

FINAL REPORT

Study Title

Oral (Gavage) Acute Dose Time of Peak Cholinesterase Depression Study of Malathion
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.

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Study Completed On

29 February 2008
(Final Report)

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Laboratory Project ID

Charles River Laboratories Preclinical Services Protocol Number: TQC00032

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

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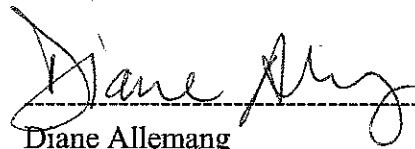
These data are the property of Cheminova A/S and as such, are considered to be confidential for all purposes other than compliance with FIFRA Section 10. Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality, which may exist under any other statute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

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study does not meet the requirements of 40 CFR Part 160, and differs in the following ways:

- 1) The Testing Facility's Quality Assurance Unit did not audit the protocol, the raw data or the report, and did not perform critical phase inspections for the study.
- 2) Samples of the test substance formulation were not analyzed.

Sponsor/Submitter:

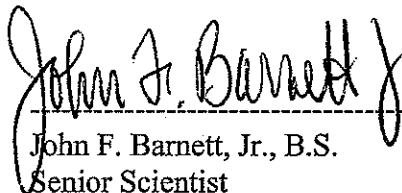


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5th March 2008

Study Director:



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Senior Scientist
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Date

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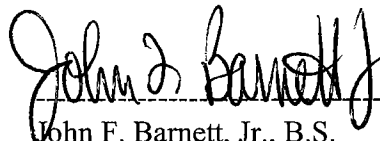
STUDY DIRECTOR STATEMENT

This study was conducted using good scientific practices and according to the SOPs of the Testing Facility. The Testing Facility Quality Assurance Unit (QAU) did not audit the protocol, raw data, or the report, and did not perform critical phase inspections for the study. The Testing Facility performed an independent Quality Control review of the cholinesterase data and the cholinesterase tables that are included in this report.

As a pilot time-of-peak effect investigation it was not necessary to conduct this study in full compliance with all aspects of the regulations cited below^{a,b,c}; however, this study was conducted using the same facilities and procedures which are subjected to routine inspection under the Testing Facility's Quality Assurance program.

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 the raw data. Those deviations that occurred did not affect the quality or integrity of the study.

Study Director:


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


Date

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

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1. ABSTRACT

The objective of this study was to determine the time of peak cholinesterase inhibition after acute dosing of postnatal day 11 (PND 11) rat pups with Malathion on erythrocyte and brain acetyl cholinesterase activity when the pups are sampled at various time points.

Pups from fifteen litters were assigned to the study. Eight pups of each sex were assigned to Group I (vehicle control) and forty pups of each sex were assigned to Group II (150 mg/kg).

Suspensions of the test substance, malathion, 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 the test substance and the vehicle and was adjusted on the basis of individual body weights recorded just prior to dosage administration.

Checks for viability were made twice daily. Clinical observations were recorded daily before dosage administration, by chance after dosage administration and immediately prior to sacrifice. Body weights were recorded the day after arrival, 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 30, 60, 80, 100 and 150 minutes postdosage for the pups assigned to the acute malathion dosage groups and at 60 minutes postdosage for the pups assigned to the vehicle dosage group. These samples were then analyzed to determine red blood cell (RBC) and brain cholinesterase activity.

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 day 1 postpartum (day 1 of lactation) in the Standard Operating Procedures of the Testing Facility. Throughout the protocol and the raw data, the day of birth was designated day 1 postpartum (day 1 of lactation) and all subsequent ages of the F1 generation rats and days of the lactation period were determined and cited accordingly. In the text of this report, as well as the summary and individual tables, the day of birth has been adjusted so that the day of birth and all subsequent postpartum days match the EPA guideline.

No mortality occurred in the male or female pups.

Seventeen male pups and fifteen female pups at 150 mg/kg were observed with whole body tremors, head tremors or body jerks or a combination of those observations. The adverse clinical observations occurred anywhere between 16 minutes and 143 minutes after dosage administration for both of the sexes. No additional adverse clinical signs were observed in the male or female pups.

RBC and brain cholinesterase inhibition was observed in the 150 mg/kg male and female pups at all time points evaluated compared with the vehicle controls. The greatest amount of brain cholinesterase inhibition (69.6% and 68.7% in the male and female pups, respectively) and RBC cholinesterase inhibition (75.8% and 78.0% in the male and female pups, respectively) was observed at 60 minutes postdosage.

After consultation with EPA scientists, Cheminova and EPA agreed that the time of peak effect for malaoxon was 60 minutes post dose (refer to EPA letter to Cheminova dated December 6, 2007, in ADDENDUM 4).

2. OBJECTIVE

The objective of this study was to determine the time of peak cholinesterase inhibition after acute dosing of postnatal day 11 (PND 11) rat pups with Malathion on erythrocyte and brain acetyl cholinesterase activity when the pups were sampled at various timepoints.

3. METHODS^a

The test substance was malathion (synonymous with Fyfanon Technical). Malathion (lot number 9010501) is a clear, colorless liquid. The malathion was received from the Sponsor on 16 October 2007. The expiration date is 9 November 2008. A Certificate of Analysis for the test substance is available in the Protocol (ADDENDUM 1, Attachment 2). The test substance was stored frozen (-20°C), protected from light. The vehicle, corn oil (lot number 126K0117), a viscous yellow liquid, was received from Sigma-Aldrich, Inc., St Louis, MO, on 26 July 2007, and stored at room temperature. The expiration date is July 2012. A Certificate of Analysis for the vehicle is available in ADDENDUM 2. Formulations (suspensions) of the test substance in corn oil were prepared in the morning prior to dosing at the Testing Facility and stored refrigerated (2°C to 8°C), protected from light. Duplicate concentration samples (0.5 mL each) were taken from the middle of each concentration after preparation. These samples were retained refrigerated (2°C to 8°C), protected from light at the Testing Facility for possible future evaluation. Homogeneity and stability data for prepared formulations in the corn oil vehicle bracketing the concentration tested in this study have been confirmed in a previous study⁽¹⁾.

Pups from fifteen litters were assigned to two dosage groups (eight pups of each sex in Group I and forty pups of each sex in Group II). Assignment to cholinesterase time points was documented in the raw data. Pups were administered the test substance and/or vehicle on postnatal day 11 (PND 11) using a 0.5 mL Hamilton syringe. The dosage levels were based on body weights recorded prior to dosage administration. Prepared formulations were stirred continuously during dosage administration.

Dosage Group	Number of Pups per Sex	Test Substance	Dosage (mg/kg) ^a	Concentration (mg/mL)	Dosage Volume (mL/kg)
I	8	Corn Oil	0 (Vehicle)	0	5
II	40	Malathion	150	30	5

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

-
- a. Detailed descriptions of all procedures used in the conduct of this study are provided in the appropriate sections of this report and in the attached protocol. Deviations from the Protocol and the Standard Operating Procedures of the Testing Facility are available in the raw data.

Checks for viability were made twice daily. The litters were observed for dead pups at least twice daily. The pups in each litter were counted once daily until the day of dosage administration. Clinical observations were recorded on the day of delivery, PNDs 1, 4 and 7, the day of randomization, prior to dosage administration, by chance after dosing and just prior to sacrifice. Body weights were recorded on the day of delivery, PNDs 1, 4 and 7, the day of randomization and on the day of dosage.

After dosage administration on PND 11, whole blood samples were collected (0.2 to 0.5 mL) from each of the pups assigned for cholinesterase assay at the appropriate timepoints following decapitation (without anesthesia). The samples were collected at 60 minutes postdosage from Group I and 30, 60, 80, 100 and 150 minutes postdosage from Group II (timing began with the gavage of the pup and ended with decapitation for blood collection). Whole blood was collected into 1.3 mL EDTA-coated (lavender-top) tubes. Collected blood was placed on cold packs on a tilter until processed. Blood samples were processed and analyzed for RBC cholinesterase levels according to the Study Specific Procedure located in Attachment 5 of the protocol (ADDENDUM 1) on the day of collection (within two hours of sample collection).

After blood sample collection, the brain was excised, and the weight was recorded. The brains were stored in saline on ice until assayed for cholinesterase levels according to the Study Specific Procedure located in Attachment 5 of the protocol (ADDENDUM 1). All brains were processed and analyzed for cholinesterase levels on the day of collection (within two hours of sample collection). The pups were then discarded without further evaluation.

4. RESULTS

4.1. Mortality and Clinical Observations (Summaries - Tables 1 and 2; Individual Data - Tables 9 and 10)

All male and female pups survived until scheduled sacrifice.

A total of seventeen male pups and fifteen female pups were observed with adverse clinical observations after dosage administration. In the male pups, ten pups were observed with whole body tremors; five pups with whole body tremors and head tremors; one pup with whole body tremors and body jerks; and one pup with head tremors. In the female pups, six pups were observed with whole body tremors; five pups with whole body tremors and head tremors; two pups with body jerks; one pup with whole body tremors, head tremors and body jerks; and one pup with head tremors. These observations occurred between 16 minutes and 143 minutes after dosage administration for both of the sexes.

No additional adverse clinical signs were observed in the male or female pups.

4.2. Body Weights (Summaries - Tables 3 and 4; Individual Data - Tables 11 and 12)

Body weights were generally comparable among the 150 mg/kg dosage group and the 0 (Vehicle) mg/kg dosage group for both the male and female pups.

4.3. Brain Cholinesterase Levels (Summaries - Tables 5 and 6; Individual Data - Tables 13 and 14)

As summarized in Text Table 1, brain cholinesterase levels were decreased at all intervals examined after dosage as compared with the vehicle control rats evaluated 60 minutes after dosage. The largest cholinesterase inhibition observed at 150 mg/kg occurred at 60 minutes postdosage (69.6% and 68.7% decreases in the male and female pups, respectively), with comparable, but slightly smaller, decreases at 100 and 150 minutes (the values were between 57.9% and 65.3%). Both sexes also had smaller decreases at the 80 minute interval (29.3% decrease for the male pups and 36.4% decrease for the female pups).

Text Table 1. PND 11 Pups, Brain Cholinesterase Levels - Time-of-Peak Effect - Malathion

Time Postdosage	Group	Dosage (mg/kg)	Mean ChE U/G \pm S.D. (n) ^a	Percent Decrease Compared with Control
Male Pups				
60 Minutes	I	0 (Vehicle)	5.932 \pm 0.239 (8)	--
30 Minutes	II	150	3.083 \pm 1.824 (8)	48.0%
60 Minutes	II	150	1.804 \pm 1.210 (8)	69.6%
80 Minutes	II	150	4.191 \pm 1.637 (8)	29.3%
100 Minutes	II	150	2.059 \pm 0.769 (8)	65.3%
150 Minutes	II	150	2.353 \pm 1.194 (8)	60.3%
Female Pups				
60 Minutes	I	0 (Vehicle)	6.234 \pm 0.379 (8)	--
30 Minutes	II	150	2.976 \pm 2.163 (8)	52.3%
60 Minutes	II	150	1.953 \pm 1.798 (8)	68.7%
80 Minutes	II	150	3.962 \pm 1.408 (8)	36.4%
100 Minutes	II	150	2.625 \pm 1.411 (8)	57.9%
150 Minutes	II	150	2.403 \pm 0.956 (8)	61.5%

a. n = The number of PND 11 pups evaluated for cholinesterase levels.

4.4. Red Blood Cell (RBC) Cholinesterase Levels (Summaries - Tables 7 and 8; Individual Data - Tables 15 and 16)

As summarized in Text Table 2, RBC cholinesterase levels were decreased at all intervals examined after dosage as compared with the vehicle control rats evaluated 60 minutes after dosage. The largest cholinesterase inhibition observed at the 150 mg/kg dose occurred at 60 minutes postdosage (75.8% and 78.0% decreases in the male and female pups, respectively), with comparable, but slightly smaller, decreases at 100 and 150 minutes postdosage (the values were between 72.2% and 75.9%). Both sexes had smaller decreases at the 80 minute interval (47.2% decrease for the male pups and 55.3% decrease for the female pups).

Text Table 2. PND 11 Pups, RBC Cholinesterase Levels - Time-of-Peak Effect - Malathion

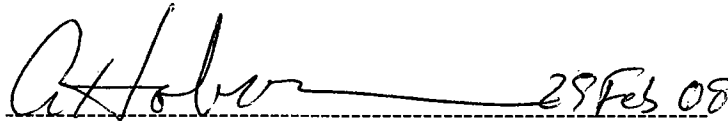
Time Postdosage	Group	Dosage (mg/kg)	Mean ChE U/mL \pm S.D. (n) ^a	Percent Decrease Compared with Control
Male Pups				
60 Minutes	I	0 (Vehicle)	2.011 \pm 0.226 (8)	--
30 Minutes	II	150	0.757 \pm 0.182 (8)	62.4%
60 Minutes	II	150	0.487 \pm 0.242 (8)	75.8%
80 Minutes	II	150	1.061 \pm 0.515 (8)	47.2%
100 Minutes	II	150	0.555 \pm 0.141 (8)	72.4%
150 Minutes	II	150	0.559 \pm 0.236 (8)	72.2%
Female Pups				
60 Minutes	I	0 (Vehicle)	2.192 \pm 0.181 (8)	--
30 Minutes	II	150	0.783 \pm 0.439 (8)	64.3%
60 Minutes	II	150	0.483 \pm 0.401 (8)	78.0%
80 Minutes	II	150	0.980 \pm 0.429 (8)	55.3%
100 Minutes	II	150	0.596 \pm 0.212 (8)	72.8%
150 Minutes	II	150	0.529 \pm 0.301 (8)	75.9%

a. n = The number of PND 21 pups evaluated for cholinesterase levels.

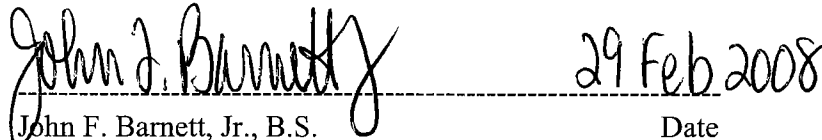
5. CONCLUSION - MALATHION

Based on these data, a 60 minute time-of-peak effect would appear to be adequate to ensure the maximal or close to maximal response to cholinesterase inhibition by malathion in both red blood cell and brain compartments for both male and female pups.

After consultation with EPA scientists, Cheminova and EPA agreed that the time of peak effect for malaoxon was 60 minutes post dose (see ADDENDUM 4).

 28 Feb 08

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

 29 Feb 2008

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

6. REFERENCE

- 1) Fulcher, S.M. Malathion developmental neurotoxicity study in the CD rat by oral gavage administration. Huntingdon Life Sciences Ltd. Study No. CHV 066/013331; MRID 45646401; 21 March, 2002. Cambridgeshire, England: Huntingdon Life Sciences, Ltd.

PROTOCOL TQCC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

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

DOSAGE GROUP TEST SUBSTANCE DOSAGE (MG/KG)a	I CORN OIL 0 (VEHICLE)	II MALATHION 150
PUPS TESTED	8	40
MORTALITY	0	0
WHOLE BODY: TREMORS b	0	16
HEAD: TREMORS c	0	6
BODY JERKS d	0	1
a. Dosage occurred on postnatal day 11. b. Observed 17 to 138 minutes after dosage administration. c. Observed 57 to 143 minutes after dosage administration. d. Observed 140 minutes after dosage administration.		

PROTOCOL TQCC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 2 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - JUVENILE FEMALE PUPS

DOSAGE GROUP TEST SUBSTANCE DOSAGE (MG/KG)a	I CORN OIL 0 (VEHICLE)	II MALATHION 150
PUPS TESTED	8	40
MORTALITY	0	0
WHOLE BODY: TREMORS b	0	12
HEAD: TREMORS c	0	7
BODY JERKS d	0	3
a. Dosage occurred on postnatal day 11. b. Observed 16 to 77 minutes after dosage administration. c. Observed 54 to 139 minutes after dosage administration. d. Observed 55 to 94 minutes after dosage administration.		

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 3 (PAGE 1): BODY WEIGHTS - SUMMARY - JUVENILE MALE PUPS

DOSAGE GROUP		I	II
TEST SUBSTANCE		CORN OIL	MALATHION
DOSAGE (MG/KG)a		0 (VEHICLE)	150
PUPS TESTED	N	8	40
BODY WEIGHT (G)			
PND 11	MEAN±S.D.	18.7 ± 2.0	21.6 ± 2.8

PND = POSTNATAL DAY

a. Dosage occurred on postnatal day 11.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 4 (PAGE 1): BODY WEIGHTS - SUMMARY - JUVENILE FEMALE PUPS

DOSAGE GROUP		I	II
TEST SUBSTANCE		CORN OIL	MALATHION
DOSAGE (MG/KG)a		0 (VEHICLE)	150
PUPS TESTED	N	8	40
BODY WEIGHT (G)			
PND 11	MEAN±S.D.	17.0 ± 2.7	21.2 ± 2.4

PND = POSTNATAL DAY

a. Dosage occurred on postnatal day 11.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 5 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - JUVENILE MALE PUPS

DOSAGE GROUP	I				II	
TEST SUBSTANCE	CORN OIL				MALATHION	
DOSAGE (MG/KG)a	0 (VEHICLE)				150	
<u>30 MINUTES POSTDOSAGE:</u>						
PUPS TESTED	N	-			8	
BRAIN WEIGHT (G)	MEAN±S.D.				0.866	± 0.103
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.				3.083	± 1.824
% INHIBITION b	%				48.0	
<u>60 MINUTES POSTDOSAGE:</u>						
PUPS TESTED	N	8			8	
BRAIN WEIGHT (G)	MEAN±S.D.	0.866	±	0.100	0.934	± 0.062
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	5.932	±	0.239	1.804	± 1.210
% INHIBITION b	%				69.6	
<u>80 MINUTES POSTDOSAGE:</u>						
PUPS TESTED	N	-			8	
BRAIN WEIGHT (G)	MEAN±S.D.				0.930	± 0.027
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.				4.191	± 1.637
% INHIBITION b	%				29.3	
a. Dosage occurred on postnatal day 11.						
b. Value derived from comparison to the Vehicle Group, 60 minutes postdosage value.						

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 5 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - SUMMARY - JUVENILE MALE PUPS

DOSAGE GROUP	I	II
TEST SUBSTANCE	CORN OIL	MALATHION
DOSAGE (MG/KG) ^a	0 (VEHICLE)	150
<u>100 MINUTES POSTDOSAGE:</u>		
PUPS TESTED	N	8
BRAIN WEIGHT (G)	MEAN±S.D.	0.980 ± 0.044
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.059 ± 0.769
% INHIBITION ^b	%	65.3
<u>150 MINUTES POSTDOSAGE:</u>		
PUPS TESTED	N	8
BRAIN WEIGHT (G)	MEAN±S.D.	0.985 ± 0.036
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.353 ± 1.194
% INHIBITION ^b	%	60.3
a. Dosage occurred on postnatal day 11.		
b. Value derived from comparison to the Vehicle Group, 60 minutes postdosage value.		

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 6 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - SUMMARY - JUVENILE FEMALE PUPS

DOSAGE GROUP		I			II		
TEST SUBSTANCE		CORN OIL			MALATHION		
DOSAGE (MG/KG)a		0 (VEHICLE)			150		
<u>30 MINUTES POSTDOSAGE:</u>							
PUPS TESTED	N	-			8		
BRAIN WEIGHT (G)	MEAN±S.D.				0.868	±	0.098
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.				2.976	±	2.163
% INHIBITION b	%				52.3		
<u>60 MINUTES POSTDOSAGE:</u>							
PUPS TESTED	N	8			8		
BRAIN WEIGHT (G)	MEAN±S.D.	0.824	±	0.080	0.886	±	0.054
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	6.234	±	0.379	1.953	±	1.798
% INHIBITION b	%				68.7		
<u>80 MINUTES POSTDOSAGE:</u>							
PUPS TESTED	N	-			8		
BRAIN WEIGHT (G)	MEAN±S.D.				0.907	±	0.044
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.				3.962	±	1.408
% INHIBITION b	%				36.4		

a. Dosage occurred on postnatal day 11.

b. Value derived from comparison to the Vehicle Group, 60 minutes postdosage value.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 6 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - SUMMARY - JUVENILE FEMALE PUPS

DOSAGE GROUP	I	II
TEST SUBSTANCE	CORN OIL	MALATHION
DOSAGE (MG/KG) ^a	0 (VEHICLE)	150
<u>100 MINUTES POSTDOSAGE:</u>		
PUPS TESTED	N	8
BRAIN WEIGHT (G)	MEAN±S.D.	0.938 ± 0.051
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.625 ± 1.411
% INHIBITION ^b	%	57.9
<u>150 MINUTES POSTDOSAGE:</u>		
PUPS TESTED	N	8
BRAIN WEIGHT (G)	MEAN±S.D.	0.961 ± 0.045
CHOLINESTERASE LEVELS (UNITS/G)	MEAN±S.D.	2.403 ± 0.956
% INHIBITION ^b	%	61.5

a. Dosage occurred on postnatal day 11.

b. Value derived from comparison to the Vehicle Group, 60 minutes postdosage value.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 7 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - JUVENILE MALE PUPS

DOSAGE GROUP	I				II	
TEST SUBSTANCE	CORN OIL				MALATHION	
DOSAGE (MG/KG)a	0 (VEHICLE)				150	
<u>30 MINUTES POSTDOSAGE:</u>						
PUPS TESTED	N	-			8	
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.				0.757	± 0.182
% INHIBITION b	%				62.4	
<u>60 MINUTES POSTDOSAGE:</u>						
PUPS TESTED	N	8			8	
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.	2.011	±	0.226	0.487	± 0.242
% INHIBITION b	%				75.8	
<u>80 MINUTES POSTDOSAGE:</u>						
PUPS TESTED	N	-			8	
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.				1.061	± 0.515
% INHIBITION b	%				47.2	

a. Dosage occurred on postnatal day 11.

b. Value derived from comparison to the Vehicle Group, 60 minutes postdosage value.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 7 (PAGE 2): RBC CHOLINESTERASE LEVELS - SUMMARY - JUVENILE MALE PUPS

DOSAGE GROUP		I	II
TEST SUBSTANCE		CORN OIL	MALATHION
DOSAGE (MG/KG) ^a		0 (VEHICLE)	150
<u>100 MINUTES POSTDOSAGE:</u>			
PUPS TESTED	N	-	8
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.		0.555 ± 0.141
% INHIBITION ^b	%		72.4
<u>150 MINUTES POSTDOSAGE:</u>			
PUPS TESTED	N	-	8
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.		0.559 ± 0.236
% INHIBITION ^b	%		72.2
a. Dosage occurred on postnatal day 11.			
b. Value derived from comparison to the Vehicle Group, 60 minutes postdosage value.			

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 8 (PAGE 1): RBC CHOLINESTERASE LEVELS - SUMMARY - JUVENILE FEMALE PUPS

DOSAGE GROUP	I			II	
TEST SUBSTANCE	CORN OIL			MALATHION	
DOSAGE (MG/KG)a	0 (VEHICLE)			150	
<u>30 MINUTES POSTDOSAGE:</u>					
PUPS TESTED	N	-		8	
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.			0.783 ± 0.439	
% INHIBITION b	%			64.3	
<u>60 MINUTES POSTDOSAGE:</u>					
PUPS TESTED	N	8		8	
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.	2.192 ± 0.181	0.483 ± 0.401		
% INHIBITION b	%			78.0	
<u>80 MINUTES POSTDOSAGE:</u>					
PUPS TESTED	N	-		8	
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.			0.980 ± 0.429	
% INHIBITION b	%			55.3	

a. Dosage occurred on postnatal day 11.

b. Value derived from comparison to the Vehicle Group, 60 minutes postdosage value.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 8 (PAGE 2): RBC CHOLINESTERASE LEVELS - SUMMARY - JUVENILE FEMALE PUPS

DOSAGE GROUP		I	II
TEST SUBSTANCE		CORN OIL	MALATHION
DOSAGE (MG/KG) ^a		0 (VEHICLE)	150
<u>100 MINUTES POSTDOSAGE:</u>			
PUPS TESTED	N	-	8
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.		0.596 ± 0.212
% INHIBITION ^b	%		72.8
<u>150 MINUTES POSTDOSAGE:</u>			
PUPS TESTED	N	-	8
CHOLINESTERASE LEVELS (UNITS/ML)	MEAN±S.D.		0.529 ± 0.301
% INHIBITION ^b	%		75.9
a. Dosage occurred on postnatal day 11.			
b. Value derived from comparison to the Vehicle Group, 60 minutes postdosage value.			

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 9 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - JUVENILE MALE PUPS

DOSAGE GROUP I		CORN OIL	0 (VEHICLE) MG/KG
PUP #	DESCRIPTION		
8401	NO ADVERSE FINDINGS		
8402	NO ADVERSE FINDINGS		
8403	NO ADVERSE FINDINGS		
8501	NO ADVERSE FINDINGS		
8502	NO ADVERSE FINDINGS		
8503	NO ADVERSE FINDINGS		
8601	NO ADVERSE FINDINGS		
8602	NO ADVERSE FINDINGS		

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 9 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - JUVENILE MALE PUPS

DOSAGE GROUP II			MALATHION	150 MG/KG
PUP #			DESCRIPTION	
8603	PND(11)		WHOLE BODY: TREMORS (28 MINUTES AFTER DOSAGE ADMINISTRATION)	
8701	PND(11)		WHOLE BODY: TREMORS (27 MINUTES AFTER DOSAGE ADMINISTRATION)	
8702			NO ADVERSE FINDINGS	
8703			NO ADVERSE FINDINGS	
8801	PND(11)		WHOLE BODY: TREMORS (19 MINUTES AFTER DOSAGE ADMINISTRATION)	
8802			NO ADVERSE FINDINGS	
8803			NO ADVERSE FINDINGS	
8901			NO ADVERSE FINDINGS	
8902			NO ADVERSE FINDINGS	
8903	PND(11)		WHOLE BODY: TREMORS (31 MINUTES AFTER DOSAGE ADMINISTRATION)	
9001			NO ADVERSE FINDINGS	
9002	PND(11)		WHOLE BODY: TREMORS (34 MINUTES AND 41 MINUTES AFTER DOSAGE ADMINISTRATION)	
9003			NO ADVERSE FINDINGS	
9101			NO ADVERSE FINDINGS	
9102			NO ADVERSE FINDINGS	
9103	PND(11)		WHOLE BODY: TREMORS (17 MINUTES AFTER DOSAGE ADMINISTRATION)	
9201			NO ADVERSE FINDINGS	
9202			NO ADVERSE FINDINGS	
9203			NO ADVERSE FINDINGS	
9301			NO ADVERSE FINDINGS	
9302			NO ADVERSE FINDINGS	
9303			NO ADVERSE FINDINGS	
9401			NO ADVERSE FINDINGS	
9402			NO ADVERSE FINDINGS	
9403			NO ADVERSE FINDINGS	
9501			NO ADVERSE FINDINGS	
9502			NO ADVERSE FINDINGS	
9503	PND(11)		WHOLE BODY: TREMORS (65 MINUTES AFTER DOSAGE ADMINISTRATION)	
9601	PND(11)		WHOLE BODY: TREMORS (54 MINUTES AFTER DOSAGE ADMINISTRATION)	
9602			NO ADVERSE FINDINGS	
9603			NO ADVERSE FINDINGS	

PND = POSTNATAL DAY

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 9 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - JUVENILE MALE PUPS

DOSAGE GROUP II				MALATHION	150 MG/KG
PUP #				DESCRIPTION	
9604	PND(11)	HEAD: TREMORS (79 MINUTES AFTER DOSAGE ADMINISTRATION)	
9701	PND(11)	WHOLE BODY: TREMORS (77 MINUTES AFTER DOSAGE ADMINISTRATION)	
	PND(11)	HEAD: TREMORS (143 MINUTES AFTER DOSAGE ADMINISTRATION)	
9702	PND(11)	WHOLE BODY: TREMORS (74 MINUTES AFTER DOSAGE ADMINISTRATION)	
	PND(11)	BODY JERKS (140 MINUTES AFTER DOSAGE ADMINISTRATION)	
9703	PND(11)	WHOLE BODY: TREMORS (71 MINUTES AFTER DOSAGE ADMINISTRATION)	
9704	PND(11)	WHOLE BODY: TREMORS (66 MINUTES AFTER DOSAGE ADMINISTRATION)	
	PND(11)	HEAD: TREMORS (85 MINUTES AFTER DOSAGE ADMINISTRATION)	
9801	PND(11)	WHOLE BODY: TREMORS (24 MINUTES AND 63 MINUTES AFTER DOSAGE ADMINISTRATION)	
	PND(11)	HEAD: TREMORS (89 MINUTES AND 141 MINUTES AFTER DOSAGE ADMINISTRATION)	
9802	PND(11)	WHOLE BODY: TREMORS (60 MINUTES AND 138 MINUTES AFTER DOSAGE ADMINISTRATION)	
9803	PND(11)	WHOLE BODY: TREMORS (25 MINUTES AFTER DOSAGE ADMINISTRATION)	
	PND(11)	HEAD: TREMORS (57 MINUTES, 84 MINUTES AND 135 MINUTES AFTER DOSAGE ADMINISTRATION)	
9804	PND(11)	WHOLE BODY: TREMORS (34 MINUTES AND 81 MINUTES AFTER DOSAGE ADMINISTRATION)	
	PND(11)	HEAD: TREMORS (133 MINUTES AFTER DOSAGE ADMINISTRATION)	
PND = POSTNATAL DAY					

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 10 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

DOSAGE GROUP I	CORN OIL	0 (VEHICLE) MG/KG
PUP #	DESCRIPTION	
8404	NO ADVERSE FINDINGS	
8405	NO ADVERSE FINDINGS	
8406	NO ADVERSE FINDINGS	
8504	NO ADVERSE FINDINGS	
8505	NO ADVERSE FINDINGS	
8506	NO ADVERSE FINDINGS	
8604	NO ADVERSE FINDINGS	
8605	NO ADVERSE FINDINGS	

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 10 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

DOSAGE GROUP II			MALATHION	150 MG/KG
PUP #			DESCRIPTION	
8606	PND(11)		WHOLE BODY: TREMORS (28 MINUTES AFTER DOSAGE ADMINISTRATION)	
8704			NO ADVERSE FINDINGS	
8705			NO ADVERSE FINDINGS	
8706			NO ADVERSE FINDINGS	
8804			NO ADVERSE FINDINGS	
8805			NO ADVERSE FINDINGS	
8806			NO ADVERSE FINDINGS	
8904			NO ADVERSE FINDINGS	
8905	PND(11)		WHOLE BODY: TREMORS (21 MINUTES AFTER DOSAGE ADMINISTRATION)	
8906	PND(11)		WHOLE BODY: TREMORS (25 MINUTES AND 47 MINUTES AFTER DOSAGE ADMINISTRATION)	
9004			NO ADVERSE FINDINGS	
9005			NO ADVERSE FINDINGS	
9006			NO ADVERSE FINDINGS	
9104			NO ADVERSE FINDINGS	
9105	PND(11)		WHOLE BODY: TREMORS (16 MINUTES AFTER DOSAGE ADMINISTRATION)	
9106			NO ADVERSE FINDINGS	
9204			NO ADVERSE FINDINGS	
9205			NO ADVERSE FINDINGS	
9206			NO ADVERSE FINDINGS	
9304			NO ADVERSE FINDINGS	
9305	PND(11)		WHOLE BODY: TREMORS (46 MINUTES AFTER DOSAGE ADMINISTRATION)	
9306			NO ADVERSE FINDINGS	
9404	PND(11)		WHOLE BODY: TREMORS (30 MINUTES AFTER DOSAGE ADMINISTRATION)	
9405			NO ADVERSE FINDINGS	
9406	PND(11)		BODY JERKS (94 MINUTES AFTER DOSAGE ADMINISTRATION)	
9504			NO ADVERSE FINDINGS	
9505			NO ADVERSE FINDINGS	
9506			NO ADVERSE FINDINGS	
9605			NO ADVERSE FINDINGS	
9606	PND(11)		WHOLE BODY: TREMORS (77 MINUTES AFTER DOSAGE ADMINISTRATION)	
	PND(11)		HEAD: TREMORS (54 MINUTES AFTER DOSAGE ADMINISTRATION)	
9607			NO ADVERSE FINDINGS	
9608	PND(11)		HEAD: TREMORS (80 MINUTES AFTER DOSAGE ADMINISTRATION)	
9705			NO ADVERSE FINDINGS	

PND = POSTNATAL DAY

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 10 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

DOSAGE GROUP II			MALATHION	150 MG/KG
PUP #				DESCRIPTION
9706	PND(11)	WHOLE BODY: TREMORS (24 MINUTES AFTER DOSAGE ADMINISTRATION)
	PND(11)	HEAD: TREMORS (75 MINUTES AND 136 MINUTES AFTER DOSAGE ADMINISTRATION)
9707	PND(11)	WHOLE BODY: TREMORS (73 MINUTES AFTER DOSAGE ADMINISTRATION)
	PND(11)	HEAD: TREMORS (91 MINUTES AND 138 MINUTES AFTER DOSAGE ADMINISTRATION)
	PND(11)	BODY JERKS (55 MINUTES AFTER DOSAGE ADMINISTRATION)
9708	PND(11)	BODY JERKS (68 MINUTES AFTER DOSAGE ADMINISTRATION)
9805	PND(11)	WHOLE BODY: TREMORS (42 MINUTES AND 60 MINUTES AFTER DOSAGE ADMINISTRATION)
	PND(11)	HEAD: TREMORS (90 MINUTES AFTER DOSAGE ADMINISTRATION)
9806	PND(11)	WHOLE BODY: TREMORS (57 MINUTES AFTER DOSAGE ADMINISTRATION)
	PND(11)	HEAD: TREMORS (139 MINUTES AFTER DOSAGE ADMINISTRATION)
9807	PND(11)	WHOLE BODY: TREMORS (34 MINUTES AND 55 MINUTES AFTER DOSAGE ADMINISTRATION)
	PND(11)	HEAD: TREMORS (136 MINUTES AFTER DOSAGE ADMINISTRATION)
9808				NO ADVERSE FINDINGS

PND = POSTNATAL DAY

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 11 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - JUVENILE MALE PUPS

PUP #	DOSAGE GROUP I	CORN OIL	0 (VEHICLE) MG/KG
PND 11			
8401	19.2		
8402	19.6		
8403	21.0		
8501	20.7		
8502	19.3		
8503	18.2		
8601	15.0		
8602	16.6		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 11 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - JUVENILE MALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
PND 11			
8603	13.8		
8701	25.2		
8702	22.1		
8703	25.1		
8801	19.3		
8802	18.7		
8803	18.3		
8901	24.4		
8902	25.5		
8903	23.3		
9001	17.0		
9002	16.6		
9003	18.0		
9101	22.9		
9102	22.3		
9103	21.5		
9201	21.5		
9202	22.9		
9203	21.6		
9301	21.8		
9302	23.0		
9303	21.9		
9401	22.8		
9402	24.5		
9403	22.2		
9501	26.5		
9502	25.1		
9503	24.0		
9601	24.5		
9602	22.5		
9603	22.8		
9604	21.3		
9701	22.7		
9702	21.1		
9703	21.6		
9704	22.1		
9801	17.2		
9802	19.4		
9803	19.3		
9804	18.4		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 12 (PAGE 1): BODY WEIGHTS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

PUP #	DOSAGE GROUP I	CORN OIL	0 (VEHICLE) MG/KG
PND 11			
8404	18.8		
8405	18.4		
8406	18.4		
8504	19.2		
8505	18.3		
8506	17.7		
8604	12.9		
8605	12.5		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 12 (PAGE 2): BODY WEIGHTS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
PND 11			
8606	15.0		
8704	22.5		
8705	22.5		
8706	23.0		
8804	18.6		
8805	18.5		
8806	17.7		
8904	24.1		
8905	22.4		
8906	23.7		
9004	17.6		
9005	17.3		
9006	17.4		
9104	21.9		
9105	22.0		
9106	21.0		
9204	23.7		
9205	23.0		
9206	22.8		
9304	21.3		
9305	21.1		
9306	22.0		
9404	23.2		
9405	22.4		
9406	21.1		
9504	23.9		
9505	24.7		
9506	24.0		
9605	22.3		
9606	22.2		
9607	23.2		
9608	21.8		
9705	22.1		
9706	22.3		
9707	21.8		
9708	22.3		
9805	18.4		
9806	18.7		
9807	17.0		
9808	18.1		

PND = POSTNATAL DAY

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 13 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE MALE PUPS

PUP #	DOSAGE GROUP I	CORN OIL	0 (VEHICLE) MG/KG
	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
	60 MINUTES POSTDOSAGE		
8401	0.964	5.869	
8402	0.926	6.094	
8403	0.965	6.371	
8501	0.915	5.850	
8502	0.842	5.906	
8503	0.857	6.045	
8601	0.670	5.713	
8602	0.791	5.604	

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 13 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE MALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
30 MINUTES POSTDOSAGE			
8603	0.687	X	LOW
	0.687	0.719	
8701	0.756	4.699	
8702	0.986	3.975	
8703	0.972	1.198	
8801	0.864	X	LOW
	0.864	1.049	
8802	0.928	3.566	
8803	0.870	4.030	
8901	0.866	5.425	
60 MINUTES POSTDOSAGE			
8902	0.975	4.544	
8903	1.010	1.787	
9001	0.931	1.631	
9002	0.816	0.859	
9003	0.870	1.370	
9101	0.943	1.300	
9102	0.957	2.232	
9103	0.967	X	LOW
	0.967	0.710	
80 MINUTES POSTDOSAGE			
9201	0.918	5.445	
9202	0.918	1.728	
9203	0.894	4.286	
9301	0.933	5.681	
9302	0.933	6.227	
9303	0.971	4.756	
9401	0.964	2.753	
9402	0.906	2.654	

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.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 13 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE MALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
100 MINUTES POSTDOSAGE			
9403	0.919	3.280	
9501	1.034	2.740	
9502	0.989	2.008	
9503	0.998	1.957	
9601	1.027	1.035	
9602	1.002	1.078	
9603	0.927	1.938	
9604	0.946	2.439	
150 MINUTES POSTDOSAGE			
9701	1.036	2.649	
9702	0.986	4.528	
9703	0.944	3.403	
9704	0.972	2.356	
9801	0.936	1.210	
9802	0.974	X	DNR
	0.974	1.735	
9803	1.020	2.116	
9804	1.011	0.830	

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.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 14 (PAGE 1): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

PUP #	DOSAGE GROUP I	CORN OIL	0 (VEHICLE) MG/KG
	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
	60 MINUTES POSTDOSAGE		
8404	0.887	6.694	
8405	0.932	6.796	
8406	0.838	6.151	
8504	0.845	6.463	
8505	0.871	5.832	
8506	0.797	5.950	
8604	0.698	5.820	
8605	0.724	6.167	

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 14 (PAGE 2): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
30 MINUTES POSTDOSAGE			
8606	0.677	X	LOW
	0.677	0.692	
8704	0.949	1.215	
8705	0.879	X	LOW
	0.879	1.037	
8706	0.976	X	LOW
	0.976	1.068	
8804	0.881	5.828	
8805	0.798	4.932	
8806	0.835	4.904	
8904	0.948	4.135	
60 MINUTES POSTDOSAGE			
8905	0.927	1.082	
8906	0.914	0.817	
9004	0.805	1.148	
9005	0.854	6.127	
9006	0.830	1.485	
9104	0.873	2.787	
9105	0.924	X	LOW
	0.924	0.863	
9106	0.962	1.318	
80 MINUTES POSTDOSAGE			
9204	0.937	3.313	
9205	0.852	2.259	
9206	0.955	3.949	
9304	0.930	5.483	
9305	0.869	6.036	
9306	0.847	3.019	
9404	0.926	2.591	
9405	0.942	5.043	

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.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 14 (PAGE 3): BRAIN CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
	BRAIN (G)	FINAL CHOLINESTERASE (UNITS/G)	FOOTNOTE
100 MINUTES POSTDOSAGE			
9406	0.918	5.113	
9504	0.902	4.571	
9505	0.967	1.817	
9506	0.939	2.199	
9605	1.049	1.977	
9606	0.891	1.301	
9607	0.937	1.700	
9608	0.900	2.320	
150 MINUTES POSTDOSAGE			
9705	1.032	2.034	
9706	0.969	2.144	
9707	0.961	2.646	
9708	0.960	4.529	
9805	0.944	2.363	
9806	0.988	1.345	
9807	0.870	2.458	
9808	0.962	X	DNR
	0.962	1.703	

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.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 15 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE MALE PUPS

PUP #	DOSAGE GROUP I	CORN OIL	0 (VEHICLE) MG/KG
FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
60 MINUTES POSTDOSAGE			
8401	1.956		
8402	2.280		
8403	1.613		
8501	2.235		
8502	1.922		
8503	2.173		
8601	2.081		
8602	1.826		

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 15 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE MALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
30 MINUTES POSTDOSAGE			
8603	X	LOW	
	0.675		
8701	0.655		
8702	0.645		
8703	X	DNR	
	0.677		
8801	X	LOW	
	0.522		
8802	0.998		
8803	0.854		
8901	1.028		
60 MINUTES POSTDOSAGE			
8902	0.993		
8903	0.379		
9001	0.379		
9002	0.301		
9003	0.354		
9101	X	DNR	
	0.660		
9102	0.558		
9103	0.275		
80 MINUTES POSTDOSAGE			
9201	1.432		
9202	0.451		
9203	1.051		
9301	1.227		
9302	2.065		
9303	0.887		
9401	0.645		
9402	0.733		

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 TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 15 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE MALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
100 MINUTES POSTDOSAGE			
9403	0.786		
9501	0.474		
9502	X	DNR	
	0.630		
9503	0.496		
9601	X	DNR	
	0.471		
9602	0.364		
9603	0.508		
9604	X	DNR	
	0.712		
150 MINUTES POSTDOSAGE			
9701	0.717		
9702	0.972		
9703	X	DNR	
	0.770		
9704	0.450		
9801	X	DNR	
	0.358		
9802	X	DNR	
9802	0.313		
9803	0.527		
9804	X	DNR	
	0.367		

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

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 16 (PAGE 1): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

PUP #	DOSAGE GROUP I	CORN OIL	0 (VEHICLE) MG/KG
FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
60 MINUTES POSTDOSAGE			
8404	2.458		
8405	2.109		
8406	1.955		
8504	2.386		
8505	2.129		
8506	2.354		
8604	X	DNR	
	X	DNR	
	2.081		
8605	2.066		

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.

PROTOCOL TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 16 (PAGE 2): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
30 MINUTES POSTDOSAGE			
8606	X	LOW	
	0.332		
8704	X	LOW	
	0.453		
8705	X	DNR	
	0.545		
8706	X	LOW	
	0.518		
8804	1.711		
8805	0.922		
8806	0.948		
8904	0.837		
60 MINUTES POSTDOSAGE			
8905	0.292		
8906	0.237		
9004	0.219		
9005	1.444		
9006	0.372		
9104	0.519		
9105	X	DNR	
	0.444		
9106	0.339		
80 MINUTES POSTDOSAGE			
9204	0.701		
9205	0.502		
9206	0.860		
9304	1.408		
9305	1.743		
9306	X	DNR	
	1.052		
9404	0.540		
9405	1.032		

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 TQC00032: ORAL (GAVAGE) ACUTE DOSE TIME OF PEAK CHOLINESTERASE DEPRESSION STUDY OF MALATHION IN JUVENILE RATS

TABLE 16 (PAGE 3): RBC CHOLINESTERASE LEVELS - INDIVIDUAL DATA - JUVENILE FEMALE PUPS

PUP #	DOSAGE GROUP II	MALATHION	150 MG/KG
FINAL CHOLINESTERASE (UNITS/ML)		FOOTNOTE	
100 MINUTES POSTDOSAGE			
9406	1.023		
9504	0.785		
9505	X	DNR	
	0.555		
9506	0.405		
9605	0.419		
9606	X	DNR	
	0.492		
9607	0.613		
9608	0.474		
150 MINUTES POSTDOSAGE			
9705	0.330		
9706	0.398		
9707	0.506		
9708	1.238		
9805	0.571		
9806	0.296		
9807	0.404		
9808	0.492		

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.

ADDENDUM 1 - PROTOCOL



FINAL PROTOCOL

Charles River Laboratories Study No. TQC00032

**Oral (Gavage) Acute Dose Time of Peak Cholinesterase Depression
Study of Malathion 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

17 October 2007

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1. STUDY NUMBER

TQC00032

2. STUDY TITLE

Oral (Gavage) Acute Dose Time of Peak Cholinesterase Depression Study of Malathion in Juvenile Rats

3. PURPOSE

The objective of this study is to determine the time of peak cholinesterase inhibition after acute dosing of postnatal day 11 (PND 11) rat pups with Malathion on erythrocyte and brain acetyl cholinesterase activity when the pups are sampled at various timepoints.

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
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1600 Wilson Blvd., Suite 700
Arlington, VA 22209
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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.

10. REGULATORY COMPLIANCE

This study will be conducted using good scientific practices and according to the SOPs of the Testing Facility. The Testing Facility Quality Assurance Unit (QAU) will not audit the protocol, the raw data or the report and will not perform critical phase inspections for the study. The Testing Facility will perform an independent Quality Control review of the cholinesterase data and the cholinesterase tables to be included in the final study report.

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

11. PROPOSED STUDY SCHEDULE

See Attachment 1 to the protocol.

12. TEST SUBSTANCE AND VEHICLE

12.1. Identification

12.1.1. Test Substance

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
Expiration Date:	9 November 2008 (received at the Testing Facility on 16 October 2007)

The Sponsor will provide to the Testing Facility documentation or certification of the identity, composition, strength, purity and stability of each of the test substance (Certificate of Analysis). This documentation will be included in the final report. The Certificate of Analysis is attached to this protocol (ATTACHMENT 2). The Study Monitor'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. The bulk test substance will be handled in a chemical fume hood. Gloves will be washed with soap and water or sprayed with an appropriate cleaning solution prior to removal and then disposed of in a biohazard container. For all other activities, standard safety precautions will be followed. The Material Safety Data Sheet (MSDS) is attached to the protocol (ATTACHMENT 3).

12.3. Storage

Bulk Test Substance:	Frozen (approximately -20°C), protected from light.
Vehicle:	Room temperature.
Prepared Formulation:	Refrigerated (2°C - 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 at least once at the Testing Facility.

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

13.2. Adjustment for Purity

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

13.3. Testing Facility Reserve Samples

No reserve samples of the test substance or vehicle will be retained.

14. ANALYSES

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

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

14.1. Bulk Test Substance Stability

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

14.1.1. Analyses of Prepared Formulations

14.1.1.1. Concentration and Homogeneity

Concentration samples of the prepared formulation will be collected on the day of preparation. The test substance samples will be stored refrigerated at the Testing Facility for possible future analyses. Duplicate samples (0.5 mL each) will be taken from the middle of each concentration on the day of preparation. The disposition of these samples will be documented in the raw data.

14.1.1.2. Stability

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

15. DISPOSITION

Unused prepared formulations will be discarded at the Testing Facility. Any concentration and homogeneity samples will be discarded at the Testing Facility following issue of the final report. 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 one gestation day 18 (DG 18) female rats.

16.2.2. Neonatal Rats

F1 generation population
selected for study: Fifteen litters.

16.3. Body Weight and Age

There will be twenty one DG 18 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.

The 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 usage on study (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 Care and Use of Laboratory Animals*¹.

17.1. Housing

Upon arrival, the female rats will be housed in a nesting box for the remainder of the gestation period and 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. Feed

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 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. RANDOMIZATION**18.1. Adults**

The female rats will be naturally bred at the Supplier's facility by breeder male rats of the same source and strain. The day of delivery will be designated day 1 of lactation (postpartum). The female rats will be allowed to deliver their litters at the Testing Facility.

18.2. F1 Generation

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 usage on study (day 11 postpartum), an appropriate number of pups from the fifteen litters assigned to study will be used to provide 8 pups/sex for the control group and 40 pups/sex for the 150 mg/kg malathion dosage group. If possible 3 pups/sex/litter will be assigned to the study; however, it may be necessary to select more pups from a

given litter to compensate for others that may be of insufficient litter size. Assignment to cholinesterase timepoints will be documented in the raw data. The pups will be of good general health (no adverse clinical signs) following physical examination of the pups and adequate body weights.

19. ADMINISTRATION

19.1. 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.

19.2. Method and Frequency

19.2.1. Adults

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

19.2.2. F1 Generation

Pups will be administered the test substance and/or vehicle on day 11 postpartum using a 0.5 mL Hamilton syringe. The doses will be based on body weights recorded prior to dosage administration. Prepared formulations will be stirred continuously during dosage administration.

19.3. Rationale for Dosage Selection

Dosages were selected by the Sponsor on the basis of previous toxicity studies conducted with malathion. The doses selected for use on this study will cause marked reduction in the cholinesterase levels of the day 11 postpartum pups without causing mortality. This will allow for sufficient evaluation of the time of peak cholinesterase depression.

19.4. Dosage Levels, Concentrations and Dosage Volumes

Dosage Group	Number of Pups per Sex	Test Substance	Dosage (mg/kg) ^a	Concentration (mg/mL)	Dosage Volume (mL/kg)	Batch Number
I	8	Corn Oil	0 (Vehicle)	0	5	B-TQC00032-A(Day.Month.Year)
II	40	Malathion	150	30	5	B-TQC00032-B(Day.Month.Year)

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

20. TESTS, ANALYSES AND MEASUREMENTS - ADULTS

Viability observations will be recorded at least twice daily. Clinical observations and body weights will be recorded on the day of randomization of the pups. Clinical observations may be recorded more frequently than cited above. Maternal observations will be recorded on days 1, 4 and 7 postpartum and on the day of randomization of the pups (observed abnormal behavior recorded daily). 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.

20.1. Method of Sacrifice - Adults

The dams will be sacrificed by carbon dioxide asphyxiation.

20.2. Necropsy - Adults**20.2.1. Scheduled Sacrifice of Adults with Litters Assigned to Study**

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

20.2.2. Scheduled Sacrifice of Adults with Litters Not Assigned to Study

Dams with litters not assigned to the study placed into the Testing Facility General Population and used for method development, training or will be assigned to internal research projects. Only as a last resort will these rats be humanely euthanized without use.

20.2.3. Adults 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.

20.2.4. Adults 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.

21. TESTS, ANALYSES AND MEASUREMENTS - PUPS

21.1. 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.

21.2. 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 just 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.

21.3. 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.

22. CHOLINESTERASE ASSAY

22.1. 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 (collected from 8 pups/sex/timepoint) from Group II will be collected at 30, 60, 80, 100 and 150 minutes postdosage from the male and female pups and from Group I at 60 minutes postdosage (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. All samples will be labeled with protocol number, date of collection, pup number, dosage group, dosage level, day of study, species, sex, timepoint and storage conditions.

The blood and brain samples will be analyzed for cholinesterase levels the same day that they are collected (within 2 hours of sample collection).

22.1.1. RBC

Approximately 0.40 to 0.60 mLs of whole blood will be collected into 1.3 mL EDTA-coated (lavender-top) tubes. Blood samples will be stored mixed on cold packs on a tilter until being processed for RBC cholinesterase levels according to the Testing Facility's Standard Operating Procedure.

22.1.2. Brains

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

23. METHOD OF SACRIFICE

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

24. NECROPSY

24.1. 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.

24.2. Pups Not Selected for Study

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

24.3. Pups Found Dead or Unscheduled Sacrifice After 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. Tissues may be retained at the discretion of the Study Director.

25. STATISTICAL EVALUATION

Averages and percentages will be calculated. Additional procedures and/or analyses may be performed if deemed appropriate.

26. DATA ACQUISITION, VERIFICATION AND STORAGE

Data 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 97/2000/2005/XP*), *Quattro Pro 8*, *The SAS System* (version 6.12) and/or *Softmax® Pro* (version 4.0).

Data will be hand- and/or computer-recorded. 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.

27. RECORDS TO BE MAINTAINED

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

28. KEY PERSONNEL

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

29. REPORT

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

An unaudited report will be prepared including: abstract, summary of methods, results and conclusion; table of contents; copy of the protocol; amendments; summary and individual tables; and reports of supporting data (if appropriate).

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

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.

30. ANIMAL WELFARE

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

Adverse observations will be promptly reported to the Study Director and veterinary staff. The veterinarian may make recommendations regarding treatment of the animal(s) in addition to those already agreed upon and/or alteration of study procedures to ensure the well-being of the animal(s) should unanticipated responses or circumstances occur. All recommendations shall be discussed with the Study Director and the recommendations

and subsequent actions properly documented in the study record. Treatment of the animal(s) may occur without notification of the Sponsor when such treatment as determined by the Study Director does not adversely affect the study objectives.

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

31. 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.

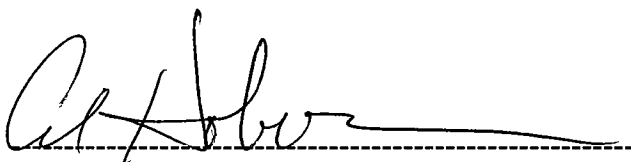
The signature of the Sponsor's representative below is assurance that the study is not an unnecessary duplication of previous work. Documentation for the necessity of this study may be obtained from the Sponsor. No alternative procedures were available to meet the stated purposes of the study.

32. 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; 1996.
- 2) U.S. Environmental Protection Agency (1997). A set of scientific issues being considered by the agency concerning the office of pesticide programs (OPP) cholinesterase inhibition policy. Scientific Advisory Panel (SAP) June, 1997, Meeting.
- 3) Lassiter.TL., Barone.S Jr., and Padilla.S. Ontogenetic differences in the regional and cellular acetylcholinesterase and butyrylcholinesterase activity in the rat brain. Dev Brain Res 1998; 105 :109-123.

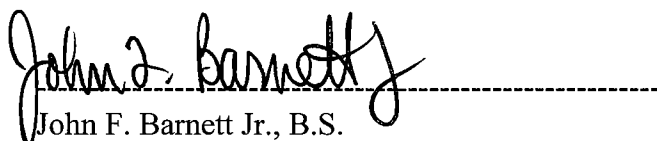
33. PROTOCOL APPROVAL

33.1. For the Testing Facility



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

17-Oct-07
Date

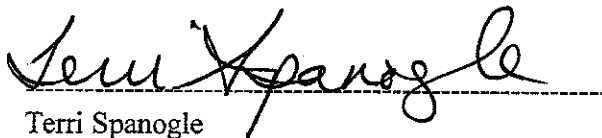


John F. Barnett Jr., B.S.
Senior Scientist
Study Director

17 Oct 2007
Date

33.2. For the Sponsor¹

Sponsor approval received via email.

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

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

A handwritten date "18 October 2007" is written in cursive script over a horizontal dashed line.

Date

1. Date of Sponsor Approval: 16 October 2007

**ATTACHMENT 1 -
STUDY SCHEDULE**

PROPOSED SCHEDULE^a

09 OCT 07	Time-Mated Females Arrive - Acclimation Begins.
23 OCT 07	Proposed Experimental Start Date
23 OCT 07	Dosage, Sacrifice and Cholinesterase Evaluation - Day 11 Postpartum.
30 OCT 07	Quality Control Reviewed Cholinesterase Tables.
20 NOV 07	Unaudited Draft Report.
Date the Study Director Signs the Final Report.	Study Completion Date.

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

**ATTACHMENT 2 -
CERTIFICATE OF ANALYSIS**



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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:		CAS-Name: Butanedioic acid,			
Malathion		(dimethoxyphosphinothioyl)			
CAS No.: 121-75-5		thio)-, diethyl ester			
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: Dec 5, 2006		Signature: Barbara Hinz			



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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				
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.				
Date: <u>December 5, 2006</u>		Signature: <u>Barbara Hinz</u> Barbara Hinz		

**ATTACHMENT 3 -
MATERIAL SAFETY DATA SHEET**



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

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GHB/September 2005
 Replaces version GHB/January 2002

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SAFETY DATA SHEET

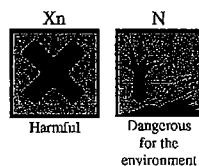
FYFANON[®] TECHNICAL

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)-\text{CH}_2\text{COOC}_2\text{H}_5 \\ \\ \text{CH}_3\text{O} \end{array} $

2.2. Typical content 96-97%



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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, pin-point pupils, tightness in chest, laboured breathing, nervousness, sweating, watering of eyes, drooling or frothing of mouth and nose, muscle spasms and coma.

4.2. Emergency and first aid procedures General

Exposed persons must receive prompt medical treatment. When any of the signs of exposure occurs, call a doctor (physician), clinic or hospital immediately. Explain that the victim has been exposed to malathion, an organophosphorus insecticide, and describe his/her condition. Immediately remove the victim from the area where the product is present.

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

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

Inhalation

If experiencing any discomfort, immediately remove from exposure. Get medical attention immediately if symptoms develop.

Ingestion

If the exposed person is conscious, make him/her vomit quickly. Make the exposed person rinse mouth and drink 1 or 2 glasses of water or milk if available. Let him/her induce vomiting by touching the back of the throat with a finger. Repeat until vomit is clear. Never give anything by mouth to an unconscious person. Get medical attention immediately.

Eye contact

Immediately flush with much water or eyewash solution, occasionally opening eyelids, until no evidence of chemical remains. Remove contact lenses after a few minutes and flush

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



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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

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



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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
9.12. Partition coefficient n-octanol/water	K _{ow} = 560
9.13. pH	When equal amounts of Fyfanon® and distilled water are dispersed at 20°C, the pH measured in the water phase is 3.7-3.8.
9.14. Flash point	163°C (Pensky-Martens closed tester; see, however, 10.1.)
9.15. Autoignition temperature	278°C
9.16. Explosive properties	Not explosive
9.17. Oxidising properties	Not oxidising

10. ♣ STABILITY AND REACTIVITY

10.1. Thermal decomposition	Fyfanon® will decompose rapidly when heated to temperatures above 140°C, significantly increasing the risk of explosion. Direct local heating such as electric heating or by steam must be avoided.
-----------------------------------	---

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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^{a)}
 - Skin LD₅₀, acute dermal, rat: > 2000 mg/kg
 - Inhalation LC₅₀, inhalation, rat: > 5.2 mg/l/4 h
- ^{a)} Values from 1000 to 2830 mg/kg are mentioned in literature as well as in WHO Data Sheet No. 29, VBC/DS/77.29
- 11.2. Irritancy Slightly irritating to eyes and skin.
- 11.3. Allergic sensitisation In animal tests mixed results were obtained:
 Magnusson-Kligman maximisation test: positive
 Buehler test: negative
 Local Lymph Node Assay: negative.
 The meaning of these results for humans cannot be fully evaluated.
- 11.4. Carcinogenicity IARC evaluation: The available data provide no evidence that **malathion** is likely to present a carcinogenic risk to humans.
- 11.5. Effects on reproduction No effects on fertility are found for **malathion** in rats and rabbits at maternal non-toxic doses.
- 11.6. Teratogenicity No indications of teratogenic effects of **malathion** are found.
- 11.7. Mutagenicity **Malathion** is not mutagenic.

12. ♣ ECOLOGICAL INFORMATION

- 12.1. Ecotoxicity **Malathion** is very toxic to fish, aquatic invertebrates, aquatic life stages of amphibians and insects. It is less toxic to aquatic plants, birds and soil macro- and microorganisms.

The ecotoxicity is measured to be:

- Fish Rainbow trout (*Oncorhynchus mykiss*) 96 h-LC₅₀: 0.18 mg/l
 37-day NOEC: 21 µg/l
- Invertebrates Daphnids (*Daphnia magna*) 48 h-EC₅₀: 0.72 µg/l
 21-day NOEC: 0.06 µg/l
- Algae Green algae (*Selenastrum capricornutum*) 72-h IC₅₀: 4.06 mg/l
- Birds Bobwhite quail (*Colinus virginianus*) LD₅₀: 359 mg/kg
 5-day dietary LC₅₀: 3497 mg/kg
- Mallard duck (*Anas platyrhynchos*) LD₅₀: 1485 mg/kg

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
 DK-7620 Lemvig
 Denmark
 Phone (+45) 98 90 96 90
 Fax (+45) 98 90 96 91
 www.cheminova.com
 CVR-No. DK 12 76 00 43

GHB/September 2005

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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

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



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

Cheminova A/S
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 CVR-No. DK 12 76 00 43

GHB/September 2005

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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

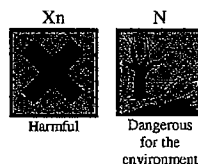
15. ♣ REGULATORY INFORMATION

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 PROCEDURE**

ATTACHMENT 4**TEST SUBSTANCE PREPARATION PROCEDURE**

Test Substance: Malathion (synonymous with Fyfanon Technical)

Vehicle: Corn Oil

A. Purpose:

The purpose of this procedure is to provide a method for the preparation of dosage formulations of the test substance for oral (gavage) administration to juvenile rats on Study no. TQC00032.

B. General Information:

1. All formulation containers will be labeled and color-coded. Each label will specify the study number, test substance identification, batch number, concentration, dosage level, dosage group, preparation date, expiration date, and storage conditions.
2. Formulations (suspensions) of the 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:
 - ☒ Double nitrile gloves, uniform/lab coat, goggles or safety glasses with side shields
 - ☐ Dust-Mist/HEPA-filtered Mask
 - ☐ Half-Face Respirator
 - ☒ Full-Face Respirator/Positive Pressure Hood
 - ☒ Tyvek[®] Suit
 - ☐ Full Face Shield
 - ☒ Bulk TA/S will be handled in a chemical fume hood
 - ☒ Gloves will be washed with soap and water or sprayed with an appropriate cleaning solution prior to removal and then disposed of in a biohazard container.
5. The test substance 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. The container will be dried completely before preparation of the dosage formulations.

1. Weigh the required amount of test substance into an appropriately sized and labeled, pre-calibrated container (See TA/S PREPARATION CALCULATIONS).
2. QS ad with vehicle to the required volume in the pre-calibrated container (See TA/S PREPARATION CALCULATIONS).
3. Add a magnetic stir bar to the container, place the container on a magnetic stir plate and thoroughly mix the formulation. Continue to mix the formulation prior to and during sampling, aliquotting and/or dosage administration.
4. Aliquot the formulation into an appropriately sized and labeled container for dosage administration. If the preparation is not used on the day of preparation, the aliquot will be stored refrigerated and protected from light; the formulation will be stored at room temperature and protected from light when used.
5. On the day of administration, remove the aliquot from the refrigerator and allow the aliquot to equilibrate to room temperature for at least 30 minutes prior to dosage administration, if necessary. 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.

6. Repeat steps C1 through C5 for each concentration of the test substance.

Version: TQC00032(25 SEP 07) # of pages: 3

Prepared By: Patricia A Garbely Date: 17 OCT 2007

Approved By: John J. Barnett Date: 17 Oct 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 50 mL polypropylene container containing chilled 25.0 mL (\pm 0.5 mL) of 0.1% Tween 80[®] buffer.
2. The brain is homogenized approximately 60 seconds on wet ice (wet ice is defined as ice with water). Homogenizer must be cooled for approximately 1 minute 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 (10 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: John J. for John Gullinakis Date: 17 Oct 2007
 Approved By: John J. Barnett Date: 17 Oct 2007

ADDENDUM 2 - CERTIFICATE OF ANALYSIS

**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 OIL

NOT 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

ADDENDUM 3 - ENVIRONMENTAL AND HUSBANDRY REPORTS

TEMPERATURE AND RELATIVE HUMIDITY REPORT

ARGUS

Temperature and Relative Humidity Report Location: Room 11 Protocol Number: TQC00032			
Range of Dates: 09-Oct-2007 14:07 to 23-Oct-2007 14:59			
Target Range: Species: Rat Total Number of Days: Total Number of Hours: Total Number of Data Points: Mean (± SD): Maximum: Median: Minimum: Number of Points in Range (%): Number of Points High (%): Number of Points Low (%):	Temperature 64°F to 79°F 15 336.5 337 72.1 (± 0.9) 73.4 72.4 69.8 337 (100.0) 0 (0.0) 0 (0.0)	Relative Humidity 30% to 70% 15 336.5 337 52.0 (± 9.5) 66.8 53.3 33.3 337 (100.0) 0 (0.0) 0 (0.0)	

Report Generated: 31-Oct-2007 at 14:24

COMMENTS: _____

REVIEWED BY: Chester Rivera DATE: 10-31-07

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: L0718954-2
 Lot Code: JUN 28 07 3B
 Entered: 7/17/2007

Assay	Analysis	Units
PROTEIN	20.9	%
FAT (ACID HYDRO.)	5.98	%
FIBER (CRUDE)	4.48	%
ARSENIC	LESS THAN 0.2	PPM
CADMIUM	0.0675	PPM
CALCIUM	0.9252	%
LEAD	0.182	PPM
MERCURY	LESS THAN 0.025	PPM
PHOSPHORUS	0.6564	%
SELENIUM	0.498	PPM

ORGANOPHOSPHATES	PPM	ORGANOPHOSPHATES	PPM
Diazinon	LESS THAN 0.02	Disulfoton	LESS THAN 0.02
Ethion	LESS THAN 0.02	Malathion	LESS THAN 0.02
Methyl Parathion	LESS THAN 0.02	Parathion	LESS THAN 0.02
Thimet	LESS THAN 0.02	Thiodan	LESS THAN 0.02
Trithion	LESS THAN 0.02		

PESTICIDES AND PCB	PPM	PESTICIDES AND PCB	PPM
Aldrin	LESS THAN 0.02	Alpha-BHC	LESS THAN 0.02
Beta-BHC	LESS THAN 0.02	Chlordane	LESS THAN 0.02
DDE	LESS THAN 0.02	DDT	LESS THAN 0.02
Delta-BHC	LESS THAN 0.02	Dieldrin	LESS THAN 0.02
Endrin	LESS THAN 0.02	HCB	LESS THAN 0.02
Heptachlor	LESS THAN 0.02	Heptachlor Epoxide	LESS THAN 0.02
Lindane	LESS THAN 0.02	Methoxychlor	LESS THAN 0.02

REVIEWED BY

Eve Pendleton

20 Nov 2007

Approved
 [Signature]
 11-26-07

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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.

REVIEWED BY
Elin Anderson
20 Nov 2007

Approved
M. H.
29 Nov 07

EXACT COPY

WATER ANALYSES



QC Laboratories

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: 917950

Sample Number L2446398-1
Sample Description DRINKING WATER - ANALYTICAL
Received Temp: 38 F Iced (Y/N): Y

Samp. Date/Time/Temp 10/05/07 11:02am NA F
Sampled by Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	< 0.2 mg/l	mg/l	10/05/07 11:02AM CU
COLIFORM-MF	SM 9222B	TNTC W/O COLIFORMS col/100ml	1. col/100ml	10/05/07 04:37PM AM
E. COLI CONFIRM	SM 9221E + MUG	NEG col/100ml	1. col/100ml	10/06/07 12:00PM AMD
STANDARD PLATE COUNT	SM 9215B	>5800 col/ml	1. col/ml	10/05/07 04:37PM AMD

Sample Number L2446398-2
Sample Description DRINKING WATER - FILL STATION
Received Temp: 38 F Iced (Y/N): Y

Samp. Date/Time/Temp 10/05/07 11:08am NA F
Sampled by Customer Sampled

Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	1.0 mg/l	mg/l	10/05/07 11:08AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/05/07 04:37PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/05/07 04:37PM AMD

- A result of "ND" indicates the concentration of the analyte tested was either not detected or below the RLs.
- Definitions: ND=not detected; NEG=negative; POS=positive; COL=colonies; RLs=laboratory reporting limits; L/A=laboratory accident; TNTC=too numerous to count
- A result marked with "DRY" indicates that the result was calculated and reported on a dry weight basis.
- All analysis, except field tests are conducted in Southampton, PA unless otherwise identified.
- The test "pH lab" is analyzed upon receipt at the laboratory, the result will not be suitable for regulatory purposes.
- Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
- QC 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: 895213

Thomas J. Hines, President

Approved
10-29-07

① Retested mv 10-29-07

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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5/25/19/NA/2007

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 917950

Sample Number	Sample Description	Received Temp:	Samp. Date/Time/Temp	Sampled by
L2446398-3	DRINKING WATER - ROOM 12 RACK 109 Iced (Y/N): Y	38 F	10/05/07 11:12am NA F	Customer Sampled
Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.5 mg/l	mg/l	10/05/07 11:12AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/05/07 04:37PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/05/07 04:37PM AMD
Sample Number	Sample Description	Received Temp:	Samp. Date/Time/Temp	Sampled by
L2446398-4	DRINKING WATER - FORMULATION Iced (Y/N): Y	38 F	10/05/07 11:17am NA F	Customer Sampled
Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	< 0.2 mg/l	mg/l	10/05/07 11:17AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/05/07 04:37PM AMD
STANDARD PLATE COUNT	SM 9215B	231 col/ml	1. col/ml	10/05/07 04:37PM AMD
Sample Number	Sample Description	Received Temp:	Samp. Date/Time/Temp	Sampled by
L2446398-5	DRINKING WATER - ROOM 51 RACK 09410 Iced (Y/N): Y	38 F	10/05/07 11:24am NA F	Customer Sampled
Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.9 mg/l	mg/l	10/05/07 11:24AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/05/07 04:37PM AMD
STANDARD PLATE COUNT	SM 9215B	<1 col/ml	1. col/ml	10/05/07 04:37PM AMD

- A result of "ND" indicates the concentration of the analyte tested was either not detected or below the RLs.
- Definitions: ND=not detected; NEG=negative; POS=positive; COL=colonies; RLs=laboratory reporting limits; L/A=laboratory accident; TNTC=too numerous to count
- A result marked with "DRY" indicates that the result was calculated and reported on a dry weight basis.
- All analysis, except field tests are conducted in Southampton, PA unless otherwise identified.
- The test "PH lab" is analyzed upon receipt at the laboratory, the result will not be suitable for regulatory purposes.
- Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
- QC 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 2 of 4

Serial Number: 895213

Thomas J. Hines, President

① Retested m/l 11-12-07

Approved
m/l 11-12-07

EXACT COPY
S25 19NW2007

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 917950

Sample Number	Sample Description	Samp. Date/Time/Temp	Sampled by	
L2446398-6	DRINKING WATER - H-2 Received Temp: 38 F Iced (Y/N): Y	10/05/07 11:38am NA F	Customer Sampled	
Parameter	Method	Result	RLs	Test Date, Time, Analyst
CHLORINE RESIDUAL	SM 4500-CL-G	0.4 mg/l	mg/l	10/05/07 11:38AM CU
COLIFORM-MF	SM 9222B	<1 col/100ml	1. col/100ml	10/05/07 04:37PM AMD
STANDARD PLATE COUNT	SM 9215B	135 col/ml	1. col/ml	10/05/07 04:37PM AMD

L2446398-1:

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.

L2446398-2:

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.

L2446398-3:

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.

L2446398-4:

- A result of "ND" indicates the concentration of the analyte tested was either not detected or below the RLS.
- Definitions: ND=not detected; NEG=negative; POS=positive; COL=colonies; RLS=laboratory reporting limits; L/A=laboratory accident; TNTC=too numerous to count
- A result marked with "DRY" indicates that the result was calculated and reported on a dry weight basis.
- All analysis, except field tests are conducted in Southampton, PA unless otherwise identified.
- The test "pH lab" is analyzed upon receipt at the laboratory, the result will not be suitable for regulatory purposes.
- Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
- QC 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 3 of 4

Serial Number: 895213

Thomas J. Hines, President
Approved: *[Signature]*
11-12-07

① Retested MW 11-12-07

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8/15/19 NOV 2007

QC Laboratories

Analytical Report



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

P.O. No:
PWSID No:

Inv. No: 917950

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.

L2446398-5:

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.

L2446398-6:

1. A water supply is considered bacteriologically "SAFE" if no Coliform bacteria are detected. To be considered "SAFE" your report should indicate "<1 col/100ml" or "NEG" for the Coliform Test. If your report indicates a positive result "POS" or a value of one (1) or greater then your supply is "UNSAFE FOR DRINKING" contact your local Health Dept. or QC for advice.

- A result of "ND" indicates the concentration of the analyte tested was either not detected or below the RLs.
 - Definitions: ND=not detected; NEG=negative; POS=positive; COL=colonies; RLs=laboratory reporting limits; L/A=laboratory accident; TNTC=too numerous to count
 - A result marked with "DRY" indicates that the result was calculated and reported on a dry weight basis.
 - All analysis, except field tests are conducted in Southampton, PA unless otherwise identified.
 - The test "pH lab" is analyzed upon receipt at the laboratory, the result will not be suitable for regulatory purposes.
 - Actual times of analysis for parameters reported <24 hrs are available upon request. All testing is completed within the required holding time unless otherwise noted.
 - QC 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 4 of 4

Serial Number: 895213

Thomas J. Hines
Thomas J. Hines, President

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8/23/9/11/2007

Analysis Report



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 No.	Analysis Name	CAS Number	As Received Result	As Received		Dilution Factor
				Limit of Quantitation	Units	
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

Retest Requested on 9/10/07

Lancaster Laboratories, Inc.
2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
717-656-2300 Fax: 717-656-2681

10/24/07

Approved

[Signature]

8-9-07

Exact copy
Jem 25 Oct 2007

2216 Rev. 3/27/06

Analysis Report



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

Charles River Laboratories

Reported: 07/26/2007 at 19:47

57 Union Street

Discard: 08/03/2007

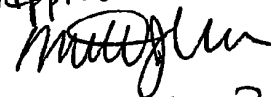
Worcester MA 01608

19051

CAT No.	Analysis Name	CAS Number	As Received		Units	Dilution Factor
			Result	Limit of Quantitation		
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-T	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 No.	Analysis Name	Method	Analysis		Analyst	Dilution Factor
			Trial#	Date and Time		
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 PE	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.
 2425 New Holland Pike
 PO Box 12425
 Lancaster, PA 17605-2425
 717-656-2300 Fax: 717-656-2681

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2216 Rev. 3/27/06

Jem 7/30/2007

Analysis Report



Page 3 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: 08/03/2007

Charles 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

Lancaster Laboratories, Inc.
 2425 New Holland Pike
 PO Box 12425
 Lancaster, PA 17605-2425
 717-656-2300 Fax: 717-656-2681

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2216 Rev. 3/27/06

Jem 25 Oct 2007

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 01608

81007

I 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-DDD	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

Lancaster Laboratories, Inc.
2425 New Holland Pike
PO Box 12425
Lancaster, PA 17605-2425
717-656-2300 Fax: 717-656-2681① This result is below the
the federal drinking water
standard of 2mg/liter, w 6-502Acceptable
10-5-07

2216 Rev. 3/27/06

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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

Reported: 09/13/2007 at 12:47

Discard: 09/28/2007

Charles River Laboratories

57 Union Street

Worcester MA 01608

81007

CAT			As Received	As Received		
No.	Analysis Name	CAS Number	Result	Limit of Quantitation	Units	Dilution Factor
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				Analysis		
No.	Analysis Name	Method	Trial#	Date and Time	Analyst	Dilution Factor
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

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

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Analysis Report



Page 1 of 3

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					
PCB-1260	< 17.0	17.0	ug/kg	90		65-137		
Batch number: 072420005A	Sample number(s): 5141313							
2,4-D	< 17.0	17.0	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	< 17.0	17.0	ug/kg					
Toxaphene	< 33.0	33.0	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

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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 MAX	BKG Conc	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	20
Selenium	94	92	75-125	1	20	2.69	2.95	9 (1)	20
Barium	98	101	75-125	2	20	115.	125.	8	20
Cadmium	94	93	75-125	2	20	< 0.500	< 0.500	12 (1)	20
Chromium	84 (2)	75 (2)	75-125	1	20	100.	128.	24*	20
Lead	-39 (2)	-246 (2)	75-125	10	20	265.	394.	39*	20
Silver	96	95	75-125	0	20	< 0.500	< 0.500	200* (1)	20
Batch number: 072425711002	Sample number(s): 5141313 UNSPK: P141423 BKG: P141423								
Mercury	93	88	80-120	4	20	< 0.0943	< 0.0938	33* (1)	20
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	88	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

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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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ADDENDUM 4 - ENVIRONMENTAL PROTECTION AGENCY 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.

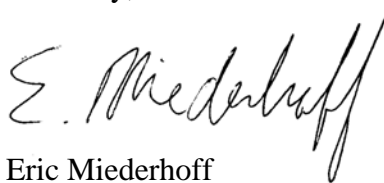
Design Parameters:

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 initial "E" 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