

FINAL REPORT

Study Title

Oral (Gavage) Acute 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

12 March 2008
(Final Report)

Performing Laboratory

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Subcontracting Facilities

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Sponsor

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Denmark

Laboratory Project ID

Charles River Laboratories Preclinical Services Protocol Number: TQC00017

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:

March 13, 2008

Signature:



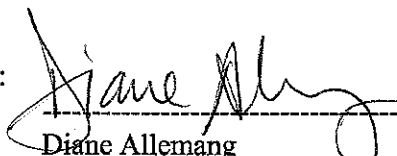
These data are the property of Cheminova A/S and as such, are considered to be confidential for all purposes other than compliance with FIFRA Section 10. Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality, which may exist under any other statute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

1. GOOD LABORATORY PRACTICE COMPLIANCE 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 (APPENDIX 2) and/or the raw data. Those deviations that occurred did not affect the quality or integrity of the study.

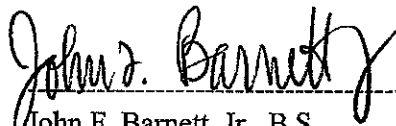
Sponsor/Submitter:


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

Date

March 13, 2008

Study Director:


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

Date

12 Mar 2008

-
- 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].

2. QUALITY ASSURANCE STATEMENT

Protocol: TQC00017

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

		<u>Date(s) Findings Submitted to:</u>	
Date(s) of Inspection	Phase(s) Inspected	Study Director	Study Director Management
24 JAN 06 22 JUN 07 12 NOV 07	Protocol	24 JAN 06 22 JUN 07 12 NOV 07	24 JAN 06 22 JUN 07 12 NOV 07
04 DEC 07	Amendment 1	04 DEC 07	04 DEC 07
10 DEC 07	Amendment 2	10 DEC 07	10 DEC 07
26 DEC 07	Amendment 3	26 DEC 07	26 DEC 07
05 FEB 08	Amendment 4	05 FEB 08	05 FEB 08
04 DEC 07	Test Substance Preparation	05 DEC 07	05 DEC 07
04 DEC 07	Test Article Administration	07 DEC 07	07 DEC 07
04 DEC 07	Blood/Brain Collection	07 DEC 07	07 DEC 07
07 DEC 07	Cholinesterase Evaluation	07 DEC 07	07 DEC 07
07 & 08 JAN 08	Formulation Data	08 JAN 08	08 JAN 08
08 JAN 08	In-Life Data	09 JAN 08	09 JAN 08

Date(s) Findings Submitted to:

Date(s) of Inspection	Phase(s) Inspected	Study Director	Study Director Management
08 JAN 08	Necropsy Data	09 JAN 08	09 JAN 08
14 JAN 08	Cholinesterase Data	23 JAN 08	23 JAN 08
09, 21-22 JAN 08	Tables	24 JAN 08	24 JAN 08
17 & 18 JAN 08	Methods	21 JAN 08	21 JAN 08
24 JAN 08	Results	24 JAN 08	24 JAN 08
25 JAN 08	Summary	25 JAN 08	25 JAN 08
11, 12 MAR 08	Revised Report	12 MAR 08	12 MAR 08

The QA Statements provided by the following Test Sites have been reviewed.

Test Site(s)	Phase	QA Statement Location
Charles River Laboratories, Preclinical Services, Massachusetts	Concentration and Homogeneity Analyses	Appendix 4

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.

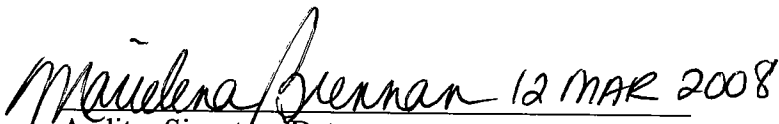

Auditor Signature/Date

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3. SUMMARY AND CONCLUSION

The objective of this study was to compare the effect of acute dosing of young pre-weanling rats with Malathion and Malaoxon on erythrocyte and brain acetyl cholinesterase activity when the pups were sampled at the time of peak effect. The study was designed to provide data for both compounds that can be compared using the Environmental Protection Agency's (EPA) benchmark dose modeling methodology.

3.1. Summary

Twenty-four litters with six male and six female pups per litter were assigned to this 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. The pups from the twelve litters assigned to the malathion dosage groups were administered one of the following dosages: 0 (Vehicle), 10, 25, 50, 100 and 150 mg/kg corresponding to Groups I through VI for malathion. The pups from the other twelve litters were assigned to the vehicle control and malaoxon dosage groups: 0 (Vehicle), 1.0, 3.5, 7.0, 10.0 and 12.5 mg/kg corresponding to Groups I through VI for malaoxon. Suspensions of the test substances in the vehicle, corn oil, or the vehicle alone were administered via oral gavage once to the pups on postnatal day 11 (PND 11^a). 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, by chance after dosage administration and prior to sacrifice. Body weights were recorded on the day of randomization and prior to dosage administration.

After dosage administration on PND 11, whole blood samples were collected from each of the pups following decapitation (without anesthesia), and the brains were removed. The samples were collected at 60 minutes postdosage for the pups assigned to both the malaoxon and malathion dosage groups as well as the pups assigned to the vehicle dosage groups. These samples were then analyzed for red blood cell (RBC) and brain cholinesterase levels.

All pups were then discarded without further evaluation.

-
- 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 postnatal day 1 (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 postnatal day 1 (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 postnatal days match the EPA guideline.

No mortality occurred in the malaoxon or malathion dosage groups.

In the pups administered malaoxon, slight whole body tremors were observed in male and female pups at 10.0 mg/kg and the male pups at 12.5 mg/kg. The male and female pups administered malathion were observed with slight or moderate whole body tremors at 100 and 150 mg/kg, and the female pups at 150 mg/kg were also observed with body jerks.

No effects on body weights were observed in either the malaoxon or malathion dosage groups.

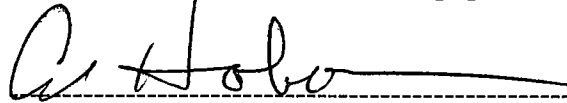
Brain cholinesterase levels in the pups administered malaoxon were reduced or statistically significantly reduced in the male pups at 7.0 mg/kg and higher and the female pups at 10 and 12.5 mg/kg compared with controls. The male and female pups administered malaoxon at dosage levels of 3.5 mg/kg and higher also had statistically significantly reduced RBC cholinesterase levels compared with controls.

Brain cholinesterase levels were statistically significantly reduced in both the male and female pups administered malathion at dosage levels of 100 and 150 mg/kg as compared with the vehicle control groups. RBC cholinesterase levels were statistically significantly reduced in both the male and female pups administered malathion at dosage levels of 50 mg/kg and higher, and also in the female pups administered 25 mg/kg compared with controls.

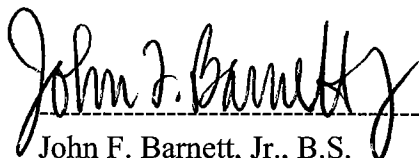
3.2. Conclusion

Acute oral administration of malaoxon to male and female pups on PND 11 resulted in slight whole body tremors at dosages of 10 and 12.5 mg/kg. Brain cholinesterase activity was reduced or statistically significantly reduced at dosage levels of 7.0 mg/kg and higher in the male pups and at 10.0 and 12.5 mg/kg in the female pups. There were also statistically significant reductions in RBC cholinesterase activity observed at dosages of 3.5 mg/kg and higher in both male and female pups.

Acute oral administration of malathion to male and female pups on PND 11 resulted in slight or moderate whole body tremors at 100 and 150 mg/kg, and body jerks at 150 mg/kg in the female pups. Brain cholinesterase activity was statistically significantly reduced at dosage levels of 100 and 150 mg/kg in the male and female pups. There was also a statistically significant reduction in RBC cholinesterase activity observed at 50, 100 and 150 mg/kg in both the male and female pups and at 25 mg/kg in female pups.

 12-MAR-08

Alan M. Hoberman, Ph.D., DABT, Fellow ATS Date
Director of Research

 12 Mar 2008

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

4. DESCRIPTION OF TEST PROCEDURES

4.1. Conduct of Study

4.1.1. Sponsor

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

4.1.2. Testing Facility

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

4.1.3. Study Number

TQC00017

4.1.4. Objective of the Study

The objective of this study was to compare the effect of acute dosing of young pre-weanling rats with Malathion and Malaoxon on erythrocyte and brain acetyl cholinesterase activity when the pups were sampled at the time of peak effect. The study was designed to provide data for both compounds that can be compared using EPA's benchmark dose modeling methodology.

4.1.5. 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. The study design was discussed with and approved by EPA as required by the Generic Data Call-In (DCI) issued in October, 2004 (GDCI-057701-24675).

4.1.6. Ownership of the Study

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

4.1.7. Study Monitor

Judith Hauswirth, Ph.D. (Toxicology Consultant)

4.1.8. Sponsor's Representative

Terri Spanogle (Senior Scientist, Cheminova, Inc., 1600 Wilson Blvd, Suite 700, Arlington, VA 22209, USA)

4.1.9. Study Director

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

4.1.10. Principal Scientist

Julian Gulbinski III, B.S., M.B.A. (Scientist)

4.1.11. Technical Performance

4.1.12. Charles River Laboratories Preclinical Services

4.1.12.1. Pennsylvania

Matthew J. Vaneman, B.S. (Director of Operations)
Daniel E. Fisher, B.S. (Study Supervisor)
Michael R. Mason, B.A. (Research Technician)
Jessica Y. Chan, B.S. (Necropsy Laboratory Technician)
Eurika L. Gray, B.S. (Formulation Laboratory Technician)

4.1.12.2. Massachusetts

Peggy Buxton, B.S. (Principal Investigator) - Concentration and homogeneity analyses

4.1.13. Report Preparation

John F. Barnett, Jr., B.S.
Emily J. Wash, B.A. (Study Coordinator)
Scott A. Johnson, B.S. (Study Coordinator)

4.1.14. Report Review

Alan M. Hoberman, Ph.D., DABT, Fellow ATS (Director of Research)

4.1.15. Date Protocol Signed

3 December 2007

4.1.16. Dates of Technical Performance

Experimental Start Date (EPA)	04 DEC 07
Experimental Start Date (OECD)	04 DEC 07
Experimental Completion Date (OECD/EPA)	18 DEC 07

4.1.16.1. Malaoxon

Rat Arrival	20 NOV 07
Dosage, Sacrifice and Cholinesterase Evaluation - (PND ^a 11)	04 DEC 07

4.1.16.2. Malathion

Rat Arrival	20 NOV 07
Dosage, Sacrifice and Cholinesterase Evaluation - (PND 11)	07 DEC 07

4.1.17. Records Maintained

The original report, raw data and reserve samples of the bulk test substances 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. Unused prepared formulations were 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.

a. PND is an abbreviation used for postnatal day.

4.2. Test Substance and Vehicle Information

Test Substance Information			
Malaoxon			
Description:	Clear liquid	Purity:	97.7%
Storage:	Frozen (at least -20°C), protected from light	Supplier:	Sponsor
Batch Number	CAS Number	Date Received	Retest Date
849-BSe-42C	1634-78-2	22 DEC 05	04 MAR 09
Malathion (synonymous with Fyfanon Technical)			
Description:	Clear liquid	Purity:	96.0%
Storage:	Frozen (at least -20°C), protected from light	Supplier:	Sponsor
Lot Number	CAS Number	Date Received	Retest Date
9010501	121-75-5	16 OCT 07	09 NOV 08

Vehicle Information						
Name	Description	Lot Number	Supplier	Date Received	Storage	Expiration Date
Corn Oil	Clear, yellow-green liquid	126K0117	Sigma Aldrich, Inc. ^a	27 AUG 07	RT	JUL 12

a. Sigma Aldrich, Inc., St. Louis, MO, USA

RT - Room Temperature

Sampling				
Bulk Test Substance Reserve				
Sample Size: 0.5 g				
Test Substance	Lot Number	Date Sampled	Storage Conditions	Date Archived
Malathion	9010501	08 JAN 08	F, PL	09 JAN 08
Malaoxon	849-BSe-42C	08 JAN 08	F, PL	09 JAN 08
Vehicle Reserve				
Sample Size: 5 mL				
Name	Date Sampled	Storage Conditions	Date Archived	
Corn oil	08 JAN 08	RT	09 JAN 08	
Concentration and Homogeneity ^a				
Sample Size: 1.0 mL				
Malathion				
Date Sampled	Date Shipped	Recipient	Shipping Conditions	Purpose
07 DEC 07	10 DEC 07	Charles River Laboratories, MA ^b	R, PL	C, H
Malaoxon				
Date Sampled	Date Shipped	Recipient	Shipping Conditions	Purpose
04 DEC 07	04 DEC 07	Charles River Laboratories, MA ^b	R, PL	C, H

- a. 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 analytical laboratory; the remaining samples were retained at the Testing Facility as backup samples and stored refrigerated (2°C to 8°C). Only concentration analyses were performed on the samples from the vehicle group.

- b. Charles River Laboratories Preclinical Services, Shrewsbury, MA, USA

RT - Room temperature

F - Frozen (at least -20°C)

R - Refrigerated (2°C to 8°C) on cold packs

PL - Protected from light

C - Concentration

H - Homogeneity

4.2.1. Special Handling Instructions

Double nitrile gloves, full faced positive pressure hood, appropriate eye protection and Tyvek[®] suit were worn during formulation preparation and dosage administration. 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.

4.2.2. 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 1.

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. A Certificate of Analysis is available in APPENDIX 3.

4.3. Test Substance Preparation and Storage Conditions

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

4.3.1. Analytical Results

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)⁴ and HLS Report CHV 066/013331 (MRID 45646401)⁵] and were not determined during the conduct of this study. Results of concentration and homogeneity analyses are available in APPENDIX 4.

4.4. Test System

4.4.1. Species/Strain

Crl:CD(SD) Rat

4.4.2. Supplier (Source)

Charles River Laboratories, Inc., Portage, MI, USA.

4.4.3. 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.)

4.4.4. 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.

4.4.5. Test System Data

Number of Dams ^a	51
Weight (g) the Day After Arrival	230 - 369
Number of Pups Assigned to Study	288
Date of Birth	24 NOV 07 - 26 NOV 07
Weight (g) at Study Assignment (PND 11)	8.2 - 24.6

4.4.6. Method of Randomization**4.4.6.1. Dams**

The female rats were naturally bred at the Supplier's facility by breeder male rats of the same source and strain. The female rats were shipped to arrive at the Testing Facility on gestation days 16 and 18 (DGs 16 and 18). The day of pup delivery was designated day 0 of lactation (postnatal).

4.4.6.2. F1 Generation Pups

On PNDs 9 or 10, twenty-four litters of approximately twelve pups per litter (six males and six females) were 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 six 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 when there was an insufficient number of male and/or female pups within the litter.

a. See APPENDIX 2 (DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY, Item 1).

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
Male Paw Tattoo 2	1.0 mg/kg
Male Paw Tattoo 3	3.5 mg/kg
Male Paw Tattoo 4	7.0 mg/kg
Male Paw Tattoo 5	10.0 mg/kg
Male Paw Tattoo 6	12.5 mg/kg
Female Paw Tattoo 7	0 (Vehicle) mg/kg
Female Paw Tattoo 8	1.0 mg/kg
Female Paw Tattoo 9	3.5 mg/kg
Female Paw Tattoo 10	7.0 mg/kg
Female Paw Tattoo 11	10.0 mg/kg
Female Paw Tattoo 12	12.5 mg/kg

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
Male Paw Tattoo 2	10 mg/kg
Male Paw Tattoo 3	25 mg/kg
Male Paw Tattoo 4	50 mg/kg
Male Paw Tattoo 5	100 mg/kg
Male Paw Tattoo 6	150 mg/kg
Female Paw Tattoo 7	0 (Vehicle) mg/kg
Female Paw Tattoo 8	10 mg/kg
Female Paw Tattoo 9	25 mg/kg
Female Paw Tattoo 10	50 mg/kg
Female Paw Tattoo 11	100 mg/kg
Female Paw Tattoo 12	150 mg/kg

4.4.7. System of Identification

4.4.7.1. Dams

Female rats were assigned temporary animal numbers at receipt. The rats were permanently identified using Monel[®] self-piercing ear tags 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.

4.4.8. Neonatal Rats

On PNDs 9 or 10, pups selected for study were individually identified by tattoo using a syringe and needle with AIMS Black Pigment #242, AIMS, Inc. (Lot No. D0407A; Expiration Date 30 April 2009), Piscataway, NJ, USA 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.

4.5. Husbandry

4.5.1. Research Facility Registration

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

4.5.2. Study Room

The study room was maintained under conditions of positive airflow relative to a hallway and independently supplied with a minimum of ten changes per hour of 100% fresh air that had been passed through 99.97% HEPA filters. Room temperature and humidity were monitored constantly throughout the study. Room temperature was targeted at 64°F to 79°F (18°C to 26°C); relative humidity was targeted at 30% to 70%^a.

4.5.3. Housing

Each dam with a litter of male and female pups was housed in a common nesting box during the postnatal period. All cage sizes and housing conditions were in compliance with the *Guide for the Care and Use of Laboratory Animals*⁽⁶⁾.

4.5.4. Light

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

4.5.5. Sanitization

Cages were changed once during the study. Bedding was changed as often as necessary to keep the rats dry and clean.

4.5.6. Diet

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

4.5.7. 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 5.

a. See APPENDIX 5 (ENVIRONMENTAL AND HUSBANDRY REPORTS).

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

4.5.8. 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 nesting boxes. Chlorine was added to the processed water as a bacteriostat.

4.5.9. 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 5.

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.

4.5.10. Nesting Material

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

4.5.11. 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 5.

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.

4.6. Methods

4.6.1. Dosage Levels, Concentrations and Dosage Volumes

4.6.1.1. Malaoxon

Dosage Group	Number of Pups per Dosage Group		Dosage ^a (mg/kg)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Assigned Neonatal Rat Numbers	
	Male	Female				Male Rats	Female Rats
I	12	12	0 (Vehicle)	0 (Vehicle)	5	5101, 5201, 5301, 5401, 5501, 5601, 5701, 5801, 5901, 6001, 6101, 6201	5107, 5207, 5307, 5407, 5507, 5607, 5707, 5807, 5907, 6007, 6107, 6207
II	12	12	1.0	0.2	5	5102, 5202, 5302, 5402, 5502, 5602, 5702, 5802, 5902, 6002, 6102, 6202	5108, 5208, 5308, 5408, 5508, 5608, 5708, 5808, 5908, 6008, 6108, 6208
III	12	12	3.5	0.7	5	5103, 5203, 5303, 5403, 5503, 5603, 5703, 5803, 5903, 6003, 6103, 6203	5109, 5209, 5309, 5409, 5509, 5609, 5709, 5809, 5909, 6009, 6109, 6209
IV	12	12	7.0	1.4	5	5104, 5204, 5304, 5404, 5504, 5604, 5704, 5804, 5904, 6004, 6104, 6204	5110, 5210, 5310, 5410, 5510, 5610, 5710, 5810, 5910, 6010, 6110, 6210
V	12	12	10.0	2.0	5	5105, 5205, 5305, 5405, 5505, 5605, 5705, 5805, 5905, 6005, 6105, 6205	5111, 5211, 5311, 5411, 5511, 5611, 5711, 5811, 5911, 6011, 6111, 6211
VI	12	12	12.5	2.5	5	5106, 5206, 5306, 5406, 5506, 5606, 5706, 5806, 5906, 6006, 6106, 6206	5112, 5212, 5312, 5412, 5512, 5612, 5712, 5812, 5912, 6012, 6112, 6212

a. The test substance was considered 100% pure for the purpose of dosage calculations.

4.6.1.2. Malathion

Dosage Group	Number of Pups per Dosage Group		Dosage ^a (mg/kg)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Assigned Neonatal Rat Numbers	
	Male	Female				Male Rats	Female Rats
I	12	12	0 (Vehicle)	0	5	6301, 6401, 6501, 6601, 6701, 6801, 6901, 7001, 7101, 7201, 7301, 7401	6307, 6407, 6507, 6607, 6707, 6807, 6907, 7007, 7107, 7207, 7307, 7407
II	12	12	10	2	5	6302, 6402, 6502, 6602, 6702, 6802, 6902, 7002, 7102, 7202, 7302, 7402	6308, 6408, 6508, 6608, 6708, 6808, 6908, 7008, 7108, 7208, 7308, 7408
III	12	12	25	5	5	6303, 6403, 6503, 6603, 6703, 6803, 6903, 7003, 7103, 7203, 7303, 7403	6309, 6409, 6509, 6609, 6709, 6809, 6909, 7009, 7109, 7209, 7309, 7409
IV	12	12	50	10	5	6304, 6404, 6504, 6604, 6704, 6804, 6904, 7004, 7104, 7204, 7304, 7404	6310, 6410, 6510, 6610, 6710, 6810, 6910, 7010, 7110, 7210, 7310, 7410
V	12	12	100	20	5	6305, 6405, 6505, 6605, 6705, 6805, 6905, 7005, 7105, 7205, 7305, 7405	6311, 6411, 6511, 6611, 6711, 6811, 6911, 7011, 7111, 7211, 7311, 7411
VI	12	12	150	30	5	6306, 6413 ^b , 6506, 6606, 6706, 6806, 6906, 7006, 7106, 7206, 7306, 7406	6312, 6412, 6512, 6612, 6712, 6812, 6912, 7012, 7112, 7212, 7312, 7412

a. The test substance was considered 100% pure for the purpose of dosage calculations.

b. Pup 6406 was excluded from study due to adverse condition and replaced with pup 6413.

4.6.2. Rationale for Dosage Selection

This study is a repeat of a recently conducted study with malathion and malaoxon by Huntingdon Life Sciences, Ltd. (HLS) (Huntingdon Life Sciences Report No. CHV 112/053810; January 17, 2006; MRID 46756705). The results of the HLS study have come under question by the EPA and thus, the study is being repeated. Dose levels tested in this study are different from the dose levels tested in the HLS study. The rationale for dosage selection for this study is as follows:

The malathion dosage levels for the pups were selected by the Sponsor based on available toxicological data from a cholinesterase study in adult and juvenile rats (Huntingdon Life Sciences Report No. CHV 067/012452) and the results of a BMD analysis of the cholinesterase data. The sampling time point of 60 minutes after dose administration was selected by the Sponsor based on the results of a time-to-peak effect study (Charles River Laboratories Study Nos. TQC00021 and TQC00032).

The malaoxon dosage levels for the pups were selected by the Sponsor based on the results of a recently conducted dosage range-finding cholinesterase study in juvenile rats (Charles River Laboratories Study No. TQC00022) and the results of a BMD analysis of the cholinesterase data. The sampling time point of 60 minutes after dose administration was selected by the Sponsor based on the results of a time-to-peak effect study (Charles River Laboratories Study Nos. TQC00021 and TQC00031).

The dosage levels and the time-to-peak effect for malathion and malaoxon in this study were agreed upon by the EPA (see the EPA approval letter dated December 6, 2007, in APPENDIX 6).

4.6.3. 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 human exposure.

4.6.4. Method and Frequency of Administration

Pups were administered the test substance and/or vehicle on PND 11. Dosages were adjusted for body weights recorded prior to administration. Dosage administration occurred at approximately the same time each day. Prepared formulations were stirred continuously during dosage administration.

4.6.5. Method of Study Performance

4.6.5.1. 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.

4.6.5.2. F1 Generation Pups

Checks for viability were made twice daily. The litters were observed for dead pups at least twice daily and were counted once daily until the day of dosage administration. Clinical observations were recorded on the day of delivery, PNDs 1, 4, and 7, on the day of randomization, prior to dosage administration and one or more times prior to sacrifice^a. Pups were weighed on PNDs 1, 4, and 7, on the day of randomization and on the day of dosage. Maternal behavior was recorded on PNDs 1, 4 and 7 and on the day of randomization, and any observed abnormal behavior was recorded daily.

On the day of dosage (PND 11), whole blood samples (approximately 0.05 to 0.60 mLs each)^b were collected (within 10 seconds) from each of the pups assigned for cholinesterase assay^(7,8). The whole blood samples were collected from each pup following decapitation. The samples were collected at 60 minutes postdosage from the male and female pups assigned to the Malathion and Malaoxon dosage groups (timing began with the gavage of the rat and ended with decapitation for blood collection). The time of each decapitation and blood collection were recorded in the raw data. All samples were labeled with the rat number^c.

After blood sample collection, the brain was carefully excised from the skull and placed in a weighing boat on ice water prior to processing for cholinesterase evaluation^d. All brains were processed and analyzed for cholinesterase levels on the day of collection. The pups were then discarded without further evaluation.

The blood and brain samples were analyzed for cholinesterase levels within 2 hours after sample collection (the time of analysis was documented in the raw data)^e.

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- a. See APPENDIX 2, item 2.
 - b. See APPENDIX 2, items 3 through 5.
 - c. See APPENDIX 2, item 6.
 - d. See APPENDIX 2, item 7.
 - e. See APPENDIX 2, items 8 and 9.

4.6.5.2.1. RBC

Approximately 0.05 to 0.60 mLs of whole blood were collected into 1.3 mL EDTA-coated (lavender-top) tubes and placed on a rotator device under an ice pack until being processed for RBC cholinesterase levels according to the Study Specific Procedure located in Attachment 5 of the protocol^a. Cholinesterase assays were conducted on the day of blood collection.

4.6.5.2.2. Brains

The brain was weighed and was recorded to three decimal places. The brains were placed into chilled 0.1% Tween 80[®] buffer and stored on ice water until being assayed for cholinesterase levels according to the Study Specific Procedure located in ATTACHMENT 5 of the protocol. Cholinesterase assays were conducted on the day of brain collection.

4.6.6. Gross Necropsy

4.6.6.1. Dams

On postpartum day 11, all dams were sacrificed by carbon dioxide asphyxiation and discarded without further evaluation.

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

One of the dams with no surviving pups was sacrificed by carbon dioxide asphyxiation after the last pup was found dead or missing (presumed cannibalized). Carcasses were discarded without further evaluation.

4.6.6.2. F1 Generation Pups

Pups that died before dosage administration were discarded without further evaluation. All pups not selected for study were sacrificed by an intraperitoneal injection of sodium pentobarbital and discarded without further evaluation.

All pups assigned to the study were sacrificed by decapitation without anesthesia on PND 11. Sacrifice was immediately followed by blood collection and brain dissection, and the pups were then discarded without further evaluation. All other pups were sacrificed by an intraperitoneal injection of sodium pentobarbital (pups \leq 11 days of age).

a. See APPENDIX 2, item 10. The procedures set forth in the Study Specific Procedure were recommended by EPA scientists in a conference call between the EPA and the Sponsor on 19 July 2007, and subsequent discussions in early August 2007.

4.6.7. Data Collection and Statistical Analyses

4.6.7.1. 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* and the *Vivarium Temperature and Relative Humidity Monitoring System*. 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 97/2000/2003/XP*), and *Softmax® Pro* (version 4.0).

4.6.7.2. 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.

5. RESULTS - MALAOXON

5.1. Analytical Results (APPENDIX 4)

Dosing suspensions of malaoxon prepared in corn oil were analyzed and were found to be acceptable and homogeneous under the conditions of the study. All prepared formulations used for dose administration were analyzed and were found to be 12.0, -2.7, -3.5, -2.5, and -3.5 of the targeted concentrations for the 0.2 mg/mL, 0.7 mg/mL, 1.4 mg/mL, 2 mg/mL and 2.5 mg/mL formulations, respectively. The homogeneity values obtained were 1.0%, 0.6%, 0.7%, 0.2% and 1.1% RSD for the 0.2 mg/mL, 0.7 mg/mL, 1.4 mg/mL, 2 mg/mL and 2.5 mg/mL formulations, respectively. The analytical report can be found in APPENDIX 4.

5.2. Mortality and Clinical Observations (Summaries - Tables A1 and A2; Individual Data - Tables A9 and A10)

All pups survived until scheduled sacrifice.

Slight whole body tremors were observed in one male pup and three female pups at 10 mg/kg and two male pups at 12.5 mg/kg. These clinical signs were observed between 33 and 57 minutes postdosage. No additional adverse clinical signs were observed in the male or female pups.

5.3. Body Weights (Summaries - Tables A3 and A4; Individual Data - Tables A11 and A12)

The body weights were generally comparable among the test substance dosage groups and the 0 (Vehicle) mg/kg dosage groups for both the male and female pups.

5.4. Brain Cholinesterase Levels (Summaries - Tables A5 and A6; Individual Data - Tables A13 and A14)

As summarized in Text Table 1, brain cholinesterase levels were reduced or statistically significantly reduced ($p \leq 0.01$) in the male pups at 7.0 mg/kg and higher and the female pups at 10 and 12.5 mg/kg when compared with the vehicle control groups. The brain cholinesterase levels were comparable with the vehicle control group values for the male pups at dosages up to and including 3.5 mg/kg and the female pups at dosages up to and including 7.0 mg/kg.

Text Table 1: Malaoxon Brain Cholinesterase Levels			
Group	Dosage (mg/kg)	Mean ChE ChE U/G \pm S.D. (n)	Percent Decrease Compared with Controls
Male Pups			
I	0 (Vehicle)	5.144 \pm 0.558 (12)	--
II	1.0	5.272 \pm 0.401 (12)	a
III	3.5	4.650 \pm 0.995 (12)	9.6%
IV	7.0	3.817 \pm 0.980 (12)**	25.8%
V	10.0	2.841 \pm 1.574 (12)**	44.8%
VI	12.5	3.953 \pm 1.191 (10)	23.2%
Female Pups			
I	0 (Vehicle)	5.144 \pm 0.542 (12)	--
II	1.0	5.068 \pm 0.618 (12)	1.5%
III	3.5	4.654 \pm 1.375 (12)	9.5%
IV	7.0	4.310 \pm 1.150 (12)	16.2%
V	10.0	2.659 \pm 1.336 (12)**	48.3%
VI	12.5	2.504 \pm 1.270 (12)**	51.3%

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

a. No inhibition occurred; value was 2.5% greater than the control value.

5.5. Red Blood Cell (RBC) Cholinesterase Levels (Summaries - Tables A7 and A8; Individual Data - Tables A15 and A16)

As summarized in Text Table 2, both male and female pups administered malaoxon at dosages of 3.5 mg/kg and higher had statistically significantly reduced ($p \leq 0.01$) RBC cholinesterase levels when compared with the vehicle control group. The values in both the male and female pups at 1.0 mg/kg were comparable to the vehicle control group values.

Text Table 2: Malaoxon RBC Cholinesterase Levels			
Group	Dosage (mg/kg)	Mean ChE ChE U/mL \pm S.D. (n)	Percent Decrease Compared with Controls
Male Pups			
I	0 (Vehicle)	2.320 \pm 0.543 (12)	--
II	1.0	1.893 \pm 0.535 (12)	18.4%
III	3.5	1.129 \pm 0.397 (12)**	51.3%
IV	7.0	0.634 \pm 0.243 (12)**	72.7%
V	10.0	0.549 \pm 0.209 (11)**	76.3%
VI	12.5	1.051 \pm 0.764 (9)**	54.7%
Female Pups			
I	0 (Vehicle)	2.127 \pm 0.486 (12)	--
II	1.0	1.770 \pm 0.382 (12)	16.8%
III	3.5	1.196 \pm 0.666 (12)**	43.8%
IV	7.0	0.733 \pm 0.272 (12)**	65.5%
V	10.0	0.553 \pm 0.322 (10)**	74.0%
VI	12.5	0.491 \pm 0.341 (11)**	76.9%

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

6. CONCLUSION - MALAOXON

Acute oral administration of malaoxon to male and female pups on PND 11 resulted in slight whole body tremors at dosages of 10 and 12.5 mg/kg. Brain cholinesterase activity was reduced or statistically significantly reduced at dosages of 7.0 mg/kg and higher in the male pups and at 10.0 and 12.5 mg/kg in the female pups. There were also statistically significant reductions in RBC cholinesterase activity observed at dosages of 3.5 mg/kg and higher in both male and female pups.

7. RESULTS - MALATHION

7.1. Analytical Results (APPENDIX 4)

Dosing suspensions of malathion prepared in corn oil were analyzed and were found to be acceptable and homogeneous under the conditions of the study. All prepared formulations used for dose administration were analyzed and were found to be -7.7%, -5.4%, 1.2%, 1.1%, and -3.4% of the targeted concentrations for the 2 mg/mL, 5 mg/mL, 10 mg/mL, 20 mg/mL and 30 mg/mL formulations, respectively. The homogeneity values obtained were 1.4%, 1.0%, 2.8%, 1.2% and 0.6% RSD for the 2 mg/mL, 5 mg/mL, 10 mg/mL, 20 mg/mL and 30 mg/mL formulations, respectively. The analytical report can be found in APPENDIX 4.

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

All pups survived until scheduled sacrifice.

Slight or moderate whole body tremors were observed in five male pups and one female pup at 100 mg/kg and five male pups and seven female pups at 150 mg/kg. Three female pups (two of which were observed with tremors) in the 150 mg/kg dosage group were also observed with body jerks. These clinical signs were observed between 41 and 57 minutes postdosage.

One female pup in the 10 mg/kg dosage group was observed with red perianal substance at 57 minutes postdosage. This adverse clinical sign was considered to be unrelated to the test substance because it occurred in only one pup and the incidence was not dosage dependent.

7.3. Body Weights (Summaries - Tables B3 and B4; Individual Data - Tables B11 and B12)

The body weights were generally comparable among the test substance dosage groups and the 0 (Vehicle) mg/kg dosage groups for both the male and female pups.

7.4. Brain Cholinesterase Levels
(Summaries - Tables B5 and B6; Individual Data - Tables B13 and B14)

As summarized in Text Table 3, brain cholinesterase levels were statistically significantly reduced ($p \leq 0.05$ to $p \leq 0.01$) in both the male and female pups administered malathion at dosages of 100 and 150 mg/kg when compared with the vehicle control groups. The brain cholinesterase levels were comparable with the vehicle control group values for both the male and female pups at dosages up to and including 50 mg/kg.

Text Table 3: Malathion Brain Cholinesterase Levels			
Group	Dosage (mg/kg)	Mean ChE ChE U/G \pm S.D. (n)	Percent Decrease Compared with Controls
Male Pups			
I	0 (Vehicle)	5.112 \pm 0.580 (12)	--
II	10	5.198 \pm 0.491 (12)	a
III	25	5.108 \pm 0.436 (12)	0.1%
IV	50	4.379 \pm 0.816 (12)	14.3%
V	100	3.327 \pm 1.152 (12)**	34.9%
VI	150	2.822 \pm 1.366 (12)**	44.8%
Female Pups			
I	0 (Vehicle)	4.982 \pm 0.446 (11)	--
II	10	5.107 \pm 0.356 (12)	b
III	25	4.861 \pm 0.485 (12)	2.4%
IV	50	4.655 \pm 0.690 (12)	6.6%
V	100	2.888 \pm 1.633 (12)*	42.0%
VI	150	1.760 \pm 1.509 (12)**	64.7%

a. No inhibition occurred; value was 1.7% greater than the control value.

b. No inhibition occurred; value was 2.5% greater than the control value.

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

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

7.5. Red Blood Cell (RBC) Cholinesterase Levels (Summaries - Tables B7 and B8; Individual Data - Tables B15 and B16)

As summarized in Text Table 4, RBC cholinesterase levels were statistically significantly reduced ($p \leq 0.01$) in both the male and female pups administered malathion at dosages of 50 mg/kg and higher as compared with the vehicle control groups. There was also a statistically significant reduction ($p \leq 0.05$) in the RBC cholinesterase levels for the female pups in the 25 mg/kg dosage group when compared with the vehicle control group.

Text Table 4: Malathion RBC Cholinesterase Levels			
Group	Dosage (mg/kg)	Mean ChE ChE U/mL \pm S.D. (n)	Percent Decrease Compared with Controls
Male Pups			
I	0 (Vehicle)	2.044 \pm 0.309 (12)	--
II	10	1.947 \pm 0.272 (12)	4.7%
III	25	1.747 \pm 0.324 (11)	14.5%
IV	50	1.246 \pm 0.497 (11)**	39.0%
V	100	1.042 \pm 0.500 (10)**	49.0%
VI	150	0.669 \pm 0.390 (11)**	67.3%
Female Pups			
I	0 (Vehicle)	2.173 \pm 0.169 (12)	--
II	10	1.944 \pm 0.287 (11)	10.5%
III	25	1.780 \pm 0.322 (11)*	18.1%
IV	50	1.550 \pm 0.398 (12)**	28.7%
V	100	0.801 \pm 0.639 (11)**	63.1%
VI	150	0.483 \pm 0.349 (10)**	77.8%

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

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

8. CONCLUSION - MALATHION

Acute oral administration of malathion to male and female pups on PND 11 resulted in slight or moderate whole body tremors at 100 and 150 mg/kg, and body jerks at 150 mg/kg in the female pups. Brain cholinesterase activity was statistically significantly reduced at dosages of 100 and 150 mg/kg in the male and female pups. There was also a statistically significant reduction in RBC cholinesterase activity observed at 50, 100 and 150 mg/kg in both the male and female pups and at 25 mg/kg in the female pups.

9. REFERENCES

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PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A1 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - MALAOXON - MALE PUPS

DOSAGE GROUP	I	II	III	IV	V	VI
TEST SUBSTANCE	VEHICLE	MALAOXON	MALAOXON	MALAOXON	MALAOXON	MALAOXON
DOSAGE (MG/KG)	0	1.0	3.5	7.0	10.0	12.5
PUPS TESTED	12	12	12	12	12	12
MORTALITY	0	0	0	0	0	0
WHOLE BODY: TREMORS a	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	2/ 2

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

a. Observed within 1 hour after dosage administration.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A2 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - MALAOXON - FEMALE PUPS

DOSAGE GROUP	I	II	III	IV	V	VI
TEST SUBSTANCE	VEHICLE	MALAOXON	MALAOXON	MALAOXON	MALAOXON	MALAOXON
DOSAGE (MG/KG)	0	1.0	3.5	7.0	10.0	12.5
PUPS TESTED	12	12	12	12	12	12
MORTALITY	0	0	0	0	0	0
WHOLE BODY: TREMORS a	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3	0/ 0

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

a. Observed within 1 hour after dosage administration.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A3 (PAGE 1): BODY WEIGHTS - SUMMARY - MALAOXON - MALE PUPS

DOSAGE GROUP		I	II	III	IV	V	VI
TEST SUBSTANCE		VEHICLE	MALAOXON	MALAOXON	MALAOXON	MALAOXON	MALAOXON
DOSAGE (MG/KG)		0	1.0	3.5	7.0	10.0	12.5
PUPS TESTED	N	12	12	12	12	12	12
BODY WEIGHT (G)							
PND 11	MEAN±S.D.	19.7 ± 1.5	19.4 ± 1.9	19.5 ± 1.8	19.6 ± 1.6	18.6 ± 1.6	19.2 ± 1.6

PND = POSTNATAL DAY

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A4 (PAGE 1): BODY WEIGHTS - SUMMARY - MALAOXON - FEMALE PUPS

DOSAGE GROUP		I	II	III	IV	V	VI
TEST SUBSTANCE		VEHICLE	MALAOXON	MALAOXON	MALAOXON	MALAOXON	MALAOXON
DOSAGE (MG/KG)		0	1.0	3.5	7.0	10.0	12.5
PUPS TESTED	N	12	12	12	12	12	12
BODY WEIGHT (G)							
PND 11	MEAN±S.D.	18.9 ± 1.8	18.4 ± 1.3	18.3 ± 1.8	18.6 ± 1.8	17.6 ± 2.1	17.5 ± 2.1
PND = POSTNATAL DAY							

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A5 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALAOXON - MALE PUPS

DOSAGE GROUP		I	II	III	IV
TEST SUBSTANCE		VEHICLE	MALAOXON	MALAOXON	MALAOXON
DOSAGE (MG/KG)		0	1.0	3.5	7.0
PUPS TESTED	N	12	12	12	12
BRAIN WEIGHT (G)	MEAN±S.D.	0.906 ± 0.093	0.910 ± 0.108	0.914 ± 0.096	0.877 ± 0.101
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	5.144 ± 0.558	5.272 ± 0.401	4.650 ± 0.995	3.817 ± 0.980**
% INHIBITION a	%		-2.5	9.6	25.8

a. Value derived from comparison to the Vehicle Group.

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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A5 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALAOXON - MALE PUPS

DOSAGE GROUP		V	VI
TEST SUBSTANCE		MALAOXON	MALAOXON
DOSAGE (MG/KG)		10.0	12.5
PUPS TESTED	N	12	12
INCLUDED IN ANALYSES	N	12	10a
BRAIN WEIGHT (G)	MEAN±S.D.	0.835 ± 0.142	0.880 ± 0.128
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.841 ± 1.574**	3.953 ± 1.191
% INHIBITION b	%	44.8	23.2

- a. Excludes values for sample results that did not meet the acceptability criterion.
b. Value derived from comparison to the Vehicle Group.
** Statistically significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A6 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALAOXON - FEMALE PUPS

DOSAGE GROUP		I	II	III	IV
TEST SUBSTANCE		VEHICLE	MALAOXON	MALAOXON	MALAOXON
DOSAGE (MG/KG)		0	1.0	3.5	7.0
PUPS TESTED	N	12	12	12	12
BRAIN WEIGHT (G)	MEAN±S.D.	0.949 ± 0.055	0.940 ± 0.054	0.934 ± 0.063	0.949 ± 0.063
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	5.144 ± 0.542	5.068 ± 0.618	4.654 ± 1.375	4.310 ± 1.150
% INHIBITION a	%		1.5	9.5	16.2

a. Value derived from comparison to the Vehicle Group.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A6 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALAOXON - FEMALE PUPS

DOSAGE GROUP		V	VI
TEST SUBSTANCE		MALAOXON	MALAOXON
DOSAGE (MG/KG)		10.0	12.5
PUPS TESTED	N	12	12
BRAIN WEIGHT (G)	MEAN±S.D.	0.914 ± 0.074	0.917 ± 0.073
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.659 ± 1.336**	2.504 ± 1.270**
% INHIBITION a	%	48.3	51.3

a. Value derived from comparison to the Vehicle Group.
 ** Statistically significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A7 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - MALAOXON - MALE PUPS

DOSAGE GROUP		I	II	III	IV
TEST SUBSTANCE		VEHICLE	MALAOXON	MALAOXON	MALAOXON
DOSAGE (MG/KG)		0	1.0	3.5	7.0
PUPS TESTED	N	12	12	12	12
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.320 ± 0.543	1.893 ± 0.535	1.129 ± 0.397**	0.634 ± 0.243**
% INHIBITION a	%		18.4	51.3	72.7

a. Value derived from comparison to the Vehicle Group.

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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A7 (PAGE 2): RBC CHOLINESTERASE LEVELS - SUMMARY - MALAOXON - MALE PUPS

DOSAGE GROUP		V	VI
TEST SUBSTANCE		MALAOXON	MALAOXON
DOSAGE (MG/KG)		10.0	12.5
PUPS TESTED	N	12	12
INCLUDED IN ANALYSES	N	11a	9a
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	0.549 ± 0.209**	1.051 ± 0.764**
% INHIBITION b	%	76.3	54.7

- a. Excludes values for sample results that did not meet the acceptability criterion.
b. Value derived from comparison to the Vehicle Group.
** Statistically significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A8 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - MALAOXON - FEMALE PUPS

DOSAGE GROUP		I	II	III	IV
TEST SUBSTANCE		VEHICLE	MALAOXON	MALAOXON	MALAOXON
DOSAGE (MG/KG)		0	1.0	3.5	7.0
PUPS TESTED	N	12	12	12	12
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.127 ± 0.486	1.770 ± 0.382	1.196 ± 0.666**	0.733 ± 0.272**
% INHIBITION a	%		16.8	43.8	65.5

a. Value derived from comparison to the Vehicle Group.

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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A8 (PAGE 2): RBC CHOLINESTERASE LEVELS - SUMMARY - MALAOXON - FEMALE PUPS

DOSAGE GROUP		V	VI
TEST SUBSTANCE		MALAOXON	MALAOXON
DOSAGE (MG/KG)		10.0	12.5
PUPS TESTED	N	12	12
INCLUDED IN ANALYSES	N	10a	11a
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	0.553 ± 0.322**	0.491 ± 0.341**
% INHIBITION b	%	74.0	76.9

- a. Excludes values for sample results that did not meet the acceptability criterion.
b. Value derived from comparison to the Vehicle Group.
** Statistically significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A9 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

PUP #	DESCRIPTION
DOSAGE GROUP I	VEHICLE 0 MG/KG
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 II	MALAOXON 1.0 MG/KG
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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A9 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

PUP #	DESCRIPTION
DOSAGE GROUP III	MALAOXON 3.5 MG/KG
5103	NO ADVERSE FINDINGS
5203	NO ADVERSE FINDINGS
5303	NO ADVERSE FINDINGS
5403	NO ADVERSE FINDINGS
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 IV	MALAOXON 7.0 MG/KG
5104	NO ADVERSE FINDINGS
5204	NO ADVERSE FINDINGS
5304	NO ADVERSE FINDINGS
5404	NO ADVERSE FINDINGS
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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A9 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

PUP #	DESCRIPTION	
DOSAGE GROUP V	MALAOXON	10.0 MG/KG
5105	NO ADVERSE FINDINGS	
5205	NO ADVERSE FINDINGS	
5305	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (33 MINUTES AFTER DOSAGE ADMINISTRATION)
5405	NO ADVERSE FINDINGS	
5505	NO ADVERSE FINDINGS	
5605	NO ADVERSE FINDINGS	
5705	NO ADVERSE FINDINGS	
5805	NO ADVERSE FINDINGS	
5905	NO ADVERSE FINDINGS	
6005	NO ADVERSE FINDINGS	
6105	NO ADVERSE FINDINGS	
6205	NO ADVERSE FINDINGS	
DOSAGE GROUP VI	MALAOXON	12.5 MG/KG
5106	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (57 MINUTES AFTER DOSAGE ADMINISTRATION)
5206	NO ADVERSE FINDINGS	
5306	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (52 MINUTES AFTER DOSAGE ADMINISTRATION)
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	

PND = POSTNATAL DAY

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A10 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

PUP #	DESCRIPTION
DOSAGE GROUP I	VEHICLE 0 MG/KG
5107	NO ADVERSE FINDINGS
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	NO ADVERSE FINDINGS
6107	NO ADVERSE FINDINGS
6207	NO ADVERSE FINDINGS
DOSAGE GROUP II	MALAOXON 1.0 MG/KG
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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A10 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

PUP #	DESCRIPTION
DOSAGE GROUP III	MALAOXON 3.5 MG/KG
5109	NO ADVERSE FINDINGS
5209	NO ADVERSE FINDINGS
5309	NO ADVERSE FINDINGS
5409	NO ADVERSE FINDINGS
5509	NO ADVERSE FINDINGS
5609	NO ADVERSE FINDINGS
5709	NO ADVERSE FINDINGS
5809	NO ADVERSE FINDINGS
5909	NO ADVERSE FINDINGS
6009	NO ADVERSE FINDINGS
6109	NO ADVERSE FINDINGS
6209	NO ADVERSE FINDINGS
DOSAGE GROUP IV	MALAOXON 7.0 MG/KG
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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A10 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

PUP #	DESCRIPTION	
DOSAGE GROUP V	MALAOXON	10.0 MG/KG
5111	NO ADVERSE FINDINGS	
5211	NO ADVERSE FINDINGS	
5311	NO ADVERSE FINDINGS	
5411	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (35 MINUTES AFTER DOSAGE ADMINISTRATION)
5511	NO ADVERSE FINDINGS	
5611	PND(11)	WHOLE BODY: TREMORS (54 MINUTES AFTER DOSAGE ADMINISTRATION)
5711	NO ADVERSE FINDINGS	
5811	NO ADVERSE FINDINGS	
5911	NO ADVERSE FINDINGS	
6011	NO ADVERSE FINDINGS	
6111	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (56 MINUTES AFTER DOSAGE ADMINISTRATION)
6211	NO ADVERSE FINDINGS	
DOSAGE GROUP VI	MALAOXON	12.5 MG/KG
5112	NO ADVERSE FINDINGS	
5212	NO ADVERSE FINDINGS	
5312	NO ADVERSE FINDINGS	
5412	NO ADVERSE FINDINGS	
5512	NO ADVERSE FINDINGS	
5612	NO ADVERSE FINDINGS	
5712	NO ADVERSE FINDINGS	
5812	NO ADVERSE FINDINGS	
5912	NO ADVERSE FINDINGS	
6012	NO ADVERSE FINDINGS	
6112	NO ADVERSE FINDINGS	
6212	NO ADVERSE FINDINGS	

PND = POSTNATAL DAY

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A11 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

PND 11			
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
5101	19.0		
5201	19.2		
5301	19.5		
5401	18.6		
5501	16.5		
5601	21.1		
5701	21.0		
5801	21.7		
5901	19.6		
6001	21.3		
6101	20.5		
6201	18.0		
PUP #	DOSAGE GROUP II	MALAOXON	1.0 MG/KG
5102	18.5		
5202	17.5		
5302	22.0		
5402	19.0		
5502	17.8		
5602	20.3		
5702	19.3		
5802	22.9		
5902	19.4		
6002	19.9		
6102	19.9		
6202	16.1		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A11 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

PND 11			
PUP #	DOSAGE GROUP III	MALAOXON	3.5 MG/KG
5103	17.7		
5203	18.8		
5303	21.2		
5403	19.8		
5503	16.8		
5603	21.1		
5703	17.9		
5803	21.4		
5903	20.7		
6003	21.1		
6103	20.7		
6203	16.8		
PUP #	DOSAGE GROUP IV	MALAOXON	7.0 MG/KG
5104	18.5		
5204	19.9		
5304	20.8		
5404	19.8		
5504	18.4		
5604	20.8		
5704	20.3		
5804	21.9		
5904	19.6		
6004	19.7		
6104	20.5		
6204	15.6		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A11 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

PND 11			
PUP #	DOSAGE GROUP V	MALAOXON	10.0 MG/KG
5105	18.0		
5205	20.2		
5305	19.9		
5405	19.7		
5505	16.1		
5605	19.5		
5705	19.9		
5805	18.9		
5905	15.8		
6005	18.9		
6105	19.6		
6205	16.9		
PUP #	DOSAGE GROUP VI	MALAOXON	12.5 MG/KG
5106	19.0		
5206	19.2		
5306	19.2		
5406	19.8		
5506	16.8		
5606	19.8		
5706	19.5		
5806	21.2		
5906	18.6		
6006	21.9		
6106	19.6		
6206	16.0		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A12 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

PND 11			
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
5107	18.1		
5207	18.5		
5307	20.0		
5407	18.9		
5507	16.3		
5607	19.8		
5707	17.5		
5807	19.5		
5907	18.6		
6007	19.7		
6107	23.1		
6207	16.6		
PUP #	DOSAGE GROUP II	MALAOXON	1.0 MG/KG
5108	18.8		
5208	18.3		
5308	19.8		
5408	20.1		
5508	16.0		
5608	19.2		
5708	17.5		
5808	18.7		
5908	17.9		
6008	18.8		
6108	19.6		
6208	16.4		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A12 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

PND 11			
PUP #	DOSAGE GROUP III	MALAOXON	3.5 MG/KG
5109	16.9		
5209	18.7		
5309	19.0		
5409	17.8		
5509	15.6		
5609	19.7		
5709	18.9		
5809	21.2		
5909	19.1		
6009	19.0		
6109	19.1		
6209	14.6		
PUP #	DOSAGE GROUP IV	MALAOXON	7.0 MG/KG
5110	16.8		
5210	19.2		
5310	19.1		
5410	17.7		
5510	17.4		
5610	18.4		
5710	17.8		
5810	21.5		
5910	18.8		
6010	20.4		
6110	20.9		
6210	15.1		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A12 (PAGE 3): BODY WEIGHTS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

PND 11			
PUP #	DOSAGE GROUP V	MALAOXON	10.0 MG/KG
5111	18.3		
5211	15.7		
5311	19.3		
5411	17.9		
5511	15.2		
5611	19.7		
5711	18.7		
5811	15.7		
5911	18.2		
6011	19.2		
6111	20.0		
6211	13.5		
PUP #	DOSAGE GROUP VI	MALAOXON	12.5 MG/KG
5112	16.6		
5212	19.3		
5312	19.7		
5412	17.2		
5512	14.1		
5612	20.5		
5712	17.6		
5812	16.8		
5912	17.9		
6012	19.7		
6112	17.5		
6212	13.6		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A13 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
5101	0.998	4.540	
	0.998	5.469a	
5201	0.945	5.614	
	0.945	4.997a	
5301	0.850	5.413	
5401	0.942	4.882	
5501	0.886	4.965	
5601	1.009	5.682	
5701	0.902	4.537	
	0.902	4.614a	
5801	0.685	4.185	
	0.685	5.200a	
5901	0.889	5.213	
	0.889	5.077a	
6001	0.961	6.088	
6101	0.996	5.566	
6201	0.808	5.037	
PUP #	DOSAGE GROUP II	MALAOXON	1.0 MG/KG
5102	0.835	4.341	
5202	0.908	5.771	
5302	1.004	X	DNR
	1.004	5.130	
5402	0.954	5.120	
5502	0.917	5.133	
5602	0.967	5.020	
5702	0.974	5.228	
5802	0.877	X	DNR
	0.877	5.592	
5902	0.959	5.490	
6002	0.945	5.512	
6102	0.978	5.816	
6202	0.602	5.112	

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

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

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A13 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP III	MALAOXON	3.5 MG/KG
5103	0.947	1.866	
5203	0.940	5.060	
5303	0.965	3.758	
5403	0.969	4.558	
5503	0.848	5.376	
5603	0.944	5.204	
5703	0.930	4.736	
5803	0.928	4.813	
5903	0.715	5.594	
6003	1.088	4.686	
6103	0.917	5.239	
6203	0.777	4.915	
PUP #	DOSAGE GROUP IV	MALAOXON	7.0 MG/KG
5104	0.894	3.650	
5204	0.882	5.227	
5304	0.819	X	LOW
	0.819	X	DNR
	0.819	X	DNR
	0.819	1.764	
5404	0.978	3.205	
5504	0.914	3.523	
5604	0.959	3.570	
5704	0.917	4.156	
5804	0.912	4.530	
5904	0.963	3.691	
	0.963	4.061a	
6004	0.893	4.947	
6104	0.782	2.798	
6204	0.610	4.748	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A13 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP V	MALAOXON	10.0 MG/KG
5105	0.892	1.848	
5205	0.993	2.924	
5305	0.911	X	DNR
	0.911	1.005	LOW a
	0.911	X	LOW
5405	1.002	0.801	LOW a
	1.002	0.725b	
	1.002	1.717b	
	1.002	1.232b	
5505	0.875	3.322	
5605	0.912	1.031	LOW a
5705	0.991	2.927	
5805	0.789	2.312	
5905	0.677	5.729	
	0.677	5.515b	
6005	0.636	4.549	
6105	0.732	4.760	
6205	0.611	2.882	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Extrapolated data.

b. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A13 (PAGE 4): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP VI	MALAOXON	12.5 MG/KG
5106	0.847	X	LOW a
	0.847	X	LOW a
	0.847	X	LOW a
5206	0.938	2.495	
5306	0.955	4.073	
	0.955	5.107b	
5406	0.970	4.732	
	0.970	5.408b	
5506	0.841	X	LOW a
	0.841	X	LOW a
	0.841	X	LOW a
	0.841	X	LOW a
5606	0.988	4.409	
5706	0.886	2.887	
5806	0.934	3.143	
5906	0.647	5.598	
	0.647	5.609b	
6006	0.928	5.002	
6106	0.910	5.006	
6206	0.639	2.189	

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.

a. Below quantitative level.

b. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A14 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
	DOSAGE GROUP I	VEHICLE	0 MG/KG
5107	0.922	4.306	
	0.922	5.403a	
5207	0.966	6.346	
	0.966	5.601a	
5307	0.987	4.300	
	0.987	X	DNR
	0.987	X	DNR
5407	0.972	4.947	
5507	0.858	5.567	
5607	1.004	5.020	
5707	0.912	5.165	
5807	0.954	5.320	
5907	1.003	5.288	
6007	0.988	5.347	
6107	0.984	5.173	
6207	0.841	4.945	
PUP #	DOSAGE GROUP II	MALAOXON	1.0 MG/KG
5108	0.906	3.901	
5208	0.955	5.997	
5308	0.962	4.132	
5408	1.029	5.028	
5508	0.874	5.128	
5608	0.996	4.752	
5708	0.909	4.988	
5808	0.918	5.488	
5908	0.947	5.830	
6008	0.976	5.274	
6108	0.969	5.444	
6208	0.834	4.853	

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

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

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A14 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP III	MALAOXON	3.5 MG/KG
5109	0.902	3.520	
5209	0.922	6.199	
5309	0.948	X	LOW
	0.948	X	LOW
	0.948	0.731	
5409	0.954	5.036	
5509	0.865	5.066	
5609	0.972	4.730	
5709	0.960	5.267	
5809	0.944	5.061	
5909	1.012	5.054	
6009	0.992	4.944	
6109	0.956	5.422	
6209	0.777	4.819	
PUP #	DOSAGE GROUP IV	MALAOXON	7.0 MG/KG
5110	0.859	3.158	
5210	0.966	5.960	
5310	0.999	4.385	
5410	0.953	X	DNR
	0.953	X	LOW
	0.953	X	DNR
	0.953	1.330	
5510	0.932	4.277	
5610	0.985	4.144	
5710	0.998	4.782	
5810	0.966	5.137	
5910	0.956	4.940	
6010	0.989	4.782	
6110	0.993	4.299	
6210	0.791	4.521	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A14 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP V	MALAOXON	10.0 MG/KG
5111	0.885	X	DNR
	0.885	X	LOW
	0.885	0.646	
5211	0.792	2.841	
5311	0.909	X	LOW
	0.909	X	LOW
	0.909	0.813	
5411	0.957	2.284	
5511	0.860	2.018	
5611	1.013	1.815	
5711	0.966	5.059	
5811	0.925	3.630	
5911	0.991	4.175	
6011	0.920	X	LOW
	0.920	X	LOW
	0.920	2.442	
6111	0.969	2.236	
6211	0.777	3.945	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A14 (PAGE 4): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP VI	MALAOXON	12.5 MG/KG
5112	0.862	1.398	
5212	0.938	3.284	
5312	0.998	4.211	
	0.998	5.253a	
5412	0.946	X	LOW
	0.946	0.844	
5512	0.842	X	DNR
	0.842	X	DNR
	0.842	0.727	LOW b
5612	0.997	2.626	
5712	0.936	3.293	
5812	0.962	2.171	
5912	0.966	1.379	
6012	0.933	X	LOW
	0.933	X	LOW
	0.933	4.251	
6112	0.877	3.839	
6212	0.747	2.028	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

b. Extrapolated data.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A15 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
5101	2.019	a	
5201	2.581		
5301	1.813		
5401	3.015		
	3.205b		
5501	2.378		
5601	1.444	c	
5701	X	DNR	
	1.512		
5801	2.335		
5901	2.489		
6001	X	DNR	
	X	HIGH	
	3.200		
6101	2.392		
6201	X	DNR	
	2.660		

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

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

HIGH = REPORTED VALUE IS ABOVE THE HIGHEST STANDARD.

- Values for pup 5101 first run (1.431 units/mL) and second run (2.607 units/mL) were not within 25% acceptability criteria of each other; Values averaged.
- Repeat analysis performed; value excluded from summarization and statistical analyses.
- Values for pup 5601 first run (1.833 units/mL) and second run (1.054 units/mL) were not within 25% acceptability criteria of each other; Values averaged.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A15 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP II	MALAOXON
		1.0 MG/KG
5102	1.723	
5202	2.067	
5302	1.480	
5402	1.999	
5502	1.816	
5602	X	DNR
	2.102	
5702	0.658	a
5802	1.546	
5902	1.890	
6002	2.397	
6102	2.228	
6202	2.811	
PUP #	DOSAGE GROUP III	MALAOXON
		3.5 MG/KG
5103	X	LOW
	0.427	
5203	0.966	
5303	0.477	
5403	1.051	
5503	1.438	
5603	1.360	
5703	1.048	
5803	1.001	
5903	1.497	
6003	1.063	
6103	1.663	
6203	X	DNR
	1.559	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Values for pup 5702 first run (0.542 units/mL) and second run (0.774 units/mL) were not within 25% acceptability criteria of each other; Values averaged.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A15 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP IV	MALAOXON 7.0 MG/KG
5104	1.104	
5204	0.636	
5304	0.213	LOW a
	X	DNR
	X	DNR
5404	X	LOW
	X	DNR
	0.577	
5504	0.378	
5604	0.367	
5704	X	DNR
	0.640	
5804	0.684	
5904	0.720	b
6004	0.887	
6104	0.584	
6204	X	DNR
	0.817	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Extrapolated data.

b. Values for pup 5904 first run (0.558 units/mL) and second run (0.882 units/mL) were not within 25% acceptability criteria of each other; Values averaged.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A15 (PAGE 4): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP V	MALAOXON	10.0 MG/KG
5105	X	DNR	
	X	DNR	
	0.558		
5205	X	LOW	
	0.574		
5305	X	DNR	
	X	DNR	
	0.620		
5405	X	DNR	
	X	LOW	
	0.375		
5505	X	DNR	
	X	DNR	
	X	DNR	
5605	0.242	LOW a	
	X	DNR	
	X	DNR	
5705	X	DNR	
	0.419		
5805	X	LOW	
	X	DNR	
	0.531		
5905	1.002		
6005	0.793		
6105	0.533		
6205	X	DNR	
	0.394		

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Extrapolated data.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A15 (PAGE 5): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - MALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP VI	MALAOXON	12.5 MG/KG
5106	X	DNR	
	X	LOW a	
	X	DNR	
5206	X	DNR	
	X	DNR	
	X	DNR	
	X	DNR	
5306	1.526		
5406	2.304		
	2.380b		
5506	X	LOW c	
	X	LOW c	
	X	LOW c	
5606	X	DNR	
	0.971		
	1.219b		
5706	X	LOW	
	0.363		
5806	X	DNR	
	X	DNR	
	0.035	LOW d	
5906	1.792		
	1.621b		
6006	0.525		
6106	1.485		
6206	0.460		

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Negative values can not be extrapolated.

b. Repeat analysis performed; value excluded from summarization and statistical analyses.

c. Below quantitative level.

d. Extrapolated data.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A16 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
5107	1.870		
5207	2.942		
	2.642a		
5307	1.724		
	1.530a		
5407	3.049		
	2.650a		
5507	2.333		
5607	1.618		
5707	1.773		
5807	1.665		
5907	2.115		
6007	1.868		
6107	2.506		
6207	X	DNR	
	2.062		
PUP #	DOSAGE GROUP II	MALAOXON	1.0 MG/KG
5108	1.201		
5208	2.337		
5308	X	DNR	
	1.997		
5408	2.175		
5508	1.798		
5608	1.538		
5708	1.356		
5808	1.382		
5908	1.907		
6008	1.577		
6108	2.317		
6208	1.659		

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

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

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A16 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP III		MALAOXON 3.5 MG/KG
5109	0.360		
5209	1.569		
5309	X		DNR
	0.284		LOW a
	X		DNR
5409	2.802		
5509	1.119		
5609	1.275		
5709	1.220		
	X		DNR
	X		DNR
	X		LOW
5809	0.724		
5909	0.972		
6009	1.102		
6109	X		DNR
	1.147		
6209	1.778		

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Extrapolated data.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A16 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP IV	MALAOXON	7.0 MG/KG
5110	0.747		
5210	0.861		
5310	1.369		
5410	0.435	LOW a	
	X	LOW	
	X	DNR	
5510	0.463		
5610	0.539		
5710	0.558		
5810	X	DNR	
	0.517		
5910	1.007		
6010	0.836		
6110	X	DNR	
	0.612		
6210	0.855		

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Extrapolated data.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A16 (PAGE 4): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP	V	MALAOXON
			10.0 MG/KG
5111		X	DNR
		X	DNR
		X	DNR
5211		X	LOW
		0.424	
5311		X	LOW a
		X	LOW a
		X	LOW a
5411		0.660	b
5511		X	DNR
		X	DNR
		0.477	
5611		0.419	
5711		1.371	
5811		0.261	LOW c
		X	DNR
5911		X	DNR
		X	DNR
		X	DNR
		0.745	
6011		X	LOW
		0.468	
6111		0.344	LOW c
		X	DNR
6211		X	LOW
		0.361	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Below quantitative level.

b. Values for pup 5411 first run was low, second run (0.435 units/mL) and third run (0.885 units/mL) were not within 25% acceptability criteria of each other; Values averaged.

c. Extrapolated data.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE A16 (PAGE 5): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - MALAOXON - FEMALE PUPS

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP VI	MALAOXON	12.5 MG/KG
5112	X	DNR	
	X	DNR	
	0.237	LOW a	
5212	X	DNR	
	0.399		
5312	1.189		
5412	0.354	LOW a	
	X	DNR	
5512	X	DNR	
	0.079	LOW a	
	X	LOW	
5612	X	DNR	
	X	DNR	
	0.569		
5712	X	LOW	
	0.444		
5812	0.212	LOW a	
	X	DNR	
5912	X	DNR	
	X	LOW	
	X	LOW	
	0.459		
6012	X	DNR	
	0.401		
6112	X	DNR	
	X	DNR	
6212	1.053		

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Extrapolated data.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

DOSAGE GROUP	I	II	III	IV	V	VI
TEST SUBSTANCE	VEHICLE	MALATHION	MALATHION	MALATHION	MALATHION	MALATHION
DOSAGE (MG/KG)	0	10	25	50	100	150
PUPS TESTED	12	12	12	12	12	12
MORTALITY	0	0	0	0	0	0
WHOLE BODY: TREMORS a	0/ 0	0/ 0	0/ 0	0/ 0	5/ 5	5/ 5

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

a. Observed within 1 hour of dosage administration.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

DOSAGE GROUP TEST SUBSTANCE DOSAGE (MG/KG)	I VEHICLE 0	II MALATHION 10	III MALATHION 25	IV MALATHION 50	V MALATHION 100	VI MALATHION 150
PUPS TESTED	12	12	12	12	12	12
MORTALITY	0	0	0	0	0	0
WHOLE BODY: TREMORS a	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	7/ 7
BODY JERKS a	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
RED PERIANAL SUBSTANCE a	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0

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

a. Observed within 1 hour after dosage administration.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

DOSAGE GROUP		I	II	III	IV	V	VI
TEST SUBSTANCE		VEHICLE	MALATHION	MALATHION	MALATHION	MALATHION	MALATHION
DOSAGE (MG/KG)		0	10	25	50	100	150
PUPS TESTED	N	12	12	12	12	12	12
BODY WEIGHT (G)							
PND 11	MEAN±S.D.	20.1 ± 3.9	20.5 ± 3.1	18.7 ± 4.6	20.0 ± 2.7	18.9 ± 3.7	20.3 ± 4.3
PND = POSTNATAL DAY							

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

DOSAGE GROUP		I	II	III	IV	V	VI
TEST SUBSTANCE		VEHICLE	MALATHION	MALATHION	MALATHION	MALATHION	MALATHION
DOSAGE (MG/KG)		0	10	25	50	100	150
PUPS TESTED	N	12	12	12	12	12	12
BODY WEIGHT (G)							
PND 11	MEAN±S.D.	18.6 ± 3.9	19.2 ± 3.6	19.3 ± 3.3	19.4 ± 3.3	18.8 ± 3.9	18.8 ± 2.7
PND = POSTNATAL DAY							

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

DOSAGE GROUP		I	II	III	IV
TEST SUBSTANCE		VEHICLE	MALATHION	MALATHION	MALATHION
DOSAGE (MG/KG)		0	10	25	50
PUPS TESTED	N	12	12	12	12
BRAIN WEIGHT (G)	MEAN±S.D.	0.918 ± 0.109	0.942 ± 0.114	0.875 ± 0.128	0.908 ± 0.095
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	5.112 ± 0.580	5.198 ± 0.491	5.108 ± 0.436	4.379 ± 0.816
% INHIBITION a	%		-1.7	0.1	14.3

a. Value derived from comparison to the Vehicle Group.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B5 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALATHION - MALE PUPS

DOSAGE GROUP		V	VI
TEST SUBSTANCE		MALATHION	MALATHION
DOSAGE (MG/KG)		100	150
PUPS TESTED	N	12	12
BRAIN WEIGHT (G)	MEAN±S.D.	0.897 ± 0.119	0.911 ± 0.120
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	3.327 ± 1.152**	2.822 ± 1.366**
% INHIBITION a	%	34.9	44.8

a. Value derived from comparison to the Vehicle Group.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

DOSAGE GROUP		I	II	III	IV
TEST SUBSTANCE		VEHICLE	MALATHION	MALATHION	MALATHION
DOSAGE (MG/KG)		0	10	25	50
PUPS TESTED	N	11b	12	12	12
BRAIN WEIGHT (G)	MEAN±S.D.	0.932 ± 0.100	0.910 ± 0.096	0.916 ± 0.109	0.892 ± 0.094
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	4.982 ± 0.446	5.107 ± 0.356	4.861 ± 0.485	4.655 ± 0.690
% INHIBITION a	%		-2.5	2.4	6.6

a. Value derived from comparison to the Vehicle Group.

b. Excludes values for pup 6807, which had a sample result beyond expected range.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B6 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - SUMMARY - MALATHION - FEMALE PUPS

DOSAGE GROUP		V	VI
TEST SUBSTANCE		MALATHION	MALATHION
DOSAGE (MG/KG)		100	150
PUPS TESTED	N	12	12
BRAIN WEIGHT (G)	MEAN±S.D.	0.900 ± 0.123	0.908 ± 0.079
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.888 ± 1.633*	1.760 ± 1.509**
% INHIBITION a	%	42.0	64.7

a. Value derived from comparison to the Vehicle Group.

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

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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

DOSAGE GROUP		I	II	III	IV
TEST SUBSTANCE		VEHICLE	MALATHION	MALATHION	MALATHION
DOSAGE (MG/KG)		0	10	25	50
PUPS TESTED	N	12	12	12	12
INCLUDED IN ANALYSES	N	12	12	11a	11a
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.044 ± 0.309	1.947 ± 0.272	1.747 ± 0.324	1.246 ± 0.497**
% INHIBITION b	%		4.7	14.5	39.0

- a. Excludes values for sample results that did not meet the acceptability criterion.
b. Value derived from comparison to the Vehicle Group.
** Statistically significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B7 (PAGE 2): RBC CHOLINESTERASE LEVELS - SUMMARY - MALATHION - MALE PUPS

DOSAGE GROUP		V	VI
TEST SUBSTANCE		MALATHION	MALATHION
DOSAGE (MG/KG)		100	150
PUPS TESTED	N	12	12
INCLUDED IN ANALYSES	N	10a	11a
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	1.042 ± 0.500**	0.669 ± 0.390**
% INHIBITION b	%	49.0	67.3

- a. Excludes values for sample results that did not meet the acceptability criterion.
b. Value derived from comparison to the Vehicle Group.
** Statistically significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

DOSAGE GROUP		I	II	III	IV
TEST SUBSTANCE		VEHICLE	MALATHION	MALATHION	MALATHION
DOSAGE (MG/KG)		0	10	25	50
PUPS TESTED	N	12	12	12	12
INCLUDED IN ANALYSES	N	12	11a	11a	12
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.173 ± 0.169	1.944 ± 0.287	1.780 ± 0.322*	1.550 ± 0.398**
% INHIBITION b	%		10.5	18.1	28.7

a. Excludes values for sample results that did not meet the acceptability criterion.

b. Value derived from comparison to the Vehicle Group.

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

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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

TABLE B8 (PAGE 2): RBC CHOLINESTERASE LEVELS - SUMMARY - MALATHION - FEMALE PUPS

DOSAGE GROUP		V	VI
TEST SUBSTANCE		MALATHION	MALATHION
DOSAGE (MG/KG)		100	150
PUPS TESTED	N	12	12
INCLUDED IN ANALYSES	N	11a	10a
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	0.801 ± 0.639**	0.483 ± 0.349**
% INHIBITION b	%	63.1	77.8

- a. Excludes values for sample results that did not meet the acceptability criterion.
b. Value derived from comparison to the Vehicle Group.
** Statistically significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PUP #	DESCRIPTION
DOSAGE GROUP I	VEHICLE 0 MG/KG
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	MALATHION 10 MG/KG
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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PUP #	DESCRIPTION
DOSAGE GROUP III	MALATHION 25 MG/KG
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	MALATHION 50 MG/KG
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

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PUP #		DESCRIPTION	
DOSAGE GROUP V		MALATHION	100 MG/KG
6305		NO ADVERSE FINDINGS	
6405		NO ADVERSE FINDINGS	
6505	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (47 MINUTES AFTER DOSAGE ADMINISTRATION)	
6605	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (46 MINUTES AFTER DOSAGE ADMINISTRATION)	
6705		NO ADVERSE FINDINGS	
6805	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (48 MINUTES AFTER DOSAGE ADMINISTRATION)	
6905		NO ADVERSE FINDINGS	
7005	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (49 MINUTES AFTER DOSAGE ADMINISTRATION)	
7105	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (46 MINUTES AFTER DOSAGE ADMINISTRATION)	
7205		NO ADVERSE FINDINGS	
7305		NO ADVERSE FINDINGS	
7405		NO ADVERSE FINDINGS	
DOSAGE GROUP VI		MALATHION	150 MG/KG
6306		NO ADVERSE FINDINGS	
6413	PND(11)	WHOLE BODY: TREMORS - SLIGHT (47 MINUTES AFTER DOSAGE ADMINISTRATION)	
6506	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (44 MINUTES AFTER DOSAGE ADMINISTRATION)	
6606		NO ADVERSE FINDINGS	
6706		NO ADVERSE FINDINGS	
6806	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (50 MINUTES AFTER DOSAGE ADMINISTRATION)	
6906		NO ADVERSE FINDINGS	
7006		NO ADVERSE FINDINGS	
7106	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - MODERATE (50 MINUTES AFTER DOSAGE ADMINISTRATION)	
7206		NO ADVERSE FINDINGS	
7306	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (45 MINUTES AFTER DOSAGE ADMINISTRATION)	
7406		NO ADVERSE FINDINGS	

PND = POSTNATAL DAY

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PUP #	DESCRIPTION
DOSAGE GROUP I	VEHICLE 0 MG/KG
6307	NO ADVERSE FINDINGS
6407	NO ADVERSE FINDINGS
6507	NO ADVERSE FINDINGS
6607	NO ADVERSE FINDINGS
6707	NO ADVERSE FINDINGS
6807	NO ADVERSE FINDINGS
6907	NO ADVERSE FINDINGS
7007	NO ADVERSE FINDINGS
7107	NO ADVERSE FINDINGS
7207	NO ADVERSE FINDINGS
7307	NO ADVERSE FINDINGS
7407	NO ADVERSE FINDINGS
DOSAGE GROUP II	MALATHION 10 MG/KG
6308 PND(11)	RED PERIANAL SUBSTANCE (57 MINUTES AFTER DOSAGE ADMINISTRATION)
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	NO ADVERSE FINDINGS
7108	NO ADVERSE FINDINGS
7208	NO ADVERSE FINDINGS
7308	NO ADVERSE FINDINGS
7408	NO ADVERSE FINDINGS

PND = POSTNATAL DAY

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PUP #	DESCRIPTION
DOSAGE GROUP III	MALATHION 25 MG/KG
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
DOSAGE GROUP IV	MALATHION 50 MG/KG
6310	NO ADVERSE FINDINGS
6410	NO ADVERSE FINDINGS
6510	NO ADVERSE FINDINGS
6610	NO ADVERSE FINDINGS
6710	NO ADVERSE FINDINGS
6810	NO ADVERSE FINDINGS
6910	NO ADVERSE FINDINGS
7010	NO ADVERSE FINDINGS
7110	NO ADVERSE FINDINGS
7210	NO ADVERSE FINDINGS
7310	NO ADVERSE FINDINGS
7410	NO ADVERSE FINDINGS

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PUP #	DESCRIPTION	
DOSAGE GROUP V	MALATHION	100 MG/KG
6311	NO ADVERSE FINDINGS	
6411	NO ADVERSE FINDINGS	
6511	NO ADVERSE FINDINGS	
6611	NO ADVERSE FINDINGS	
6711	NO ADVERSE FINDINGS	
6811	NO ADVERSE FINDINGS	
6911	NO ADVERSE FINDINGS	
7011	PND(11)	WHOLE BODY: TREMORS - CONTINUOUS - SLIGHT (48 MINUTES AFTER DOSAGE ADMINISTRATION)
7111	NO ADVERSE FINDINGS	
7211	NO ADVERSE FINDINGS	
7311	NO ADVERSE FINDINGS	
7411	NO ADVERSE FINDINGS	
DOSAGE GROUP VI	MALATHION	150 MG/KG
6312	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (57 MINUTES AFTER DOSAGE ADMINISTRATION)
6412	PND(11)	WHOLE BODY: TREMORS - CONTINUOUS - SLIGHT (48 MINUTES AFTER DOSAGE ADMINISTRATION)
6512	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (42 MINUTES AFTER DOSAGE ADMINISTRATION)
6612	NO ADVERSE FINDINGS	
6712	NO ADVERSE FINDINGS	
6812	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (47 MINUTES AFTER DOSAGE ADMINISTRATION)
	PND(11)	BODY JERKS (47 MINUTES AFTER DOSAGE ADMINISTRATION)
6912	NO ADVERSE FINDINGS	
7012	NO ADVERSE FINDINGS	
7112	PND(11)	BODY JERKS (47 MINUTES AFTER DOSAGE ADMINISTRATION)
7212	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - MODERATE (41 MINUTES AFTER DOSAGE ADMINISTRATION)
7312	PND(11)	WHOLE BODY: TREMORS - INTERMITTENT - SLIGHT (42 MINUTES AFTER DOSAGE ADMINISTRATION)
7412	PND(11)	WHOLE BODY: TREMORS - CONTINUOUS - MODERATE (46 MINUTES AFTER DOSAGE ADMINISTRATION)
	PND(11)	BODY JERKS (46 MINUTES AFTER DOSAGE ADMINISTRATION)

PND = POSTNATAL DAY

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PND 11			
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
6301	17.7		
6401	20.4		
6501	18.5		
6601	14.9		
6701	13.9		
6801	21.0		
6901	24.8		
7001	23.0		
7101	16.0		
7201	23.5		
7301	22.9		
7401	25.1		
PUP #	DOSAGE GROUP II	MALATHION	10 MG/KG
6302	22.7		
6402	18.6		
6502	18.2		
6602	16.1		
6702	22.1		
6802	14.8		
6902	22.9		
7002	21.9		
7102	20.9		
7202	23.7		
7302	25.1		
7402	19.2		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PND 11			
PUP #	DOSAGE GROUP III	MALATHION	25 MG/KG
6303	17.4		
6403	13.3		
6503	18.9		
6603	12.6		
6703	15.0		
6803	14.8		
6903	24.4		
7003	24.3		
7103	15.1		
7203	22.0		
7303	22.0		
7403	24.8		
PUP #	DOSAGE GROUP IV	MALATHION	50 MG/KG
6304	21.6		
6404	18.0		
6504	18.0		
6604	16.9		
6704	16.0		
6804	21.3		
6904	23.3		
7004	22.6		
7104	18.3		
7204	24.2		
7304	21.4		
7404	19.0		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PND 11			
PUP #	DOSAGE GROUP V	MALATHION	100 MG/KG
6305	17.6		
6405	13.1		
6505	16.8		
6605	16.1		
6705	16.2		
6805	23.7		
6905	23.5		
7005	14.9		
7105	18.3		
7205	23.9		
7305	22.3		
7405	20.5		
PUP #	DOSAGE GROUP VI	MALATHION	150 MG/KG
6306	24.3		
6413	23.5		
6506	16.3		
6606	12.8		
6706	15.4		
6806	21.7		
6906	23.9		
7006	14.7		
7106	20.2		
7206	23.9		
7306	21.7		
7406	25.1		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PND 11			
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
6307	20.7		
6407	15.4		
6507	18.3		
6607	14.6		
6707	14.4		
6807	13.2		
6907	21.2		
7007	20.3		
7107	15.9		
7207	23.2		
7307	21.0		
7407	25.6		
PUP #	DOSAGE GROUP II	MALATHION	10 MG/KG
6308	16.2		
6408	19.2		
6508	16.5		
6608	14.9		
6708	15.4		
6808	17.1		
6908	23.4		
7008	19.6		
7108	17.5		
7208	22.9		
7308	22.1		
7408	25.8		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PND 11			
PUP #	DOSAGE GROUP III	MALATHION	25 MG/KG
6309	18.3		
6409	13.8		
6509	17.4		
6609	15.6		
6709	15.4		
6809	19.3		
6909	20.8		
7009	20.5		
7109	19.8		
7209	22.3		
7309	23.8		
7409	24.2		
PUP #	DOSAGE GROUP IV	MALATHION	50 MG/KG
6310	22.7		
6410	12.7		
6510	17.2		
6610	20.2		
6710	13.6		
6810	20.3		
6910	22.8		
7010	20.8		
7110	20.0		
7210	21.8		
7310	21.0		
7410	19.2		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PND 11			
PUP #	DOSAGE GROUP V	MALATHION	100 MG/KG
6311	17.3		
6411	18.6		
6511	20.3		
6611	16.6		
6711	14.2		
6811	16.1		
6911	23.2		
7011	10.9		
7111	20.7		
7211	23.7		
7311	21.9		
7411	22.0		
PUP #	DOSAGE GROUP VI	MALATHION	150 MG/KG
6312	18.3		
6412	16.6		
6512	20.9		
6612	14.4		
6712	13.8		
6812	19.3		
6912	21.6		
7012	17.5		
7112	20.1		
7212	21.8		
7312	20.8		
7412	20.9		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
DOSAGE GROUP I	VEHICLE	0 MG/KG	
6301	0.883	6.190	
	0.883	X	DNR
	0.883	5.675a	
6401	0.953	5.778	
6501	0.832	4.988	
	0.832	4.915a	
6601	0.786	4.020	
	0.786	3.756a	
6701	0.734	5.540	
6801	0.930	4.875	
6901	0.993	5.234	
7001	0.897	4.751	
7101	0.856	4.598	
7201	1.068	4.806	
7301	0.996	5.073	
7401	1.092	5.496	
PUP #	DOSAGE GROUP II	MALATHION	10 MG/KG
6302	0.979	6.393	
6402	0.829	5.280	
6502	0.828	4.974	
6602	0.807	4.526	
6702	0.936	4.819	
6802	0.810	5.372	
6902	0.942	5.040	
7002	0.898	4.692	
7102	1.054	5.322	
7202	1.083	4.955	
7302	1.147	5.457	
7402	0.992	5.545	

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

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

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP III	MALATHION	25 MG/KG
6303	0.812	5.835	
6403	0.770	4.247	
6503	0.881	5.134	
	0.881	5.133a	
6603	0.726	4.859	
6703	0.817	4.864	
6803	0.671	5.685	
6903	0.936	5.053	
7003	0.921	5.251	
7103	0.853	5.358	
7203	1.010	4.617	
7303	0.977	5.303	
7403	1.125	5.095	
PUP #	DOSAGE GROUP IV	MALATHION	50 MG/KG
6304	1.029	4.730	
6404	0.914	3.100	
6504	0.752	5.651	
	0.752	5.571a	
6604	0.866	4.339	
6704	0.849	4.409	
6804	0.761	3.352	
6904	0.897	4.778	
7004	0.892	4.510	
7104	0.924	4.058	
7204	1.069	3.238	
7304	0.984	5.167	
7404	0.954	5.212	

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP V	MALATHION	100 MG/KG
6305	0.871	4.688	
	0.871	4.518a	
6405	0.813	3.100	
6505	0.767	4.964	
6605	0.793	2.827	
6705	0.848	3.782	
6805	0.977	1.509	
6905	0.940	2.773	
7005	0.695	4.666	
7105	0.926	1.399	
7205	1.031	3.322	
7305	1.086	3.902	
7405	1.014	2.987	
PUP #	DOSAGE GROUP VI	MALATHION	150 MG/KG
6306	1.052	1.693	
6413	0.993	0.720	
6506	0.767	4.780	
6606	0.758	4.269	
6706	0.822	2.226	
6806	0.950	3.938	
6906	0.901	2.493	
7006	0.709	4.124	
7106	0.976	0.537	
7206	0.943	2.829	
7306	0.986	3.330	
7406	1.077	2.922	

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

PUP #	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
	DOSAGE GROUP I	VEHICLE	0 MG/KG
6307	0.982	4.962	
6407	0.852	5.526	
6507	0.999	4.950	
	0.999	5.212a	
6607	0.833	4.240	
	0.833	X	DNR
	0.833	4.361a	
6707	0.813	4.788	
6807	0.692b	2.077c	
6907	0.901	5.246	
7007	0.850	4.624	
7107	0.874	X	DNR
	0.874	4.395	
7207	1.045	5.085	
7307	0.975	5.611	
7407	1.125	5.379	
PUP #	DOSAGE GROUP II	MALATHION	10 MG/KG
6308	0.850	5.411	
6408	0.995	5.228	
6508	0.811	5.677	
6608	0.790	4.845	
6708	0.822	4.974	
6808	0.877	5.152	
6908	0.944	4.935	
7008	0.842	4.568	
7108	0.895	4.552	
7208	0.978	5.142	
7308	1.009	5.591	
7408	1.102	5.210	

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

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

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

b. Value was excluded from summarization and statistical analyses.

c. Sample result beyond expected range; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP III	MALATHION	25 MG/KG
6309	0.905	5.237	
6409	0.760	4.379	
6509	0.784	5.197	
6609	0.827	4.714	
6709	0.839	4.721	
6809	0.894	3.740	
6909	0.947	5.686	
7009	0.868	4.702	
7109	0.969	4.857	
7209	1.041	4.973	
7309	1.080	5.098	
7409	1.079	5.023	
PUP #	DOSAGE GROUP IV	MALATHION	50 MG/KG
6310	1.012	4.887	
6410	0.731	4.432	
6510	0.760	4.916	
6610	0.936	5.113	
6710	0.797	4.999	
	0.797	4.920a	
6810	0.923	4.590	
6910	0.898	4.969	
7010	0.824	3.907	
7110	0.903	5.189	
7210	1.022	2.787	
7310	0.958	5.101	
7410	0.935	4.974	

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

BRAIN (G)		FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
PUP #	DOSAGE GROUP V	MALATHION	100 MG/KG
6311	0.928	0.706	
6411	0.957	2.948	
6511	0.853	4.791	
6611	0.849	2.434	
6711	0.839	3.555	
6811	0.798	0.534	
6911	0.915	1.076	
7011	0.603	4.456	
7111	0.976	2.281	
7211	1.050	2.201	
7311	1.006	5.387	
7411	1.024	4.282	
PUP #	DOSAGE GROUP VI	MALATHION	150 MG/KG
6312	0.907	0.930	
6412	0.909	0.921	
6512	1.030	0.558	
6612	0.800	4.385	
	0.800	4.287a	
6712	0.810	2.194	
6812	0.887	X	LOW
	0.887	0.638	
6912	0.888	4.374	
7012	0.784	3.597	
7112	0.964	0.711	
7212	0.966	X	LOW
	0.966	0.546	
7312	0.948	0.733	
7412	1.001	1.533	

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.

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
6301	1.818		
6401	2.191		
6501	1.673		
	1.779a		
6601	2.131		
6701	1.743		
	X	DNR	
	2.209a		
	1.897a		
6801	2.225		
6901	2.150		
7001	1.914		
7101	2.416		
7201	2.166		
7301	1.535		
7401	2.562		
PUP #	DOSAGE GROUP II	MALATHION	10 MG/KG
6302	1.504		
6402	2.156		
6502	1.848		
6602	1.913		
6702	1.680		
6802	1.889		
6902	1.663		
7002	2.035		
7102	2.073		
7202	1.878		
7302	2.226		
7402	2.495		

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

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

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP III	MALATHION
		25 MG/KG
6303	1.821	
6403	1.569	
6503	1.982	
	2.306a	
6603	Xb	
6703	1.577	
6803	2.001	
6903	1.331	
7003	1.762	
7103	2.237	
7203	1.199	
7303	2.117	
7403	1.623	

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

- a. Repeat analysis performed; value excluded from summarization and statistical analyses.
- b. Insufficient sample for analysis.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP IV	MALATHION
		50 MG/KG
6304	1.029	
6404	0.720	
6504	1.620	
	1.782a	
6604	Xb	
6704	1.628	
6804	X	DNR
	X	DNR
	0.741	
6904	1.108	
7004	1.360	
7104	1.284	
7204	X	DNR
	X	DNR
	X	DNR
	0.451	
7304	2.141	
7404	1.623	

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

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

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

b. Insufficient sample for analysis.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP V	MALATHION
6305	1.723	
	1.709a	
6405	Xb	
6505	1.441	
6605	0.611	
6705	0.955	
6805	X	DNR
	X	DNR
	X	DNR
	X	LOW
6905	0.798	
7005	1.697	
7105	X	DNR
	0.329	
7205	0.793	
7305	1.466	
7405	0.604	

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

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

LOW = REPORTED VALUE IS BELOW THE LOWEST STANDARD.

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

b. Insufficient sample for analysis.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP VI	MALATHION 150 MG/KG
6306	X	DNR
	0.492	
6413	X	DNR
	0.339	
6506	1.477	
6606	Xa	
6706	0.540	
6806	0.330	
6906	0.444	
7006	1.064	
7106	X	DNR
	0.226	
7206	X	DNR
	0.701	
7306	X	DNR
	X	DNR
	1.108	
7406	0.642	

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

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

a. Insufficient sample for analysis.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
PUP #	DOSAGE GROUP I	VEHICLE	0 MG/KG
6307	2.093		
6407	2.309		
6507	2.226		
	2.140a		
6607	1.995		
6707	2.043		
6807	2.401		
6907	2.113		
7007	2.166		
7107	2.173		
7207	1.859		
7307	2.455		
7407	2.238		
PUP #	DOSAGE GROUP II	MALATHION	10 MG/KG
6308	1.791		
6408	2.126		
6508	1.626		
6608	Xb		
6708	1.844		
6808	2.314		
6908	1.559		
7008	1.829		
7108	2.347		
7208	1.943		
7308	2.312		
7408	1.697		

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

a. Repeat analysis performed; value excluded from summarization and statistical analyses.

b. Insufficient sample for analysis.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)			FOOTNOTE
PUP #	DOSAGE GROUP III		MALATHION 25 MG/KG
6309	1.573		
6409	1.819		
6509	1.556		
6609	Xa		
6709	1.505		
6809	1.187		
6909	1.712		
7009	1.999		
	2.050b		
7109	2.109		
7209	1.750		
7309	2.068		
7409	2.297		
PUP #	DOSAGE GROUP IV		MALATHION 50 MG/KG
6310	1.202		
6410	1.420		
6510	1.542		
6610	1.637		
6710	1.487		
6810	1.321		
6910	1.675		
7010	1.359		
7110	2.018		
7210	0.740		
7310	2.029		
7410	2.168		

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

a. Insufficient sample for analysis.

b. Repeat analysis performed; value excluded from summarization and statistical analyses.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP V	MALATHION
6311	0.167	
6411	0.622	
6511	X	DNR
	1.290	
6611	X	DNR
	0.294	
6711	0.867	
6811	X	DNR
	0.338	
6911	X	DNR
	0.235	
7011	Xa	
7111	X	DNR
	0.552	
7211	X	DNR
	0.619	
7311	2.057	
7411	X	DNR
	1.773	

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

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

a. Insufficient sample for analysis.

PROTOCOL TQC00017: ORAL (GAVAGE) ACUTE DOSE COMPARATIVE CHOLINESTERASE STUDY OF MALATHION AND MALAOXON IN JUVENILE RATS

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

FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE
PUP #	DOSAGE GROUP VI	MALATHION 150 MG/KG
6312	0.173	
6412	X	DNR
	0.773	
6512	X	DNR
	0.325	
6612	Xa	
6712	0.294	
6812	X	DNR
	X	DNR
	0.374	
6912	1.267	
7012	0.752	
7112	X	DNR
	X	DNR
	X	DNR
7212	X	DNR
	X	DNR
	0.278	
7312	0.152	
7412	X	DNR
	0.440	

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

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

a. Insufficient sample for analysis.

APPENDIX 1 - PROTOCOL AND AMENDMENTS



FINAL PROTOCOL

Charles River Laboratories Study No. TQC00017

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

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

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

3 December 2007

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1. STUDY NUMBER

TQC00017

2. STUDY TITLE

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

3. OBJECTIVE

The objective of this study is to compare the effect of acute dosing of young pre-weanling rats with Malathion and Malaoxon on erythrocyte and brain acetyl cholinesterase activity when the pups are sampled at the time of peak effect.

4. TESTING FACILITY

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

5. STUDY DIRECTOR

John F. Barnett, Jr., B.S. (Senior Scientist)
Address as cited above for Testing Facility.
Direct Tel: 215.957.2284
E-mail: john.barnettjr@crl.com

6. SPONSOR

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

7. SPONSOR'S REPRESENTATIVE

Terri Spanogle
Senior Scientist
Cheminova, Inc.
1600 Wilson Blvd., Suite 700
Arlington, VA 22209
USA
Tel: 703.373.8883
Fax: 703.373.8887
E-mail: tls.us@cheminova.com

8. STUDY MONITOR

Judith Hauswirth, Ph.D.
Toxicology Consultant

9. 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].

10. 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 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. All procedures conducted by the Test Site will be specifically defined by the protocol, or will be described in detail in the Standard Operating Procedures of the Test Site. The QAU for this facility 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 archival location of any records generated by this facility will be identified 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.

11. PROPOSED STUDY SCHEDULE

See Attachment 1 to the protocol.

12. TEST SUBSTANCES AND VEHICLES

12.1. Identification

12.1.1. Test Substances

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

Lot Number:	9010501
Purity:	96.0%
CAS Number:	121-75-5
Reanalysis Date:	9 November 2008 (received at the Testing Facility on 16 October 2007)

Malaoxon

Batch/Lot Number:	849-BSe-42C
Purity:	97.7%
CAS Number:	1634-78-2
Reanalysis Date:	4 March 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 and Malaoxon 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.

12.1.2. 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.

12.2. 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).

12.3. Storage

Bulk Test Substances:	Malathion - Frozen (at least -20°C), protected from light. Malaoxon - Frozen (at least -20°C), protected from light.
Vehicle:	Room temperature.
Prepared Formulations:	Refrigerated (2°C to 8°C) and 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.

13. FORMULATION

13.1. Frequency of Preparation

Formulations (suspensions) will be prepared in the morning prior to dosing for each test substance at the Testing Facility.

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

13.2. Adjustment for Purity

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

13.3. Testing Facility Reserve Samples

The Testing Facility will reserve a sample of approximately 0.5 g of each lot of bulk test substances and approximately 5 mL of the vehicle used during the course of the study. Samples will be stored under the previously cited conditions.

14. 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.

14.1. Acceptance Criteria

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

1) concentration results will be considered acceptable if the difference between the actual mean value and the targeted concentration is $\leq 15\%$; 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 $\leq 5\%$. Results obtained outside of the criteria will be

considered Out of Specification (OOS) and procedures for investigation and notification will be followed in the applicable laboratory Standard Operating Procedure covering OOS results.

14.2. Analyses of Prepared Formulations

14.2.1. 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.

14.2.2. 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 has been provided to the Study Director.

14.3. Shipping Instructions

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

Principal Investigator: Peggy Buxton, B.S.
Charles River Laboratories
Preclinical Services, Massachusetts
334 South Street
Shrewsbury, MA 01545
USA
Tel: 508.925.6423
Fax: 508.925.6701
E-mail: peggy.buxton@crl.com

The recipient will be notified in advance of sample shipment.

15. DISPOSITION

Unused 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.

16. TEST SYSTEM

16.1. 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.

16.2. Number

16.2.1. Adult Rats

F0 generation population
acclimated:

Twenty-four gestation day 16 (DG 16) female rats
and twenty-four DG 18 female rats.

16.2.2. Neonatal Rats

F1 generation population
selected for study:

Twelve litters of six male and six female pups will
be administered Malaoxon and twelve additional
litters of six male and six female rats will be
administered Malathion.

16.3. Body Weight and Age

There will be twenty-four DG 18 female rats and twenty-four DG 16 female rats ordered to arrive at the Testing Facility. 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.

16.4. Sex

Dams will be used only to nurse the pups and are not considered part of the Test System. Male and female pups will be given the test substance and/or the vehicle. Equal numbers of male and female pups from each litter will be used (when possible).

16.5. Source

Charles River Laboratories, Inc.

F0 generation female rats will be shipped in filtered cartons by air freight and/or truck from Charles River Laboratories, Inc., to the Testing Facility.

16.6. Identification

16.6.1. Adult Rats

Female rats are assigned temporary animal numbers at receipt. The rats will be permanently identified using Monel[®] self-piercing ear tags.

16.6.2. Neonatal Rats

Prior to day 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.

17. ANIMAL HUSBANDRY

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

17.1. Housing

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

17.2. 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.

17.3. 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%.

17.4. Light

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

17.5. Diet

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

17.6. Water

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

17.7. 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.

18. 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. Within this protocol and the final report, the day of birth will be designated day 0 postpartum (day 0 of lactation). However, in the study data the day of birth will be designated day 1 postpartum 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.

19. RANDOMIZATION

19.1. 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 0 of lactation (postpartum). The female rats will be allowed to deliver their litters at the Testing Facility.

19.2. Pups

To ensure that the appropriate number of male and female pups are assigned to each dosage group, pups may be cross-fostered. These instances will be documented appropriately in the raw data and indicated in the final report.

Prior to day 11 postpartum, twenty-four litters of approximately twelve pups per litter (six males and six 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 the six 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 Malaoxon dosage groups will be assigned to the following dosage group:

Paw Tattoo	Dosage Group Assignment
Male Paw Tattoo 1	0 (Vehicle) mg/kg
Male Paw Tattoo 2	1.0 mg/kg
Male Paw Tattoo 3	3.5 mg/kg
Male Paw Tattoo 4	7.0 mg/kg
Male Paw Tattoo 5	10.0 mg/kg
Male Paw Tattoo 6	12.5 mg/kg
Female Paw Tattoo 7	0 (Vehicle) mg/kg
Female Paw Tattoo 8	1.0 mg/kg
Female Paw Tattoo 9	3.5 mg/kg
Female Paw Tattoo 10	7.0 mg/kg
Female Paw Tattoo 11	10.0 mg/kg
Female Paw Tattoo 12	12.5 mg/kg

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

Paw Tattoo	Dosage Group Assignment
Male Paw Tattoo 1	0 (Vehicle) mg/kg
Male Paw Tattoo 2	10 mg/kg
Male Paw Tattoo 3	25 mg/kg
Male Paw Tattoo 4	50 mg/kg
Male Paw Tattoo 5	100 mg/kg
Male Paw Tattoo 6	150 mg/kg
Female Paw Tattoo 7	0 (Vehicle) mg/kg
Female Paw Tattoo 8	10 mg/kg
Female Paw Tattoo 9	25 mg/kg
Female Paw Tattoo 10	50 mg/kg
Female Paw Tattoo 11	100 mg/kg
Female Paw Tattoo 12	150 mg/kg

20. ADMINISTRATION

20.1. 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.

20.2. Method and Frequency

20.2.1. Dams

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

20.2.2. Pups

Pups will be administered the test substance and/or vehicle on day 11 postpartum. The doses will be based on body weights recorded prior to dosage administration. Prepared formulations will be stirred continuously during dosage administration.

20.3. Rationale for Dosage Selection

This study is a repeat of a recently conducted study with malathion and malaoxon by Huntingdon Life Sciences, Ltd. (HLS) (Huntingdon Life Sciences Report No. CHV 112/053810; January 17, 2006; MRID 46756705). The results of the HLS study have come under question by the EPA and thus, the study is being repeated. Dose levels tested in this study are different from the dose levels tested in the HLS study. The rationale for dosage selection for this study is as follows:

The malathion dosages for the pups were selected by the Sponsor based on available toxicological data from a cholinesterase study in adult and juvenile rats (Huntingdon Life Sciences Report No. CHV 067/012452) and the results of a BMD analysis of the cholinesterase data. The sampling time point of 60 minutes after dose administration was selected by the Sponsor based on the results of a time-to-peak effect study (Charles River Laboratories Study Nos. TQC00021 and TQC00032).

The malaoxon dosages for the pups were selected by the Sponsor based on the results of a recently conducted dosage range-finding cholinesterase study in juvenile rats (Charles River Laboratories Study No. TQC00022) and the results of a BMD analysis of the cholinesterase data. The sampling time point of 60 minutes after dose administration was selected by the Sponsor based on the results of a time-to-peak effect study (Charles River Laboratories Study Nos. TQC00021 and TQC00031).

20.4. Dosage Levels, Concentrations and Dosage Volumes**20.4.1. Malaoxon**

Dosage Group	Number of Pups per Dosage Group		Dosage ^a (mg/kg)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Batch Number
	Male	Female				
I	12	12	0 (Vehicle)	0 (Vehicle)	5	B-TQC00017-A(Day.Month.Year)
II	12	12	1.0	0.2	5	B-TQC00017-B(Day.Month.Year)
III	12	12	3.5	0.7	5	B-TQC00017-C(Day.Month.Year)
IV	12	12	7.0	1.4	5	B-TQC00017-D(Day.Month.Year)
V	12	12	10.0	2.0	5	B-TQC00017-E(Day.Month.Year)
VI	12	12	12.5	2.5	5	B-TQC00017-F(Day.Month.Year)

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

20.4.2. Malathion

Dosage Group	Number of Pups per Dosage Group		Dosage ^a (mg/kg)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Batch Number
	Male	Female				
I	12	12	0 (Vehicle)	0	5	B-TQC00017-A(Day.Month.Year)
II	12	12	10	2	5	B-TQC00017-G(Day.Month.Year)
III	12	12	25	5	5	B-TQC00017-H(Day.Month.Year)
IV	12	12	50	10	5	B-TQC00017-I(Day.Month.Year)
V	12	12	100	20	5	B-TQC00017-J(Day.Month.Year)
VI	12	12	150	30	5	B-TQC00017-K(Day.Month.Year)

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

21. 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.

22. METHOD OF SACRIFICE - DAMS

The dams will be sacrificed by carbon dioxide asphyxiation.

23. NECROPSY - DAMS

23.1. Scheduled Sacrifice of Dams with Litters Assigned to Study

On day 11 postpartum, dams will be sacrificed by carbon dioxide asphyxiation and discarded without further evaluation.

23.2. 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.

23.3. 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.

23.4. Dams Unscheduled Sacrifice or Found Dead

Dams that die or are sacrificed before scheduled termination will be discarded without further evaluation. Litters from these dams will be excluded from the study.

24. TESTS, ANALYSES AND MEASUREMENTS - PUPS

24.1. Viability

All Periods:

Gestating and lactating female rats will be evaluated at least twice daily for viability. Once the pups are delivered, the litters will be observed for dead pups at least twice daily and the pups in each litter will be counted once daily until the day of dosage administration.

24.2. Clinical Observations and/or General Appearance

Acclimation Period:	The pups in each litter will be evaluated on the day of delivery and on postpartum days 1, 4, 7 and on the day of randomization.
Predosage Period:	The pups in each litter will be evaluated on the day of randomization.
Dosage Period:	Prior to dosage administration and one or more times prior to sacrifice.
Maternal Behavior:	Days 1, 4 and 7 postpartum and on the day of randomization. Observed abnormal behavior recorded daily.

Clinical observations may be recorded more frequently than cited above.

24.3. Body Weights

Acclimation Period:	The pups in each litter will be weighed on postpartum days 1, 4, 7 and on the day of randomization.
Dosage Period:	On the day of dosage.

25. CHOLINESTERASE ASSAY**25.1. Blood and Brain Sample Collection**

On the day of dosage (day 11 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} (See ATTACHMENT 5). The whole blood samples will be collected (within 10 seconds and does not require documentation in the raw data) from each pup following decapitation. The whole blood samples will be collected at 60 minutes postdosage from the male and female pups assigned to the Malathion and 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 at minimum with protocol number, date of collection, rat number, dosage group, dosage level, day of study, species, generation, sex, timepoint and storage conditions.

After blood sample collection, the brain will be carefully excised from the skull and placed in a weighing boat on ice prior to processing for cholinesterase evaluation.

The blood and brain samples will be analyzed for cholinesterase levels within 2 hours after sample collection (the time of analysis will be documented in the raw data).

25.1.1. RBC

Approximately 0.40 to 0.60 mLs of whole blood will be collected into 1.2 mL EDTA-coated (lavender-top) tubes and placed on a rotator device under an ice pack until being processed for RBC cholinesterase levels according to the Study Specific Procedure located in Attachment 5 of the protocol.

25.1.2. Brains

The brain will be weighed and the weight recorded to three decimal places. The brains will be placed into the chilled 0.1% Tween 80® buffer and stored on ice until being assayed for cholinesterase levels according to the Study Specific Procedure located in Attachment 5 of the protocol.

26. 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 11 days of age).

27. NECROPSY - PUPS

27.1. Scheduled Sacrifice

Pups assigned to the study will be sacrificed by decapitation on day 11 postpartum. Sacrifice will be immediately followed by blood collection and brain dissection, and the pups will then be discarded without further evaluation.

27.2. Pups Found Dead Before Dosage Administration on Day 11 Postpartum or Unscheduled Sacrifice

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

27.3. 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.

27.4. 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.

28. 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 ($p \leq 0.05$), the interval with the largest value will be compared with values at each of the other intervals using Dunnett's test.

29. 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 97/2000/2003/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.

30. RECORDS TO BE MAINTAINED

Protocol, Amendments and Deviations.
Study Schedules
Test Substance, Vehicle and/or Reagent Receipt, Preparation and Use.
Animal Acquisition.
Randomization Schedules.
Timing of dosing, sacrifice, sample collection, sample processing and sample analysis.
Treatment (if prescribed by Staff Veterinarian).
General Comments.
Clinical Observations and/or General Appearance.
Body Weights.
Organ 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.

31. KEY PERSONNEL

Director of Research: Alan M. Hoberman, Ph.D., DABT, Fellow ATS
Senior Scientist and Study Director: John F. Barnett, Jr., B.S.
Manager of Study Management: Monica L. Davis, B.S., ALAT
Director of Operations: Matthew J. Vaneman, B.S.
Chair, Institutional Animal Care and Use Committee: Joseph W. Lech, B.S., LAT
Associate Director of Regulatory Compliance: Nancy A. Catricks, M.S.
Attending Veterinarian: Dena C. Lebo, V.M.D., Division Veterinarian
Scientist, Cholinesterase Evaluations: Julian Gulbinski, B.S, M.B.A

32. 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 an electronic 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 will be retained at the Testing Facility.

33. 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 Animals¹, 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's Representative 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's Representative will be informed by the Study Director of any such event as soon as possible.

34. 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.

35. REFERENCES

- (1) Institute of Laboratory Animal Resources Commission on Life Sciences and the National Research Council. *Guide for the care and use of laboratory animals*. Washington (D.C.): National Academy Press.
- (2) (=Scientific Advisory Panel). A set of scientific issues being considered by the Agency concerning the Office of Pesticide Programs (OPP) Cholinesterase Inhibition Policy; 1997 June. Washington (D.C.): U.S. Environmental Protection Agency.
- (3) Lassiter TL, Barone SJr, Padilla S. Ontogenetic differences in the regional and cellular acetylcholinesterase and butyrylcholinesterase activity in the rat brain. *Dev Brain Res* 1998;105:109-23.

36. PROTOCOL APPROVAL

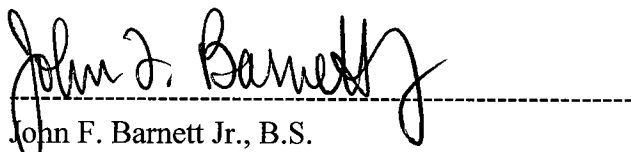
36.1. Testing Facility



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

3 Dec 07

Date

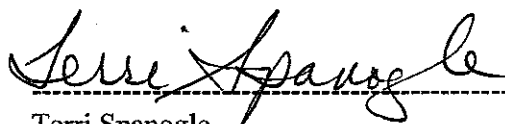


John F. Barnett Jr., B.S.
Senior Scientist
Study Director

03 Dec 2007

Date

36.2. Sponsor^a

A handwritten signature in cursive script, reading "Terri Spanogle", written over a horizontal dashed line.

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

A handwritten date "6 December 2007" written in cursive script, positioned above a horizontal dashed line.

Date

a. Date of Sponsor Approval: 3 December 2007

**ATTACHMENT 1 -
PROPOSED STUDY SCHEDULE**

PROPOSED STUDY SCHEDULE^a

20 NOV 07	Time-Mated Females Arrive - Acclimation Begins.
04 DEC 07	Proposed Experimental Start Date
04 DEC 07	Malaoxon - Dosage, Sacrifice and Cholinesterase Evaluation - Day 11 Postpartum.
07 DEC 07	Malathion - Dosage, Sacrifice and Cholinesterase Evaluation - Day 11 Postpartum.
27 DEC 07	Quality Assurance Reviewed Cholinesterase Tables.
10 JAN 08	Proposed Audited Draft Report and Proposed Experimental End Date
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 9
DK-7620 Lønng
Denmark

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Fax (+45) 96 90 96 91
www.cheminova.com
CVR-No. DK 12 76 00 43

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 X	The article is stable at least 4 years from date
In deep freezer X	of analysis/last date of reanalysis when stored at
Additional Comments:	
recommended conditions.	
ACTIVE INGREDIENT IDENTIFICATION	
Common Name/ISO-Name:	Malaoxon
CAS No.:	1634-78-2
Empirical Formula:	C ₁₀ H ₁₉ O ₇ PS
Molecular Weight:	314.3
Identified by means of:	
CAS-Name:	Butanedioic acid, [(dimethoxyphosphinyl)thio]-, diethyl ester
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: ³¹ P-NMR	
Analytical Report (incl. amendments): REP 029-07	
Date of analysis/reanalysis (yy/mm/dd)	050304
-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 FIFRA 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



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Denmark

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Fax (+45) 96 90 96 91
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CVR-No. DK12760043

BATCH ANALYTICAL CERTIFICATE

ARTICLE IDENTIFICATION			
Article Name: Pyfanon 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 _____			
Additional Comments:			
ACTIVE INGREDIENT IDENTIFICATION			
Common Name/ISO-Name: Malathion		CAS-Name: Butanedioic acid, ((dimethoxyphosphinothioyl)thio)-, diethyl ester	
CAS No.: 121-75-5			
Empirical Formula: C ₁₀ H ₁₉ O ₆ PS ₂		Structural Formula:	
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			
Content of Isomalathion: 0.29% w/w			
Analytical Method: VAM 001-02 and VAM 005-03			
Analytical Report (incl. amendments): TEM 010-02			
Date of analysis/ reanalysis (yy-mm-dd)	021024	041103	061109
-for article stored at -	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 FIFRA 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: December 5, 2006		Signature: Barbara Hinz	

**ATTACHMENT 3 -
MATERIAL SAFETY DATA SHEETS**

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

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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

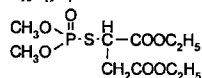
DK-7620 Lemvig

Denmark

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

2. COMPOSITION/INFORMATION ON INGREDIENTS

Common Name Malaoxon
CAS Name Butanedioic acid, [(dimethoxyphosphinyl)thio]-, diethyl ester
Other Name(s) S-1,2-Bis(ethoxycarbonyl)ethyl O,O-dimethyl phosphorothioate
CAS No. 1634-78-2
EU Classification T;R24/25
Molecular Weight 314.29
Empirical Formula C₁₀H₁₉O₇PS
Structural Formula



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

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

Cholinesterase Inhibition – Treatment

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 nor implied, on the part of Cheminova Agro A/S.

Name: Malaoxon
Material Type: Analytical Standard
Cheminova 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 absorptive 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/Hygienic 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	0.5-1.0 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 Cheminova Agro A/S.

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

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10. 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.
S28-36/37-45: 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 Cheminova Agro A/S.



Product no. 300
Product name **FYFANON® TECHNICAL**
ISO name Malathion

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

Phone (+45) 96 90 96 90
Fax (+45) 96 90 96 91
www.cheminova.com
CVR-No. DK 12 76 00 43

GHB/September 2005
Replaces version GHB/January 2002

Page 1 of 9

SAFETY DATA SHEET

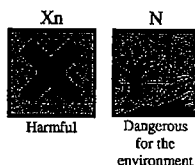
FYFANON® TECHNICAL

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 telephone no. (+45) 97 83 53 53

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 phosphorodithioate |
| 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{CH}_3\text{O}-\text{P}(=\text{S})-\text{S}-\text{CH}(\text{COOC}_2\text{H}_5)_2 \\ \\ \text{CH}_3\text{O} \end{array} $ |
- 2.2. Typical content 96-97%

Safety data sheet according to 91/155/EEC as amended



Product no. 300
Product name FYFANON® TECHNICAL
ISO name Malathion

Cheminova A/S
P.O. Box 9
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CVR-No. DK 12 76 00 43

GHB/September 2005

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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, pinpoint 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

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ISO name Malathion

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

6. ♣ ACCIDENTAL RELEASE MEASURES

- 6.1. Personal protection Observe all protection and safety precautions when cleaning up

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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.

6.2. Steps to be taken in case of spill

It is recommended to have a predetermined plan for the handling of spills.

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.

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.



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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	2002	TWA 15 mg/m ³ total dust; skin notation
	ACGIH (USA) TLV	2005	TWA 10 mg/m ³ ; skin notation; BEI
	EU, 2000/39/EC	2000	Not established
	Germany, MAK	2004	TWA 15 mg/m ³ measured as inhalable fraction of the aerosol CEILING 60 mg/m ³ BAT
	HSE (UK) OEL	2003	8-hr TWA 10 mg/m ³ ; skin notation

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

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

Respiratory protection The product 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

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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 K _{ow} = 560
9.12. Partition coefficient n-octanol/water	
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.
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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 LD₅₀, acute oral, rat: approx. 5500 mg/kg^{*)}
 - Skin LD₅₀, acute dermal, rat: > 2000 mg/kg
 - Inhalation LC₅₀, 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.
- 11.4. Carcinogenicity The meaning of these results for humans cannot be fully evaluated. 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

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- Earthworms *Eisenia foetida foetida* 14-day LC₅₀: 613 mg/kg soil
 - Bees Honey bees (*Apis mellifera*) LD₅₀, acute oral: 0.38 µg/bee
 - Honey bees (*Apis mellifera*) LD₅₀, 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

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Packaging group III
Marine pollutant (P/PP) Marine pollutant

IATA/CAO CLASSIFICATION

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

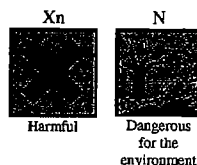
15. ♣ REGULATORY INFORMATION

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 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 TQC00017.

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 at least once at the Testing Facility.
3. Formulations will be administered at a final dosage volume of 5 mL/kg.
4. Safety:
 - X Double nitrile gloves, uniform/lab coat, goggles or safety glasses with side shields
 - ___ Dust-Mist/HEPA-filtered Mask
 - ___ Half-Face Respirator
 - X Full-Face Respirator/Positive Pressure Hood
 - X Tyvek[®] Suit
 - ___ Full Face Shield
 - X Bulk TA/S will be handled in a chemical fume hood
 - X 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.

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 preparation of other dosage formulations (if dilutions and/or serial dilutions are required) aliquotting and/or dosage administration.
4. If necessary, aliquot the formulation into an appropriately sized and labeled container for dosage administration. Add a magnetic stir bar to the container, place the container on a magnetic stir plate and mix the formulation thoroughly prior to and during dosage administration.
5. Repeat steps C1 through C4 for each concentration of each test substance.

6. 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:

Mark A. Coker

03 DEC .07

Approved by:

John J. Burnett

Date:

03 Dec 2007

ATTACHMENT 5 -
STUDY-SPECIFIC PROCEDURE FOR THE CHOLINESTERASE
EVALUATION OF PND 11 RAT PUP BRAINS AND RBCs

Purpose: This Study Specific Procedure describes the steps used to evaluate cholinesterase levels in rat pup brain tissue and red blood cells that differ with the Standard Operating Procedures of the Testing Facility.

NOTE: All buffers, reagents, standards and reference materials are to be made according to Testing Facility's SOPs.

I. SAMPLE PROCESSING

A. BRAIN SAMPLE PROCESSING:

1. The brain is transferred into an individual 15 mL polypropylene container containing chilled 5.0 mL (\pm 0.5 mL) of 0.1% Tween 80[®] buffer.
2. The brain is homogenized at least 30 seconds on wet ice (wet ice is defined as ice with water). Homogenizer must be rinsed with R.O. Deionized water prior to next use to prevent heat build up.
3. Analyze the brain samples according to section II and III below. Brain samples may be analyzed no more than three times to achieve an acceptable result (See section V).

B. BLOOD SAMPLE PROCESSING

1. For whole blood samples less than 1 mL, the sample should be processed in the container in which it was received to minimize blood loss from transfer.
2. Centrifuge the samples for approximately (5 min., 3 to 6°C, 2500 rpm).
3. Remove the plasma and the interface layer from the packed red blood cells.
4. Discard the plasma.

5. Perform a secondary dilution by transferring 0.040 mL of the packed RBC's into a vial containing 0.860 mL of 0.1% Tween buffer and mix well by inversion (this will achieve a dilution factor of 22.5).
6. Sonicate each diluted sample using a MiSonoix 3000 sonicator equipped with a micro tip. Sonicate each sample for 5 seconds at a power setting of 0.5 watts on wet ice.
7. Analyze the diluted RBC sample according to section II and III below.

II. PLATE SET-UP and INSTRUMENT PARAMETERS

A PLATE SET-UP (NOTE: all samples are to be mixed prior to analysis)

1. Standards, blanks and test samples are run in duplicate.
2. Place 0.010 mL (10 mcL) of each standard or prepared test sample into two individual wells. The location of the sample is to be entered into the SOFTmax template and verified. The SOFTMax template will include the location of all standards, blanks and samples (sample addition will be documented on the Run Documentation Form).
3. Place 0.250 mL of 0.65mM DTNB into each well including the blank wells (DTNB addition is recorded on the Run Documentation Form).
4. Incubate the plate for 10 minutes at 37°C (incubation is usually done in the instrument). The incubation times will be recorded on the Run Documentation Form.
5. The plate is removed from the instrument and 0.100 mL of 3.5mM ATC is added to each well, including the blank wells, the plate is returned to the instrument and the run is started by activating the READ icon.

B. INSTRUMENT PARAMETERS FOR BRAIN AND RBC SAMPLES

PARAMETER	SETTING
Mode:	Kinetic
Run Time:	12 minutes
Intervals:	15 seconds
Detection:	435nm
Auto-mix:	Before first read: Off Between Reads : Off
AutoCalibrate:	On
Lag Time	180 Seconds (3 minutes)
Strips:	Read entire plate
OD Min:	0.0a
OD Max:	2.0 ^a
Incubator Temperature:	37°
Kinetic Reduction:	Vmax
Data Mode:	Absorbance
Display:	with reduced number

- a. The recommended Min and Max values may change based on response magnitude of response and or baseline drift.

III. SAMPLE ANALYSIS

- Once the samples have been processed, they are analyzed by the *SPECTRAmax 190* and recorded using SOFTMax® PRO 4.0 software according to the set-up parameters as outlined in II.
- SOFTMax® PRO 4.0 will automatically add a time and date stamp to each file as part of the file name. This will serve as the unique identifier of each analysis.

IV. CALCULATIONS & ACCEPTANCE CRITERIA

A. Calculations

- The kinetics are automatically reduced to a slope or a Vmax as reported by SOFTMax® PRO 4.0. Each plot is manually checked by the operator to ensure good kinetics, (i.e. linear). Samples with results that are less than the Lower Limit of Quantification (LLOD) are documented in the raw data as “low”. Samples with

results that are greater than the Upper Limit of Quantification (ULOD) are documented in the raw data as “High”. High samples may be diluted and reanalyzed.

B. Acceptance Criteria

1. Correlation Coefficient for the standard curve must not be less than 0.975. If the correlation coefficient is less than 0.975, then it is considered a failed run, and all samples on that plate should be repeated.
2. Standard Curve - The back-calculated concentrations of the calibration standards must be within $\pm 15\%$ (or $\pm 20\%$ for the LLOQ) of their theoretical concentrations. Standards that do not meet the appropriate criteria may be excluded by masking, as long as no more than 20% of the standards are “masked” (i.e., dropped). The LLOQ and ULOQ are then re-defined by SOFTmax® Pro according to the remaining standards.
3. Sample Replication - All samples are analyzed in duplicate. Brain sample duplicates must replicate within 85% of each other in order to be accepted. RBC sample duplicates need to replicate within 80% of each other in order to be accepted. Samples that do not meet these criteria will be labeled by SOFTmax® Pro as “does not replicate” and the sample should be reanalyzed. Samples should not be repeated more than two additional times. If there is insufficient sample to be re-analyzed, then the results are footnoted.
4. Samples that are below the LLOQ are labeled “low”. Any samples that have been labeled as “low” are to be repeated; however these samples should not be analyzed more than three times to achieve an initial acceptable result.
5. Samples that are above the ULOQ for the assay are labeled as “high”. Any sample that generates a “high” result may be re-analyzed or diluted as described in section I, then re-analyzed. Diluted samples which produce unacceptable results may be analyzed up to three times to achieve an initial acceptable result (RBC samples may be analyzed no more than three times to achieve an acceptable result). However, if the initial analysis is

below the limit of quantification (i.e., “low”), the sample will be re-analyzed “as is” because this is the lowest dilution factor achievable. If there are three “low” results the sample will be reported as below the quantifiable limit (BQL). Estimated values are generated by the data collection system and may be used, but need to be identified.

V. DATA COLLECTION AND FINAL REPORTING

A. Data Collection

1. Data Files - Once a set has been analyzed it is automatically saved into the appropriate study file on the network (see preference function in the edit menu). Once the data file has been saved the file is printed and initialed and dated as raw data.
2. Exported Data - Once the data has been saved and printed it may be exported into an “excel” format. This is done by selecting the appropriate SOFTmax file and selecting the export function under the “File” menu.

B. Retest Criteria

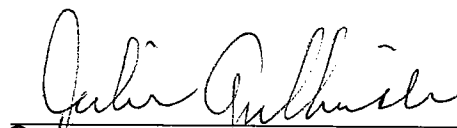
1. Any initial acceptable sample may be re-tested as long as the rationale for testing is documented in the General Comments and is subsequently approved by the Study Director (retesting is done after an initial result has been acquired, and may be done in addition to the three analyses limit).
2. Any sample that is retested must generate acceptable results (based on SOFTMax® PRO 4.0 Acceptance Criteria).
 - a. If the acceptable result is less than or equal to $\pm 25\%$ of the original sample, then the original sample is considered “confirmed” and is used (the second sample result is reported but not used in the group averages).
 - b. If the acceptable result is greater than $\pm 25\%$ of the original sample, then the original sample is considered “contradicted” and a third analysis will be conducted.

- c. If the third analysis is less than or equal to $\pm 25\%$ of the original sample, then the original sample is considered "confirmed" and is used in the group average (the second and third sample results are reported but not used in the group averages). If the third analysis is less than or equal to $\pm 25\%$ of the second analysis, then the second analysis is considered "confirmed" and is used in the group average (the first and the third sample results are reported but not used in the group averages).
- d. If neither the first analysis nor the second analysis is confirmed, then all data will be reported but none of the result from this sample will be used in the group average.

VI. REFERENCES

1. Ellman, G.L., Courtney, K.D., Andres, V.Jr. and Featherstone, R.M. (1961). A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochem Pharmac.*, 7, 88-95
2. Lawson, A.A. and Barr, R.D. (1987) Acetylcholinesterase in red blood cells. *American Journal of Hematology*, 26, 101-112

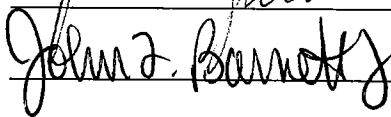
Prepared By:



Date:

03 Dec 2007

Approved By:



Date:

03 Dec 2007



Amendment 1

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

Charles River Laboratories Preclinical Services Study No. TQC00017

Item No. 1.

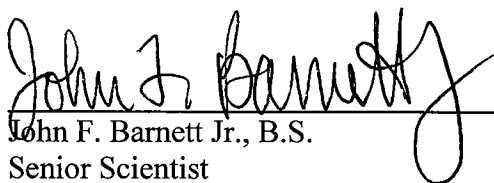
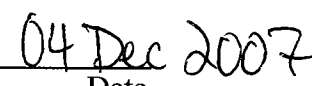
Protocol Section: Blood and Brain Sample Collection (page 19 of the protocol)

Effective Date: The effective date is the date of Study Director signature.

Change: The time between decapitation and completion of blood sample collection will be recorded in the raw data. The time will be recorded using a stop watch.

Justification: This change was made at the Sponsor's request.

STUDY DIRECTOR SIGNATURE

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



Amendment 2

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

Charles River Laboratories Preclinical Services Study No. TQC00017

Item No. 1.

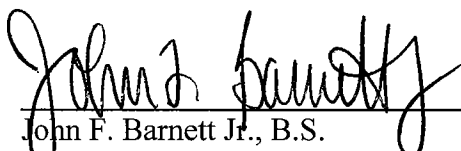
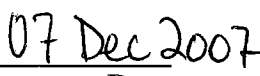
Protocol Section: Concentration and Homogeneity (page 10 of the protocol)

Effective Date: The effective date is the date of Study Director signature.

Change: Only concentration analyses will be performed on the samples from the vehicle group, rather than concentration and homogeneity analyses.

Justification: This change was made to clarify the protocol.

STUDY DIRECTOR SIGNATURE

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



Amendment 3

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

Charles River Laboratories Preclinical Services Study No. TQC00017

Item No. 1.

Protocol Section: Final Report (page 23 of the protocol)

Effective Date: The effective date is the date of Study Director signature.

Changes: A comprehensive draft final report will be prepared, rather than a summary of methods and results. The report will be formatted to comply with EPA's PR Notice 86-5 report formatting requirements. The report will include the following:

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

Justification: This change was made to correct the report format for this study.

Amendment No. 3

Page 2 of 2

Testing Facility Study No. TQC00017

Item No. 2.

Protocol Section: Final Report (page 23 of the protocol)

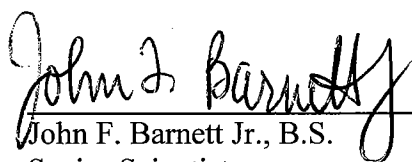
Effective Date: The effective date is the date of Study Director signature.

Changes: The last sentence in the last paragraph of this section should state:

The hard copy of the report with original signatures retained at the Testing Facility will be considered the GLP-compliant original.

Justification: This change is being made to correct this statement in the protocol.

STUDY DIRECTOR SIGNATURE



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

27 Dec 2007
Date



Amendment 4

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

Charles River Laboratories Preclinical Services Study No. TQC00017

Item No. 1.

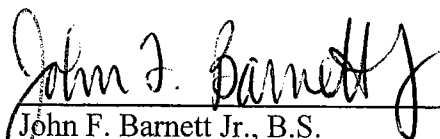

Protocol Section: Analyses (page 9 of the protocol)

Effective Date: The effective date is the date of Study Director signature.

Changes: Analyses of dosing suspensions will be performed by the Charles River Laboratories' facility in Shrewsbury, MA, rather than Worcester, MA.

Justification: This change was made to change the location of dosing suspension analyses.

STUDY DIRECTOR SIGNATURE

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

**APPENDIX 2 - 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 20 November 2007, a total of 51 dams were received at the Testing Facility rather than 48, as stated in the protocol. This deviation did not adversely affect the outcome or interpretation of the study because a sufficient number of dams and pups were available for the study to be conducted.
2. On 4 December 2007 (PND 11), postdosage clinical observations were inadvertently not recorded for male pup 5502 and female pup 5508 in the 1.0 mg/kg/day Malaoxon group. Both rats appeared normal at the next observation. This deviation does not adversely affect the outcome or interpretation of the study because sufficient information is available to evaluate this parameter.
3. On PND 11 (4 December 2007), an insufficient amount of blood was collected from the following F1 generation Malaoxon-treated male pups:

Dosage Group	Pup Number	Actual Volume Collected
0 (Vehicle) mg/kg/day	5101	0.2 mL
	5501	0.3 mL
	5701	0.2 mL
	6101	0.35 mL
1 mg/kg/day	5702	0.2 mL
	6202	0.35 mL
3.5 mg/kg/day	5503	0.3 mL
	5703	0.35 mL
	5803	0.3 mL
	5903	0.35 mL
	6003	0.3 mL
	6203	0.35 mL
7 mg/kg/day	5704	0.2 mL
10 mg/kg/day	5505	0.3 mL
	5705	0.3 mL
	6105	0.2 mL
	6205	0.3 mL
12.5 mg/kg/day	5706	0.2 mL
	6206	0.3 mL

These deviations did not adversely affect the outcome or interpretation of the study because the samples contained an adequate amount of blood for analysis (except the sample from rat #5505).

4. On PND 11 (4 December 2007), an insufficient amount of blood was collected from the following F1 generation Malaoxon-treated female pups:

Dosage Group	Pup Number	Actual Volume Collected
0 (Vehicle) mg/kg/day	5207	0.3 mL
	5707	0.3 mL
1 mg/kg/day	5208	0.3 mL
	5808	0.3 mL
	6008	0.3 mL
	6108	0.3 mL
3.5 mg/kg/day	5109	0.3 mL
	5309	0.3 mL
	5509	0.3 mL
	6209	0.2 mL
7 mg/kg/day	5210	0.3 mL
	5310	0.3 mL
	5610	0.3 mL
	6210	0.3 mL
10 mg/kg/day	5211	0.2 mL
	5511	0.3 mL
	5711	0.3 mL
	5811	0.3 mL
	6011	0.3 mL
	6111	0.3 mL
12.5 mg/kg/day	6211	0.2 mL
	5112	0.3 mL
	5512	0.3 mL
	5612	0.3 mL
	5712	0.3 mL
	5812	0.3 mL
	5912	0.3 mL
	6012	0.2 mL
	6112	0.3 mL
	6212	0.3 mL

These deviations did not adversely affect the outcome or interpretation of the study because the samples contained an adequate amount of blood for analysis (except the sample from rat #6112).

5. On PND 11 (7 December 2007), an insufficient amount of blood was collected from the following F1 generation Malathion-treated pups:

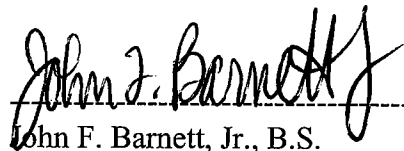
Dosage Group	Pup Number	Pup Sex	Actual Volume Collected
10 mg/kg/day	6608	Female	0.3 mL
25 mg/kg/day	6603	Male	0.05 mL
	6609	Female	0.3 mL
50 mg/kg/day	6604	Male	0.1 mL
	6410	Female	0.3 mL
100 mg/kg/day	6405	Male	0.3 mL
	6311	Female	0.3 mL
	6611	Female	0.3 mL
150 mg/kg/day	6406	Male	0.1 mL
	6606		0.3 mL
	6612	Female	0.3 mL

These deviations did not adversely affect the outcome or interpretation of the study because although 7 of the above listed samples could not be analyzed due to an insufficient amount of blood there were a sufficient number of samples with an adequate amount of blood for analysis.

6. On PND 11 (4 and 7 December 2007), the blood sample tubes were labeled with only the rat number, rather than at minimum with protocol number, date of collection, rat number, dosage group, dosage level, day of study, species, generation, sex, timepoint and storage conditions. This deviation did not adversely affect the outcome or interpretation of the study because appropriate identification was provided on the sample collection tubes to distinguish the animal providing the sample.
7. On PND 11 (4 and 7 December 2007), brain samples for all male and female pups were diluted twice in order to make sure the results were within the acceptable range for analysis according to SOP; however, the protocol requires only a single dilution. These deviations did not adversely affect the outcome or interpretation of the study because the procedure was necessary to assure the samples would be within an acceptable range. This procedure was approved by the Study Director; however, appropriate documentation was not provided at the time of the initial approval.
8. On PND 11 (4 December 2007), for runs 2, 4, 5, 6, 7 and 25 of the cholinesterase data, more than four standards needed to be masked in order to get an acceptable standard curve. This deviation did not adversely affect the outcome or interpretation of the study because documentation of this procedure was provided and all dosage groups were handled in a similar manner.

9. On PND 11 (4 December 2007), all RBC samples from pups 6201 to 6212 were analyzed approximately 2.5 hours from sample collection. This deviation did not adversely affect the outcome or interpretation of the study because the extra time was required for the samples to be prepared and analyzed and presumably did not effect the results of the analyses.
10. On PND 11 (7 December 2007), the revolutions per minute (rpms) at which the samples were spun were not listed on the blood sample processing form. This deviation did not adversely affect the outcome or interpretation of the study because it is presumed that the appropriate settings were used for the study.

All deviations are documented in the raw data.



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

12 Mar 2008

Date

APPENDIX 3 - CERTIFICATE OF ANALYSIS

Certificate Of Analysis

Page 1 of 1

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

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

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 OILNOT MORE THAN 0.001% (AS LEAD)
102 TO 130**LOT 126K0117 RESULTS**

CLEAR YELLOW-GREEN LIQUID

1.2 ML *

<0.001% *

127 *

* SUPPLIER INFORMATION

JANUARY 2007

Rodney Burbach, Supervisor
Analytical Services
St. Louis, Missouri USA

APPENDIX 4 - ANALYTICAL REPORT



FINAL REPORT

**Formulation Sample Analysis
for the Determination of Malathion and Malaoxon in Corn Oil**

Test Site Project No. TQC00017AA
Testing Facility Study No. TQC00017

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

TEST SITE:

Charles River Laboratories
Preclinical Services
334 South Street
Shrewsbury, MA 01545
USA

TESTING FACILITY:

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

SPONSOR:

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

March 11, 2008

Page 1 of 56

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7.	DATA COLLECTION AND STATISTICAL METHODS	10
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Final Report
Test Site Project No. TQC00017AA

Page 4
Testing Facility Study No. TQC00017

1. REPORT REVIEW AND APPROVAL SIGNATURE

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

P Buxton

11 MAR 2008

Peggy Buxton, BS
Principal Investigator
Scientist, Laboratory Sciences

Date

Final Report
Test Site Project No. TQC00017AA

Page 5
Testing Facility Study No. TQC00017

2. COMPLIANCE STATEMENT

This project, conducted at Charles River Laboratories Preclinical Services, Massachusetts, complied with the following regulations:

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

P. Buxton

11 MAR 2008

Peggy Buxton, BS
Principal Investigator
Scientist, Laboratory Sciences

Date

Final Report
Test Site Project No. TQC00017AA

Page 6
Testing Facility Study No. TQC00017

3. QUALITY ASSURANCE STATEMENT

This project has been inspected by the Quality Assurance Unit to assure conformance with the following good laboratory practice regulations: U.S. Environmental Protection Agency. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), Good Laboratory Practice Standards, Final Rule, 40 CFR 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 Practice [C(97)186/Final]. Reports were submitted in accordance with standard operating procedures as follows:


QA INSPECTION DATES

Dates of Inspection	Phases Inspected	Dates Findings Submitted to:			
		Principal Investigator	Principal Investigator Management	Study Director	Study Director Management
11-Dec-2007	Laboratory Procedure	14-Dec-2007	20-Dec-2007	8-Feb-2008	8-Feb-2008
18-Dec-2007	Laboratory Procedure	19-Dec-2007	20-Dec-2007	8-Feb-2008	8-Feb-2008
29-30-Jan-2008	Data and Report	1-Feb-2008	5-Feb-2008	8-Feb-2008	8-Feb-2008
11-Mar-2008	Final Report	11-Mar-08	11-Mar-2008	11-Mar-2008	11-Mar-2008

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.



Anne M. Biedrzycki, BA, MLA
Quality Assurance Auditor



Date

Final Report
Test Site Project No. TQC00017AA

Page 7
Testing Facility Study No. TQC00017

4. RESPONSIBLE PERSONNEL

Principal InvestigatorPeggy Buxton, BS
Laboratory Sciences

Associate Director - Formulation Analysis..... Dominic Moore, BSc, MRSC
Laboratory Sciences

DirectorRichard Norlin, MS
Laboratory Sciences

Technical Writer Kathleen Ferguson, BS
Report Services

5. SUMMARY

The purpose of this project was to determine the concentration and homogeneity of Malathion and Malaoxon in dose formulations from Study No. TQC00017 titled “Oral (Gavage) Acute Dose Comparative Cholinesterase Study of Malathion and Malaoxon in Juvenile Rats.”

Samples of dose formulations were analyzed for Malathion by gas chromatography with flame ionization detection. The method was validated for the analysis of dose formulations at concentrations ranging from 0.58 mg/mL to 38 mg/mL of Malathion in corn oil.

Samples of dose formulations were analyzed for Malaoxon by gas chromatography with flame ionization detection. The method was validated for the analysis of dose formulations at concentrations ranging from 0.020 mg/mL to 2.5 mg/mL of Malaoxon in corn oil.

Results for all dose formulations met the acceptance criteria for concentration ($\leq 15\%$ difference from nominal concentration) and homogeneity ($\leq 5\%$ relative standard deviation).

6. MATERIALS AND METHODS

6.1. Analytical Reference Standards

Identity:	Malathion (Fyfanon [®] Technical)
Manufacturer:	Cheminova A/S
Batch number:	9010501
Purity:	96.0% w/w (100% assumed for use)
Expiration date:	November 9, 2008
Storage conditions:	-20°C ± 5°C, protected from light

Identity:	Malaoxon
Manufacturer:	Cheminova A/S
Batch number:	849-BSe-42C
Purity:	97.7% (100% assumed for use)
Expiration date:	March 4, 2009 (when refrigerated)
Storage conditions:	-20°C ± 5°C, protected from light

The characterization of the analytical reference standards is the responsibility of the Sponsor, as is the method of synthesis, fabrication or derivation, and stability determination. Certificates of Analysis are contained in [Appendix 1](#).

6.2. Sample Receipt and Storage

Two shipments of samples were received from Charles River Laboratories Preclinical Services (Horsham, Pennsylvania) on December 5 and 11, 2007. The samples were received packaged on ice packs and in satisfactory condition. Samples were stored at 5°C ± 3°C, protected from light, and analyzed within the established stability period (15 days).

6.3. Sample Analysis

Samples of dose formulations were analyzed for Malathion according to the validated method described in Charles River Laboratories Preclinical Services Laboratory Method (LM) MALA00 for the “Analysis of Malathion in Corn Oil Dose Formulations by GC-FID,” which was validated in Charles River Laboratories Preclinical Services, Massachusetts Project Number TQC00018AX. A copy of the most recent version of the LM is contained in [Appendix 2](#).

Samples of dose formulations were analyzed for Malaoxon according to the validated method described in Charles River Laboratories Preclinical Services LM MLXN00 for the “Analysis of Malaoxon in Corn Oil Dose Formulations by GC-FID,” which was validated in Charles River Laboratories Preclinical Services, Massachusetts Project Number TQC00019AX. A copy of the most recent version of the LM is contained in [Appendix 3](#).

7. DATA COLLECTION AND STATISTICAL METHODS

TotalChrom[®], Version 6.2.1 (PerkinElmer[®]) software was used for acquisition of GC data, assessment of system suitability, and integration of the peak area of the analyte. After integration of the peak areas, data were exported to a verified Excel[®] (Microsoft[®]) spreadsheet. The Excel spreadsheet was used for regression analysis and calculation of Malathion and Malaoxon concentrations and descriptive statistics.

8. MAINTENANCE OF RAW DATA AND RECORDS

The original Final Report and raw data will be stored in the archives of the Testing Facility located in Horsham, Pennsylvania.

9. RESULTS

Concentration and homogeneity results are summarized in [Table 1](#). Results and conclusions for each analytical run are provided in the Dose Formulation Analysis Reports, which are contained in [Appendix 4](#).

9.1. Concentration

Mean measured Malathion and Malaoxon concentrations for all dose formulations were within the acceptable limits ($\leq 15\%$ difference from nominal concentration).

9.2. Homogeneity

The relative standard deviation (RSD) of the mean of the average concentration values for the top, middle, and bottom of each dose formulation was calculated to assess homogeneity. Homogeneity was acceptable ($\leq 5\%$ RSD) for all Malathion and Malaoxon dose formulations.

10. REFERENCES

1. Savage, D. Method validation to support analysis of Malathion in corn oil for Cheminova A/S. Charles River Laboratories Preclinical Services Massachusetts. Project Number TQC00018AX; August 18, 2006.
2. Savage, D. Method validation to support analysis of Malaoxon in corn oil for Cheminova A/S. Charles River Laboratories Preclinical Services Massachusetts. Project Number TQC00019AX; August 18, 2006.

TABLES

Table 1 Summary of Malathion and Malaoxon Concentration and Homogeneity Results

Analyte	Group	Nominal Concentration (mg/mL)	Mean Measured Concentration (mg/mL)	Mean Bias (%)	Homogeneity (%RSD)
Malathion	I	0	ND	NA	—
	II	2	1.846	-7.7	1.4
	III	5	4.732	-5.4	1.0
	IV	10	10.12	1.2	2.8
	V	20	20.22	1.1	1.2
	VI	30	28.97	-3.4	0.6
Malaoxon	I	0	ND	NA	—
	II	0.2	0.2239	12.0	1.0
	III	0.7	0.6811	-2.7	0.6
	IV	1.4	1.351	-3.5	0.7
	V	2.0	1.951	-2.5	0.2
	VI	2.5	2.412	-3.5	1.1

ND None detected.
 NA Not applicable.
 — Not required.

APPENDICES

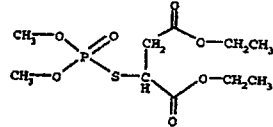
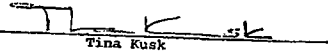
APPENDIX 1
CERTIFICATES OF ANALYSIS



Cheminova A/S
P.O. Box 9
DK-7820 Lemvig
Denmark

Phone (+45) 96 90 96 90
Fax (+45) 96 90 96 91
www.cheminova.com
CVR-No. DK12760043

BATCH ANALYTICAL CERTIFICATE

ARTICLE IDENTIFICATION	
Article Name:	Malaoxon
Manufacturer:	Cheminova A/S
Reg. Dept. Code:	-
Batch No.:	849-BSe-42c
Origin of Production:	Commercial <input type="checkbox"/> ; Pilot plant <input type="checkbox"/> ; Laboratory <input checked="" type="checkbox"/> ;
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 <input checked="" type="checkbox"/>	The article is stable at least 4 years from date of analysis/last date of reanalysis when stored at recommended conditions.
In deep freezer <input checked="" type="checkbox"/>	
Additional Comments:	
ACTIVE INGREDIENT IDENTIFICATION	
Common Name/ISO-Name:	Malaoxon
CAS No.:	1634-78-2
Empirical Formula:	C ₁₀ H ₁₉ O ₇ PS
Molecular Weight:	314.3
Identified by means of:	<div style="display: flex; justify-content: space-between;"> <div> <p>CAS-Name: Butanedioic acid, [(dimethoxyphosphinyl)thio]-, diethyl ester</p> <p>Structural Formula:</p>  </div> <div> <p>NMR <input checked="" type="checkbox"/> ; IR <input checked="" type="checkbox"/> ; UV <input checked="" type="checkbox"/> ; MS <input checked="" type="checkbox"/> ; Other Methods:</p> </div> </div>
ANALYTICAL DATA	
Certified Purity/Content of a.i.: 97.7% w/w	
Analytical Method: ³¹ P-NMR	
Analytical Report (incl. amendments): REP 029-07	
Date of analysis/reanalysis (yy/mm/dd)	050304
-for article stored at -	Cheminova A/S
GLP-COMPLIANCE	
<p>The identification and determination of purity/content of active ingredient were performed at Cheminova A/S and conducted in accordance with FIFRA 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.</p>	
Date: April 25, 2005	Signature:  Tina Kusk



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

Phone (+45) 96 90 96 90
Fax (+45) 96 90 96 91
www.cheminova.com
CVR-No. DK 12 76 00 43

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	
In deep freezer <input type="checkbox"/>		of analysis/last date of reanalysis when stored at	
Additional Comments:		recommended conditions.	
ACTIVE INGREDIENT IDENTIFICATION			
Common Name/ISO-Name:	Malathion	CAS-Name:	Butanedioic acid, ((dimethoxyphosphinothioyl)thio)-, diethyl ester
CAS No.:	121-75-5		
Empirical Formula:	C ₁₀ H ₁₉ O ₆ PS ₂	Structural Formula:	
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 Content of Isomalathion: 0.29% w/w. Analytical Method: VAM 001-02 and VAM 005-03 Analytical Report (incl. amendments): TEM 010-02			
Date of analysis/ reanalysis (yyymmdd)	021024	041103	061109
-for article stored at -	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 FIFRA 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:	December 5, 2006	Signature:	 Barbara Hinz



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CVR-No. DK 12 76 00 43

BATCH ANALYTICAL CERTIFICATE
TEST/REFERENCE ARTICLE

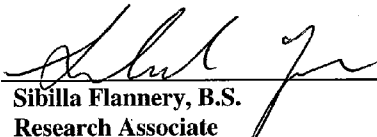
<u>Addendum</u>				
Article Name: Pyfanon Technical				
Batch No.: 9010501				
ANALYTICAL DATA				
Impurities:		Reference, Analytical Report: TEM 010-02		
CAS No.	CAS name/other name; (Cheminova name)	% by weight	Analytical method	Date of analysis (yy-mm-dd)
23060-14-2	Butanedioic acid mercapto- diethylester (ME + H ₂ S)	0.08	VAM 006-02	021022
GLP - COMPLIANCE				
<p>The identification and determination of the impurities were performed at Cheminova A/S and conducted in accordance with FIFRA 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.</p>				
Date: <u>December 5, 2006</u>		Signature: <u>Barbara Hinz</u> Barbara Hinz		


APPENDIX 2
LABORATORY METHOD MALA00



LM Number:	MALA00	Revision Number:	05
Effective Date:	February 04, 2008	Page	1 Of 14

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

Prepared By:  05 Feb 2008
Sibilla Flannery, B.S. Date
Research Associate

Reviewed By:  05 FEB 2008
Peggy Buxton, B.S. Date
Scientist

Authorized By  05 February 2008
Dominic Moore, BSc MSRC Date
Associate Director, Laboratory Sciences

LM Number:	MALA00	Revision Number:	05
Effective Date:	February 04, 2008	Page	2 Of 14

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:

NOTE: Concentrations have not been corrected for purity.

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 100)	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°C ± 5°C	19 hours
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.

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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.

6.2 Preparation of Stocks, Working Stocks, Standards and Blanks

Dilution schemes other than those listed in the tables below may be utilized with Project Scientist approval as long as the ratios remain the same.

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

6.2.1 Preparation of Stocks

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	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

6.3 Sample Preparation

Dilution schemes other than those listed in the tables below may be utilized with Project Scientist approval as long as the sample concentration is within the validated range of the method.

Store diluted samples at 5°C ± 3°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

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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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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 GC system described below, adjusting the solvent ratio if necessary, to approximate the retention time listed below. Refer to the SOP for Chromatographic System Suitability.

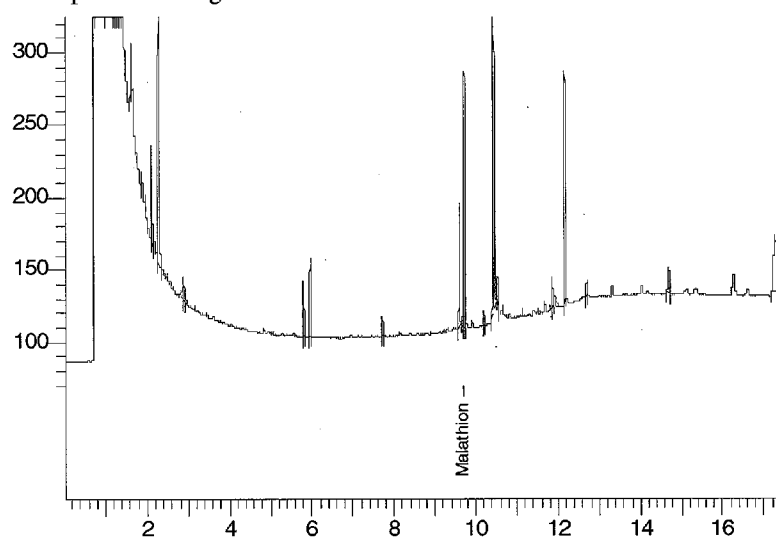
6.5.1 Instrumental

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.
- 6.6.5 Compute the correlation coefficient for the standard curve.

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- 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: (mean concentration found – theoretical concentration) x 100 / theoretical concentration.
- 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: (low value / high value) ≥ 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.
- 7.3 From Revision 01 to Revision 02:
 - 7.3.1 Added note regarding purity in Section 2.
- 7.4 From Revision 02 to Revision 03:
 - 7.4.1 Section 6.2 and 6.3: Added notes to allow adjustment to dilution schemes with Project Scientist approval.
 - 7.4.2 Added batch and reagent paperwork to LM.
 - 7.4.3 Section 6.4.1: Updated to state ≥ 2 system checks.
- 7.5 From Revision 03 to Revision 04:
 - 7.5.1 Section 2: Updated standard dilution table to read "1 in 100" instead of "1 in 1000" which was originally a typo.
- 7.6 From Revision 04 to Revision 05:
 - 7.6.1 Section 2: Updated the Stability Table with Process Stability result.
 - 7.6.2 Section 6.5: Corrected to indicate "GC" system instead of HPLC.

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BATCH AND REAGENT PAPERWORK

'Preparation of Reagents', 'Calibration Standard Preparation', 'Preparation of Samples' and 'Instrument Parameters' sheets in the LM appendix will be copied from the current signed LM revision, filled out recording raw data, and placed into batch folders to be stored with the study materials.

Paperwork not included in the LM appendix may also be utilized if reviewed, approved, and initialed/dated by a Project Scientist or management, and documented/filled-out properly.

Approval for batch paperwork not included in the LM should occur the day of and/or prior to the batch if possible, but this may not always be possible, in which case posterior approval will be acceptable.

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Preparation of Reagents

Prepared by: _____ Date: _____

Batch ID: _____

NA ☐ **Diluent 1**
(100% Acetone)

ID: _____

-Dil 1

Transfer acetone to an appropriate container.

Storage Temperature: Room Temperature (22 +/- 5 deg C)

Expiration Date: _____

NA ☐ **Diluent 2**
(0.1% Corn Oil in Acetone)

ID: _____

-Dil 2

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

Storage Temperature: Room Temperature (22 +/- 5 deg C)

Expiration Date: _____ Pipette ID: _____

Materials Used:

Acetone:	Vendor: _____	Grade: _____	Strength / Purity: _____	Lot #: _____	Exp: _____
Corn Oil:	Vendor: _____	Grade: _____	Strength / Purity: _____	Lot #: _____	Exp: _____

Approved by: PAB Date: 05 FEB 2008

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Calibration Standard Preparation

Batch ID:

Analyst Initials: _____ Date: _____					
Stock Solutions					
Compound Name		Weight (mg)	Final Volume (mL)	ID	
Malathion	Stock A			-STKA	
Malathion	Stock B			-STKB	
Diluting Solution ID: _____ Correction Factor: <input type="checkbox"/> _____ <input type="checkbox"/> N/A					
Balance ID: _____ Standard Used: _____					
Working Stock Solutions					
	mL of STKA	mL of STKB	Final Volume (mL)	ID	
Working Stock A				-WSTKA	
Working Stock B				-WSTKB	
Diluting Solution ID: _____					
Matrix Matched Calibration Standards					
Standard	mL of WSTKA	mL of WSTKB	Vehicle Added (mL)	Final Volume (mL)	Standard ID
A1					-A1
B1					-B1
A2					-A2
B2					-B2
A3					-A3
B3					-B3
Blank					-Blk
Diluting Solution ID: _____ Pipette ID: _____					
Vehicle ID: _____					
Dilutions stored in unit _____					

Approved by: PAB Date: 05 FEB 2008

Batch ID:

[illegible]

Approved by: PAB Date: 05 FEB 2008

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Instrument Parameters

Batch ID:	
Analyst Initials:	Date:
Data System:	TotalChrom 6.2.1
Interface Box:	
Autosampler:	
GC:	
Detector and Temperature:	FID and 275°C
Injector and Temperature:	Capillary and 220°C
Column:	Brand Phenomenex
	Type ZB-5
	Size 30 m x 0.25 mm ID, 0.25 µm film thickness
	S/N
Liner:	Brand Restek
	Type Split w/ Wool
	Size 4.0 mm
	S/N
Instrument Conditions:	
Carrier (He) Flow Rate:	mL/min
Make-Up (He) Flow Rate:	mL/min
Split Vent Flow Rate:	mL/min
Hydrogen Flow Rate:	mL/min
Air Flow Rate:	mL/min
Purge Flow Rate:	mL/min
Injection Technique:	Split (2:1)
Sequence:	
Injection Volume	2 µL
Solvent Rinse:	Acetone*
Approved by: <u>PAB</u> Date: <u>05 FEB 2008</u>	

*Acetone: _____


APPENDIX 3
LABORATORY METHOD MLXN00

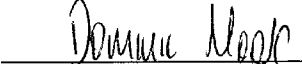


LM Number:	MLXN00	Revision Number:	05
Effective Date:	January 02, 2008	Page	1 Of 14

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

Prepared By:  02 JAN 2008
Sibilla Flannery, B.S. Date
Research Associate

Reviewed By:  02 JAN 2008
Peggy Buxton, B.S. Date
Scientist

Authorized By:  02 January 2008
Dominic Moore, BSc MSRC Date
Associate Director, Laboratory Sciences

LM Number:	MLXN00 -	Revision Number:	05
Effective Date:	January 02, 2008	Page	2 Of 14

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 [X] 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	Additional 1 in 25 Dilution
LOD	0.0007	0.007	0.018
LLOQ to ULOQ	0.017 – 0.14	0.17 – 1.4	0.43 – 3.5
Valid Sample Range	0.020 – 0.12	0.20 – 0.80	0.90 – 2.5

3 Stability

Description	Concentration Range	Storage Conditions	Time Period
Process Stability	0.00034-0.0028	22 ± 5°C	24 hours
Stability Period 1*	0.02	21°C	2 hours
Stability Period 2*	250	21°C	48 hours
Stability Period 3*	0.02-250	4°C	15 days

* Stability information provided by the Sponsor under Sponsor report number CHV 0121/053810.

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Standards should be prepared fresh for each analysis. All storage conditions are unprotected from light unless specified otherwise.

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 samples for a density of 0.915 g/mL.

6 Materials

6.1 Chemicals

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

6.2 Supplies

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

7 Procedure

7.1 Preparation of Reagents

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

7.1.1 Diluent 1 (100% Acetone)

Transfer acetone to an appropriate container.

7.1.2 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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7.2 Preparation of Stocks, Working Stocks, Standards and Blanks

Dilution schemes other than those listed in the tables below may be utilized with Project Scientist approval as long as the ratios remain the same.

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

7.2.1 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.

7.2.2 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

7.2.3 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

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7.2.4 Preparation of Blank

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

7.3 Sample Preparation

Dilution schemes other than those listed in the tables below may be utilized with Project Scientist approval as long as the sample concentration is within the validated range of the method.

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

7.3.1 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 2.5	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
From 0.9 to 2.5	1	25	diluent 2

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7.4 Analytical Run Sequence and Composition

7.4.1 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)

7.4.2 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.

7.5 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.

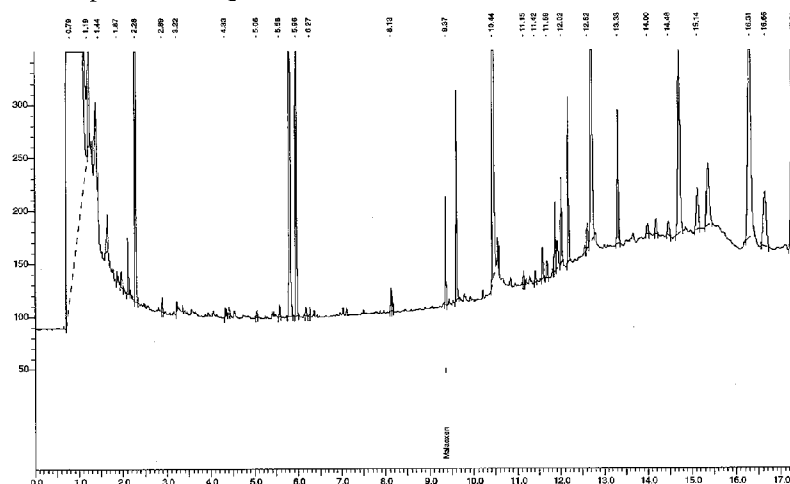
7.5.1 Instrumental

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

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Pre-injection Solvent Washes: 3
Post-injection Solvent Washes: 3
Sample Washes: 3
Sample Pumps: 3

7.5.2 Example Chromatogram for B3 Standard



7.6 Calculations

- 7.6.1 Chromatograms will be automatically integrated and visually inspected for an acceptable integration. Manual baselines will be performed when necessary.
- 7.6.2 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.
- 7.6.3 Calculate the concentration of the six spiked standards from the actual stock concentration, in terms of milligram of Malaoxon per milliliter.
- 7.6.4 Compute the unweighted linear regression relating the peak areas of the standards to their respective Malaoxon concentrations, without blank correction.
- 7.6.5 Compute the correlation coefficient for the standard curve.
- 7.6.6 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.

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7.6.7 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 (ND).

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

7.7 Acceptance Criteria

7.7.1 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.

7.7.2 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.

7.7.3 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.

7.7.4 Check Standards

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

7.7.5 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 .

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7.7.6 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 $\pm 15.0\%$.

8 Revision History

- 8.1 Method validation performed under project TQC00019AX.
- 8.2 From Revision 00 to Revision 01:
 - 8.2.1 Corrected spelling of Malaoxon throughout document.
 - 8.2.2 Added Stability in Section 2. Stability was provided by the Sponsor.
- 8.3 From Revision 01 to Revision 02:
 - 8.3.1 Section 2: Changed the Sponsor report number in the stability table footnote from "CHV 066/013331" to "CHV 0121/053810".
- 8.4 From Revision 02 to Revision 03:
 - 8.4.1 Corrected Stability in Section 2. Stability provided by the Sponsor.
- 8.5 From Revision 03 to Revision 04:
 - 8.5.1 Section 7.2 and 7.3: Added note to allow changes to the dilution schemes with Project Scientist approval.
 - 8.5.2 Added Batch and Reagent Paperwork to LM.
 - 8.5.3 Section 7.4.1: Updated to state ≥ 2 system checks.
- 8.6 From Revision 04 to Revision 05:
 - 8.6.1 Section 2 and 7.3.1: Updated dilution scheme to include samples up to and including 2.5 mg/mL.

LM Number:	MLXN00	Revision Number:	05
Effective Date:	January 02, 2008	Page	10 Of 14

APPENDIX I BATCH AND REAGENT PAPERWORK

'Preparation of Reagents', 'Calibration Standard Preparation', 'Preparation of Samples' and 'Instrument Parameters' sheets in the LM appendix will be copied from the current signed LM revision, filled out recording raw data, and placed into batch folders to be stored with the study materials.

Paperwork not included in the LM appendix may also be utilized if reviewed, approved, and initialed/dated by a Project Scientist or management, and documented/filled-out properly.

Approval for batch paperwork not included in the LM should occur the day of and/or prior to the batch if possible, but this may not always be possible, in which case posterior approval will be acceptable.

LM Number:	MLXN00	Revision Number:	05
Effective Date:	January 02, 2008	Page	11 Of 14

Preparation of Reagents

Prepared by: _____ Date: _____

Batch ID: _____

NA ☐ **Diluent 1**
(100% Acetone)

ID: _____

-Dil 1

Transfer acetone to an appropriate container.

Storage Temperature: Room Temperature (22 +/- 5 deg C)

Expiration Date: _____

NA ☐ **Diluent 2**
(2% Corn Oil in Acetone)

ID: _____

-Dil 2

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

Storage Temperature: Room Temperature (22 +/- 5 deg C) Pipette ID: _____

Expiration Date: _____

Materials Used:

Acetone:	Vendor: _____	Grade: _____	Strength / Purity: _____	Lot #: _____	Exp: _____
Corn Oil:	Vendor: _____	Grade: _____	Strength / Purity: _____	Lot #: _____	Exp: _____

Approved by: PAB Date: 02 JAN 2008

LM Number:	MLXN00	Revision Number:	05	-
Effective Date:	January 02, 2008	Page	12	Of 14

Calibration Standard Preparation

Batch ID:

Analyst Initials: _____ Date: _____					
Stock Solutions					
Compound Name		Weight (mg)	Final Volume (mL)	ID	
Malaoxon	Stock A			-STKA	
Malaoxon	Stock B			-STKB	
Diluting Solution ID: _____			Correction Factor: <input type="checkbox"/> _____ <input type="checkbox"/> N/A		
Balance ID: _____		Standard Used: _____			
Working Stock Solutions					
	mL of STKA	mL of STKB	Final Volume (mL)	ID	
Working Stock A				-WSTKA	
Working Stock B				-WSTKB	
Diluting Solution ID: _____					
Matrix Matched Calibration Standards					
Standard	mL of WSTKA	mL of WSTKB	Vehicle Added (mL)	Final Volume (mL)	Standard ID
A1					-A1
B1					-B1
A2					-A2
B2					-B2
A3					-A3
B3					-B3
Blank					-Blk
Diluting Solution ID: _____			Pipette ID: _____		
Vehicle ID: _____					
Dilutions stored in unit _____					

Approved by: PAB Date: 02 JAN 2008

Sample Preparation

Approved by: PAB Date: 02 JAN 2008

LM Number:	MLXN00	Revision Number:	- 05
Effective Date:	January 02, 2008	Page	14 Of 14

Instrument Parameters

Batch ID:	
Analyst Initials:	Date:
Data System:	TotalChrom 6.2.1
Interface Box:	
Autosampler:	
GC:	
Detector and Temperature:	FID and 275°C
Injector and Temperature:	Capillary and 220°C
Column:	Brand Phenomenex
	Type ZB-5
	Size 30 m x 0.25 mm ID, 0.25 µm film thickness
	S/N
Liner:	Brand Restek
	Type Split w/ Wool
	Size 4.0 mm
	S/N
Instrument Conditions:	
Carrier (He) Flow Rate:	mL/min
Make-Up (He) Flow Rate:	mL/min
Split Vent Flow Rate:	mL/min
Hydrogen Flow Rate:	mL/min
Air Flow Rate:	mL/min
Purge Flow Rate:	mL/min
Injection Technique:	Split (2:1)
Sequence:	
Injection Volume	2 µL
Solvent Rinse:	Acetone*

Approved by: PAB Date: 02 JAN 2008

*Acetone: _____

APPENDIX 4
DOSE FORMULATION ANALYSIS REPORTS

Final Report
Test Site Project No. TQC00017AA

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Testing Facility Study No. TQC00017

DOSE FORMULATION ANALYSIS REPORT

Sponsor: Cheminova A/S
Study Facility: Charles River Laboratories Preclinical Services, Pennsylvania
Protocol Number: TQC00017
Analyte: Malaoxon
Analytical Facility: Charles River Laboratories Preclinical Services, Massachusetts
Batch ID: TQC00017AA-1-001-1
Sampling Criteria: Start of Study Concentration and Homogeneity Analysis
Vehicle: Corn Oil
Storage Conditions: 5°C ± 3°C
Laboratory Method: MLXN00 Rev 04
Analysis Date: December 11, 2007
Notes: Samples were corrected for a corn oil density of 0.915 g/mL.

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

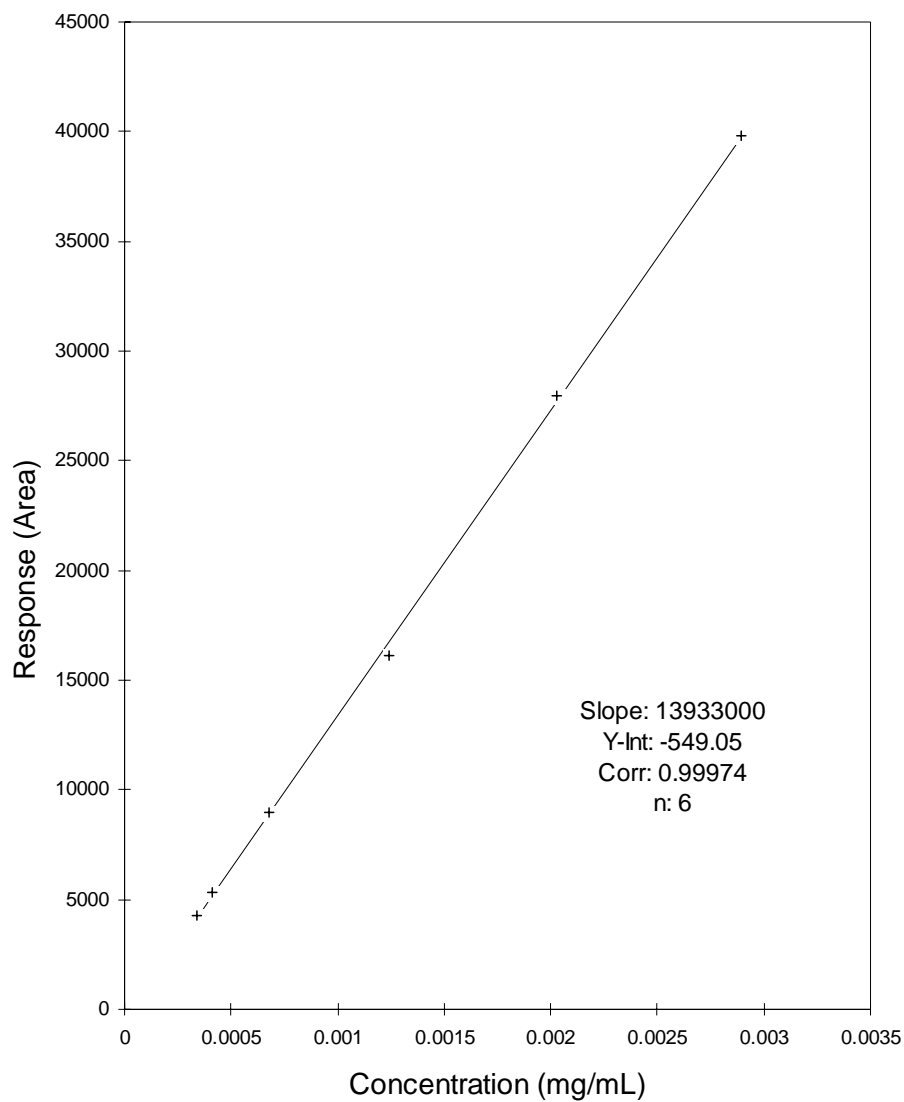
CALIBRATION STANDARDS

Standard Description	Nominal Conc.	Response Area	Calculated Conc.	% Bias	X = Exclude	Criteria Limit	Standard Pass/Fail
Cal Std A1	0.0003379	4242	0.0003439	+1.8		5%	PASS
Cal Std B1	0.0004134	5355	0.0004237	+2.5		5%	PASS
Cal Std A2	0.0006758	8970	0.0006832	+1.1		5%	PASS
Cal Std B2	0.001240	16091	0.001194	-3.7		5%	PASS
Cal Std A3	0.002027	27985	0.002048	+1.0		5%	PASS
Cal Std B3	0.002894	39786	0.002895	0.0		5%	PASS

CHECK STANDARDS

Standard Description	Nominal Conc.	Response Area	Dilution Factor	Conc. Found	% Bias	Criteria Limit	Standard Pass/Fail
Cal Std A3	0.002027	28015	1	0.002050	+1.1	5.0%	PASS
Cal Std A3	0.002027	26845	1	0.001966	-3.0	5.0%	PASS
Cal Std A3	0.002027	28398	1	0.002078	+2.5	5.0%	PASS
Cal Std A3	0.002027	27515	1	0.002014	-0.6	5.0%	PASS

Project Number: TQC00017AA
Analysis of Malaoxon in Corn Oil
Batch ID: TQC00017AA-1-001-1



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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 Middle	12/04/07	0	A	0	53.54	ND		
			B	0	54.91	ND		
Group II Top	12/04/07	0.2	A	5907	525.3	0.2227	0.2251	+12.6
			B	6027	526.7	0.2275		
Group II Middle	12/04/07	0.2	A	5989	520.8	0.2236	0.2213	+10.7
			B	5840	521.8	0.2189		
Group II Bottom	12/04/07	0.2	A	6246	522.0	0.2329	0.2254	+12.7
			B	5674	533.1	0.2179		
Group III Top	12/04/07	0.7	A	18810	538.1	0.6841	0.6765	-3.4
			B	18280	540.9	0.6688		
Group III Middle	12/04/07	0.7	A	18648	541.1	0.6821	0.6820	-2.6
			B	18603	542.1	0.6818		
Group III Bottom	12/04/07	0.7	A	18618	542.7	0.6831	0.6849	-2.2
			B	18953	536.2	0.6867		
Group IV Top	12/04/07	1.4	A	15073	1328	1.363	1.362	-2.7
			B	15080	1325	1.360		
Group IV Middle	12/04/07	1.4	A	14771	1312	1.320	1.345	-3.9
			B	15041	1337	1.369		
Group IV Bottom	12/04/07	1.4	A	15430	1327	1.392	1.347	-3.8
			B	14477	1319	1.302		
Group V Top	12/04/07	2	A	21492	1308	1.894	1.951	-2.5
			B	21887	1362	2.007		
Group V Middle	12/04/07	2	A	21087	1345	1.911	1.948	-2.6
			B	22268	1324	1.985		
Group V Bottom	12/04/07	2	A	22284	1303	1.954	1.955	-2.3
			B	21686	1339	1.955		
Group VI Top	12/04/07	2.5	A	26322	1351	2.384	2.391	-4.4
			B	26520	1349	2.398		
Group VI Middle	12/04/07	2.5	A	27268	1316	2.404	2.405	-3.8
			B	27011	1329	2.406		
Group VI Bottom	12/04/07	2.5	A	26641	1330	2.374	2.441	-2.4
			B	24176	1544	2.507		

HOMOGENEITY

Sample Description	Nominal Sample Conc.	Grand Mean Conc.	% RSD	% Error
Group II	0.2	0.2239	1.0	12.0
Group III	0.7	0.6811	0.6	-2.7
Group IV	1.4	1.351	0.7	-3.5
Group V	2	1.951	0.2	-2.5
Group VI	2.5	2.412	1.1	-3.5

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Test Site Project No. TQC00017AA

Testing Facility Study No. TQC00017

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

ACTIONS TAKEN: None.

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Testing Facility Study No. TQC00017

DOSE FORMULATION ANALYSIS REPORT

Sponsor: Cheminova A/S
Study Facility: Charles River Laboratories Preclinical Services, Pennsylvania
Protocol Number: TQC00017
Analyte: Malathion
Analytical Facility: Charles River Laboratories Preclinical Services, Massachusetts
Batch ID: TQC00017AA-1-002-1
Sampling Criteria: Start of Study Concentration and Homogeneity Analysis
Vehicle: Corn Oil
Storage Conditions: 5°C ± 3°C
Laboratory Method: MALA00 Rev 03
Analysis Date: December 18, 2007
Notes: Samples were corrected for a corn oil density of 0.915 g/mL.

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

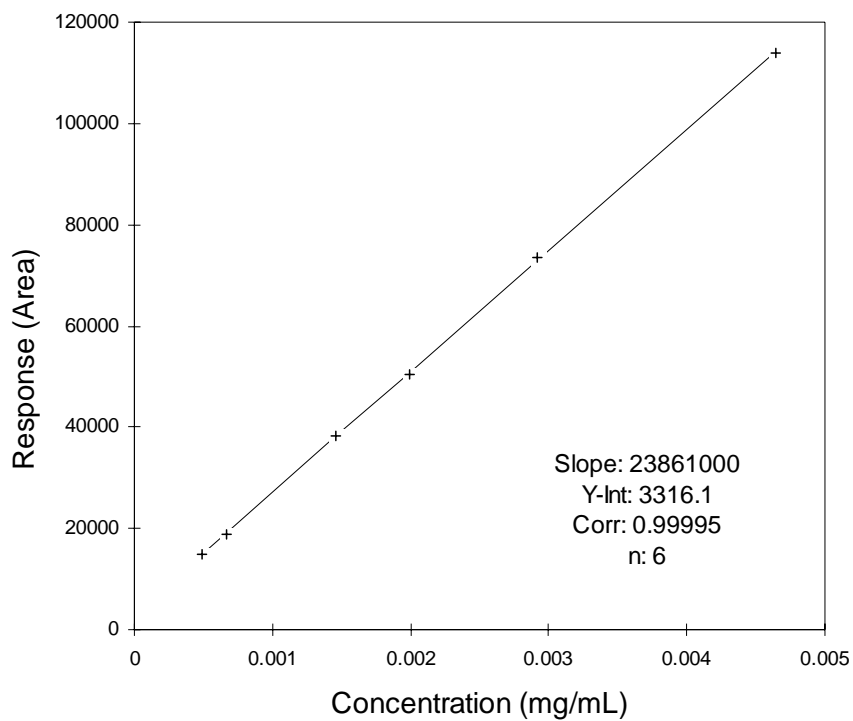
CALIBRATION STANDARDS

Standard Description	Nominal Conc.	Response Area	Calculated Conc.	% Bias	X = Exclude	Criteria Limit	Standard Pass/Fail
Cal Std A1	0.0004862	14975	0.0004886	+0.5		5%	PASS
Cal Std B1	0.0006640	18824	0.0006499	-2.1		5%	PASS
Cal Std A2	0.001459	38389	0.001470	+0.8		5%	PASS
Cal Std B2	0.001992	50582	0.001981	-0.6		5%	PASS
Cal Std A3	0.002917	73482	0.002941	+0.8		5%	PASS
Cal Std B3	0.004648	113943	0.004636	-0.3		5%	PASS

CHECK STANDARDS

Standard Description	Nominal Conc.	Response Area	Dilution Factor	Conc. Found	% Bias	Criteria Limit	Standard Pass/Fail
Check Std A3	0.002917	70079	1	0.002798	-4.1	5.0%	PASS
Check Std A3	0.002917	69492	1	0.002773	-4.9	5.0%	PASS
Check Std A3	0.002917	69647	1	0.002780	-4.7	5.0%	PASS
Check Std A3	0.002917	69541	1	0.002775	-4.9	5.0%	PASS

Project Number: TQC00017AA
Analysis of Malathion in Corn Oil
Batch ID: TQC00017AA-1-002-1



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Test Site Project No. TQC00017AA

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SAMPLES

<u>Sample Description</u>	<u>Prep Date</u>	<u>Nominal Sample Conc.</u>	<u>Replicate</u>	<u>Response Area</u>	<u>Total Dilution Factor</u>	<u>Density Corrected mg/mL</u>	<u>Mean mg/mL Found</u>	<u>% Bias</u>
Group I Middle	12/07/07	0	A	0	1093	ND		
			B	0	1111	ND		
Group II Top	12/07/07	2	A	48053	1070	1.835	1.844	-7.8
			B	48373	1073	1.853		
Group II Middle	12/07/07	2	A	48004	1072	1.837	1.822	-8.9
			B	45179	1125	1.807		
Group II Bottom	12/07/07	2	A	50192	1044	1.877	1.872	-6.4
			B	49257	1059	1.866		
Group III Top	12/07/07	5	A	26561	5366	4.783	4.730	-5.4
			B	25874	5407	4.677		
Group III Middle	12/07/07	5	A	26623	5342	4.774	4.781	-4.4
			B	26995	5273	4.788		
Group III Bottom	12/07/07	5	A	26148	5288	4.630	4.686	-6.3
			B	26660	5296	4.741		
Group IV Top	12/07/07	10	A	50837	5389	9.821	9.921	-0.8
			B	53070	5253	10.02		
Group IV Middle	12/07/07	10	A	51970	5374	10.03	10.44	+4.4
			B	57587	5212	10.85		
Group IV Bottom	12/07/07	10	A	52660	5257	9.948	9.984	-0.2
			B	52555	5309	10.02		
Group V Top	12/07/07	20	A	55063	10190	20.22	20.47	+2.3
			B	50682	11410	20.72		
Group V Middle	12/07/07	20	A	58955	9333	19.91	19.97	-0.2
			B	51612	10810	20.02		
Group V Bottom	12/07/07	20	A	51877	10990	20.46	20.23	+1.2
			B	45409	12390	19.99		
Group VI Top	12/07/07	30	A	75866	10440	29.06	28.79	-4.0
			B	72894	10690	28.52		
Group VI Middle	12/07/07	30	A	73635	10560	28.46	29.10	-3.0
			B	76249	10630	29.73		
Group VI Bottom	12/07/07	30	A	76314	10360	29.00	29.03	-3.2
			B	75404	10510	29.05		

HOMOGENEITY

<u>Sample Description</u>	<u>Nominal Sample Conc.</u>	<u>Grand Mean Conc.</u>	<u>% RSD</u>	<u>% Error</u>
Group II	2	1.846	1.4	-7.7
Group III	5	4.732	1.0	-5.4
Group IV	10	10.12	2.8	1.2
Group V	20	20.22	1.2	1.1
Group VI	30	28.97	0.6	-3.4

Final Report

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Test Site Project No. TQC00017AA

Testing Facility Study No. TQC00017

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

ACTIONS TAKEN: None.

APPENDIX 5 - ENVIRONMENTAL AND HUSBANDRY REPORTS

TEMPERATURE AND RELATIVE HUMIDITY REPORTS

ARGUS

Temperature and Relative Humidity Report Location: Room 17 Protocol Number: TQC00017			
Range of Dates: 20-Nov-2007 14:18 to 07-Dec-2007 18:59			
Target Range: Species: Rat Total Number of Days: Total Number of Hours: Total Number of Data Points:	Temperature 64°F to 79°F	Relative Humidity 30% to 70%	
	18	18	
	412.25	412.25	
	413	413	
Mean (± SD):	67.6 (± 0.5)	38.7	(± 7.6)
Maximum:	68.6	58.1	
Median:	67.6	36.6	
Minimum:	66.0	28.1	
Number of Points in Range (%):	413 (100.0)	376	(91.0)
Number of Points High (%):	0 (0.0)	0	(0.0)
Number of Points Low (%):	0 (0.0)	37	(9.0)

Report Generated: 24-Dec-2007 at 13:40

COMMENTS: _____

REVIEWED BY: John J. Barnett DATE: 23 Jun 2008

ARGUS**Relative Humidity Deviations Report**
Location: Room 17**Protocol Number: TQC00017****Range of Dates: 20-Nov-2007 14:18 to 07-Dec-2007 18:59****Humidity Target Range:** 30% to 70%
Species: Rat

Date	Time	R.H.	Date	Time	R.H.
23-Nov-2007	20:00	29.5 L	24-Nov-2007	22:00	29.1 L
23-Nov-2007	21:00	29.5 L	24-Nov-2007	23:00	29.0 L
23-Nov-2007	22:00	29.6 L	25-Nov-2007	00:00	29.2 L
23-Nov-2007	23:00	29.1 L	25-Nov-2007	01:00	28.9 L
24-Nov-2007	00:00	28.9 L	25-Nov-2007	02:00	28.9 L
24-Nov-2007	01:00	28.4 L	25-Nov-2007	03:00	29.4 L
24-Nov-2007	02:00	28.4 L	25-Nov-2007	04:00	29.4 L
24-Nov-2007	03:00	28.4 L	25-Nov-2007	05:00	29.4 L
24-Nov-2007	04:00	28.4 L	25-Nov-2007	06:00	29.4 L
24-Nov-2007	05:00	28.1 L	25-Nov-2007	07:00	29.5 L
24-Nov-2007	06:00	28.1 L	01-Dec-2007	18:00	29.7 L
24-Nov-2007	07:00	28.2 L	01-Dec-2007	19:00	29.5 L
24-Nov-2007	08:00	28.7 L	01-Dec-2007	20:00	29.2 L
24-Nov-2007	09:00	29.8 L	01-Dec-2007	21:00	28.7 L
24-Nov-2007	18:00	29.8 L	01-Dec-2007	22:00	28.3 L
24-Nov-2007	19:00	29.4 L	01-Dec-2007	23:00	28.5 L
24-Nov-2007	20:00	29.2 L	02-Dec-2007	00:00	28.3 L
24-Nov-2007	21:00	29.3 L	02-Dec-2007	01:00	28.4 L

H = Value out of range - High L = Value out of range - Low
R.H. = Relative Humidity (%)

Report Generated: 24-Dec-2007 at 13:40

☒ These deviations did not adversely affect the outcome or interpretation of the study.

☐ The following deviation(s) impacted on the outcome of the study as described:

Study Director: _____

John D. Barnett J

Date: _____

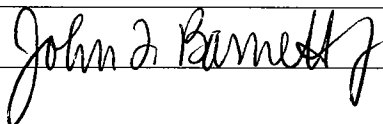
11 Jan 2008

ARGUS**Relative Humidity Deviations Report**
Location: Room 17**Protocol Number: TQC00017****Range of Dates: 20-Nov-2007 14:18 to 07-Dec-2007 18:59****Humidity Target Range:** 30% to 70%
Species: Rat

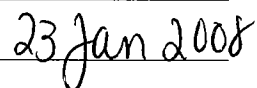
Date	Time	R.H.	Date	Time	R.H.
02-Dec-2007	02:00	29.3 L			

H = Value out of range - High L = Value out of range - Low
R.H. = Relative Humidity (%)**Report Generated: 24-Dec-2007 at 13:40**☒ These deviations did not adversely affect the outcome or interpretation of the study.☐ The following deviation(s) impacted on the outcome of the study as described:

Study Director:



Date:



FEED ANALYSES

Certified Papers Retrieval

Page 1 of 2



Return to Certified Analysis Retrieval

Product Code: 5002M
 Product Desc: CERTIFIED RODENT DIET MEAL
 Lab Number: L0723386-3
 Lot Code: SEP 25 07 3C
 Entered: 10/11/2007

Assay	Analysis	Units
PROTEIN	21.0	%
FAT (ACID HYDRO.)	6.05	%
FIBER (CRUDE)	4.56	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.0539	PPM
CALCIUM	1.01	%
LEAD	0.165	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.691	%
SELENIUM	0.368	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	0.03
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

Approved
MTH
12-13-07

http://www.labdiet.com/certified/pwa_spc002.asp

12/13/2007

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TMM rjanos

Certified Papers Retrieval

Page 2 of 2

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.

Approved
M. J. Jones
12-13-07

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Thm n Jones

http://www.labdiet.com/certified/pwa_spc002.asp

12/13/2007

WATER ANALYSES



Analytical Report



MATTHEW VANEMAN
CHARLES RIVER LAB
905 SHEEHY DRIVE
HORSHAM, PA 19044

Regarding:

MATTHEW VANEMAN
CHARLES RIVER LAB
905 SHEEHY DRIVE
HORSHAM, PA 19044

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

P.O. No:
PWSID No:

Inv. No: 924072

Sample Number L2467485-1
Sample Description DRINKING WATER- ANALYTICAL
Received Temp: 40 F Iced (Y/N): Y

Samp. Date/Time/Temp 11/02/07 11:15am NA F
Sampled by Customer Sampled

Parameter	Method	Result	RLS	Test Date, Time, Analyst
CHLORINE RESIDUAL LOW LEVEL- FIELD	SM 4500-CL-G	< 0.02 mg/l		11/02/07 11:15AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/02/07 04:11PM AMD
STANDARD PLATE COUNT	SM 9215B	15 col/ml	1. col/ml	11/02/07 04:11PM AMD

Sample Number L2467485-2
Sample Description DRINKING WATER- FILL STATION
Received Temp: 40 F Iced (Y/N): Y

Samp. Date/Time/Temp 11/02/07 11:20am NA F
Sampled by Customer Sampled

Parameter	Method	Result	RLS	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	1.50 mg/l	mg/l	11/02/07 11:20AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/02/07 04:11PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	11/02/07 04:11PM AMD

- A result of "ND" indicates the concentration of the analyte tested was either not detected or below the RLS.
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- QC NELAP ID's: PA 09-00131, NJ PA166, FL E87954, NY 11223, CT PH-0768, DE PA-018, KY 90228, MD 206, EPA PA00018, Bioassay: PA 09-03574, NJ PA034, FL E87953, KS E10373, SC 89020001.
- QC STATE ID's: Wind Gap, NJ PA001, PA 48-01334, E RUTHERFORD NJ02015, Vineland NJ06005; Reading PA 06-03543.
- All samples are collected as "grab" samples unless otherwise identified.
- MCL= is the EPA recommended "maximum contaminant level" for a parameter. PLS=customer specific permit limits.
Regulatory authorities are assessing substantial fines for testing omissions. Please track your sample collections and results on a weekly, monthly, or quarterly basis to ensure compliance. QC's internet program "LIVE ACCESS" will provide you with real-time access to collection dates and results. Please contact Customer Service for further information on acquiring LIVE ACCESS.

Page 1 of 4

Serial Number: 902818

Thomas J. Hines, President

① Retest for October and monthly for November
M/Van
11-12-07

Approved
M/Van
11-12-07
Amw 11-12-07

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

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THM 11/20/08

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 924072

Sample Number L2467485-3
Sample Description DRINKING WATER- ROOM 13 - RACK #1347
Received Temp: 40 F Iced (Y/N): Y

Sample Date/Time/Temp 11/02/07 11:25am NA F
Sampled by Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.45 mg/l	mg/l	11/02/07 11:25AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/02/07 04:11PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	11/02/07 04:11PM AMD

Sample Number L2467485-4
Sample Description DRINKING WATER- ROOM 47 RACK #C-8
Received Temp: 40 F Iced (Y/N): Y

Sample Date/Time/Temp 11/02/07 11:30am NA F
Sampled by Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.75 mg/l	mg/l	11/02/07 11:30AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/02/07 04:11PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	11/02/07 04:11PM AMD

Sample Number L2467485-5
Sample Description DRINKING WATER- FORMULATION
Received Temp: 40 F Iced (Y/N): Y

Sample Date/Time/Temp 11/02/07 11:35am NA F
Sampled by Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL LOW LEVEL-FIELD	SM 4500-CL-G	< 0.02 mg/l		11/02/07 11:35AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/02/07 04:11PM AMD
STANDARD PLATE COUNT	SM 9215B	136 col/ml	1. col/ml	11/02/07 04:11PM AMD

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Page 2 of 4

Serial Number: 902818

Thomas J. Hines
Thomas J. Hines, President

- ① retest requested and results of weekly chlorine testing have been reviewed and appear to be appropriate. Mmm 11-12-07
- ② Analysis considered retest for October and November. Mmm 11-12-07

Approved
Mmm 11-12-07

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mmmsan08

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 924072

Sample Number L2467485-6	Sample Description DRINKING WATER	Received Temp: 40 F	Iced (Y/N): Y	Samp. Date/Time/Temp 11/02/07 11:48am NA F	Sampled by Customer Sampled
Parameter	Method	Result	RLs	Test Date, Time, Analyst	
CHLORINE RESIDUAL	SM 4500-CL-G	0.54 mg/l	mg/l	11/02/07 11:48AM CU	
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	11/02/07 04:11PM AMD	
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	11/02/07 04:11PM AMD	

L2467485-1:

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.

L2467485-2:

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.

L2467485-3:

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.

L2467485-4:

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 - 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 NELAP ID's: PA 09-00131, NJ PA166, FL E87954, NY 11223, CT PH-0768, DE PA-018, KY 90228, MD 206, EPA PA00018, Bioassay: PA 09-03574, NJ PA034, FL E87953, KS E10373, SC 89020001.
 - QC STATE ID's: Wind Gap, NJ PA001, PA 48-01334; E RUTHERFORD NJ02015; Vineland NJ06005; Reading PA 06-03543.
 - All samples are collected as "grab" samples unless otherwise identified.
 - MCL= is the EPA recommended "maximum contaminant level" for a parameter. PLs=customer specific permit limits.
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Serial Number: 902818

① Retest for October and
monthly for November.

11-12-07

Approved: Thomas J. Hines, President
11-12-07

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TMM 12/20/08

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 924072

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.

L2467485-5:

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.

L2467485-6:

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.

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 - QC STATE ID's: Wind Gap, NJ PA001, PA 48-01334; E RUTHERFORD NJ02015; Vineland NJ06005; Reading PA 06-03543.
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Page 4 of 4

Serial Number: 902818

Thomas J. Hines
Thomas J. Hines, President

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THM175anos



Analytical Report



MATTHEW VANEMAN
CHARLES RIVER LAB
905 SHEEHY DRIVE
HORSHAM, PA 19044

Regarding:

MATTHEW VANEMAN
CHARLES RIVER LAB
905 SHEEHY DRIVE
HORSHAM, PA 19044

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

P.O. No:
PMSID No:

Inv. No: 932153

Sample Number	Sample Description	Received Temp	Samp. Date/Time/Temp	Sampled by
L2495000-1	DRINKING WATER - ANALYTICAL Received Temp: 37 F Iced (Y/N): Y		12/07/07 02:45pm NA F	Customer Sampled
Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL LOW LEVEL- FIELD	SM 4500-CL-G	< 0.02 mg/l		12/07/07 02:45PM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	12/07/07 03:49PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	12/07/07 03:49PM AMD

Sample Number	Sample Description	Received Temp	Samp. Date/Time/Temp	Sampled by
L2495000-2	DRINKING WATER - ROOM #24 RACK #64 Received Temp: 37 F Iced (Y/N): Y		12/07/07 02:45pm NA F	Customer Sampled
Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.6 mg/l	mg/l	12/07/07 02:45PM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	12/07/07 03:49PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	12/07/07 03:49PM AMD

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- QC NELAP ID's: PA 09-00131, NJ PA166, FL E87964, NY 11223, CT PH-0768, DE PA-018, KY 90228, MD 206, EPA PA00018, Bioassay: PA 09-03574, NJ PA034, FL E87963, KS E10373, SC 89020001.
- QC STATE ID's: Wind Gap, NJ PA001, PA 48-01334; E RUTHERFORD NJ02015; Vineland NJ06005; Reading PA 06-03543.
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Page 1 of 4

Serial Number: 913665

Thomas J. Hines, President

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11/17/2008

Approved
1-7-08

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

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 932153

Sample Number L2495000-3	Sample Description DRINKING WATER - ROOM #43 RACK #131 Received Temp: 37 F Iced (Y/N): Y	Samp. Date/Time/Temp 12/07/07 02:45pm NA F	Sampled by Customer Sampled
Parameter CHLORINE RESIDUAL COLIFORM-MF STANDARD PLATE COUNT	Method SM 4500-CL-G SM 9222B SM 9215B	Result 0.6 mg/l <1 col/100ml <1 col/ml	RLs mg/l 1. col/100ml 1. col/ml
Test Date, Time, Analyst 12/07/07 02:45PM CU 12/07/07 03:49PM AMD 12/07/07 03:49PM AMD			
Sample Number L2495000-4	Sample Description DRINKING WATER - FILL STATION Received Temp: 37 F Iced (Y/N): Y	Samp. Date/Time/Temp 12/07/07 02:45pm NA F	Sampled by Customer Sampled
Parameter CHLORINE RESIDUAL COLIFORM-MF STANDARD PLATE COUNT	Method SM 4500-CL-G SM 9222B SM 9215B	Result 0.7 mg/l <1 col/100ml <1 col/ml	RLs mg/l 1. col/100ml 1. col/ml
Test Date, Time, Analyst 12/07/07 02:45PM CU 12/07/07 03:49PM AMD 12/07/07 03:49PM AMD			
Sample Number L2495000-5	Sample Description DRINKING WATER - FORMULATIONS Received Temp: 37 F Iced (Y/N): Y	Samp. Date/Time/Temp 12/07/07 02:45pm NA F	Sampled by Customer Sampled
Parameter CHLORINE RESIDUAL LOW LEVEL- FIELD COLIFORM-MF STANDARD PLATE COUNT	Method SM 4500-CL-G SM 9222B SM 9215B	Result < 0.02 mg/l <1 col/100ml <1 col/ml	RLs Test Date, Time, Analyst 12/07/07 02:45PM CU 12/07/07 03:49PM AMD 12/07/07 03:49PM AMD

Approved
[Signature]
1-7-08

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Thomas J. Hines
Thomas J. Hines, President

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Tom Hines

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 932153

Sample Number L2495000-6
Sample Description DRINKING WATER - RABBIT LAB
Received Temp: 37 F Iced (Y/N): Y

Sample Date/Time/Temp
12/07/07 02:45pm NA F

Sampled by
Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.5 mg/l	mg/l	12/07/07 02:45PM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	12/07/07 03:49PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	12/07/07 03:49PM AMD

L2495000-1:

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.

L2495000-2:

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L2495000-3:

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L2495000-4:

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- QC STATE ID's: Wind Gap, NJ PA001, PA 48-01334; E RUTHERFORD NJ02015; Vineland NJ06005; Reading PA 06-03543.
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Page 3 of 4

Serial Number: 913665

Approved *Thomas J. Hines*
1-7-08
Thomas J. Hines, President

EXACT COPY

THM 175ar08

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 932153

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L2495000-5:

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L2495000-6:

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 - 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 NELAP ID's: PA 09-00131, NJ PA166, FL E87954, NY 11223, CT PH-0768, DE PA-018, KY 90228, MD 206, EPA PA00018, Bioassay: PA 09-03574, NJ PA034, FL E87953, KS E10373, SC 89020001.
 - QC STATE ID's: Wind Gap, NJ PA001, PA 48-01334; E RUTHERFORD NJ02015; Vineland NJ06005; Reading PA 06-03543.
 - All samples are collected as "grab" samples unless otherwise identified.
 - MCL- is the EPA recommended "maximum contaminant level" for a parameter. PLS=customer specific permit limits.
- Regulatory authorities are assessing substantial fines for testing omissions. Please track your sample collections and results on a weekly, monthly, or quarterly basis to ensure compliance. QC's internet program 'LIVE ACCESS' will provide you with real-time access to collection dates and results. Please contact Customer Service for further information on acquiring LIVE ACCESS.

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Serial Number: 913665

Approved
1-7-08
Thomas J. Hines, President

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mm 12 Jan 08

Analysis Report



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MM 170507

Page 1 of 3

Lancaster Laboratories Sample No. WW 5105153

Sample #1 905 Analytical Lab Grab Water Sample
Semi-Annual

Collected: 07/17/2007 10:28 by JH

Account Number: 02423

Submitted: 07/17/2007 17:30
Reported: 07/26/2007 at 19:47
Discard: 08/03/2007Charles River Laboratories
57 Union Street
Worcester MA 01608

19051

CAT			As Received	As Received		
No.	Analysis Name	CAS Number	Result	Limit of Quantitation	Units	Dilution Factor
00259	Mercury	7439-97-6	< 0.00020	0.00020	mg/l	1
07035	Arsenic	7440-38-2	< 0.0200	0.0200	mg/l	1
07036	Selenium	7782-49-2	< 0.0200	0.0200	mg/l	1
07046	Barium	7440-39-3	< 0.0050	0.0050	mg/l	1
07049	Cadmium	7440-43-9	< 0.0050	0.0050	mg/l	1
07051	Chromium	7440-47-3	< 0.0150	0.0150	mg/l	1
07055	Lead	7439-92-1	< 0.0150	0.0150	mg/l	1
07066	Silver	7440-22-4	< 0.0050	0.0050	mg/l	1
07072	Zinc	7440-66-6	< 0.0200	0.0200	mg/l	1
00224	Chloride	16887-00-6	2.6	2.0	mg/l	5
00226	Ortho-Phosphate as P	7723-14-0	0.037	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	< 0.0099	0.0099	ug/l	1
00454	Heptachlor	76-44-8	< 0.050	0.050	ug/l	1
00455	Aldrin	309-00-2	< 0.020	0.020	ug/l	1
00469	Dieldrin	60-57-1	< 0.020	0.020	ug/l	1
00477	Endrin	72-20-8	< 0.020	0.020	ug/l	1
00478	p,p-DDT	50-29-3	< 0.020	0.020	ug/l	1
00638	Endrin Aldehyde	7421-93-4	< 0.099	0.099	ug/l	1
01902	Alpha BHC	319-84-6	< 0.0099	0.0099	ug/l	1
01903	Beta BHC	319-85-7	< 0.024	0.024	ug/l	1
01904	Delta BHC	319-86-8	< 0.024	0.024	ug/l	1
01905	Heptachlor Epoxide	1024-57-3	< 0.024	0.024	ug/l	1
01906	p,p-DDE	72-55-9	< 0.020	0.020	ug/l	1
01907	p,p-DDD	72-54-8	< 0.020	0.020	ug/l	1
01908	Chlordane	57-74-9	< 0.50	0.50	ug/l	1
01909	Toxaphene	8001-35-2	< 0.99	0.99	ug/l	1
01910	Endosulfan I	959-98-8	< 0.0099	0.0099	ug/l	1
01911	Endosulfan II	33213-65-9	< 0.020	0.020	ug/l	1
01912	Endosulfan Sulfate	1031-07-8	< 0.040	0.040	ug/l	1
01913	PCB-1016	12674-11-2	< 0.50	0.50	ug/l	1
01914	PCB-1221	11104-28-2	< 0.50	0.50	ug/l	1
01915	PCB-1232	11141-16-5	< 0.50	0.50	ug/l	1
01916	PCB-1242	53469-21-9	< 0.50	0.50	ug/l	1

① Retest Requested on 9/10/07 / M. J. H.

Lancaster Laboratories, Inc.
2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
717-656-2300 Fax: 717-656-2681

10/4/07

Approved

M. J. H.

8-9-07

2216 Rev. 3/27/06

Analysis Report



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MAY 17 2007

Page 2 of 3

Lancaster Laboratories Sample No. WW 5105153

Sample #1 905 Analytical Lab Grab Water Sample
Semi-Annual

Collected: 07/17/2007 10:28 by JH

Account Number: 02423

Submitted: 07/17/2007 17:30
Reported: 07/26/2007 at 19:47
Discard: 08/03/2007Charles River Laboratories
57 Union Street
Worcester MA 01608

19051

CAT			As Received	As Received		
No.	Analysis Name	CAS Number	Result	Limit of Quantitation	Units	Dilution Factor
01917	PCB-1248	12672-29-6	< 0.50	0.50	ug/l	1
01918	PCB-1254	11097-69-1	< 0.50	0.50	ug/l	1
01919	PCB-1260	11096-82-5	< 0.50	0.50	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	93-76-5	< 0.050	0.050	ug/l	1
05287	Dalapon	75-99-0	< 1.3	1.3	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	MCP	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
08103	Pentachlorophenol	87-86-5	< 0.050	0.050	ug/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-037

All QC is compliant unless otherwise noted. Please refer to the Quality Control Summary for overall QC performance data and associated samples.

Approved

 8-9-07

Laboratory Chronicle

CAT				Analysis		
No.	Analysis Name	Method	Trial#	Date and Time	Analyst	Dilution Factor
00259	Mercury	SW-846 7470A	1	07/20/2007 04:13	Damary Valentin	1
07035	Arsenic	SW-846 6010B	1	07/23/2007 15:01	Joanne M Gates	1
07036	Selenium	SW-846 6010B	1	07/23/2007 15:01	Joanne M Gates	1
07046	Barium	SW-846 6010B	1	07/23/2007 15:01	Joanne M Gates	1
07049	Cadmium	SW-846 6010B	1	07/23/2007 15:01	Joanne M Gates	1
07051	Chromium	SW-846 6010B	1	07/23/2007 15:01	Joanne M Gates	1
07055	Lead	SW-846 6010B	1	07/26/2007 16:01	Eric L Eby	1
07066	Silver	SW-846 6010B	1	07/23/2007 15:01	Joanne M Gates	1
07072	Zinc	SW-846 6010B	1	07/23/2007 15:01	Joanne M Gates	1
00224	Chloride	EPA 300.0	1	07/18/2007 13:26	Ashley M Heckman	5
00226	Ortho-Phosphate as P	SM20 4500 PB	1	07/19/2007 01:50	Daniel S Smith	1
00228	Sulfate	EPA 300.0	1	07/18/2007 13:26	Ashley M Heckman	5
00368	Nitrate Nitrogen	EPA 300.0	1	07/18/2007 13:26	Ashley M Heckman	5

Lancaster Laboratories, Inc.
7425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
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Analysis Report



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Lancaster Laboratories Sample No. WW 5105153

Sample #1 905 Analytical Lab Grab Water Sample
Semi-Annual

Collected: 07/17/2007 10:28 by JH

Account Number: 02423

Submitted: 07/17/2007 17:30
Reported: 07/26/2007 at 19:47
Discard: 08/03/2007Charles River Laboratories
57 Union Street
Worcester MA 01608

19051							
01504	Fluoride	EPA 300.0	1	07/18/2007 13:26	Ashley M Heckman	5	
01505	Bromide	EPA 300.0	1	07/18/2007 13:26	Ashley M Heckman	5	
01506	Nitrite Nitrogen	EPA 300.0	1	07/18/2007 13:26	Ashley M Heckman	5	
00178	Pesticides/PCB's in Water	EPA 608	1	07/18/2007 23:34	Lindsey K Lafferty	1	
01856	Herbicides in Water	SW-846 8151A	1	07/24/2007 22:32	John W Perkins	1	
00816	Water Sample Herbicide Extract	SW-846 8151A	1	07/20/2007 16:45	Karen L Beyer	1	
00817	Water Sample Pest. Extraction	EPA 608	1	07/18/2007 09:30	Denise L Trimby	1	
01848	WW SW846 ICP Digest (tot rec)	SW-846 3005A	1	07/20/2007 14:50	Mirit S Shenouda	1	
05713	WW SW846 Hg Digest	SW-846 7470A	1	07/19/2007 18:30	Nelli S Markaryan	1	

Approved

 8-9-07

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 2425 New Holland Pike
 PO Box 12425
 Lancaster, PA 17605-2425
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Analysis Report



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Lancaster Laboratories Sample No. WN 5105152

Sample #2 905 Formulation Lab Grab Water Sample
Semi-Annual

Collected: 07/17/2007 10:35 by JH

Account Number: 02423

Submitted: 07/17/2007 17:30

Charles River Laboratories

Reported: 07/26/2007 at 19:47

57 Union Street

Discard: 08/03/2007

Worcester MA 01608

29051

CAT			As Received	As Received		
No.	Analysis Name	CAS Number	Result	Limit of	Units	Dilution
00259	Mercury	7439-97-6	< 0.00020	0.00020	mg/l	1
07035	Arsenic	7440-38-2	< 0.0200	0.0200	mg/l	1
07036	Selenium	7782-49-2	< 0.0200	0.0200	mg/l	1
07046	Barium	7440-39-3	< 0.0050	0.0050	mg/l	1
07049	Cadmium	7440-43-9	< 0.0050	0.0050	mg/l	1
07051	Chromium	7440-47-3	< 0.0150	0.0150	mg/l	1
07055	Lead	7439-92-1	< 0.0150	0.0150	mg/l	1
07066	Silver	7440-22-4	< 0.0050	0.0050	mg/l	1
07072	Zinc	7440-66-6	< 0.0200	0.0200	mg/l	1
00224	Chloride	16887-00-6	< 2.0	2.0	mg/l	5
00226	Ortho-Phosphate as P	7723-14-0	0.056	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	< 0.050	0.050	ug/l	1
00455	Aldrin	309-00-2	< 0.020	0.020	ug/l	1
00469	Dieldrin	60-57-1	< 0.020	0.020	ug/l	1
00477	Endrin	72-20-8	< 0.020	0.020	ug/l	1
00478	p,p-DDT	50-29-3	< 0.020	0.020	ug/l	1
00638	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	< 0.024	0.024	ug/l	1
01904	Delta BHC	319-86-8	< 0.024	0.024	ug/l	1
01905	Heptachlor Epoxide	1024-57-3	< 0.024	0.024	ug/l	1
01906	p,p-DDE	72-55-9	< 0.020	0.020	ug/l	1
01907	p,p-DDD	72-54-8	< 0.020	0.020	ug/l	1
01908	Chlordane	57-74-9	< 0.50	0.50	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	< 0.020	0.020	ug/l	1
01912	Endosulfan Sulfate	1031-07-8	< 0.040	0.040	ug/l	1
01913	PCB-1016	12674-11-2	< 0.50	0.50	ug/l	1
01914	PCB-1221	11104-28-2	< 0.50	0.50	ug/l	1
01915	PCB-1232	11141-16-5	< 0.50	0.50	ug/l	1
01916	PCB-1242	53469-21-9	< 0.50	0.50	ug/l	1

Lancaster Laboratories, Inc.
2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
717-656-2300 Fax: 717-656-2681

Approved
① Re-test requested
W 9-10-07 8-9-07

2216 Rev. 3/27/06

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MAY 17 2008

Analysis Report



Page 2 of 3

Lancaster Laboratories Sample No. WW 5105152

Sample #2 905 Formulation Lab Grab Water Sample
Semi-Annual

Collected: 07/17/2007 10:35 by JH

Account Number: 02423

Submitted: 07/17/2007 17:30

Charles River Laboratories

Reported: 07/26/2007 at 19:47

57 Union Street

Discard: 08/03/2007

Worcester MA 01608

29051

CAT			As Received	As Received		
No.	Analysis Name	CAS Number	Result	Limit of Quantitation	Units	Dilution Factor
01917	PCB-1248	12672-29-6	< 0.50	0.50	ug/l	1
01918	PCB-1254	11097-69-1	< 0.50	0.50	ug/l	1
01919	PCB-1260	11096-82-5	< 0.50	0.50	ug/l	1
01856	Herbicides in Water					
01857	2,4-D	94-75-7	< 0.51	0.51	ug/l	1
01858	2,4,5-TP	93-72-1	< 0.051	0.051	ug/l	1
05286	2,4,5-T	93-76-5	< 0.051	0.051	ug/l	1
05287	Dalapon	75-99-0	< 1.3	1.3	ug/l	1
05288	Dinoseb	88-85-7	< 0.51	0.51	ug/l	1
05289	Dicamba	1918-00-9	< 0.31	0.31	ug/l	1
05290	MCP	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	< 0.51	0.51	ug/l	1
05293	2,4-DB	94-82-6	< 1.0	1.0	ug/l	1
08103	Pentachlorophenol	87-86-5	< 0.051	0.051	ug/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-037

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				Analysis		
No.	Analysis Name	Method	Trial#	Date and Time	Analyst	Dilution Factor
00259	Mercury	SW-846 7470A	1	07/20/2007 04:08	Damary Valentin	1
07035	Arsenic	SW-846 6010B	1	07/23/2007 14:57	Joanne M Gates	1
07036	Selenium	SW-846 6010B	1	07/26/2007 15:57	Eric L Eby	1
07046	Barium	SW-846 6010B	1	07/23/2007 14:57	Joanne M Gates	1
07049	Cadmium	SW-846 6010B	1	07/23/2007 14:57	Joanne M Gates	1
07051	Chromium	SW-846 6010B	1	07/23/2007 14:57	Joanne M Gates	1
07055	Lead	SW-846 6010B	1	07/26/2007 15:57	Eric L Eby	1
07066	Silver	SW-846 6010B	1	07/23/2007 14:57	Joanne M Gates	1
07072	Zinc	SW-846 6010B	1	07/23/2007 14:57	Joanne M Gates	1
00224	Chloride	EPA 300.0	1	07/18/2007 13:11	Ashley M Heckman	5
00226	Ortho-Phosphate as P	SM20 4500 PE	1	07/19/2007 01:50	Daniel S Smith	1
00228	Sulfate	EPA 300.0	1	07/18/2007 13:11	Ashley M Heckman	5
00368	Nitrate Nitrogen	EPA 300.0	1	07/18/2007 13:11	Ashley M Heckman	5

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2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
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Analysis Report



Page 3 of 3

Lancaster Laboratories Sample No. WW 5105152

Sample #2 905 Formulation Lab Grab Water Sample
Semi-Annual

Collected: 07/17/2007 10:35 by JH

Account Number: 02423

Submitted: 07/17/2007 17:30

Reported: 07/26/2007 at 19:47

Discard: 08/03/2007

Charles River Laboratories

57 Union Street

Worcester MA 01608

29051

01504	Fluoride	EPA 300.0	1	07/18/2007 13:11	Ashley M Heckman	5
01505	Bromide	EPA 300.0	1	07/18/2007 13:11	Ashley M Heckman	5
01506	Nitrite Nitrogen	EPA 300.0	1	07/18/2007 13:11	Ashley M Heckman	5
00178	Pesticides/PCB's in Water	EPA 608	1	07/18/2007 23:21	Lindsey K Lafferty	1
01856	Herbicides in Water	SW-846 8151A	1	07/24/2007 22:03	John W Perkins	1
00816	Water Sample Herbicide Extract	SW-846 8151A	1	07/20/2007 16:45	Karen L Beyer	1
00817	Water Sample Pest. Extraction	EPA 608	1	07/18/2007 09:30	Denise L Trimby	1
01848	NW SW846 ICP Digest (tot rec)	SW-846 3005A	1	07/20/2007 14:50	Mirit S Shenouda	1
05713	NW SW846 Hg Digest	SW-846 7470A	1	07/19/2007 18:30	Nelli S Markaryan	1

Approved

 8-9-07

Lancaster Laboratories, Inc.
 2425 New Holland Pike
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Page 1 of 1

Lancaster Laboratories Sample No. WW 5160589

Sample #1 905 Analytical Lab Grab Water Sample
(Retest)

Semi-Annual

Collected: 09/19/2007 09:47 by EA

Account Number: 02423

Submitted: 09/19/2007 17:10

Reported: 09/28/2007 at 12:41

Discard: 10/13/2007

Charles River Laboratories

57 Union Street

Worcester MA 01608

I 58 w

CAT			As Received	As Received		
No.	Analysis Name	CAS Number	Result	Limit of Quantitation	Units	Dilution Factor
00224	Chloride	16887-00-6	< 2.0	2.0	mg/l	5
00226	Ortho-Phosphate as P	7723-14-0	0.083	0.030	mg/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-00037.

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				Analysis			Dilution
No.	Analysis Name	Method	Trial#	Date and Time	Analyst		Factor
00224	Chloride	EPA 300.0	1	09/26/2007 23:05	Ashley M Heckman		5
00226	Ortho-Phosphate as P	EPA 365.3	1	09/20/2007 03:00	Daniel S Smith		1

o maxcor contacted and further testing was conducted. mv 1-21-08

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BL-215, 08

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2425 New Holland Pike
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Lancaster, PA 17605-2425
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Analysis Report



Page 1 of 1

Lancaster Laboratories Sample No. WW 5160590

Sample #2 905 Formulation Lab Grab Water Sample
(Retest)

Semi-Annual

Collected: 09/19/2007 09:50 by EA

Account Number: 02423

Submitted: 09/19/2007 17:10

Reported: 09/28/2007 at 12:41

Discard: 10/13/2007

Charles River Laboratories

57 Union Street

Worcester MA 01608

I SE w

CAT No.	Analysis Name	CAS Number	As Received	As Received	Units	Dilution Factor
			Result	Limit of Quantitation		
00224	Chloride	16887-00-6	< 2.0	2.0	mg/l	5
00226	Ortho-Phosphate as P	7723-14-0	0.033 ^①	0.030	mg/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-00037.

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	Analyst	Dilution Factor
				Date and Time		
00224	Chloride	EPA 300.0	1	09/26/2007 23:45	Ashley M Heckman	5
00226	Ortho-Phosphate as P	EPA 365.3	1	09/20/2007 03:00	Daniel S Smith	1

① macro was contacted and another testing
was conducted. mv 1-21-08


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DEF-L4Jm 08

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2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
717-656-2300 Fax: 717-656-2681

2216 Rev. 3/27/06

The following water analyses were conducted as part of the investigation into abnormally high levels of orthophosphate as P. Samples were taken before and after each RO system. The testing revealed that only system #2 (905F) continued to have excess orthophosphates. All other systems appear to have been alleviated by Marcor's onsite maintenance. Further maintenance was requested and further testing was ordered for system #2.


1-21-08

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08/24/00

Analysis Report



Page 1 of 1

Lancaster Laboratories Sample No. WW 5213681

#1 Point Before Entering RO System Grab Water
905B Lab

Semi-Annual

Collected: 11/15/2007 10:05 by EA

Account Number: 02423

Submitted: 11/15/2007 16:20

Reported: 11/23/2007 at 10:36

Discard: 12/08/2007

Charles River Laboratories
57 Union Street
Worcester MA 01608

I SE w

CAT	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
00226	Ortho-Phosphate as P	7723-14-0	0.092	0.030	mg/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-037

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	Analysis Name	Method	Trial#	Analysis Date and Time	Analyst	Dilution Factor
00226	Ortho-Phosphate as P	EPA 365.3	1	11/17/2007 08:45	Daniel S Smith	1

Approved

 1-21-08

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01/24/08 JCS

Lancaster Laboratories, Inc.
2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
717-656-2300 Fax: 717-656-2681

2216 Rev. 3/27/06

Analysis Report



Page 1 of 1

Lancaster Laboratories Sample No. WW 5213682

#2 Point Before Entering RO System Grab Water
905F

Semi-Annual

Collected: 11/15/2007 10:01 by EA

Account Number: 02423

Submitted: 11/15/2007 16:20
Reported: 11/23/2007 at 10:36
Discard: 12/08/2007Charles River Laboratories
57 Union Street
Worcester MA 01608

I SE w

CAT	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
00226	Ortho-Phosphate as P	7723-14-0	0.12	0.030	mg/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-037

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	Analysis Name	Method	Analysis Trial#	Date and Time	Analyst	Dilution Factor
00226	Ortho-Phosphate as P	EPA 365.3	1	11/17/2007 08:45	Daniel S Smith	1

Approved
[Signature]
1-21-08

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2216 Rev. 3/27/06

Analysis Report



Page 1 of 1

Lancaster Laboratories Sample No. WW 5213684

#1A Point After RO System Grab Water
Semi-Annual

Collected: 11/15/2007 10:06 by EA

Account Number: 02423

Submitted: 11/15/2007 16:20
Reported: 11/23/2007 at 10:36
Discard: 12/08/2007Charles River Laboratories
57 Union Street
Worcester MA 01608

I 5E w

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
00226	Ortho-Phosphate as P	7723-14-0	< 0.030	0.030	mg/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-037

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
00226	Ortho-Phosphate as P	EPA 365.3	1	11/17/2007 08:45	Daniel S Smith	1

Approved

 1-21-08

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2216 Rev. 3/27/06

Analysis Report



Page 1 of 1

Lancaster Laboratories Sample No. WW 5213685

#2A Point After RO System Grab Water
Semi-Annual

Collected: 11/15/2007 10:00 by EA

Account Number: 02423

Submitted: 11/15/2007 16:20
Reported: 11/23/2007 at 10:36
Discard: 12/08/2007Charles River Laboratories
57 Union Street
Worcester MA 01608

I SE w

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
00226	Ortho-Phosphate as P	7723-14-0	0.042	0.030	mg/l	1

Commonwealth of Pennsylvania Lab Certification No. 36-037

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
00226	Ortho-Phosphate as P	EPA 365.3	1	11/17/2007 08:45	Daniel S Smith	1

Approved

 1-21-08

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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 ANALYSES

Analysis Report



Page 1 of 2

Lancaster Laboratories Sample No. G5 5141313

Bedding Sample Lot# 081007

Collected: 08/28/2007

Account Number: 02423

Submitted: 08/29/2007 16:40

Reported: 09/13/2007 at 12:47

Discard: 09/28/2007

Charles River Laboratories
57 Union Street
Worcester MA 0160881007
1 5E w

CAT No.	Analysis Name	CAS Number	As Received Result	As Received Limit of Quantitation	Units	Dilution Factor
00159	Mercury	7439-97-6	< 0.0963	0.0963	mg/kg	1
06935	Arsenic	7440-38-2	< 1.96	1.96	mg/kg	1
06936	Selenium	7782-49-2	< 1.96	1.96	mg/kg	1
06946	Barium	7440-39-3	0.950	0.490	mg/kg	1
06949	Cadmium	7440-43-9	< 0.490	0.490	mg/kg	1
06951	Chromium	7440-47-3	< 1.47	1.47	mg/kg	1
06955	Lead	7439-92-1	< 1.47	1.47	mg/kg	1
06966	Silver	7440-22-4	< 0.490	0.490	mg/kg	1
01863	Appendix IX Herbicides in Soil					
04174	2,4-D	94-75-7	< 17.	17.	ug/kg	1
04176	2,4,5-TP	93-72-1	< 1.7	1.7	ug/kg	1
02033	PCBs in Soil					
01993	PCB-1016	12674-11-2	< 17.0	17.0	ug/kg	1
01994	PCB-1221	11104-28-2	< 42.0	42.0	ug/kg	1
01995	PCB-1232	11141-16-5	< 17.0	17.0	ug/kg	1
01996	PCB-1242	53469-21-9	< 23.0	23.0	ug/kg	1
01997	PCB-1248	12672-29-6	< 17.0	17.0	ug/kg	1
01998	PCB-1254	11097-69-1	< 17.0	17.0	ug/kg	1
01999	PCB-1260	11096-82-5	< 17.0	17.0	ug/kg	1
06005	Pesticides in Solids					
01218	Gamma BHC - Lindane	58-89-9	< 0.83	0.83	ug/kg	1
01219	Heptachlor	76-44-8	< 0.83	0.83	ug/kg	1
01220	Aldrin	309-00-2	< 0.83	0.83	ug/kg	1
01221	p,p-DDT	50-29-3	< 1.7	1.7	ug/kg	1
01222	Dieldrin	60-57-1	< 1.7	1.7	ug/kg	1
01223	Endrin	72-20-8	< 1.7	1.7	ug/kg	1
01859	Methoxychlor	72-43-5	< 8.3	8.3	ug/kg	1
01981	Alpha BHC	319-84-6	< 1.0	1.0	ug/kg	1
01982	Beta BHC	319-85-7	< 2.0	2.0	ug/kg	1
01983	Delta BHC	319-86-8	< 0.83	0.83	ug/kg	1
01984	Heptachlor Epoxide	1024-57-3	< 0.83	0.83	ug/kg	1
01985	p,p-DDE	72-55-9	< 1.7	1.7	ug/kg	1
01986	p,p-DDD	72-54-8	< 1.7	1.7	ug/kg	1
01987	Chlordane	57-74-9	< 17.	17.	ug/kg	1
01988	Toxaphene	8001-35-2	< 33.	33.	ug/kg	1

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① This result is below the
the federal drinking water
standard of 2 mg/liter, as 6-502

Acceptable
10-5-07

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Analysis Report



Page 2 of 2

Lancaster Laboratories Sample No. G5 5141313

Bedding Sample Lot# 081007

Collected: 08/28/2007

Account Number: 02423

Submitted: 08/29/2007 16:40

Charles River Laboratories

Reported: 09/13/2007 at 12:47

57 Union Street

Discard: 09/28/2007

Worcester MA 01608

81007

CAT No.	Analysis Name	CAS Number	As Received	As Received	Units	Dilution
			Result	Limit of Quantitation		
01989	Endosulfan I	959-98-8	< 0.83	0.83	ug/kg	1
01990	Endosulfan II	33213-65-9	< 1.7	1.7	ug/kg	1
01991	Endosulfan Sulfate	1031-07-8	< 1.7	1.7	ug/kg	1
01992	Endrin Aldehyde	7421-93-4	< 1.7	1.7	ug/kg	1

Commonwealth of Pennsylvania Lab Certification No. 36-037

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	Analyst	Dilution Factor
				Date and Time		
00159	Mercury	SW-846 7471A	1	08/31/2007 09:23	Damary Valentin	1
06935	Arsenic	SW-846 6010B	1	08/31/2007 10:57	Eric L Eby	1
06936	Selenium	SW-846 6010B	1	08/31/2007 10:57	Eric L Eby	1
06946	Barium	SW-846 6010B	1	08/31/2007 10:57	Eric L Eby	1
06949	Cadmium	SW-846 6010B	1	08/31/2007 10:57	Eric L Eby	1
06951	Chromium	SW-846 6010B	1	08/31/2007 10:57	Eric L Eby	1
06955	Lead	SW-846 6010B	1	08/31/2007 10:57	Eric L Eby	1
06966	Silver	SW-846 6010B	1	08/31/2007 10:57	Eric L Eby	1
01863	Appendix IX Herbicides in Soil	SW-846 8151A	1	08/30/2007 23:39	Michele D Hamilton	1
02033	PCBs in Soil	SW-846 8082	1	08/30/2007 22:40	Jamie L Brillhart	1
06005	Pesticides in Solids	SW-846 8081A	1	09/11/2007 15:36	Richard A Shober	1
04181	Herbicide Soil Extraction	SW-846 3550B/SW-846 8151A	1	08/30/2007 12:30	Kerrie A Greenfield	1
05708	SW SW846 ICP Digest	SW-846 3050B	1	08/30/2007 19:15	Annamaria Stipkovits	1
05711	SW SW846 Hg Digest	SW-846 7471A modified	1	08/30/2007 23:10	Annamaria Stipkovits	1
06006	PPL Pesticide Solid Extraction	SW-846 3550B	3	09/05/2007 00:35	Karen L Beyer	1

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Analysis Report



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Quality Control Summary

Client Name: Charles River Laboratories
Reported: 09/13/07 at 12:47 PM

Group Number: 1053778

Matrix QC may not be reported if site-specific QC samples were not submitted. In these situations, to demonstrate precision and accuracy at a batch level, a LCS/LCSD was performed, unless otherwise specified in the method.

Laboratory Compliance Quality Control

Analysis Name	Blank Result	Blank LOQ	Report Units	LCS %REC	LCSD %REC	LCS/LCSD Limits	RPD	RPD Max
Batch number: 072410035B	Sample number(s): 5141313							
PCB-1016	< 17.0	17.0	ug/kg	90		72-120		
PCB-1221	< 42.0	42.0	ug/kg					
PCB-1232	< 17.0	17.0	ug/kg					
PCB-1242	< 23.0	23.0	ug/kg					
PCB-1248	< 17.0	17.0	ug/kg					
PCB-1254	< 17.0	17.0	ug/kg	90		65-137		
PCB-1260	< 17.0	17.0	ug/kg					
Batch number: 072420005A	Sample number(s): 5141313							
2,4-D	< 17.	17.	ug/kg	72		40-140		
2,4,5-TP	< 1.7	1.7	ug/kg	91		44-137		
Batch number: 072425708001	Sample number(s): 5141313							
Arsenic	< 2.00	2.00	mg/kg	93		86-114		
Selenium	< 2.00	2.00	mg/kg	98		78-122		
Barium	< 0.500	0.500	mg/kg	94		91-109		
Cadmium	< 0.500	0.500	mg/kg	95		90-110		
Chromium	< 1.50	1.50	mg/kg	107		78-122		
Lead	< 1.50	1.50	mg/kg	94		91-109		
Silver	< 0.500	0.500	mg/kg	93		89-112		
Batch number: 072425711002	Sample number(s): 5141313							
Mercury	< 0.100	0.100	mg/kg	79		66-133		
Batch number: 072470011A	Sample number(s): 5141313							
Gamma BHC - Lindane	< 0.83	0.83	ug/kg	93		74-133		
Heptachlor	< 0.83	0.83	ug/kg	84		61-129		
Aldrin	< 0.83	0.83	ug/kg	93		74-137		
p,p-DDT	< 1.7	1.7	ug/kg	114		57-124		
Dieldrin	< 1.7	1.7	ug/kg	91		71-133		
Endrin	< 1.7	1.7	ug/kg	98		65-134		
Methoxychlor	< 8.3	8.3	ug/kg	107		56-168		
Alpha BHC	< 1.0	1.0	ug/kg	94		60-127		
Beta BHC	< 2.0	2.0	ug/kg	96		68-137		
Delta BHC	< 0.83	0.83	ug/kg	97		66-118		
Heptachlor Epoxide	< 0.83	0.83	ug/kg	90		72-132		
p,p-DDE	< 1.7	1.7	ug/kg	108		52-159		
p,p-DDD	< 1.7	1.7	ug/kg	108		60-153		
Chlordane	< 17.	17.	ug/kg					
Toxaphene	< 33.	33.	ug/kg					
Endosulfan I	< 0.83	0.83	ug/kg	91		71-130		
Endosulfan II	< 1.7	1.7	ug/kg	100		73-134		
Endosulfan Sulfate	< 1.7	1.7	ug/kg	101		58-133		
Endrin Aldehyde	< 1.7	1.7	ug/kg	88		40-119		

*- Outside of specification

- (1) The result for one or both determinations was less than five times the LOQ.
- (2) The unspiked result was more than four times the spike added.

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Analysis Report



Page 2 of 3

Quality Control Summary

Client Name: Charles River Laboratories
Reported: 09/13/07 at 12:47 PM

Group Number: 1053778

Sample Matrix Quality Control

Unspiked (UNSPK) = the sample used in conjunction with the matrix spike
Background (BKG) = the sample used in conjunction with the duplicate

Analysis Name	MS %REC	MSD %REC	MS/MSD Limits	RPD RPD	BKG MAX	DUP Conc	DUP RPD	Dup RPD Max
Batch number: 072410035B	Sample number(s): 5141313 UNSPK: 5141313							
PCB-1016	87	88	45-125	2	50			
PCB-1260	85	87	62-130	2	50			
Batch number: 072420005A	Sample number(s): 5141313 UNSPK: 5141313							
2,4-D	100	98	41-158	2	35			
2,4,5-TP	92	82	30-151	11	35			
Batch number: 072425708001	Sample number(s): 5141313 UNSPK: P141423 BKG: P141423							
Arsenic	114	87	75-125	12	20	16.3	15.4	6
Selenium	94	92	75-125	1	20	2.69	2.95	9 (1)
Barium	98	101	75-125	2	20	115.	125.	8
Cadmium	94	93	75-125	2	20	< 0.500	< 0.500	12 (1)
Chromium	84 (2)	75 (2)	75-125	1	20	100.	128.	24*
Lead	-39 (2)	-246 (2)	75-125	10	20	265.	394.	39*
Silver	96	95	75-125	0	20	< 0.500	< 0.500	200* (1)
Batch number: 072425711002	Sample number(s): 5141313 UNSPK: P141423 BKG: P141423							
Mercury	93	88	80-120	4	20	< 0.0943	< 0.0938	33* (1)
Batch number: 072470011A	Sample number(s): 5141313 UNSPK: 5141313							
Gamma BHC - Lindane	82	74	43-154	9	35			
Heptachlor	73	64*	70-138	12	35			
Aldrin	78	72	21-141	8	35			
p,p-DDT	73	70	62-166	4	35			
Dieldrin	93	83	68-139	11	35			
Endrin	76	74	48-188	4	35			
Methoxychlor	92	85	74-162	8	35			
Alpha BHC	85	78	25-146	8	35			
Beta BHC	88	82	31-176	7	35			
Delta BHC	83	75	68-158	10	35			
Heptachlor Epoxide	81	72	69-133	11	35			
p,p-DDE	95	89	48-175	6	35			
p,p-DDD	91	86	52-181	3	35			
Endosulfan I	81	74	41-166	8	35			
Endosulfan II	85	81	65-144	5	35			
Endosulfan Sulfate	85	78	65-154	9	35			
Endrin Aldehyde	72	65	63-125	12	35			

Surrogate Quality Control

Surrogate recoveries which are outside of the QC window are confirmed unless attributed to dilution or otherwise noted on the Analysis Report.

Analysis Name: PCBs in Soil
Batch number: 072410035B

*- Outside of specification

- (1) The result for one or both determinations was less than five times the LOQ.
- (2) The unspiked result was more than four times the spike added.

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Analysis Report



Page 3 of 3

Quality Control Summary

Client Name: Charles River Laboratories
Reported: 09/13/07 at 12:47 PM

Group Number: 1053778

Surrogate Quality Control

	Tetrachloro-m-xylene	Decachlorobiphenyl
5141313	86	85
Blank	97	91
LCS	96	93
MS	92	91
MSD	95	91

Limits: 38-132 41-160

Analysis Name: Appendix IX Herbicides in Soil
Batch number: 072420005A
2,4-Dichlorophenylacetic acid

5141313	87
Blank	74
LCS	88
MS	93
MSD	87

Limits: 22-151

Analysis Name: Pesticides in Solids
Batch number: 072470011A

	Tetrachloro-m-xylene	Decachlorobiphenyl
5141313	94	102
Blank	104	101
LCS	98	100
MS	95	84
MSD	89	95

Limits: 38-132 41-160

*- Outside of specification

- (1) The result for one or both determinations was less than five times the LOQ.
- (2) The unspiked result was more than four times the spike added.

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TMM 17 Jan 08

**APPENDIX 6 - ENVIRONMENTAL PROTECTION AGENCY (EPA)
APPROVAL LETTER**



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PESTICIDE PROGRAMS,
SPECIAL REVIEW & REGISTRATION DIVISION

December 6, 2007

Paul Whatling
Senior Manager of Regulatory Science
Cheminova, Inc.

RE: Protocols for single-dose comparative cholinesterase study with malathion and malaoxon.

Dear Paul,

On November 5, 2007 Cheminova submitted the results of a repeat cholinesterase (ChE) time to peak effect (TTPE) study with malathion. Cheminova asked the Agency to review this study and evaluate their assertion that the results of this study support a TTPE value for malathion of 60 minutes. Additionally, Cheminova presented their overall design for an upcoming comparative cholinesterase study with malathion and malaoxon, scheduled to begin on December 4, 2007. Subsequent electronic and telephonic communication between the Agency and Cheminova concerned the TTPE value for malathion, and the appropriate dose levels for the animals in the study to be treated with malathion and malaoxon. The TTPE values will be used in the comparative cholinesterase study as sampling time points. Cheminova and the Agency have reached agreement on the disputed design parameters for the comparative ChE study, the agreed upon values are summarized below.

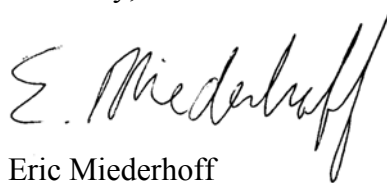
Design Parameters:

Time of Peak Effect for Malaoxon: 60 minutes for malaoxon (both RBC and brain ChE)

Time of Peak Effect for Malathion: 60 minutes for malathion (both RBC and brain ChE)

Dose Levels: Dose levels of 0, 10, 25, 50, 100, 150 mg/kg are to be used for malathion. Dose levels of 0, 1, 3.5, 7, 10, 12.5 mg/kg will be used for malaoxon.

Sincerely,

A handwritten signature in black ink, appearing to read "E. Miederhoff". The signature is fluid and cursive, with a large, stylized "M" and a long, sweeping underline.

Eric Miederhoff
Chemical Review Manager
U.S. Environmental Protection Agency
Office of Pesticide Programs
Special Review and Reregistration Division (7508P)
(703) 347-8028
Fax (703) 308-7070