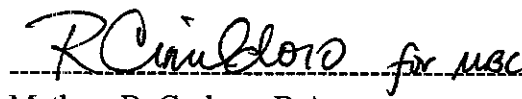
FOR THE TESTING FACILITY


for Alan M. Hoberman, Ph.D., DABT
Director of Research

27 Jan 2006
Date


John F. Barnett, Jr., B.S.
Study Director

27 Jan 2006
Date

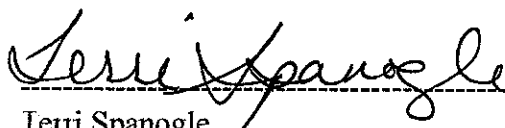

Mathew B. Carlson, B.A.
Member, Institutional Animal Care and
Use Committee

27 Jan 2006
Date

FOR THE SPONSOR

Sponsor approval received via telephone on:

27 January 2006
Date


Terri Spanogle
Sponsor's Representative
Senior Scientist
Cheminova, Inc.

1 February 2006
Date

ATTACHMENT 1
STUDY SCHEDULE

STUDY SCHEDULE^a**MALATHION**

24 JAN 06	Dams and Pups Arrive - Acclimation Begins.
30 JAN 06	Proposed Experimental Start Date
30 JAN 06 - 10 FEB 06	Dosage Administration - Pups - Days 12 through 22 postpartum.
9 FEB 06 - 10 FEB 06	Dams and Pups Sacrificed on Day 22 Postpartum.

MALAOXON

31 JAN 06	Dams and Pups Arrive - Acclimation Begins.
3 FEB 06 - 14 FEB 06	Dosage Administration - Pups - Days 12 through 22 postpartum.
13 FEB 06 - 14 FEB 06	Dams and Pups Sacrificed on Day 22 Postpartum.
APR 06	Proposed Experimental Completion Date
18 APR 06	Audited Draft Report.
Date the Study Director Signs the Final Report.	Study Completion Date.

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

ATTACHMENT 2
CERTIFICATES OF ANALYSIS



CHEMINOVA A/S
P.O. Box 3
DK-7620 Lemvig
Denmark

Phone (+45) 95 80 98 90
Fax (+45) 95 80 98 91
www.cheminova.com
CVR-No. DK12760043

BATCH ANALYTICAL CERTIFICATE

ARTICLE IDENTIFICATION	
Article Name:	Malaoxon
Manufacturer:	Cheminova A/S
Origin of Production:	Commercial <input type="checkbox"/> ; Pilot plant <input type="checkbox"/> ; Laboratory <input checked="" type="checkbox"/> ;
Reg. Dept. Code:	-
Batch No.:	849-BSE-42C
PHYSICAL PROPERTIES	
Technical Product <input type="checkbox"/> ; Preparation of technical Product <input type="checkbox"/> ; Analytical Standard <input checked="" type="checkbox"/> ; Liquid <input checked="" type="checkbox"/> ; Solid <input type="checkbox"/> ; Colour:	Colourless
Recommended Storage Conditions	
Ambient temperature in the dark	Expiry Date:
In refrigerator	The article is stable at least 4 years from date of analysis/last date of reanalysis when stored at recommended conditions.
In deep freezer	
Additional Comments:	
ACTIVE INGREDIENT IDENTIFICATION	
Common Name/ISO-Name:	Malaoxon
CAS No.:	1634-78-2
Empirical Formula:	C ₈ H ₁₉ O ₆ P ₂ S
Molecular Weight:	314.3
Identified by means of:	Structural Formula:
	NMR <input checked="" type="checkbox"/> ; IR <input checked="" type="checkbox"/> ; UV <input checked="" type="checkbox"/> ; MS <input checked="" type="checkbox"/> ; Other Methods:
ANALYTICAL DATA	
Certified Purity/Content of a.i.: 97.7% w/w	
Analytical Method: 51P-NMR	
Analytical Report (incl. amendments): REP 029-07	
Date of analysis/reanalysis (yy/mm/dd)	05/03/04
-for article stored at -	Cheminova A/S
GLP-COMPLIANCE	
The identification and determination of purity/content of active ingredient were performed at Cheminova A/S and conducted in accordance with ICH Good Laboratory Practice Standards, 40 CFR Part 160 and the OECD Principles of Good Laboratory Practices. All raw data, documentation, records, study plans, test articles, reference samples, and report are retained in the GLP archives of Cheminova A/S, Denmark.	
Date:	April 25, 2005
Signature:	Tina Kusk



CHEMINOVA A/S
P.O. Box 9
DK-7620 Lemvig
Denmark

Phone (+45) 96 96 96 90
Fax (+45) 96 96 96 91
www.cheminova.com
CVR-No. DK 12780043

BATCH ANALYTICAL CERTIFICATE

ARTICLE IDENTIFICATION						
Article Name:		Fyfanon Technical			Reg. Dept. Code:	
Manufacturer:		Cheminova A/S			Batch No : 9010501	
Origin of Production:		Commercial <input checked="" type="checkbox"/>	Pilot plant <input type="checkbox"/>	Laboratory <input type="checkbox"/>		
PHYSICAL PROPERTIES						
Technical Product <input checked="" type="checkbox"/>		Preparation of technical Product <input type="checkbox"/>	Analytical Standard <input type="checkbox"/>	Liquid <input checked="" type="checkbox"/>	Solid <input type="checkbox"/>	Colour: Pale yellowish
Recommended Storage Conditions						
Ambient temperature in the dark		Expiry Date:				
In refrigerator <input checked="" type="checkbox"/>		The article is stable at least 2 years from date of analysis/last date of reanalysis when stored at recommended conditions.				
In deep freezer <input type="checkbox"/>						
Additional Comments:						
ACTIVE INGREDIENT IDENTIFICATION						
Common Name/ISO-Name:		CAS-Name:				
Malathion		Butanedioic acid, ((dimethoxyphosphinoyl)thio)-, diethyl ester				
CAS No.:		121-75-5				
Empirical Formula:		Structural Formula:				
C ₁₀ H ₁₉ O ₆ PS ₂						
Molecular Weight:		330.4				
Identified by means of:						
NMR <input checked="" type="checkbox"/> ; IR <input checked="" type="checkbox"/> ; UV <input checked="" type="checkbox"/> ; MS <input checked="" type="checkbox"/> ; Other Methods:						
ANALYTICAL DATA						
Certified Purity/Content of a.i. : 96.0% w/w						
Analytical Method: VAM 001-02						
Analytical Report (incl. amendments): TEM 010-02						
Date of analysis/reanalysis (yy/mm/dd)	990223	000105	001206	011106	021024	041103
-for article stored at -	Cheminova A/S. Regist. storage, DK	Cheminova A/S	Cheminova A/S. Regist. storage, DK	Cheminova A/S. Regist. storage, DK	Cheminova A/S. Regist. storage, DK	Cheminova A/S. Regist. storage, DK
GLP-COMPLIANCE						
The identification and determination of purity/content of active ingredient were performed at Cheminova A/S and conducted in accordance with EUPRA Good Laboratory Practice Standards, 40 CFR Part 160 and the OECD Principles of Good Laboratory Practices. All raw data, documentation, records, study plans, test articles, reference samples, and report are retained in the GLP archives of Cheminova A/S, Denmark.						
Date: 1 November 2004		Signature: Barbara Rinz				

ATTACHMENT 3
MATERIAL SAFETY DATA SHEETS

Name: Malaoxon
Material Type: Analytical Standard
Chemnova Code: REF 029

GHB/January 1999
Page 1 of 3

MATERIAL SAFETY DATA SHEET

Malaoxon

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



Name: Malaoxon

CHEMINOVA AGRO A/S

P.O.Box 9

DK-7620 Lemvig

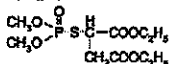
Denmark

Emergency Telephone No.: (+45) 97 83 53 53

2. COMPOSITION/INFORMATION ON INGREDIENTS

Common Name
CAS Name
Other Name(s)
CAS No.
EU Classification
Molecular Weight
Empirical Formula
Structural Formula

Malaoxon
Butanedioic acid, [(dimethoxyphosphoryl)thio]-, diethyl ester
S-1,2-Bis(ethoxycarbonyl)ethyl O,O-dimethyl phosphorothioate
1634-78-2
T/R24/25
314.29
C₁₀H₁₉O₇P₂S



3. HAZARDS IDENTIFICATION

3.1. Health Hazards (Acute and Chronic)

Malaoxon is a poison (cholinesterase inhibitor). It rapidly enters the body on contact with all skin surfaces and eyes. Clothing contaminated with material must be removed immediately and all skin washed thoroughly. Exposed persons must receive prompt medical treatment. Repeated exposures to cholinesterase inhibitors such as malaoxon may, without warning, cause increased susceptibility to doses of any cholinesterase inhibitor.

3.2. Signs and Symptoms of Exposure

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.

4. FIRST AID MEASURES

4.1. Emergency and First Aid Procedures

Call a doctor (physician), clinic or hospital immediately. Explain that the victim has been exposed to malaoxon, an organophosphorus insecticide, and describe his/her condition. Move the exposed person immediately from the area where the substance is present.

If breathing has stopped, start artificial respiration immediately and maintain until physician takes care of the exposed person.

If swallowed and the exposed person is conscious, make him/her vomit quickly. Have the exposed person drink 1 or 2 glasses of water and induce vomiting by touching the back of throat with finger. Repeat until vomit is clear. Never give anything by mouth to an unconscious person. Make the exposed person lie down and keep him/her steady. Get medical attention immediately.

In case of contact, immediately flush eyes or skin with plenty of water while removing contaminated clothing and shoes. See physician immediately.

4.2. Note to Physician

Cholinesterase Inhibition - Treatment

Malaoxon is a cholinesterase inhibitor affecting the central and peripheral nervous systems producing cardiac and respiratory depression.

Antidote: Administer atropine sulfate in large doses. TWO to FOUR mg intravenously or intramuscularly as soon as cyanosis is overcome. Repeat at 5 to 10 minute intervals until signs of atropinisation appear.

The information presented herein is believed to be accurate and reliable, but is presented without any warranty express or implied, on the part of Chemnova Agro A/S.

Name: Malaoxon
Material Type: Analytical Standard
Chemnova Code: REF 029

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		Obidoxime chloride (Toxogonin) is a pharmacological antidote and may be administered as an adjunct to, but not a substitute for, atropine, which is a symptomatic and often lifesaving antidote. DO NOT GIVE MORPHINE OR TRANQUILLIZERS.
		At first sign of pulmonary oedema the patient should be given supplemental oxygen and treated symptomatically.
		Continued absorption of malaoxon may occur and relapse may occur after initial improvement. VERY CLOSE SUPERVISION OF THE PATIENT IS INDICATED FOR AT LEAST 48 HOURS.
5.	FIRE-FIGHTING MEASURES	
5.1.	Extinguishing Media and Procedure	Dry chemical, carbon dioxide, water spray or foam.
5.2.	Hazardous Products in a Fire	The essential breakdown products are sulfur dioxide, carbon monoxide, carbon dioxide and phosphorus pentoxide.
6.	ACCIDENTAL RELEASE MEASURES	
6.1.	Personal Protection	Observe all protection and safety precautions when cleaning up spills - see 8.
6.2.	Steps to Be Taken in Case of Spill	Spills on the floor or other impervious surface should be swept up with an inert absorbent material such as hydrated lime, sawdust, Fuller's earth or other absorbent clays. Collect the contaminated absorbent, place in an appropriate container and dispose of in accordance with the instructions provided under Disposal (see 13). Rinse area with soda lye. Malaoxon can be hydrolysed in water by heating and adjusting the pH (alkaline). Malaoxon may also be disposed of through proper incineration.
7.	HANDLING AND STORAGE	
7.1.	Precautions to Be Taken in Handling	See Personal Protection - Section 8.
7.2.	Precautions to Be Taken in Storing	Store in deep freezer. The article is stable for at least 3 years from date of analysis when stored under recommended conditions.
7.3.	Fire and Explosion Precautions	---
8.	EXPOSURE CONTROLS/PERSONAL PROTECTION	
8.1.	Respiratory Protection	In case of insufficient ventilation, wear a respirator in conformity with local regulations.
	Protective Gloves	Wear chemical resistant gloves, such as barrier laminate, butyl rubber, nitrile rubber or viton.
	Eye Protection	Wear safety glasses.
	Other Protection	Wear appropriate chemical resistant clothing.
8.2.	Work/Hygiene Practices	If handled indoors, provide mechanical exhaust ventilation. 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. Before removing gloves wash them with soap and water. Always wash hands, face and arms with soap and water before smoking, eating or drinking.
9.	PHYSICAL AND CHEMICAL PROPERTIES	
9.1.	Physical State	Liquid
9.2.	Colour	Colourless
9.3.	Odour	---
9.4.	Melting Point	< 20°C
9.5.	Boiling Point	114°C
9.6.	Specific Gravity	---
9.7.	Vapour Pressure	---
9.8.	Viscosity	---
9.9.	Solubility in Water	0.5-1 g/100 ml at 20°C
9.10.	Solubility in Organic Solvents	---
9.11.	Partition Coefficient n-Octanol/Water	---
9.12.	pH	---
9.13.	Flash Point	100°C
9.14.	Autoignition Temperature	---
9.15.	Flammable Limits	---

The information presented herein is believed to be accurate and reliable, but is presented without any warranty, express nor implied, on the part of Chemnova Agro A/S.

Name: Malaoxon
 Material Type: Analytical Standard
 Chemnova Code: REF 029

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 Page 3 of 3

18. **STABILITY AND REACTIVITY**
- 10.1. **Conditions to Avoid** —
- 10.2. **Hazardous Decomposition Products** See 5.2
- 10.3. **Materials to Avoid** Strong alkalis and strong oxidizing compounds.
11. **TOXICOLOGICAL INFORMATION**
- 11.1. **Acute toxicity**
- Ingestion LD₅₀, oral, rat: 158 mg/kg
 - Skin LD₅₀, dermal, rabbit: 119 mg/kg
 - Inhalation LC₅₀, inhalation, rat: —
- 11.2. **Irritancy of Material** Unknown
- 11.3. **Carcinogenicity** Not carcinogenic
12. **ECOLOGICAL INFORMATION**
- Malaoxon is biodegradable. It undergoes rapid degradation in the environment and without problems in sewage treatment plants.
- Malaoxon is toxic to birds, fish and aquatic invertebrates. The acute toxicity is:
- Fish 48 h-LC₅₀, Perch (*Perca fluviatilis*) 150 µg/l
 - Invertebrates 24 weeks-EC₅₀, Midge (*Chironomus riparius*) 5.4 µg/l
13. **DISPOSAL CONSIDERATIONS**
- Waste Disposal Method Spill and waste disposal procedures in conformity with state and local regulations must be followed. Do not contaminate water, food or feed by storage or disposal.
14. **TRANSPORT INFORMATION**
- UN Classification Toxic Liquid, Organic, N.O.S. (Malaoxon), UN No. 2810, Class 6.1, PG II, Primary Hazard: Toxic
15. **REGULATORY INFORMATION**
- In the EU:
- T



Toxic

R24/25: Toxic in contact with skin and if swallowed.

S23-36/37-45: After contact with skin, wash immediately with plenty of water and soap. Wear suitable protective clothing and gloves. In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).
16. **OTHER INFORMATION**
-

The information presented herein is believed to be accurate and reliable, but is presented without any warranty, express nor implied, on the part of Chemnova Agro A/S.

SAFETY DATA SHEET

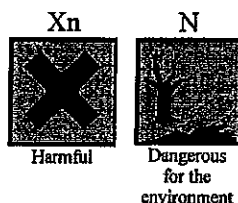
FYFANON[®] TECHNICAL

Table of contents

1 ♣	Identification of the substance/preparation and of the company/undertaking	9 ♣	Physical and chemical properties
2 ♣	Composition/information on ingredients	10 ♣	Stability and reactivity
3 ♣	Hazards identification	11 ♣	Toxicological information
4 ♣	First aid measures	12 ♣	Ecological information
5 ♣	Fire-fighting measures	13 ♣	Disposal considerations
6 ♣	Accidental release measures	14 ♣	Transport information
7 ♣	Handling and storage	15 ♣	Regulatory information
8 ♣	Exposure controls/personal protection	16 ♣	Other information

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

Emergency (+45) 97 83 53 53
telephone no.

2. ♣ COMPOSITION/INFORMATION ON INGREDIENTS

2.1. FYFANON[®]

CAS name	Butanedioic acid, [(dimethoxyphosphinothioyl)thio]-, diethyl ester
CAS no.	121-75-5
IUPAC name(s)	Diethyl (dimethoxythiophosphorylthio)succinate S-[1,2-Bis(ethoxycarbonyl)ethyl] O,O-dimethyl phosphoro-dithioate
ISO name/EU name	Malathion
EC no. (EINECS no.)	204-497-7
EU index no.	015-041-00-X
Empirical formula	C ₁₀ H ₁₉ O ₆ PS ₂
Molecular weight	330.36
Structural formula	$ \begin{array}{c} \text{S} \\ \parallel \\ \text{CH}_3\text{O}-\text{P}-\text{S}-\text{CH}-\text{COOC}_2\text{H}_5 \\ \parallel \\ \text{CH}_3\text{O} \quad \quad \quad \text{CH}_2\text{COOC}_2\text{H}_5 \end{array} $

- 2.2. Typical content 96-97%

3. ♣ HAZARDS IDENTIFICATION

3.1. CLASSIFICATION

EU classification Xn;R22 N;R50/53; see 15.1.
(according to 67/548/EEC as amended)

WHO classification Class III: Slightly hazardous

3.2. Health hazards (acute and chronic)

Fyfanon[®] (malathion) is a cholinesterase inhibitor of low mammalian toxicity. However, storage at too high temperatures may induce formation of the much more toxic and synergistic contaminant isomalathion (LD₅₀, acute 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 **Fyfanon**[®] may, without warning, cause increased susceptibility to doses of any cholinesterase inhibitor.

3.3. Environmental hazards

The substance is very toxic to aquatic organisms, see section 12.

4. ♣ FIRST AID MEASURES

4.1. Signs and symptoms of exposure

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.

4.2. Emergency and first aid procedures

General

Exposed persons must receive prompt medical treatment. When any of the signs of exposure 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 remove the victim from the area where the product is present.

Clothing contaminated with material must be removed immediately and all skin washed thoroughly.

If breathing has stopped, immediately start artificial

respiration and maintain until a physician takes charge of the exposed person.

Inhalation	If experiencing any discomfort, immediately remove from exposure. Get medical attention immediately if symptoms develop.
Ingestion	If the exposed person is conscious, make him/her vomit quickly. Make the exposed person rinse mouth and drink 1 or 2 glasses of water or milk if available. Let him/her induce vomiting by touching the back of the throat with a finger. Repeat until vomit is clear. Never give anything by mouth to an unconscious person. 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 shoes. Wash with water and soap. See physician immediately if symptoms develop.
4.3. 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.

Antidote: If symptoms (see 4.1.) 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 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 | <p>Dry chemical or carbon dioxide for small fires, water spray or foam for large fires.</p> <p>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.</p> |
| 5.2. Hazardous decomposition products in a fire | <p>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.</p> |
| 5.3. Unusual fire and explosion hazards | <p>See 10.1.</p> |

6. ♣ ACCIDENTAL RELEASE MEASURES

- | | |
|---|--|
| 6.1. Personal protection | <p>Observe all protection and safety precautions when cleaning up spills. Depending on the magnitude of the spill, this may mean wearing eye protection or face mask, coveralls, protective gloves and boots when cleaning up spills. See section 8, Personal protection.</p> |
| 6.2. Steps to be taken in case of spill | <p>It is recommended to have a predetermined plan for the handling of spills.</p> <p>Stop the source of the spill if it is safe to do so. Keep unprotected persons away from the spill area. Contain the spill to prevent any further contamination of surface, soil or water.</p> |

Spills on the floor or other impervious surface should be contained or diked and then 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. Washings must be prevented from 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.

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.

Do not contaminate water, foodstuffs, feed or seed by storage or disposal.

Store in closed, labelled containers.

- 7.3. Specific use The product is an active ingredient for the production of registered pesticides which may only be used for the applications they are registered for in accordance with a label approved by the regulatory authorities.

- 7.4. Fire and explosion precautions ---

8. ♣ EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Exposure limit values

		Year	
Malathion	OSHA (USA) PEL	200	TWA 15 mg/m ³ total dust; skin notation
		2	
	ACGIH (USA)	200	TWA 10 mg/m ³ ; skin notation; BEI
	TLV	5	
	EU, 2000/39/EC	200	Not established
		0	
Germany, MAK		200	TWA 15 mg/m ³ measured as inhalable fraction of
		4	the aerosol
			CEILING 60 mg/m ³
HSE (UK) OEL			BAT
		200	8-hr TWA 10 mg/m ³ ; skin notation
		3	

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 does not automatically present an airborne exposure concern when handled carefully due to low vapour pressure, but in the event of a discharge of the

material which produces a heavy vapour or mist, workers should put on an officially approved face mask or 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 based on the low dermal toxicity of the substance. |
| Eye protection | Wear safety glasses. It is recommended to have an eye wash fountain immediately available in the workplace. |
| Other protection | Wear coveralls or long sleeved shirt and long pants.
Wear shoes
plus socks. |
- 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 mist. Before removing gloves, wash them with water and soap. Wash thoroughly with water and soap after handling. Remove contaminated clothing immediately and wash before reuse.
- After work, take off all work clothes and shoes. Shower, using soap and water. Wear only clean clothes when leaving job. Do not wear contaminated clothing. Wash protective clothing and protective equipment with soap and water after each use. Respirator should be cleaned and filter replaced according to instructions included with respirator.
- 8.4. Environmental exposure controls
- See section 13.

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	2.85°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	16.4 cP at 40°C 30.0 cP at 25°C
9.9. Surface tension	57.8 mN/m at 20°C for a saturated solution in water
9.10. Solubility in water	148.2 mg/l at 25°C
9.11. Solubility in organic solvents	Solubility of malathion in: Acetone > 250 g/l at 20°C Methanol > 250 g/l at 20°C Ethyl acetate > 250 g/l at 20°C 1,2-Dichloroethane > 250 g/l at 20°C Xylene > 250 g/l at 20°C Heptane 57-67 g/l at 20°C
9.12. Partition coefficient n-octanol/water	K _{ow} = 560
9.13. pH	When equal amounts of Fyfanon® 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 **Fyfanon®** 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 diethyl sulphide.
- 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 iron, steel, tin plate and copper.
Fyfanon® is rapidly hydrolysed at pH > 7.0.

11. TOXICOLOGICAL INFORMATION

- 11.1. Acute toxicity The product is not considered to be harmful, neither by inhalation, in contact with skin nor if swallowed. However, it may become harmful after storage at too high temperatures, see 3.1.
- | | | |
|-------------------|--------------|--|
| Route(s) of entry | - Ingestion | LD ₅₀ , acute oral, rat: approx. 5500 mg/kg ^{*)} |
| | - Skin | LD ₅₀ , acute dermal, rat: > 2000 mg/kg |
| | - Inhalation | LC ₅₀ , inhalation, rat: > 5.2 mg/l/4 h |
- ^{*)} Values from 1000 to 2830 mg/kg are mentioned in literature as well as in WHO Data Sheet No. 29, VBC/DS/77 29
- 11.2. Irritancy Slightly irritating to eyes and skin.
- 11.3. 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.
- 11.4. Carcinogenicity IARC evaluation: The available data provide no evidence that **malathion** is likely to present a carcinogenic risk to humans.
- 11.5. Effects on reproduction No effects on fertility are found for **malathion** in rats and rabbits at maternal non-toxic doses.
- 11.6. Teratogenicity No indications of teratogenic effects of **malathion** are found.
- 11.7. 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 to be:

- | | | |
|-----------------|--|---|
| - 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
	Mallard duck (<i>Anas platyrhynchos</i>)	LD ₅₀ : 1485 mg/kg
- Earthworms	<i>Eisenia foetida foetida</i>	14-day LC ₅₀ : 613 mg/kg soil
- Bees	Honey bees (<i>Apis mellifera</i>)	LD ₅₀ , acute oral: 0.38 µg/bee
	Honey bees (<i>Apis mellifera</i>)	LD ₅₀ , topical: 0.27 µg/bee

- 12.2. Mobility Under normal conditions **malathion** is of medium mobility in soil, but is degraded rapidly.
- 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 can be removed by controlled discharge to a waste water treatment plant. Other possible methods of disposal are controlled incineration with flue gas scrubbing or removal to a licensed chemical destruction plant.
- Fyfanon®** 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.
- 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

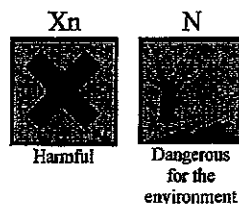
Proper shipping name	Environmentally hazardous substance, liquid, n.o.s. (Malathion)
Class	9
UN no.	3082
Packaging group	III
Marine pollutant (P/PP)	Marine pollutant

IATA/ICAO**CLASSIFICATION**

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

15. REGULATORY INFORMATION**15.1. IN THE EU****Classification and labelling**

(according to 67/548/EEC as amended):

Hazard symbols**R-phrases**

R22-50/53: Harmful if swallowed. Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

S-phrases

S24-60-61: Avoid contact with skin. 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. 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

TEST SUBSTANCE PREPARATION PROCEDURE

Test Substances: Malathion (synonymous with Fyfanon Technical) and Malaoxon

Vehicle: Corn Oil

A. Purpose:

The purpose of this procedure is to provide a method for the preparation of dosage formulations of the test substances for oral (gavage) administration to juvenile rats on Protocol TQC00013.

B. General Information:

1. All formulation containers will be labeled and color-coded. Each label will specify the protocol number, test substance identification, batch number, concentration, dosage level, dosage group, preparation date, expiration date and storage conditions.
2. Formulations (suspensions) of each test substance will be prepared once at the Testing Facility.
3. Formulations will be administered at a final dosage volume of 5 mL/kg.
4. Safety:
 - ☒ Double nitrile gloves, uniform/lab coat, goggles or safety glasses with side shields
 - ☐ Dust-Mist/HEPA-filtered Mask
 - ☐ Half-Face Respirator
 - ☒ Full-Face Respirator/Positive Pressure Hood
 - ☒ Tyvek® Suit
 - ☐ Full Face Shield
 - ☒ Bulk TA/S 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.
5. The test substances will be considered 100% pure for the purpose of dosage calculations.
6. Sampling requirements: Cited in protocol.
7. Storage: Cited in protocol.

TEST SUBSTANCE PREPARATION PROCEDURE

C. Dosage Formulation Preparation:

NOTE: Prior to dosage formulation preparation accurately measure the required amount of the appropriate vehicle (R.O. deionized water should be used for calibration purposes) in a graduated cylinder and pour the required amount of vehicle into an appropriately sized container. Carefully mark each container at the meniscus. This mark will be used during the preparation to bring the dosage formulations up to volume.

1. Weigh the required amount of test substance into an appropriately sized and labeled, pre-calibrated container (See TA/S PREPARATION CALCULATIONS).
2. QS ad with vehicle to the required volume in the pre-calibrated container (See TA/S PREPARATION CALCULATIONS).
3. Add a magnetic stir bar to the container, place the container on a magnetic stir plate and thoroughly mix the formulation. Continue to mix the formulation prior to and during sampling, preparation of other dosage formulations (if dilutions and/or serial dilutions are required), and/or aliquotting.
4. Aliquot the formulation into an appropriate number of appropriately sized and labeled containers for daily dosage administration. Aliquots will be stored refrigerated and protected from light.
5. On each day of dosage administration, remove the required number of aliquots for refrigerated storage. A magnetic stir bar will be added to each aliquot. The aliquots will be placed on a magnetic stir plate and mixed thoroughly prior to and during dosage administration.
6. Repeat steps C1 through C5 for each concentration of each test substance.

ATTACHMENT 4

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TEST SUBSTANCE PREPARATION PROCEDURE

7. NOTE: If the concentrations of the formulations are considerably low and the weigh out of the test substance into a pre-calibrated beaker will be difficult, dilutions and/or serial dilutions may be performed as necessary. If this is the case, for step C1, the appropriate amount of the appropriate stock formulation will be added to an appropriately sized and labeled, pre-calibrated beaker. All other steps will then be followed.

Written by: Patricia A GarbelyApproved by: John D. Barnett Date: 27 Jan 2006Clarification: ☒ No ☐ Yes (See attached clarification form.)Initials/Date: ARD / 15.FEB.06



PROTOCOL IQC00013

ORAL (GAVAGE) REPEAT DOSE COMPARATIVE CHOLINESTERASE STUDY
OF MALATHION AND MALAOXON IN JUVENILE RATS

Amendment 1 – 12 April 2006

1. Randomization (page 12 of the protocol):

[Effective Date: 1 February 2006] Cross-fostering will be performed if a litter has an insufficient number of male and/or female pups within the litter. If this is necessary, the cross-fostering will be documented in the raw data.

Reason for Change:

This change is being made to ensure that there are a sufficient number of male and female pups available in each litter for assignment to study because the initial shipment from the breeder included uneven litter representation.

2. Blood and Brain Sample Collection (page 16 of the protocol)

[Effective Date: 9 February 2006] The whole blood samples will be collected at 2 hours postdosage from the male and female pups assigned to the Malathion dosage groups and 30 minutes postdosage for the pups assigned to the Malaoxon dosage groups (timing begins with the gavage of the animal and ends with decapitation for blood collection).

Any revisions to this finalized amendment must be made by subsequent amendment.

905 Sheehy Drive, Bldg. A, Horsham, PA 19044 • 215.443.8710 • FAX 215.443.8587

Protocol IQC00013
Amendment 1
Page 2

Reason for Change:

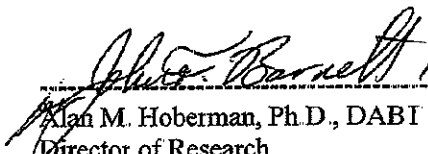
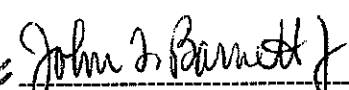
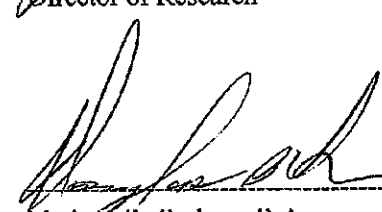
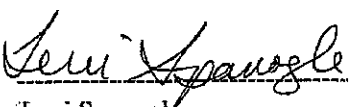
This change is being made to revise the time of blood collection from 1 hour postdosage to 30 minutes postdosage for the pups assigned to the Malaoxon dosage group.

3. RBC (page 17 of the protocol)

[Effective Date: 09 February 2006] Blood samples will be stored on cold packs rather than ice until being processed for RBC cholinesterase levels according to the Testing Facility's Standard Operating Procedure.

Reason for Change:

This change is being made to revise the storage conditions from ice to cold packs.

 Alan M. Hoberman, Ph.D., DABI Director of Research	12 Apr 2006 Date	 John F. Barnett Jr., B.S. Senior Scientist Study Director	12 Apr 2006 Date
 Mathew B. Carlson, B.A. Member, Institutional Animal Care and Use Committee	12 APR 2006 Date	 Terri Spanogle Senior Scientist Sponsor's Representative	17 April 2006 Date

Any revisions to this finalized amendment must be made by subsequent amendment.

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APPENDIX E

DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY

**DEVIATIONS FROM THE PROTOCOL AND THE STANDARD
OPERATING PROCEDURES OF THE TESTING FACILITY**

1. On postnatal days 7 through 10 of study (PNDs 7-10) (26-28 January 2006, 30 January 2006 and 3 February 2006), clinical observations were not recorded daily after the day of arrival for all pups. Clinical observations were recorded only on the day after arrival and on the day of randomization. This deviation does not adversely affect the outcome or interpretation of the study because sufficient data were collected during the acclimation period.
2. On PND 20 (12 February 2006), the postdosage check for clinical signs for female pup 5707 in the 0.1 mg/kg/day malaoxon dosage group was performed 32 minutes late. This deviation does not adversely affect the outcome or interpretation of the study because the evaluation was performed.
3. On PND 21 (10 February 2006), the postdosage check for clinical signs for female pup 7006 in the 0 (Vehicle) mg/kg/day dosage group was not performed prior to sacrifice. This deviation does not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.
4. On PND 21 (13 February 2006 and 14 February 2006), the postdosage checks for clinical signs for all male and female pups were not performed immediately before sacrifice as stated in the protocol; however, the checks for clinical signs were performed within 33 minutes before sacrifice for the pups assigned to the malathion group, and within 29 minutes before sacrifice for those assigned to the malaoxon group. This deviation does not adversely affect the outcome or interpretation of the study because the postdosage clinical signs were performed.

5. On PND 21, brain or RBC samples from the following pups were reanalyzed after an acceptable result was obtained:


Sample Type	Pup Number	Sex	Dosage Group	Day of Study	Dosage Level	Date
RBC	5808	Female	VII	PND 21	1	14 FEB 06
RBC	6101	Male	I	PND 21	0	14 FEB 06
Brain	6505	Male	V	PND 21	150	9 FEB 06
Brain	6510	Female	V	PND 21	150	9 FEB 06
Brain	6606	Female	I	PND 21	0	9 FEB 06
Brain	6607	Female	II	PND 21	5	9 FEB 06
Brain	6608	Female	III	PND 21	25	9 FEB 06
Brain	6609	Female	IV	PND 21	50	9 FEB 06
Brain	6610	Female	V	PND 21	150	9 FEB 06
Brain	6706	Female	I	PND 21	0	9 FEB 06
Brain	6801	Male	I	PND 21	0	9 FEB 06
Brain	6806	Female	I	PND 21	0	9 FEB 06
RBC	6901	Male	I	PND 21	0	10 FEB 06
Brain	6906	Female	I	PND 21	0	10 FEB 06
Brain	7002	Male	II	PND 21	5	10 FEB 06
Brain	7006	Female	I	PND 21	0	10 FEB 06
Brain	7010	Female	V	PND 21	150	10 FEB 06
RBC	7101	Male	I	PND 21	0	10 FEB 06

These deviations did not adversely affect the outcome or interpretation of the study because the samples were reanalyzed based on a request of the Study Director after his review of the data or because of improper dilution of the initial samples.

6. On PND 21 (10 February 2006) the blood sample for male pup 6905 in the 150 mg/kg/day dosage group (Group V) was dropped and could not be analyzed for RBC ChE values. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data was available to evaluate this parameter.
7. On PND 21 (13 February 2006) an insufficient amount of blood was collected for male pup 5203 in the 1 mg/kg/day dosage group (Group VII) resulting in an inability to analyze for RBC ChE levels. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data was available to evaluate this parameter.

8. On PND 21 (9 February 2006) brain samples from male pups 6601 and 6701 in the 0 (Vehicle) mg/kg/day dosage group (Group I) were inadvertently homogenized in saline rather than Tween buffer, preventing brain homogenates from being analyzed. This deviation does not adversely affect the outcome or interpretation of the study because sufficient samples were available to evaluate this parameter.
9. On PND 21 (10 February 2006) the technician processing blood samples inadvertently recorded male pup 7103 in the 25 mg/kg/day dosage group (Group II) and male pup 7204 in the 50 mg/kg/day dosage group (Group IV) twice, and did not record the processing of female pups 7107 in the 5 mg/kg/day dosage group (Group II) and 7209 in the 50 mg/kg/day dosage group (Group IV) even though blood samples were collected and processed for these two female pups. This deviation did not adversely affect the outcome or interpretation of the study because based on the data present and a review of the results it was presumed that all samples (including samples for female pups 7107 and 7209) were processed properly.

All deviations are documented in the raw data.

 21 Apr 2006
John F. Barnett, Jr. Date
Senior Scientist
Study Director

APPENDIX F
CERTIFICATE OF ANALYSIS

**SIGMA-ALDRICH****Certificate of Analysis**

Product Name Corn oil
Product Number C8267
Product Brand Sigma
CAS Number 8001-30-7
Molecular Formula
Molecular Weight

TEST**APPEARANCE****FREE FATTY ACIDS****HEAVY METALS****IODINE VALUE****QC ACCEPTANCE DATE****SPECIFICATION**CLEAR YELLOW TO YELLOW-GREEN
LIQUIDLESS THAN 2.0 ML OF 0.02 N SODIUM
HYDROXIDE REQUIRED TO
NEUTRALIZE 10 GM OF CORN OIL

NOT MORE THAN 0.001% (AS LEAD)

102 TO 130

LOT 065K0077 RESULTS

CLEAR YELLOW-GREEN LIQUID

1.0 ML *

<0.001% *

117 *

*** SUPPLIER INFORMATION**

JUNE 2005

Lori Schulz, Manager
Analytical Services
St Louis, Missouri USA

APPENDIX G
ANALYTICAL REPORT



FINAL REPORT

**FORMULATION SAMPLE ANALYSIS FOR THE
DETERMINATION OF MALATHION AND MALAOXON IN
CORN OIL FOR CHARLES RIVER LABORATORIES
PRECLINICAL SERVICES**

Project Number: TQC00013AA

Submitted to:

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

Submitted by:

Charles River Laboratories
Preclinical Services
57 Union Street
Worcester, MA 01608

Report No. TQC00013AA-06-320

Page 1 of 41

Issue Date: April 21, 2006

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11. Materials and Methods	12
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13. Results	12
13.1. Concentration	12
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Project Number: TQC00013AA
Final Report

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For Charles River Laboratories Preclinical Services

1. LIST OF APPENDICES

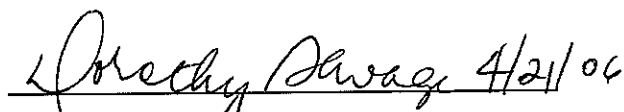
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Project Number: TQC00013AA
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2. APPROVAL

The study was performed under my overall scientific guidance and management. The report provides a full and accurate record of the raw data generated.

 4/21/06

Dorothy Savage, B.S./Date
Principal Investigator
Charles River Laboratories
Preclinical Services

Project Number: TQC00013AA
Final Report

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For Charles River Laboratories Preclinical Services

3. COMPLIANCE STATEMENT

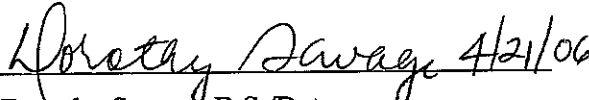
This project was conducted in compliance with the following regulations:

U.S. Environmental Protection Agency. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); Good Laboratory Practice Standards; Final Rule. 40 CFR Part 160.

Japanese Ministry of Agriculture, Forestry and Fisheries (1999). Good Laboratory Practice Standards. 11 Nousan No. 6283.

Organisation for Economic Co-operation and Development (1998). The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final].

Principal Investigator:


Dorothy Savage, B.S./Date

Project Number: TQC00013AA
 Final Report

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4. QUALITY ASSURANCE STATEMENT

This study has been inspected by the Quality Assurance Unit to assure conformance with the Good Laboratory Practice (GLP) regulations promulgated by the U.S. Environmental Protection Agency. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); Good Laboratory Practice Standards; Final Rule. 40 CFR Part 160, Japanese Ministry of Agriculture, Forestry and Fisheries (1999). Good Laboratory Practice Standards. 11 Nousan No. 6283, 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 Standard Operating Procedures as follows:

QA INSPECTION DATES

Dates Findings Submitted to:

Dates of Inspection	Phase(s) Inspected	Principal Investigator	PI Management	Study Director	Study Director Management
1/31/2006	Laboratory Procedure	1/31/2006	1/31/2006	4/7/2006	4/7/2006
4/3/2006, 4/4/2006	Data	4/4/2006	4/6/2006	4/7/2006	4/7/2006
4/3/2006, 4/4/2006	Draft Final Report	4/4/2006	4/6/2006	4/7/2006	4/7/2006
4/20/2006	Final Report	4/20/2006	4/20/2006	4/21/2006	4/21/2006

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

Mary Donohoe 4/21/06
 Mary Donohoe/Date

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5. CONTRIBUTING PERSONNEL

Principal Investigator Dorothy Savage, B.S.

Associate Director, Analytical Chemistry Richard Norlin, M.S.

Divisional Vice President

Laboratory Sciences North America Alan Bartlett, CChem, MRSC

Report Coordinator Erika L. Manyak, A.S.

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6. TEST SUBSTANCE AND ANALYTICAL REFERENCE STANDARD CHARACTERIZATION/STABILITY

Compound Malathion

Physical Description:	Clear Yellowish Liquid
Storage Conditions:	-20±5°C, Protected from light
Lot Number:	9010501
Date Received:	17-Jan-2006
Expiration/Retest Date:	30-Nov-2006
Amount Received:	1 g
Received From:	Charles River Laboratories Preclinical Services, Pennsylvania
Manufacturer/Supplier:	Cheminova A/S
Purity:	96.0%*

Compound Malaoxon

Physical Description:	Clear Liquid
Storage Conditions:	-20±5°C, Protected from light
Lot Number:	849-BSe-42C
Date Received:	17-Jan-2006
Expiration/Retest Date:	04-Mar-2009
Amount Received:	1 g
Received From:	Charles River Laboratories Preclinical Services, Pennsylvania
Manufacturer/Supplier:	Cheminova A/S
Purity:	97.7%*

* = The test substances were considered 100% pure for the purposes of dosage calculations.

6.1. Characterization and Stability

The characterization of the test substances/analytical reference standards is the responsibility of the Sponsor, as are the methods of synthesis, fabrication or derivation and stability determinations.

7. ARCHIVAL STORAGE

The original final report and raw data will be maintained for a minimum period of two years following submission of the final report in the Charles River Laboratories Preclinical Services Archives department located in Horsham, PA. The Sponsor will be notified prior to disposal of any original study data. Archival material will be indexed by Study No. TQC00013.

PART A: ANALYSIS OF MALATHION**8. MATERIALS AND METHODS**

Samples were analyzed according to the method described in Charles River Laboratories Preclinical Services, Massachusetts Laboratory Method (LM) for the "Analysis of Malathion in Corn Oil Dose Formulations by GC-FID" LM MALA00, which was validated in Charles River Laboratories Preclinical Services, Massachusetts Project # TQC00018AX. A copy of the most recent LM revision is included in Appendix B. The dose formulation samples were quantitated using Gas Chromatography with six matrix matched calibration standards. Refer to the Dose Formulation Analysis Report in Appendix A for details on the run.

All samples in this project were prepared at Charles River Laboratories Preclinical Services, Pennsylvania and shipped to Charles River Laboratories Preclinical Services, Massachusetts on cold packs. Samples were received in satisfactory condition on January 31, 2006 and were analyzed immediately upon receipt.

9. COMPUTER SOFTWARE

The GC data was acquired utilizing PerkinElmer's TotalChrom Client/Server software Version 6.2.1. TotalChrom software was used to integrate the peak areas of the analyte. Following integration, the data was exported to a verified Excel spreadsheet. The Excel spreadsheet was used to perform the regression, calculate the regression constants and calculate the concentration of the analyte in unknown samples using the peak areas of the analyte. System suitability was verified using TotalChrom software.

10. RESULTS

Refer to the Dose Formulation Analysis Report in Appendix A for details. The report consists of results and conclusions from one analysis period. Preparation and analysis dates are listed for each result along with Charles River Laboratories Preclinical Services, Pennsylvania sample identification.

10.1. Concentration

Test article samples prepared on January 30, 2006, which were used for dosing, were within acceptable limits of $\pm 15\%$ error.

10.2. Homogeneity

Homogeneity was determined for all dose formulation concentration levels. Mean concentration results from samples taken from the top, middle and bottom of the formulations were calculated. Homogeneity was calculated by determining the percent

relative standard deviation (RSD) of the three mean values. All of the results were within the acceptable range of $\leq 5\%$ RSD. The values obtained were 1.0%, 1.5%, 1.0% and 1.3% RSD for the 1 mg/mL, 5 mg/mL, 10 mg/mL and 30 mg/mL formulations, respectively.

PART B: ANALYSIS OF MALAOXON**11. MATERIALS AND METHODS**

Samples were analyzed according to the method described in Charles River Laboratories Preclinical Services, Massachusetts Laboratory Method (LM) for the "Analysis of Malaoxon in Corn Oil Dose Formulations by GC-FID" LM MLXN00, which was validated in Charles River Laboratories Preclinical Services, Massachusetts Project # TQC00019AX. A copy of the most recent LM revision is included in Appendix B. The dose formulation samples were quantitated using Gas Chromatography with six matrix matched calibration standards. Refer to the Dose Formulation Analysis Report in Appendix A for details on the run.

All samples in this project were prepared at Charles River Laboratories Preclinical Services, Pennsylvania and shipped to Charles River Laboratories Preclinical Services, Massachusetts on cold packs. Samples were received in satisfactory condition on February 3, 2006 and were analyzed immediately upon receipt.

12. COMPUTER SOFTWARE

The GC data was acquired utilizing PerkinElmer's TotalChrom Client/Server software Version 6.2.1. TotalChrom software was used to integrate the peak areas of the analyte. Following integration, the data was exported to a verified Excel spreadsheet. The Excel spreadsheet was used to perform the regression, calculate the regression constants and calculate the concentration of the analyte in unknown samples using the peak areas of the analyte. System suitability was verified using TotalChrom software.

13. RESULTS

Refer to the Dose Formulation Analysis Report in Appendix A for details. The report consists of results and conclusions from one analysis period. Preparation and analysis dates are listed for each result along with Charles River Laboratories Preclinical Services, Pennsylvania sample identification.

13.1. Concentration

Test article samples prepared on February 2, 2006, which were used for dosing, were within acceptable limits of $\pm 15\%$ error.

13.2. Homogeneity

Homogeneity was determined for all dose formulation concentration levels. Mean concentration results from samples taken from the top, middle and bottom of the formulations were calculated. Homogeneity was calculated by determining the percent

relative standard deviation (RSD) of the three mean values. All of the results were within the acceptable range of $\leq 5\%$ RSD. The values obtained were 1.1%, 2.0%, 0.9% and 0.4% RSD for the 0.02 mg/mL, 0.2 mg/mL, 0.5 mg/mL and 0.8 mg/mL formulations, respectively.

Appendix A. Dose Formulation Analysis Reports

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DOSE FORMULATION ANALYSIS REPORT

Sponsor: Cheminova A/S

Study Facility: Charles River Laboratories Preclinical Service, Pennsylvania

Protocol Number: TQC00013

Analyte: Malathion

Analytical Facility: Charles River Laboratories Preclinical Services, Massachusetts

Batch ID: TQC00013AA-1-004-1

Sampling Criteria: Start of Study Concentration and Homogeneity Analysis

Vehicle: Corn Oil

Storage Conditions: 5±3°C

Laboratory Method: LM #MALA00 Revision 00

Analysis Date: January 31, 2006

Notes: Samples were corrected for a corn oil density of 0.915 g/mL.

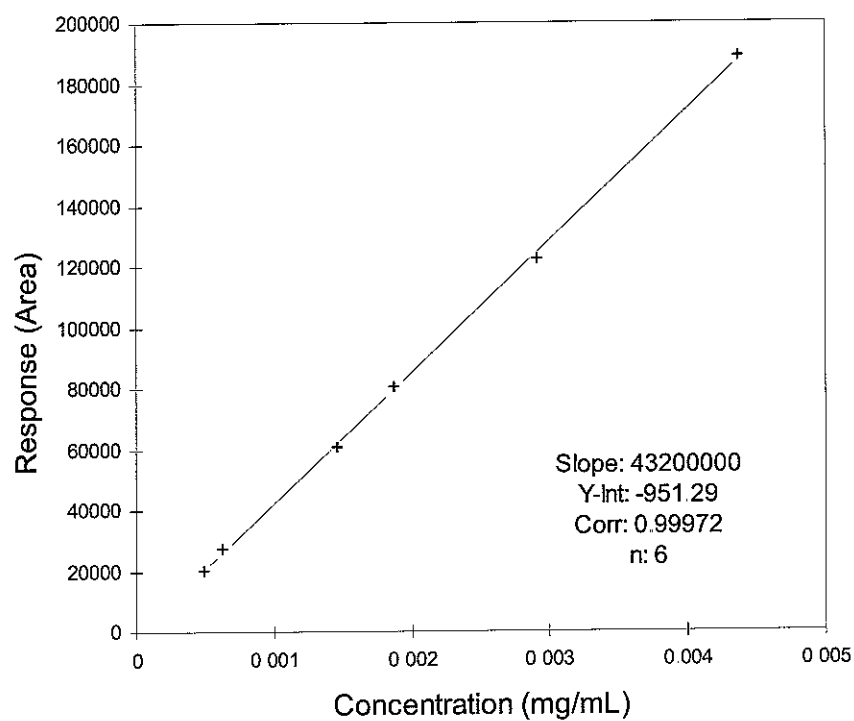
RESULTS: (Concentrations in mg/mL, ND = none detected)CALIBRATION STANDARDS

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	0.0004852	20317	0.0004923	+1.5%		5%	PASS
Cal Std B1	0.0006228	27171	0.0006510	+4.5%		5%	PASS
Cal Std A2	0.001456	60526	0.001423	-2.3%		5%	PASS
Cal Std B2	0.001868	80407	0.001883	+0.8%		5%	PASS
Cal Std A3	0.002911	122550	0.002859	-1.8%		5%	PASS
Cal Std B3	0.004360	188886	0.004394	+0.8%		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	0.002911	121790	1	0.002841	-2.4%	5.0%	PASS
Check Std A3	0.002911	121459	1	0.002834	-2.6%	5.0%	PASS
Check Std A3	0.002911	129267	1	0.003014	+3.5%	5.0%	PASS
Check Std A3	0.002911	125466	1	0.002926	+0.5%	5.0%	PASS

Project Number: TQC00013AA
Analysis of Malathion in Corn Oil
Batch ID: TQC00013AA-1-004-1



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SAMPLES

Sample Description	Prep Date	Nominal Sample Conc.	Replicate	Response Area	Total Dilution Factor	Density Corrected mg/mL	Mean mg/mL Found	% Bias
Group I Top	01/30/06	0	A	0	1029	ND		
		0	B	0	1066	ND		
Group I Mid	01/30/06	0	A	0	1044	ND		
		0	B	0	986.5	ND		
Group I Bot	01/30/06	0	A	0	1022	ND		
		0	B	0	992.4	ND		
Group II Top	01/30/06	1	A	44413	1056	1.014	1.022	+2.2%
		1	B	44455	1071	1.030		
Group II Mid	01/30/06	1	A	45934	1043	1.036	1.034	+3.4%
		1	B	46287	1031	1.031		
Group II Bot	01/30/06	1	A	45445	1041	1.023	1.013	+1.3%
		1	B	42936	1078	1.002		
Group III Top	01/30/06	5	A	44820	5262	5.101	5.063	+1.3%
		5	B	44189	5255	5.025		
Group III Mid	01/30/06	5	A	45077	5288	5.155	5.153	+3.1%
		5	B	45376	5250	5.151		
Group III Bot	01/30/06	5	A	41134	5564	4.960	5.006	+0.1%
		5	B	46035	5077	5.052		
Group IV Top	01/30/06	10	A	88879	5329	10.14	10.11	+1.1%
		10	B	87576	5374	10.08		
Group IV Mid	01/30/06	10	A	88563	5379	10.20	10.12	+1.2%
		10	B	88042	5329	10.04		
Group IV Bot	01/30/06	10	A	91877	5283	10.39	10.29	+2.9%
		10	B	87548	5429	10.18		
Group V Top	01/30/06	30	A	135009	10390	29.93	30.39	+1.3%
		30	B	137776	10500	30.85		
Group V Mid	01/30/06	30	A	131143	10460	29.26	29.69	-1.0%
		30	B	136518	10350	30.12		
Group V Bot	01/30/06	30	A	144136	9686	29.77	29.70	-1.0%
		30	B	139811	9935	29.62		

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HOMOGENEITY

Sample	Nominal	Grand		
<u>Description</u>	<u>Sample</u>	<u>Mean</u>	<u>RSD</u>	<u>%</u>
Group II	1	1.023	1.0%	2.3%
Group III	5	5.074	1.5%	1.5%
Group IV	10	10.17	1.0%	1.7%
Group V	30	29.93	1.3%	-0.2%

CONCLUSIONS: Results indicate that the formulations are within the acceptable limits of $\pm 15\%$ of theoretical concentrations. The formulations are also within the acceptable limits of $\leq 5\%$ RSD for homogeneity.

ACTIONS TAKEN: None.

Project Number: TQC00013AA

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DOSE FORMULATION ANALYSIS REPORT

Sponsor: Cheminova A/S

Study Facility: Charles River Laboratories Preclinical Services, Pennsylvania

Protocol Number: TQC00013

Analyte: Malaoxon

Analytical Facility: Charles River Laboratories Preclinical Services, Massachusetts

Batch ID: TQC00013AA-1-009-1

Sampling Criteria: Start of Study Concentration and Homogeneity Analysis

Vehicle: Corn Oil

Storage Conditions: 5±3°C

Laboratory Method: LM #MLXN00 Revision 00

Analysis Date: February 3, 2006

Notes: Samples were corrected for a corn oil density of 0.915 g/mL.

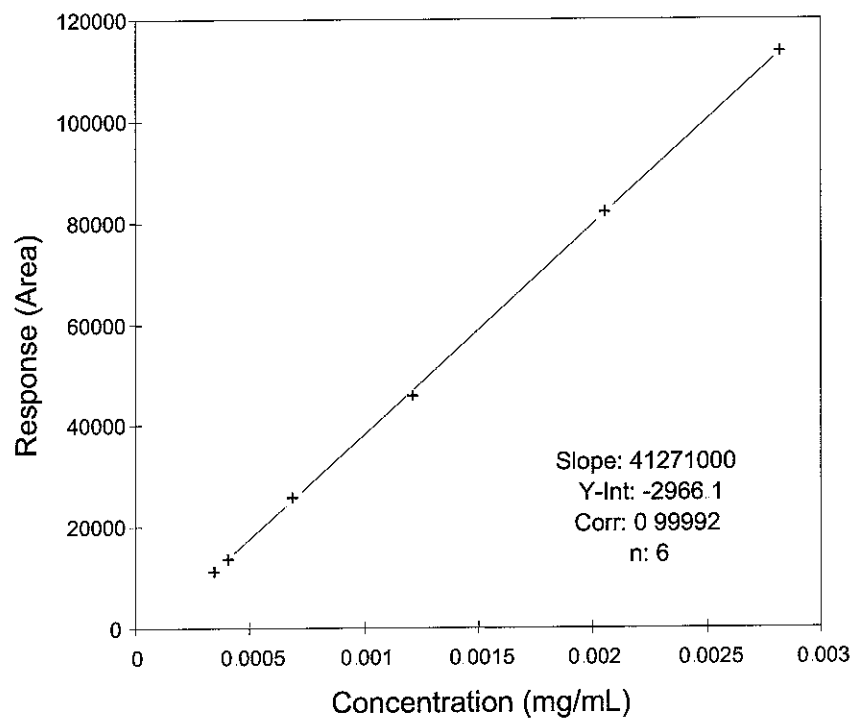
RESULTS: (Concentrations in mg/mL, ND = none detected)CALIBRATION STANDARDS

Standard Description	Nominal Conc.	Response Area	Calculated Conc.	% Bias	"X" = Exclude	Criteria Limit	Standard Pass/Fail
Cal Std A1	0.0003423	11372	0.0003474	+1.5%		5%	PASS
Cal Std B1	0.0004028	13544	0.0004000	-0.7%		5%	PASS
Cal Std A2	0.0006846	25845	0.0006981	+2.0%		5%	PASS
Cal Std B2	0.001208	45952	0.001185	-1.9%		5%	PASS
Cal Std A3	0.002054	81900	0.002056	+0.1%		5%	PASS
Cal Std B3	0.002820	113605	0.002825	+0.2%		5%	PASS

CHECK STANDARDS

Standard Description	Nominal Conc.	Response Area	Dilution Factor	Conc. Found	% Bias	Criteria Limit	Standard Pass/Fail
Check Std A3	0.002054	82013	1	0.002059	+0.2%	5.0%	PASS
Check Std A3	0.002054	84685	1	0.002124	+3.4%	5.0%	PASS
Check Std A3	0.002054	84080	1	0.002109	+2.7%	5.0%	PASS

Project Number: TQC00013AA
Analysis of Malaoxon in Corn Oil
Batch ID: TQC00013AA-1-009-1



Project Number: TQC00013AA
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SAMPLES

Sample Description	Prep Date	Nominal Sample Conc.	Replicate	Response Area	Total Dilution Factor	Density Corrected mg/mL	Mean mg/mL Found	% Bias
Group I Top	02/02/06	0	A	0	54.11	ND		
		0	B	0	53.59	ND		
Group I Mid	02/02/06	0	A	0	53.07	ND		
		0	B	0	51.98	ND		
Group I Bot	02/02/06	0	A	0	51.76	ND		
		0	B	0	51.02	ND		
Group VI Top	02/02/06	0.02	A	12414	54.63	0.01863	0.01920	-4.0%
		0.02	B	13318	54.75	0.01976		
Group VI Mid	02/02/06	0.02	A	12980	53.99	0.01909	0.01879	-6.1%
		0.02	B	12360	54.40	0.01848		
Group VI Bot	02/02/06	0.02	A	12741	54.07	0.01883	0.01898	-5.1%
		0.02	B	13127	53.60	0.01913		
Group VII Top	02/02/06	0.2	A	13353	542.7	0.1963	0.1897	-5.2%
		0.2	B	12192	544.6	0.1830		
Group VII Mid	02/02/06	0.2	A	12145	548.8	0.1839	0.1872	-6.4%
		0.2	B	12627	551.1	0.1905		
Group VII Bot	02/02/06	0.2	A	11925	560.5	0.1851	0.1822	-8.9%
		0.2	B	12427	525.0	0.1792		
Group VIII Top	02/02/06	0.5	A	40147	523.2	0.5001	0.4954	-0.9%
		0.5	B	38478	534.0	0.4906		
Group VIII Mid	02/02/06	0.5	A	37964	540.1	0.4901	0.4880	-2.4%
		0.5	B	37617	540.0	0.4859		
Group VIII Bot	02/02/06	0.5	A	39476	528.3	0.4971	0.4959	-0.8%
		0.5	B	39443	526.1	0.4947		
Group IX Top	02/02/06	0.8	A	58397	537.8	0.7316	0.7337	-8.3%
		0.8	B	59179	534.0	0.7357		
Group IX Mid	02/02/06	0.8	A	60691	524.3	0.7400	0.7338	-8.3%
		0.8	B	60903	513.8	0.7276		
Group IX Bot	02/02/06	0.8	A	61614	517.5	0.7410	0.7392	-7.6%
		0.8	B	59891	529.2	0.7374		

HOMOGENEITY

Sample	Nominal	Grand		
<u>Description</u>	<u>Sample</u>	<u>Mean</u>	<u>RSD</u>	<u>%</u>
Group VI	0.02	0.01899	1.1%	-5.1%
Group VII	0.2	0.1864	2.0%	-6.8%
Group VIII	0.5	0.4931	0.9%	-1.4%
Group IX	0.8	0.7356	0.4%	-8.1%

CONCLUSIONS: Results indicate that the formulations are within the acceptable limits of $\pm 15\%$ of theoretical concentrations. The formulations are also within the acceptable limits of $\leq 5\%$ RSD for homogeneity.

ACTIONS TAKEN: None.

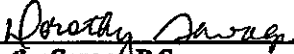
Appendix B. Laboratory Methods




LM Number:	<u>MALA00</u>	Revision Number:	<u>01</u>
Effective Date:	<u>February 24, 2006</u>	Page	<u>1</u> Of <u>9</u>

**Laboratory Method for the
Analysis of Malathion in Corn Oil Dose Formulations
by GC-FID**

Prepared By:  3/1/06
Melissa Izbicki, B.S. Date
Senior Laboratory Associate

Reviewed By:  3/1/06
Dorothy Savage, B.S. Date
Senior Scientist

Authorized By:  3/1/06
Richard D. Norlin, M.S. Date
Associate Director, Analytical Chemistry Department

LM Number:	MALA00	Revision Number:	01
Effective Date:	February 24, 2006	Page	2 Of 9

1 Purpose

The purpose of this laboratory method is to accurately determine the concentration of Malathion in Corn Oil dose formulations.

2 Scope

Analysis of Malathion in dose formulation samples with limitations as stated below.

Vehicle: Corn Oil

Sample Volume (or Amount): 1 mL

Volumetric Samples [] Gravimetric Samples [X] Both []

Concentrations Covered by Laboratory Method:

Final Injected Concentration - mg/mL

LOD	0.000033
LLOQ to ULOQ	0.0005 - 0.0045

Corresponding Concentrations - mg/mL in Corn Oil

	Standard Dilution (1 in 1000)	Additional 1 in 5 Dilution	Additional 1 in 10 Dilution
LOD	0.033	0.17	0.33
LLOQ to ULOQ	0.5 - 4.5	2.5 - 22	5.0 - 45
Valid Sample Range	0.58 - 3.8	2.9 - 19	5.8 - 38

3 Stability

Description	Concentration Range	Storage Conditions	Time Period
Process Stability	0.0005 - 0.0045 mg/mL	22 ± 5°C	TBD
Stability Period 1*	1-250 mg/mL	21°C	48 hours
Stability Period 2*	1-250 mg/mL	4°C	15 days

*Stability information provided by Sponsor under Sponsor report number CHV 066/013331. Standards should be prepared fresh for each analysis. All storage conditions are unprotected from light unless specified otherwise.

LM Number:	MALA00	Revision Number:	01
Effective Date:	February 24, 2006	Page	3 Of 9

4 Definitions/Abbreviations

GC:	Gas Chromatography
FID:	Flame Ionization Detector
ND:	None detected
N/A:	Not applicable
LOD:	Limit of Detection
LLOQ:	Lower Limit of Quantitation
ULOQ:	Upper Limit of Quantitation

5 Correction Factors

Purity:	Correct for purity as specified in protocol.
Density:	Correct for corn oil density of 0.915 g/mL.

5.1 Chemicals

Acetone, HPLC grade or equivalent
Corn Oil, Sigma, Reagent Grade or equivalent

5.2 Supplies

Volumetric flasks and pipets
Autosampler Vials, crimp top or equivalent

6 Procedure

6.1 Preparation of Reagents

Other volumes may be prepared using the same proportions. Store all reagents at room temperature and use within 14 days unless noted otherwise.

6.1.1 Diluent 1 (100% Acetone)

Transfer acetone to an appropriate container.

6.1.2 Diluent 2 (0.1% Corn Oil in Acetone)

Add 0.5 mL of corn oil to a 500 mL volumetric flask. Bring to volume with Diluent 1 and mix thoroughly.

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Effective Date:	February 24, 2006	Page	4 Of 9

6.2 Preparation of Stocks, Working Stocks, Standards and Blanks

Stocks, working stocks, standards and blanks should be stored at $5 \pm 3^\circ\text{C}$.

6.2.1 Preparation of Stocks

	Malathion weight (mg)*	Volumetric Flask (mL)	Diluent
Stock A	25 ± 1.3	100	diluent 1
Stock B	32 ± 1.6	100	diluent 1

* Record weights to the nearest 0.01 mg.

6.2.2 Preparation of Working Stocks

	Aliquot from Stock A (mL)	Aliquot from Stock B (mL)	Volumetric Flask (mL)	Diluent
Working Stock A	1	N/A	50	diluent 1
Working Stock B	N/A	1	50	diluent 1

6.2.3 Preparation of Standards

Calibration Standards	Aliquot from Working Stock A (mL)	Aliquot from Working Stock B (mL)	Corn Oil (mL)	Volumetric Flask (mL)	Diluent
A1, A2 and A3	1, 3 and 6	N/A	0.01	10	diluent 1
B1, B2 and B3	N/A	1, 3 and 7	0.01	10	diluent 1

6.2.4 Preparation of Blank

	Vehicle (mL)	Volumetric Flask (mL)	Diluent
Blank	0.01	10	diluent 1

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Effective Date:	February 24, 2006	Page	5 Of 9

6.3 Sample Preparation

Store diluted samples at $5 \pm 3^{\circ}\text{C}$.

- 6.3.1 Weigh sample vials using a balance capable of reading at least 0.001 g. Transfer each sample into individual volumetric flasks as indicated in the initial dilution table below. Triple rinse the sample vial contents with diluent 1 into the appropriate volumetric flask. Bring the volumetric flask to volume with diluent 1 and mix well. The initial dilutions may be diluted further as indicated in the tables below. Transfer an aliquot of each final dilution into individual autosampler vials. Allow sample vials to dry completely and reweigh the vials.

Initial Dilution			
Sample Concentration Ranges (mg/mL)	Sample Size (mL)	Initial Dilution Volumetric Flask Size (mL)	Diluent (Triple rinse sample vial)
0 and from 0.58 to 38	1	100	diluent 1

Second Dilution			
Sample Concentration Ranges (mg/mL)	Aliquot from Initial Dilution (mL)	Second Dilution Volumetric Flask Size (mL)	Diluent
0 and from 0.58 to 38	1	10	diluent 1

Final Dilution			
Sample Concentration Ranges (mg/mL)	Aliquot from Initial Dilution (mL)	Second Dilution Volumetric Flask Size (mL)	Diluent
0 and from 0.058 to 3.8	N/A	N/A	N/A
From 2.9 to 19	1	5	diluent 2
From 5.8 to 38	1	10	diluent 2

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Effective Date:	February 24, 2006	Page	6 Of 9

6.4 Analytical Run Sequence and Composition

6.4.1 The typical run list should follow this order

2 system checks	test injections
5 replicate injections	system suitability (B3 standard)
1 injection each	six point calibration curve
1 injection	blank
≤ 10 injections	unknown samples
1 injection	check standard (A3)

6.4.2 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.

6.5 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.

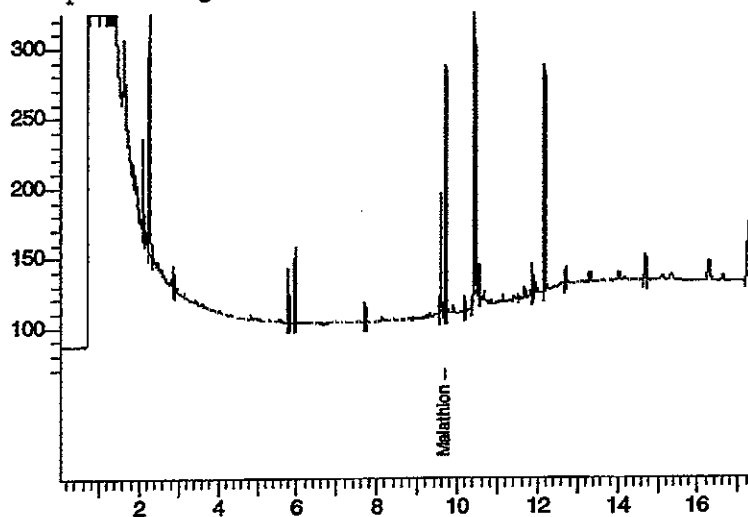
6.5.1 Instrumental

Gas Chromatograph:	Agilent, HP6890 or equivalent
Autosampler:	Agilent, HP7673 or equivalent
Carrier Gas:	Helium
Carrier Gas Flow Rate:	Approximately 5 mL/min
Hydrogen Flow to FID:	Approximately 40 mL/min
Air Flow to FID:	Approximately 450 mL/min
Helium Make-Up Flow:	Approximately 25 mL/min
Split Flow:	Approximately 21 mL/min
Septum Purge Flow:	Approximately 1.0 mL/min
Detector and Temperature:	FID at 275°C
Analytical Column:	Phenomenex, ZB-5, 30 m x 0.25 mm ID, 0.25 μm film thickness
Injection Volume:	2 μL
Oven Program:	50°C for 1 min, ramp to 280°C at 20°C/min, hold for 5 min
Injector:	Capillary
Injector Temperature:	220°C
Total Run Time:	17.5 minutes
Sampling Rate:	10 pts/s
Retention Time for Malathion:	9.7 ± 1.0 minutes
Injection Technique:	Split (split ratio 2:1)
Inlet Purge:	Purge valve on at 0.5 min

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Liner: Restek, split w/ wool, 4.0 mm id
 Rinse Solvent: Acetone
 Pre-injection Solvent Washes: 3
 Post-injection Solvent Washes: 3
 Sample Washes: 3
 Sample Pumps: 3

6.5.2 Example Chromatogram for B3 Standard



6.6 Calculations

- 6.6.1 Chromatograms will be automatically integrated and visually inspected for an acceptable integration. Manual baselines will be performed when necessary.
- 6.6.2 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.
- 6.6.3 Calculate the concentration of the six spiked standards from the actual stock concentration, in terms of milligram of Malathion per milliliter.
- 6.6.4 Compute the unweighted linear regression relating the peak areas of the standards to their respective Malathion concentrations, without blank correction.

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- 6.6.5 Compute the correlation coefficient for the standard curve.
- 6.6.6 Using the peak area of the samples and the regression equation, determine the concentration in mg/mL of Malathion. Correct for the dilution factor if necessary.
- 6.6.7 Concentrations found to be less than the LOD will be reported as <LOD. Concentrations found to be less than the LLOQ but greater than the LOD will be reported as <LLOQ. In cases, such as blank samples, where no peak is observed, the results will be reported as none detected (N.D.).
- 6.6.8 Calculate mean concentrations for replicate samples. Calculate the percent error from theoretical as: $(\text{mean concentration found} - \text{theoretical concentration}) / \text{theoretical concentration} \times 100$.
- 6.7 Acceptance Criteria
- 6.7.1 System Suitability
- The Malathion peaks in the five system suitability injections must meet the following acceptable limits: The mean tailing factor ≤ 2.0 , the relative standard deviation (%) of the peak areas $\leq 2.0\%$, and the relative standard deviation (%) of the retention time $\leq 2.0\%$. If the criteria are out of the acceptable limits, make corrections to the GC system and repeat the suitability injections.
- 6.7.2 Correlation Coefficient
- The correlation coefficient for the standard curve must not be less than 0.995. If the value does not exceed 0.995, repeat the preparation of the standard curve.
- 6.7.3 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.
- 6.7.4 Check Standards
- The back-calculated concentration for the A3 check standards must be within 5.0% of nominal theoretical concentration.
- 6.7.5 Replication of Results
- Replicate concentrations found for solution formulations must not vary by more than 10%. Acceptance is defined as: $(\text{low value} / \text{high value}) \geq 0.90$.

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6.7.6 Samples

The mean of the back-calculated concentrations for replicate samples must be within $\pm 15.0\%$ of their nominal concentration.

Refer to the Standard Operating Procedure for "Resolution and Reporting of Out of Specification Dose Formulation Analysis Results" if the percent error is greater than $\pm 15.0\%$.

7 Revision History

7.1 Method validation performed under project TQC00018AX.

7.2 From Revision 00 to Revision 01:

7.2.1 Updated stability in Section 3. Stability was provided by the Sponsor.



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**Laboratory Method for the
Analysis of Malaoxon in Corn Oil Dose Formulations
by GC-FID**

Prepared By: Erika L. Manyak 4-13-06
Erika L. Manyak
Technical Writer
Date

Reviewed By: Dorothy Savage 4/13/06
Dorothy Savage, B.S.
Senior Scientist
Date

Authorized By: Richard Norlin 4/13/06
Richard Norlin, M.S.
Associate Director, Analytical Chemistry Department
Date

LM Number:	MLXN00	Revision Number:	02
Effective Date:	April 13, 2006	Page	2 Of 9

1 Purpose

The purpose of this laboratory method is to accurately determine the concentration of Malaoxon in Corn Oil dose formulations.

2 Scope

Analysis of Malaoxon in dose formulation samples with limitations as stated below.

Vehicle: Corn Oil

Sample Volume (or Amount): 1 mL

Volumetric Samples ☐ Gravimetric Samples ☒ Both ☐

Concentrations Covered by Laboratory Method:

NOTE: Concentrations have not been corrected for purity.

Final Injected Concentration - mg/mL

LOD	0.000014
LLOQ to ULOQ	0.00034 – 0.0028

Corresponding Concentrations - mg/mL in Corn Oil

	Standard Dilution (1 in 50)	Additional 1 in 10 Dilution
LOD	0.0007	0.007
LLOQ to ULOQ	0.017 – 0.14	0.17 – 1.4
Valid Sample Range	0.020 – 0.12	0.20 – 0.80

Stability

Description	Concentration Range	Storage Conditions	Time Period
Process Stability	0.00034-0.0028	22 ± 5°C	24 hours
Stability Period 1*	0.02-250	21°C	48 hours
Stability Period 2*	0.02-250	4 °C	15 days

* Stability information provided by the Sponsor under Sponsor report number CHV 0121/053810. Standards should be prepared fresh for each analysis. All storage conditions are unprotected from light unless specified otherwise.

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3 Definitions/Abbreviations

GC:	Gas Chromatography
FID:	Flame Ionization Detector
ND:	None Detected
N/A:	Not applicable
LOD:	Limit of Detection
LLOQ:	Lower Limit of Quantitation
ULOQ:	Upper Limit of Quantitation

4 Correction Factors

Purity:	Correct for purity as specified in protocol
Density:	Correct samples for a density of 0.915 g/mL.

5 Materials

5.1 Chemicals

Acetone, HPLC Grade or equivalent
Corn Oil, Sigma, Reagent Grade or equivalent

5.2 Supplies

Volumetric flasks and pipets
Autosampler Vials, Agilent crimp top or equivalent

6 Procedure

6.1 Preparation of Reagents

Other volumes may be prepared using the same proportions. Store all reagents at room temperature and use within 14 days unless noted otherwise.

6.1.1 Diluent 1 (100% Acetone)

Transfer acetone to an appropriate container.

6.1.2 Diluent 2 (2% Corn Oil in Acetone)

Add 10 mL of corn oil to a 500 mL volumetric flask. Dilute to volume with Diluent 1 and mix thoroughly.

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6.2 Preparation of Stocks, Working Stocks, Standards and Blanks

Stocks, working stocks, standards and blanks should be stored at $5 \pm 3^\circ\text{C}$.

6.2.1 Preparation of stocks

	Malaoxon weight (mg)*	Volumetric Flask (mL)	Diluent
Stock A	34 ± 1.7	100	diluent 1
Stock B	40 ± 2.0	100	diluent 1

* Record weights to the nearest 0.01 mg.

6.2.2 Preparation of working stocks

	Aliquot from Stock A (mL)	Aliquot from Stock B (mL)	Volumetric Flask (mL)	Diluent
Working Stock A	1	N/A	100	diluent 1
Working Stock B	N/A	1	100	diluent 1

6.2.3 Preparation of standards

Calibration Standards	Aliquot from Working Stock A (mL)	Aliquot from Working Stock B (mL)	Vehicle (mL)	Volumetric Flask (mL)	Diluent
A1, A2 and A3	1, 2 and 6	N/A	0.2	10	diluent 1
B1, B2 and B3	N/A	1, 3 and 7	0.2	10	diluent 1

6.2.4 Preparation of Blank

	Vehicle (mL)	Volumetric Flask (mL)	Diluent
Blank	0.2	10	diluent 1

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6.3 Sample Preparation

Store diluted samples at $5 \pm 3^\circ\text{C}$

- 6.3.1 Weigh sample vials using a balance capable of reading at least 0.001 g. Transfer each sample into individual volumetric flasks as indicated in the initial dilution table below. Triple rinse the sample vial contents with diluent 1 into the appropriate volumetric flask. Bring the volumetric flask to volume with diluent 1 and mix well. The initial dilutions may be diluted further as indicated in the tables below. Transfer an aliquot of each final dilution into individual autosampler vials. Allow sample vials to dry completely and reweigh the vials.

Initial Dilution			
Sample Concentration Ranges (mg/mL)	Aliquot from Sample (in Duplicate) (mL)	Initial Dilution Volumetric Flask Size (mL)	Diluent
0, and from 0.020 to 0.8	1	50	diluent 1

Final Dilution			
Sample Concentration Ranges (mg/mL)	Aliquot from Initial Dilution (mL)	Final Dilution Volumetric Flask Size (mL)	Diluent
0, and from 0.020 to 0.12	N/A	N/A	N/A
From 0.2 to 0.8	1	10	diluent 2

6.4 Analytical Run Sequence and Composition

- 6.4.1 The typical run list should follow this order

2 system checks	test injections
5 replicate injections	system suitability (B3 standard)
1 injection each	six point calibration curve
1 injection	blank
≤ 10 injections	unknown samples
1 injection	check standard (A3)

- 6.4.2 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.

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6.5 Analytical Conditions

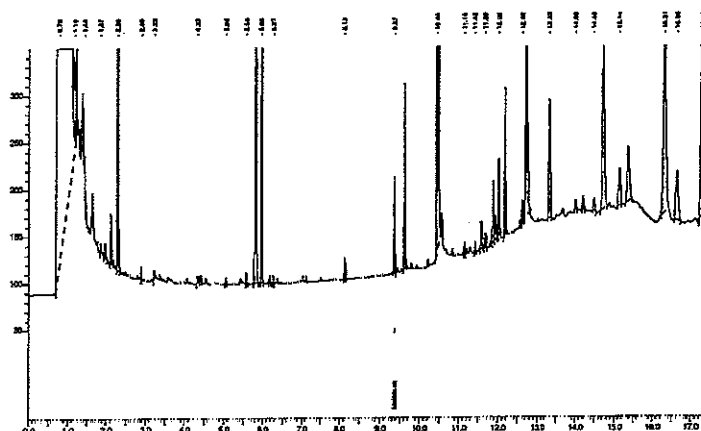
Use the GC system described below, adjusting the carrier gas flow, if necessary, to approximate the retention time listed below. Refer to the SOP for Chromatographic System Suitability.

6.5.1 Instrumental

Gas Chromatograph:	Agilent, HP6890 or equivalent
Autosampler:	Agilent, HP7673 or equivalent
Carrier Gas:	Helium
Carrier Gas Flow Rate:	Approximately 5 mL/min
Hydrogen Flow to FID:	Approximately 40 mL/min
Air Flow to FID:	Approximately 450 mL/min
Helium Make-Up Flow:	Approximately 25 mL/min
Split Flow:	Approximately 21 mL/min
Septum Purge Flow:	Approximately 1.0 mL/min
Detector and Temperature:	FID at 275°C
Analytical Column:	Phenomenex, ZB-5, 30 m x .25 mm ID, 0.25µm film thickness
Injection Volume:	2 µL
Oven Program:	50°C for 1 min, ramp to 280°C at 20°C/min, hold for 5 min
Injector:	Capillary
Injector Temperature:	220°C
Total Run Time:	17.5 minutes
Sampling Rate:	10 pts/s
Retention Time for Malaoxen:	9.4 ± 1.0 minutes
Injection Technique:	Split (split ratio 2:1)
Inlet Purge:	Purge valve on at 0.5 min
Liner:	Restek, split w/ wool, 4.0 mm id
Pre-injection Solvent Washes:	3
Post-injection Solvent Washes:	3
Sample Washes:	3
Sample Pumps:	3

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Effective Date:	April 13, 2006	Page	7 Of 9

6.5.2 Example Chromatogram for B3 Standard



6.6 Calculations

- 6.6.1 Chromatograms will be automatically integrated and visually inspected for an acceptable integration. Manual baselines will be performed when necessary.
- 6.6.2 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.
- 6.6.3 Calculate the concentration of the six spiked standards from the actual stock concentration, in terms of milligram of Malaoxon per milliliter.
- 6.6.4 Compute the unweighted linear regression relating the peak areas of the standards to their respective Malaoxon concentrations, without blank correction.
- 6.6.5 Compute the correlation coefficient for the standard curve.
- 6.6.6 Using the peak area of the samples and the regression equation, determine the concentration in mg/mL of Malaoxon. Correct for the dilution factor if necessary.
- 6.6.7 Concentrations found to be less than the LOD will be reported as <LOD. Concentrations found to be less than the LLOQ but greater than the LOD

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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).

- 6.6.8 Calculate mean concentrations for replicate samples. Calculate the percent error from theoretical as: (mean concentration found – theoretical concentration) / theoretical concentration x 100.

6.7 Acceptance Criteria

6.7.1 System Suitability

The Malaoxon peaks in the five system suitability injections must meet the following acceptable limits: The mean tailing factor ≤ 2.0 , the relative standard deviation (%) of the peak areas $\leq 2.0\%$, and the relative standard deviation (%) of the retention time $\leq 2.0\%$. If the criteria are out of the acceptable limits, make corrections to the HPLC system and repeat the suitability injections.

6.7.2 Correlation Coefficient

The correlation coefficient for the standard curve must not be less than 0.995. If the value does not exceed 0.995, repeat the preparation of the standard curve.

6.7.3 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.

6.7.4 Check Standards

The back-calculated concentration for the A3 check standards must be within 5.0% of nominal theoretical concentration.

6.7.5 Replication of Results

Replicate concentrations found for solution formulations must not vary by more than 15%. Acceptance is defined as: (low value / high value) ≥ 0.85 .

6.7.6 Samples

The mean of the back-calculated concentrations for replicate samples must be within $\pm 15.0\%$ of their nominal concentration.

Refer to the Standard Operating Procedure for "Resolution and Reporting of Out of Specification Dose Formulation Analysis Results" if the percent error is greater than $\pm 15.0\%$.

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7 Revision History

- 7.1 Method validation performed under project TQC00019AX.
- 7.2 From Revision 00 to Revision 01:
 - 7.2.1 Corrected spelling of Malaoxon throughout document.
 - 7.2.2 Added Stability in Section 2. Stability was provided by the Sponsor.
- 7.3 From Revision 01 to Revision 02:
 - 7.3.1 Section 2: Changed the Sponsor report number in the stability table footnote from "CHV 066/013331" to "CHV 0121/053810".

APPENDIX H
ENVIRONMENTAL AND HUSBANDRY REPORTS

TEMPERATURE AND RELATIVE HUMIDITY REPORT

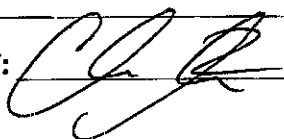
ARGUS

Temperature and Relative Humidity Report Location: Room 12 Protocol Number: TQC00013			
Range of Dates: 24-Jan-2006 13:53 to 14-Feb-2006 10:59			
Target Range: Species: Rat	Temperature 64°F to 79°F		Relative Humidity 30% to 70%
Total Number of Days: Total Number of Hours: Total Number of Data Points:	22 500.75 501		22 500.75 501
Mean (± SD):	73.8	(± 0.3)	47.9 (± 2.4)
Maximum:	74.7		55.4
Median:	73.8		47.7
Minimum:	73.0		40.8
Number of Points in Range (%):	501	(100.0)	501 (100.0)
Number of Points High (%):	0	(0.0)	0 (0.0)
Number of Points Low (%):	0	(0.0)	0 (0.0)

Report Generated: 20-Feb-2006 at 15:50

COMMENTS: _____

REVIEWED BY: _____



DATE: _____

2/20/06

FEED ANALYSES



Return to Certified Analysis Retrieval

Product Code: 5002M
 Product Desc: CERTIFIED RODENT DIET MEAL
 Lab Number: L0525308-1
 Lot Code: NOV 01 05 3A
 Entered: 11/15/2005

Exact Copy

Date 3-15-06

Assay	Analysis	Units
PROTEIN	20.7	%
FAT ACID (HYDRO.)	5.67	%
FIBER (CRUDE)	4.35	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.051	PPM
CALCIUM	0.9686	%
LEAD	0.190	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.7554	%
SELENIUM	0.336	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	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES 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

REVIEWED BY

Eve's Anderson

1/23/06

Mirex	LESS THAN 0.02	PCB	LESS THAN 0.15
AFLATOXINS	PPB Aflatoxins	LESS THAN 5	

No notes.

For additional information, please contact:

- 1) Customer Service at (314) 982-1310 -- for assay methodology
- 2) Dr. Dorrance Haught at (314) 317-5178 -- 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.

REVIEWED BY
Ellis Anderson
11/23/06

Exact Copy
Det 31586

WATER ANALYSES



Analytical Report



JOE SCHWINDT
CHARLES RIVER LAB
905 SHEEHY DRIVE
HORSHAM, PA 19044

Regarding:

JOE SCHWINDT
CHARLES RIVER LAB
905 SHEEHY DRIVE
HORSHAM, PA 19044

EXACT COPY

pg 120-06

Account No: W05899, CHARLES RIVER LAB
Project No: W05899, CHARLES RIVER LAB

P.O. No:
PWSID No:

Inv. No: 743010

Sample Number L1836573-1	Sample Description DRINKING WATER - ROOM 2 Received Temp: 34°F Iced (Y/N): Y	Samp. Date/Time/Temp 01/06/06 11:10am NA°F	Sampled by Customer Sampled
Parameter CHLORINE RESIDUAL COLIFORM-MF	Method SM 4500-CL-G SM 9222B	Result 0.60 mg/l <1 col/100ml	RLs 0.10 mg/l 1. col/100ml
		Test Date, Time, Analyst 01/06/06 11:10AM CU 01/06/06 03:49PM CSW	
Sample Number L1836573-2	Sample Description DRINKING WATER - ANALYTICAL Received Temp: 34°F Iced (Y/N): Y	Samp. Date/Time/Temp 01/06/06 11:15am NA°F	Sampled by Customer Sampled
Parameter CHLORINE RESIDUAL COLIFORM-MF	Method SM 4500-CL-G SM 9222B	Result ND mg/l <1 col/100ml	RLs 0.10 mg/l 1. col/100ml
		Test Date, Time, Analyst 01/06/06 11:15AM CU 01/06/06 03:49PM CSW	
Sample Number L1836573-3	Sample Description DRINKING WATER - FILL STATION Received Temp: 34°F Iced (Y/N): Y	Samp. Date/Time/Temp 01/06/06 11:20am NA°F	Sampled by Customer Sampled
Parameter CHLORINE RESIDUAL COLIFORM-MF	Method SM 4500-CL-G SM 9222B	Result 0.80 mg/l <1 col/100ml	RLs 0.10 mg/l 1. col/100ml
		Test Date, Time, Analyst 01/06/06 11:20AM CU 01/06/06 03:49PM CSW	
Sample Number L1836573-4	Sample Description DRINKING WATER - ROOM 38	Samp. Date/Time/Temp 01/06/06 11:25am NA°F	Sampled by Customer Sampled

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.
Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
QC certification ID's: Southampton (NELAP) PADEP 09-131, NJDEP PA166, FL E87954, Bioassay PA034, MON-NELAP labs: Wind Gap-NJ PA001, Alltest-NJ 02015, Vineland-NJ 06005; PA 68-580.
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.

*Reviewed by
J. Barone
acceptable
1/30/06*

Thomas J. Hines
Thomas J. Hines, President

EXACT COPY

ALC 2 20 06



Analytical Report



Account No: W05899, CHARLES RIVER LAB
Project No: W05899, CHARLES RIVER LAB

P.O. No:
PWSID No:

Inv. No: 743010

Received Temp: 34°F Iced (Y/N): Y

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.50 mg/l	0.10 mg/l	01/06/06 11:25AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	01/06/06 03:49PM CSW

Sample Number: L1836573-5 Sample Description: DRINKING WATER - FORMULATION
Received Temp: 34°F Iced (Y/N): Y
Samp. Date/Time/Temp: 01/06/06 11:30am NA°F
Sampled by: Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	ND mg/l	0.10 mg/l	01/06/06 11:30AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	01/06/06 03:49PM CSW

Sample Number: L1836573-6 Sample Description: DRINKING WATER - H-2
Received Temp: 34°F Iced (Y/N): Y
Samp. Date/Time/Temp: 01/06/06 11:40am NA°F
Sampled by: Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.10 mg/l	0.10 mg/l	01/06/06 11:40AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	01/06/06 03:49PM CSW

L1836573-1:

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.

L1836573-2:

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.

L1836573-3:

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.

L1836573-4:

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;
THC=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.
Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
QC certification ID's: Southampton (NELAP) PADEP 09-131, NJDEP PA166, FL E87954, Biscassay PA034, NON-NELAP Labs: Wind Gap-NJ PA001, Allentown-NJ 02015, Vineland-NJ 06005, PA 68-580.
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.

Page 2 of 3

Serial Number: 639696

Reviewed by
J. Barnett
accepted
1/30/06

Thomas J. Hines, President

1205 Industrial Blvd., P.O. Box 514, Southampton, PA 18966-0514 Phone: 215-355-3900 Fax: 215-355-7231 www.qclaboratories.com

EXACT COPY

DU 2 20 04



Analytical Report



Account No: W05899, CHARLES RIVER LAB
Project No: W05899, CHARLES RIVER LAB

P.O. No:
PWSID No:

Inv. No: 743010

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.

L1836573-5:

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.

L1836573-6:

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.
Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
QC certification ID's: Southampton (NELAP) PADEP 09-131, NJDEP PA166, FL E57954, Bioassay PA034, NCN-NELAP labs: Wind Gap-NJ PA001, Allentown-NJ 02015, Vineland-NJ 06005; PA 68-580.
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.

10 3 of 3

Serial Number: 639696

Thomas J. Hines
Thomas J. Hines, President

1205 Industrial Blvd., P.O. Box 514, Southampton, PA 18966-0514 Phone: 215-355-3900 Fax: 215-355-7231 www.qclaboratories.com



Analytical Report

EXACT COPY

AL 2:20 06



Regarding:

JOHN BARNETT SR.
CHARLES RIVER LAB
905 SHEEHY DRIVE
HORSHAM, PA 19044

JOHN BARNETT SR.
CHARLES RIVER LAB
905 SHEEHY DRIVE
HORSHAM, PA 19044

Account No: WD5899, CHARLES RIVER LAB
Project No: WD5899, CHARLES RIVER LAB

P.O. No:
PMSID No:

Inv. No: 750092

Sample Number	Sample Description	Method	Result	RLs	Test Date, Time, Analyst
L1859927-1	DRINKING WATER - ROOM 1 Received Temp: 36°F Iced (Y/N): Y	SM 4500-CL-G SM 9222B	0.80 mg/l <1 col/100ml	0.10 mg/l 1. col/100ml	02/03/06 11:41AM CU 02/03/06 04:40PM CSW
L1859927-2	DRINKING WATER - ANALYTICAL Received Temp: 36°F Iced (Y/N): Y	SM 4500-CL-G SM 9222B	ND mg/l <1 col/100ml	0.10 mg/l 1. col/100ml	02/03/06 11:46AM CU 02/03/06 04:40PM CSW
L1859927-3	DRINKING WATER - FILL STATION Received Temp: 36°F Iced (Y/N): Y	SM 4500-CL-G SM 9222B	0.20 mg/l <1 col/100ml	0.10 mg/l 1. col/100ml	02/03/06 11:50AM CU 02/03/06 04:40PM CSW
L1859927-4	DRINKING WATER - ROOM 40/41				

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.
Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
QC certification ID's: Southampton (NELAP) PADEP 09-131, NJDEP PA166, FL E87954, Bioassay PA034, NON-NELAP labs: Wind Gap-NJ PA001, Alltest-NJ 02015, Vineland-NJ 06005; PA 68-580.
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.

Page 1 of 3

Serial Number: 648581

Thomas J. Hines
Thomas J. Hines, President

Reviewed by J. Barnett 2/14/06
Room 41 is being repeated because the one colony was
thought to be from contamination 2/14/06
1205 Industrial Blvd., P.O. Box 514, Southampton, PA 18966-0514 Phone: 215-355-3900 Fax: 215-355-7231 www.qclaboratories.com



Analytical Report

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AL 2-20-06



Account No: W05899, CHARLES RIVER LAB
Project No: W05899, CHARLES RIVER LAB

P.O. No:
PWSID No:

Inv. No: 750092

Received Temp: 36°F Iced (Y/N): Y

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.70 mg/l	0.10 mg/l	02/03/06 12:00PM CU
COLIFORM-MF	SM 9222B	1 col/100ml	1. col/100ml	02/03/06 04:40PM CSW
E. COLI CONFIRM	SM 9221F	POS col/100ml	1. col/100ml	02/04/06 12:00PM CSW

Sample Number	Sample Description	Samp. Date/Time/Temp	Sampled by
L1859927-5	DRINKING WATER - FORMULATION Received Temp: 36°F Iced (Y/N): Y	02/03/06 12:05pm NA°F	Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	ND mg/l	0.10 mg/l	02/03/06 12:05PM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	02/03/06 04:40PM CSW

Sample Number	Sample Description	Samp. Date/Time/Temp	Sampled by
L1859927-6	DRINKING WATER - H-1 Received Temp: 36°F Iced (Y/N): Y	02/03/06 12:13pm NA°F	Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.20 mg/l	0.10 mg/l	02/03/06 12:13PM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	02/03/06 04:40PM CSW

L1859927-1:

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.

L1859927-2:

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.

L1859927-3:

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.

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;
TNIC=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.
Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
QC certification ID's: Southampton (NELAP) PADEP 09-131, NJDEP PA166, FL E87954, Bioassay PA034, NON-NELAP Labs: Wind Gap-NJ PA001, Alltest-NJ 02015, Vineland-NJ 06005; PA 68-580.
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.

Page 2 of 3

Serial Number: 648581

Thomas J. Hines
Thomas J. Hines, President

1205 Industrial Blvd., P.O. Box 514, Southampton, PA 18966-0514 Phone: 215-355-3900 Fax: 215-355-7231 www.qclaboratories.com



Analytical Report

INNOVATIVE
AK 2-20-06



Account No: W05899, CHARLES RIVER LAB
Project No: W05899, CHARLES RIVER LAB

P.O. No:
PMSID No:

Inv. No: 750092

L1859927-5:

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.

L1859927-6:

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.
Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
QC certification ID's: Southampton (NELAP) PADEP 09-131, NJDEP PA166, FL EB7954, Bioassay PA034. NON-NELAP labs: Wind Gap-NJ PA001, Allentown-NJ 02015, Vineland-NJ 06005; PA 68-580.
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.

Page 3 of 3

Serial Number: 648581

Thomas J. Hines
Thomas J. Hines, President

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Analysis Report



Page 1 of 3

Lancaster Laboratories Sample No. WW 4685437

Sample #1 905 Analytical Lab Grab Water Sample
Semi-Annual

Collected: 01/09/2006 13:25 by EA

Account Number: 02423

Submitted: 01/10/2006 16:15

Charles River Laboratories

Reported: 01/26/2006 at 10:44

57 Union Street

Discard: 02/03/2006

Worcester MA 01608

1-905

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
00259	Mercury	7439-97-6	< 0.00020	0.00020	ug/l	1
07035	Arsenic	7440-38-2	< 0.0200	0.0200	ug/l	1
07036	Selenium	7782-49-2	< 0.0200	0.0200	ug/l	1
07046	Barium	7440-39-3	< 0.0050	0.0050	ug/l	1
07049	Cadmium	7440-43-9	< 0.0050	0.0050	ug/l	1
07051	Chromium	7440-47-3	< 0.0150	0.0150	ug/l	1
07055	Lead	7439-92-1	< 0.0200	0.0200	ug/l	1
07066	Silver	7440-22-4	< 0.0050	0.0050	ug/l	1
07072	Zinc	7440-66-6	< 0.0200	0.0200	ug/l	1
00224	Chloride	16987-00-6	< 2.0	2.0	mg/l	5
00226	Ortho-Phosphate as P	7723-14-0	< 0.030	0.030	mg/l	1
00228	Sulfate	14808-79-8	< 5.0	5.0	mg/l	5
00368	Nitrate Nitrogen	14797-55-8	< 0.50	0.50	mg/l	5
01504	Fluoride	16984-48-8	< 0.50	0.50	mg/l	5
01505	Bromide	24959-67-9	< 2.5	2.5	mg/l	5
01506	Nitrite Nitrogen	14797-65-0	< 0.50	0.50	mg/l	5
00178	Pesticides/PCB's in Water					
00453	Gamma BHC - Lindane	58-89-9	< 0.010	0.010	ug/l	1
00454	Heptachlor	76-44-8	< 0.052	0.052	ug/l	1
00455	Aldrin	309-00-2	< 0.021	0.021	ug/l	1
00469	Dieldrin	60-57-1	< 0.031	0.031	ug/l	1
00477	Endrin	72-20-8	< 0.021	0.021	ug/l	1
00478	p,p-DDT	50-29-3	< 0.021	0.021	ug/l	1
00538	Endrin Aldehyde	7421-93-4	< 0.10	0.10	ug/l	1
01902	Alpha BHC	319-84-6	< 0.010	0.010	ug/l	1
01903	Beta BHC	319-85-7	< 0.041	0.041	ug/l	1
01904	Delta BHC	319-86-8	< 0.010	0.010	ug/l	1
01905	Heptachlor Epoxide	1024-57-3	< 0.010	0.010	ug/l	1
01906	p,p-DDD	72-55-9	< 0.021	0.021	ug/l	1
01907	p,p-DDD	72-54-8	< 0.021	0.021	ug/l	1
01908	Chlordane	57-74-9	< 0.52	0.52	ug/l	1
01909	Toxaphene	8001-35-2	< 1.0	1.0	ug/l	1
01910	Endosulfan I	959-98-8	< 0.010	0.010	ug/l	1
01911	Endosulfan II	33213-65-9	< 0.021	0.021	ug/l	1
01912	Endosulfan Sulfate	1031-07-8	< 0.021	0.021	ug/l	1
01913	PCB-1016	12674-11-2	< 0.52	0.52	ug/l	1

Lancaster Laboratories, Inc.
2425 New Holland Pike
PO Box 12425
Lancaster, PA 17405-2425
717-656-2300 Fax: 717-656-2681

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At 2 20-00

Analysis Report



Page 2 of 3

Lancaster Laboratories Sample No. WW 4685437

Sample #1 905 Analytical Lab Grab Water Sample
Semi-Annual

Collected: 01/09/2006 13:25 by EA

Account Number: 02423

Submitted: 01/10/2006 16:15
Reported: 01/26/2006 at 10:44
Discard: 02/03/2006Charles River Laboratories
57 Union Street
Worcester MA 01608

1-905

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
01914	PCB-1221	11104-28-2	< 0.52	0.52	ug/l	1
01915	PCB-1232	11141-16-5	< 0.52	0.52	ug/l	1
01916	PCB-1242	53469-21-9	< 0.52	0.52	ug/l	1
01917	PCB-1248	12673-29-6	< 0.52	0.52	ug/l	1
01918	PCB-1254	11097-69-1	< 0.52	0.52	ug/l	1
01919	PCB-1260	11096-82-5	< 0.52	0.52	ug/l	1
01856	Herbicides in Water					
01857	2,4-D	94-75-7	< 0.50	0.50	ug/l	1
01858	2,4,5-TP	93-72-1	< 0.050	0.050	ug/l	1
05286	2,4,5-T	93-75-5	< 0.050	0.050	ug/l	1
05287	Dalapon	75-99-0	< 1.2	1.2	ug/l	1
05288	Dinoseb	88-85-7	< 0.50	0.50	ug/l	1
05289	Dicamba	1918-00-9	< 0.30	0.30	ug/l	1
05290	MCPP	93-65-2	< 200.	200.	ug/l	1
05291	MCPA	94-74-6	< 1,000.	1,000.	ug/l	1
05292	2,4-DP (Dichlorprop)	120-36-5	< 0.50	0.50	ug/l	1
05293	2,4-DB	94-82-6	< 1.0	1.0	ug/l	1
04103	Pentachlorophenol	87-86-5	0.069	0.050	ug/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-037
The sample received for the nitrate/nitrite analysis was submitted
in an unpreserved container.All QC is compliant unless otherwise noted. Please refer to the Quality
Control Summary for overall QC performance data and associated samples.

Laboratory Chronicle

CAT No.	Analysis Name	Method	Trial#	Analysis Date and Time	Analyst	Dilution Factor
00259	Mercury	SW-846 7470A	1	01/19/2006 08:21	Damary Valentin	1
07035	Arsenic	SW-846 6010B	1	01/12/2006 22:11	John P Hook	1
07036	Selenium	SW-846 6010B	1	01/24/2006 07:31	Eric L Eby	1
07046	Barium	SW-846 6010B	1	01/12/2006 22:11	John P Hook	1
17049	Cadmium	SW-846 6010B	1	01/12/2006 22:11	John P Hook	1

MEMBER
ACIL

Lancaster Laboratories, Inc.
2425 New Holland Pike
PO Box 12425
Lancaster PA 17605-2425
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2216 Rev. 3/10/03

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Analysis Report



Page 3 of 3

Lancaster Laboratories Sample No. MW 4685437

Sample #1 905 Analytical Lab Grab Water Sample
Semi-Annual

Collected: 01/09/2006 13:25 by EA

Account Number: 02423

Submitted: 01/10/2006 16:15
Reported: 01/26/2006 at 10:44
Discard: 02/03/2006Charles River Laboratories
57 Union Street
Worcester MA 01608

1-905						
07051	Chromium	SW-846 6010B	1	01/12/2006 22:11	John P Hook	1
07055	Lead	SW-846 6010B	1	01/12/2006 22:11	John P Hook	1
07066	Silver	SW-846 6010B	1	01/12/2006 22:11	John P Hook	1
07072	Zinc	SW-846 6010B	1	01/12/2006 22:11	John P Hook	1
00224	Chloride	EPA 300.0	1	01/11/2006 09:48	Shannon L Phillips	5
00226	Ortho-Phosphate as P	EPA 365.3	1	01/10/2006 22:15	Daniel S Smith	1
00228	Sulfate	EPA 300.0	1	01/11/2006 09:48	Shannon L Phillips	5
00368	Nitrate Nitrogen	EPA 300.0	1	01/11/2006 09:48	Shannon L Phillips	5
01504	Fluoride	EPA 300.0	1	01/11/2006 09:48	Shannon L Phillips	5
01505	Bromide	EPA 300.0	1	01/11/2006 09:48	Shannon L Phillips	5
01506	Nitrite Nitrogen	EPA 300.0	1	01/11/2006 09:48	Shannon L Phillips	5
00178	Pesticides/PCB's in Water	EPA 608	1	01/11/2006 09:48	Shannon L Phillips	5
01856	Herbicides in Water	SW-846 8151A	1	01/14/2006 00:35	Mark E McNulty	1
00816	Water Sample Herbicide Extract	SW-846 8151A	1	01/12/2006 18:55	John W Perkins	1
			1	01/11/2006 20:55	Karen L Beyer	1
00817	Water Sample Pest Extraction	EPA 608	1	01/11/2006 17:30	Olivia I Santiago	1
01848	WW SW846 ICP Digest (tot rec)	SW-846 3005A	1	01/11/2006 20:15	James L Mertz	1
05713	WW SW846 Hg Digest	SW-846 7470A	2	01/18/2006 20:00	Nelli S Markaryan	1

Lancaster Laboratories, Inc.
2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
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Analysis Report



Page 1 of 3

Lancaster Laboratories Sample No. WW 4685438

Sample #2 905 Formulation Lab Grab Water Sample
Semi-Annual

Collected: 01/09/2006 13:00 by EA

Account Number: 02423

Submitted: 01/10/2006 16:15
Reported: 01/26/2006 at 10:44
Discard: 02/03/2006Charles River Laboratories
57 Union Street
Worcester MA 01608

2-905

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
00259	Mercury	7439-97-6	< 0.00020	0.00020	ug/l	1
07035	Arsenic	7440-38-2	< 0.0200	0.0200	ug/l	1
07036	Selenium	7782-49-2	< 0.0200	0.0200	ug/l	1
07046	Barium	7440-39-3	< 0.0050	0.0050	ug/l	1
07049	Cadmium	7440-43-9	< 0.0050	0.0050	ug/l	1
07051	Chromium	7440-47-3	< 0.0150	0.0150	ug/l	1
07055	Lead	7439-92-1	< 0.0200	0.0200	ug/l	1
07066	Silver	7440-22-4	< 0.0050	0.0050	ug/l	1
07072	Zinc	7440-66-6	< 0.0200	0.0200	ug/l	1
00224	Chloride	16887-00-6	< 2.0	2.0	ug/l	5
00226	Ortho-Phosphate as P	7723-14-0	< 0.030	0.030	ug/l	1
00228	Sulfate	14808-79-8	< 5.0	5.0	ug/l	5
00368	Nitrate Nitrogen	14797-85-8	< 0.50	0.50	ug/l	5
01504	Fluoride	16984-48-8	< 0.50	0.50	ug/l	5
01505	Bromide	24959-67-9	< 2.5	2.5	ug/l	5
01506	Nitrite Nitrogen	14797-65-0	< 0.50	0.50	ug/l	5
00178	Pesticides/PCB's in Water					
00453	Gamma BHC - Lindane	58-89-9	< 0.0095	0.0095	ug/l	1
00454	Heptachlor	76-44-8	< 0.047	0.047	ug/l	1
00455	Aldrin	309-00-2	< 0.019	0.019	ug/l	1
00469	Dieldrin	60-57-1	< 0.028	0.028	ug/l	1
00477	Endrin	72-20-8	< 0.019	0.019	ug/l	1
00478	p,p-DDT	50-29-3	< 0.019	0.019	ug/l	1
00638	Endrin Aldehyde	7421-93-4	< 0.095	0.095	ug/l	1
01902	Alpha BHC	319-84-6	< 0.0095	0.0095	ug/l	1
01903	Beta BHC	319-85-7	< 0.038	0.038	ug/l	1
01904	Delta BHC	319-86-8	< 0.0095	0.0095	ug/l	1
01905	Heptachlor Epoxide	1024-57-3	< 0.0095	0.0095	ug/l	1
01906	p,p-DDE	72-55-9	< 0.019	0.019	ug/l	1
01907	p,p-DDD	72-54-8	< 0.019	0.019	ug/l	1
01908	Chlordane	57-74-9	< 0.47	0.47	ug/l	1
01909	Toxaphene	8001-35-2	< 0.95	0.95	ug/l	1
01910	Endosulfan I	959-98-8	0.012	0.0095	ug/l	1
01911	Endosulfan II	33213-65-9	< 0.019	0.019	ug/l	1
01912	Endosulfan Sulfate	1031-07-8	< 0.019	0.019	ug/l	1
01913	PCB-1016	12674-11-2	< 0.47	0.47	ug/l	1

Lancaster Laboratories, Inc.
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PO Box 12425
Lancaster, PA 17605-2425
717-656-2300 Fax: 717-656-2681

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Analysis Report



Page 2 of 3

Lancaster Laboratories Sample No. WW 4685438

Sample #2 905 Formulation Lab Grab Water Sample
Semi-Annual

Collected: 01/09/2006 13:00 by EA

Account Number: 02423

Submitted: 01/10/2006 16:15

Charles River Laboratories

Reported: 01/26/2006 at 10:44

57 Union Street

Discard: 02/03/2006

Worcester MA 01608

2-905

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
01914	PCB-1221	11104-28-2	< 0.47	0.47	ug/l	1
01915	PCB-1232	11141-16-5	< 0.47	0.47	ug/l	1
01916	PCB-1242	53469-21-9	< 0.47	0.47	ug/l	1
01917	PCB-1248	12672-29-6	< 0.47	0.47	ug/l	1
01918	PCB-1254	11097-69-1	< 0.47	0.47	ug/l	1
01919	PCB-1260	11096-82-5	< 0.47	0.47	ug/l	1
01856	Herbicides in Water					
01857	2,4-D	94-75-7	< 0.48	0.48	ug/l	1
01858	2,4,5-TP	93-72-1	< 0.048	0.048	ug/l	1
05286	2,4,5-T	93-76-5	< 0.048	0.048	ug/l	1
05287	Dalapon	75-99-0	< 1.2	1.2	ug/l	1
05288	Dinoseb	88-85-7	< 0.48	0.48	ug/l	1
05289	Dicamba	1918-00-9	< 0.29	0.29	ug/l	1
05290	MCPP	93-65-2	< 190.	190.	ug/l	1
05291	MCPA	94-74-6	< 960.	960.	ug/l	1
05292	2,4-DP (Dichlorprop)	120-36-5	< 0.48	0.48	ug/l	1
05293	2,4-DB	94-82-6	< 0.96	0.96	ug/l	1
08103	Pentachlorophenol	87-86-5	< 0.048	0.048	ug/l	1

Commonwealth of Pennsylvania Lab Certification No. 35-037

The sample received for the nitrate/nitrite analysis was submitted
in an unpreserved containerAll QC is compliant unless otherwise noted. Please refer to the Quality
Control Summary for overall QC performance data and associated samples.

Laboratory Chronicle

CAT No.	Analysis Name	Method	Trial#	Analysis Date and Time	Analyst	Dilution Factor
00259	Mercury	SW-846 7470A	1	01/19/2006 08:22	Dawary Valentin	1
07035	Arsenic	SW-846 6010B	1	01/12/2006 22:15	John P Hook	1
07036	Selenium	SW-846 6010B	1	01/24/2006 07:35	Eric L Eby	1
07046	Barium	SW-846 6010B	1	01/12/2006 22:15	John P Hook	1
07049	Cadmium	SW-846 6010B	1	01/12/2006 22:15	John P Hook	1

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2216 Rev. 3/10/03

2007 0000

PAC 2 20 06

Analysis Report



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Lancaster Laboratories Sample No. WW 4685438

Sample #2 905 Formulation Lab Grab Water Sample
Semi-Annual

Collected: 01/09/2006 13:00 by EA

Account Number: 02423

Submitted: 01/10/2006 16:15

Reported: 01/26/2006 at 10:44

Discard: 02/03/2006

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57 Union Street
Worcester MA 01608

2-905						
07051	Chromium	SW-846 6010B	1	01/12/2006 22:15	John P Hook	1
07055	Lead	SW-846 6010B	1	01/12/2006 22:15	John P Hook	1
07066	Silver	SW-846 6010B	1	01/12/2006 22:15	John P Hook	1
07072	Zinc	SW-846 6010B	1	01/12/2006 22:15	John P Hook	1
00224	Chloride	EPA 300.0	1	01/11/2006 10:03	Shannon L Phillips	5
00226	Ortho-Phosphate as P	EPA 365.3	1	01/10/2006 22:15	Daniel S Smith	1
00228	Sulfate	EPA 300.0	1	01/11/2006 10:03	Shannon L Phillips	5
00368	Nitrate Nitrogen	EPA 300.0	1	01/11/2006 10:03	Shannon L Phillips	5
01504	Fluoride	EPA 300.0	1	01/11/2006 10:03	Shannon L Phillips	5
01505	Bromide	EPA 300.0	1	01/11/2006 10:03	Shannon L Phillips	5
01506	Nitrite Nitrogen	EPA 300.0	1	01/11/2006 10:03	Shannon L Phillips	5
00178	Pesticides/PCB's in Water	EPA 608	1	01/11/2006 10:03	Shannon L Phillips	5
01856	Herbicides in Water	SW-846 8151A	1	01/14/2006 01:56	Mark E McNulty	1
00816	Water Sample Hexbioids	SW-846 8151A	1	01/12/2006 19:57	John W Perkins	1
	Extract		1	01/11/2006 20:55	Karen L Beyer	1
00817	Water Sample Pest.	EPA 608	1	01/11/2006 17:30	Olivia I Santiago	1
	Extraction					
01848	WW SW846 ICF Digest (tot	SW-846 3005A	1	01/11/2006 20:15	James L Mertz	1
	rec)					
05713	WW SW846 Hg Digest	SW-846 7470A	2	01/18/2006 20:00	Nelli S Markaryan	1

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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 NELAC 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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BEDDING ANALYSIS



Analysis Report

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Page 1 of 2

Lancaster Laboratories Sample No. G5 4569412

Bedding Sample Lot# JUL 08 2005

Collected: 07/21/2005

Account Number: 02423

Submitted: 07/22/2005 16:15

Reported: 08/01/2005 at 16:04

Discard: 08/16/2005

Charles River Laboratories

57 Union Street

Worcester MA 01608

JUL8-

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
00159	Mercury	7439-97-6	< 0.0992	0.0992	mg/kg	1
06935	Arsenic	7440-38-2	< 2.00	2.00	mg/kg	1
06936	Selenium	7782-49-2	< 2.00	2.00	mg/kg	1
06946	Barium	7440-39-3	0.756	0.500	mg/kg	1
06949	Cadmium	7440-43-9	< 0.500	0.500	mg/kg	1
06951	Chromium	7440-47-3	< 1.50	1.50	mg/kg	1
06955	Lead	7439-92-1	< 2.00	2.00	mg/kg	1
06966	Silver	7440-22-4	< 0.500	0.500	mg/kg	1
01224	Pesticides/PCBs in Solids					
01218	Gamma BHC - Lindane	58-89-9	< 4.15	4.15	ug/kg	5
01219	Heptachlor	76-44-8	< 4.15	4.15	ug/kg	5
01220	Aldrin	309-00-2	< 4.15	4.15	ug/kg	5
01221	p,p-DDT	50-29-3	< 8.50	8.50	ug/kg	5
01222	Dieldrin	60-57-1	< 8.50	8.50	ug/kg	5
01223	Endrin	72-20-8	< 8.50	8.50	ug/kg	5
01859	Methoxychlor	72-43-5	< 41.5	41.5	ug/kg	5
01981	Alpha BHC	319-84-6	< 4.15	4.15	ug/kg	5
01982	Beta BHC	319-85-7	< 4.15	4.15	ug/kg	5
01983	Delta BHC	319-86-8	< 4.15	4.15	ug/kg	5
01984	Heptachlor Epoxide	1024-57-3	< 4.15	4.15	ug/kg	5
01985	p,p-DDE	72-55-9	< 8.50	8.50	ug/kg	5
01986	p,p-DDD	72-54-8	< 8.50	8.50	ug/kg	5
01987	Chlordane	57-74-9	< 85.0	85.0	ug/kg	5
01988	Toxaphene	8001-35-2	< 165.	165.	ug/kg	5
01989	Endosulfan I	959-98-8	< 4.15	4.15	ug/kg	5
01990	Endosulfan II	33213-65-9	< 8.50	8.50	ug/kg	5
01991	Endosulfan Sulfate	1031-07-8	< 8.50	8.50	ug/kg	5
01992	Endrin Aldehyde	7421-93-4	< 8.50	8.50	ug/kg	5
01993	PCB-1016	12674-11-2	< 85.0	85.0	ug/kg	5
01994	PCB-1221	11104-28-2	< 85.0	85.0	ug/kg	5
01995	PCB-1232	11141-16-5	< 85.0	85.0	ug/kg	5
01996	PCB-1242	53469-21-9	< 85.0	85.0	ug/kg	5
01997	PCB-1248	12672-29-6	< 165.	165.	ug/kg	5
01998	PCB-1254	11097-69-1	< 85.0	85.0	ug/kg	5
01999	PCB-1260	11096-82-5	< 165.	165.	ug/kg	5

Due to the nature of the sample extract matrix, a dilution was used for the analysis. The reporting limits were raised accordingly.

01863 Appendix IX Herbicides in Soil



Analysis Report

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Page 2 of 2

Lancaster Laboratories Sample No. G5 4569412

Bedding Sample Lot# JUL 08 2005

Collected: 07/21/2005

Account Number: 02423

Submitted: 07/22/2005 16:15
Reported: 08/01/2005 at 16:04
Discard: 08/16/2005

Charles River Laboratories
57 Union Street
Worcester MA 01608

JUL8-

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
04174	2,4-D	94-75-7	< 17.	17.	ug/kg	1
04176	2,4,5-TF	93-72-1	< 1.7	1.7	ug/kg	1
2,4,5-T was detected in the method blank above the method detection limit. Since there is no 2,4,5-T detected in this sample, this data is reported. The surrogate data is outside the QC limits due to unresolvable matrix problems evident in the sample chromatogram.						

Commonwealth of Pennsylvania Lab Certification No. 36-037

Laboratory Chronicle

CAT No.	Analysis Name	Method	Trial#	Analysis Date and Time	Analyst	Dilution Factor
00159	Mercury	SW-846 7471A	1	07/29/2005 09:30	Damary Valentin	1
06935	Arsenic	SW-846 6010B	1	07/29/2005 07:31	Joanne M Gates	1
06936	Selenium	SW-846 6010B	1	07/29/2005 07:31	Joanne M Gates	1
06946	Barium	SW-846 6010B	1	07/29/2005 07:31	Joanne M Gates	1
06949	Cadmium	SW-846 6010B	1	07/29/2005 07:31	Joanne M Gates	1
06951	Chromium	SW-846 6010B	1	07/29/2005 07:31	Joanne M Gates	1
06955	Lead	SW-846 6010B	1	07/29/2005 07:31	Joanne M Gates	1
06966	Silver	SW-846 6010B	1	07/29/2005 07:31	Joanne M Gates	1
01224	Pesticides/PCBs in Solids	SW-846 8081A/8082	1	07/28/2005 09:34	Douglas D Seitz	5
01963	Appendix IX Herbicides in Soil	SW-846 8151A	1	07/28/2005 20:30	Michele D Hamilton	1
04181	Herbicide Soil Extraction	SW-846 3550B/8151A	1	07/28/2005 02:30	David V Hershey Jr	1
05708	SW SW846 ICP Digest	SW-846 3050B	2	07/28/2005 20:20	Annamaria Stipkovits	1
05711	SW SW846 Eg Digest	SW-846 7471A modified	1	07/28/2005 22:45	Annamaria Stipkovits	1
06006	PPL Pesticide Solid Extraction	SW-846 3550B	1	07/27/2005 11:25	Lindsay K Ward	1



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

A	TIC is a possible aldol-condensation product
B	Analyte was also detected in the blank
C	Pesticide result confirmed by GC/MS
D	Compound quantitated on a diluted sample
E	Concentration exceeds the calibration range of the instrument
N	Presumptive evidence of a compound (TICs only)
P	Concentration difference between primary and confirmation columns $>25\%$
U	Compound was not detected
X,Y,Z	Defined in case narrative

Inorganic Qualifiers

B	Value is $<CDL$, but $\geq IDL$
E	Estimated due to interference
M	Duplicate injection precision not met
N	Spike sample not within control limits
S	Method of standard additions (MSA) used for calculation
U	Compound was not detected
W	Post digestion spike out of control limits
*	Duplicate analysis not within control limits
+	Correlation coefficient for MSA <0.995

Analytical test results for methods listed on the laboratories' accreditation scope meet all requirements of NELAC 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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3768.02

APPENDIX I
QUALITY ASSURANCE STATEMENT



QUALITY ASSURANCE STATEMENT

Protocol: TQC00013

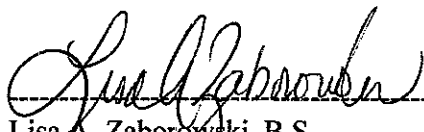
This study has been inspected by the Quality Assurance Unit to assure conformance with the Good Laboratory Practice (GLP) regulations promulgated by the U.S. Environmental Protection Agency; the Organisation for Economic Co-operation and Development; and the Japanese Ministry of Agriculture, Forestry and Fisheries. Reports were submitted in accordance with Standard Operating Procedures as follows:

QA INSPECTION DATES

Dates of Inspection	Phase(s) Inspected	Dates Findings Submitted to:	
		Study Director	Study Director Management
27 JAN 06	Protocol	27 JAN 06	27 JAN 06
30 JAN 06	Test Substance Preparation	30 JAN 06	30 JAN 06
30 JAN 06	Test Substance Administration	06 FEB 06	06 FEB 06
09 FEB 06	Sacrifice	09 FEB 06	09 FEB 06
09 FEB 06	Blood Collection	09 FEB 06	09 FEB 06
09 FEB 06	Cholinesterase Evaluation	16 FEB 06	16 FEB 06
18-19 MAR 06	Formulation Data	20 MAR 06	20 MAR 06
18-19 MAR 06	In-Life Data	22 MAR 06	22 MAR 06
18-19 MAR 06	Necropsy Data	22 MAR 06	22 MAR 06
31 MAR 06 – 03 APR 06	Cholinesterase Data	04 APR 06	04 APR 06
31 MAR 06 – 03 APR 06	Report Tables	04 APR 06	04 APR 06
04-06 APR 06	Methods	06 APR 06	06 APR 06
06 APR 06	Results	07 APR 06	07 APR 06
07 APR 06	Summary	07 APR 06	07 APR 06
18-20 APR 06 21 APR 06	Revised Report	20 APR 06 21 APR 06	20 APR 06 21 APR 06

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

 4-21-06

Lisa A. Zaborowski, B.S.
Senior Quality Assurance Auditor
Principal Auditor