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Risk Assessment Branch I, Health Effects Division (7509P) Date: June 25, 2014
EPA Reviewer: Linda Taylor, PhD **Signature:**
Risk Assessment Branch V, Health Effects Division (7509P) Date: 06-25-2014

TXR#: 0056869

DATA EVALUATION RECORD

STUDY TYPE: Special Acute Chlorpyrifos Oxon Saturated Vapor Inhalation Toxicity - [Rat]

PC CODE: 065910 **DP BARCODE:** 415447

TEST MATERIAL (PURITY): Chlorpyrifos Oxon Technical (100%)

SYNONYMS: Chlorpyrifos-ethyl oxon, oxydursban, Dowco 180

CITATION: Hotchkiss, JA, NOSE-ONLY INHALATION OF CHLORPYRIFOS-OXON VAPOR: LIMITED TOXICOKINETICS AND DETERMINATION OF TIME-DEPENDENT EFFECTS ON PLASMA, RED BLOOD CELL, BRAIN AND LUNG CHOLINESTERASE ACTIVITY IN FEMALE CD(SD):Crl RATS (2013), Toxicology & Environmental Research and Consulting, The Dow Chemical Company Midland, Michigan 48674 MRID 49210101, Unpublished.

SPONSOR: Dow AgroSciences LLC, 9330 Zionsville Road, Indianapolis, Indiana 46268

EXECUTIVE SUMMARY:

In a special acute inhalation toxicity study (MRID 49210101) designed to assess the effect of an acute inhalation exposure to a saturated vapor of chlorpyrifos oxon on cholinesterase (ChE) activity, 8 female CD(SD):Crl rats/exposure group/sacrifice time were exposed for six consecutive hours to filtered air (control) or a time-weighted average concentration of 35.3 $\mu g/m^3$ (2.58 ppb) chlorpyrifos oxon (100% purity) vapors using a flow-past nose-only inhalation exposure system. Rats were sacrificed immediately (0 hr) or at 1, 2, 4, 8, or 24 hours after the end of the exposure period. Blood and tissues were isolated and processed to determine ChE activity in red blood cells (RBC), plasma, lung, and brain tissue. Oxon and the metabolite 3,5,6-trichloro-2-pyridinol (TCP) concentrations were determined in whole blood samples from four oxon-exposed rats at each sacrifice time.

During or after oxon exposure, no clinical signs of toxicity were noted in oxon-exposed rats at any time. There were no statistically significant decreases in ChE activity in any tissue monitored. The only statistically significant changes in cholinesterase (ChE) activity were in the RBC and brain, however, increases of ChE activity occurred.

In the red blood cell samples, the ChE values for the 35.3 $\mu g/m^3$ samples at 0, 1, 2, 4, 8 and 24

hours after exposure were 93.6%, 110.6%, 113.9%, 116.5%, 102.2%, and 111.9%, respectively, of the 0 $\mu g/m^3$ control group, with none having both statistical significance and an activity decrease greater than 10%. The RBC ChE activity at 4 hours was statistically significant, however it was an increase in activity.

In the plasma samples, the ChE values for the 35.3 $\mu g/m^3$ samples at 0, 1, 2, 4, 8 and 24 hours after exposure were 103.0%, 107.5%, 101.5%, 136.7%, 101.0%, and 127.6%, respectively, of the 0 $\mu g/m^3$ control group, with none having statistical significance nor a decrease in ChE activity.

In the lung samples, the ChE values for the 35.3 $\mu g/m^3$ samples at 0, 1, 2, 4, 8 and 24 hours after exposure were 93.7%, 108.3%, 118.6%, 109.1%, 101.7% and 91.6%, respectively, of the 0 $\mu g/m^3$ control group, with none having statistical significance nor a decrease in activity greater than 10%.

In the brain samples, the ChE values for the 35.3 $\mu g/m^3$ samples at 0, 1, 2, 4, 8 and 24 hours after exposure were 100.5%, 106.2%, 102.0%, 100.9%, 101.2%, and 101.0%, respectively, of the 0 $\mu g/m^3$ control group, with none having both statistical significance and an activity decrease. The brain ChE activity at 1 hour was statistically significant, however it was an increase in activity.

At any time after exposure, no oxon was measured in the blood (lower-limit of quantitation; LLQ = 0.118 ng/g blood), however, blood TCP levels > LLQ (2.44 ng/g blood) were measured at the end of exposure and through eight hours post-exposure. No statistically significant inhibition of ChE activity by oxon was measured in RBC, plasma, lung, or brain at any time after exposure. The presence of TCP in the blood of oxon-exposed rats confirms that inhaled oxon vapor is absorbed by the respiratory tract, however, the oxon is rapidly metabolized to TCP and the oxon is not systemically bioavailable at blood levels ≥ the LLQ of 0.118 ng/g blood (3.53x10-4 nmole/g blood). The six-hour No Observed Effect Concentration (NOEC) for inhaled oxon vapor is > 35 μg oxon/m^3 air, based on the absence of statistically-significant cholinesterase inhibition in RBC, plasma, brain, or lung (the portal-of-entry tissue). The results of this study suggest that there is no cholinesterase-based hazard from inhalation of a saturated vapor concentration (35.3 $\mu g/m^3$) of chlorpyrifos oxon.

The purpose of the study was to determine pharmacokinetics and ChE inhibition in the RBC, plasma, brain and lung of rats exposed to a single dose of saturated vapor of chlorpyrifos oxon. This purpose was achieved and no meaningful ChE inhibition was observed at the saturated concentration.

This study is classified as **acceptable/non-guideline**, however, since it was a special study, it is acceptable, although it does not fulfill any guideline requirement.

COMPLIANCE - Signed and dated GLP Compliance, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Chlorpyrifos oxon

Description:

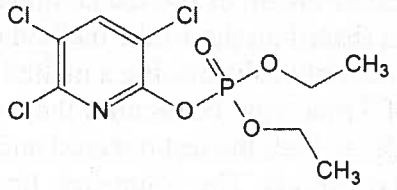
Lot #: XP3-136253-74C

Purity: 100%

Compound stability: The test atmosphere was generated and immediately delivered to the test system, therefore determination of the stability of the test material under the conditions of administration was not necessary for this study.

CAS #: 5598-15-2

Structure:



2. Vehicle: Air

3. Test animals

Species: Rat

Strain: Crl: CD(SD)

Age/weight at study initiation: Approximately 10 weeks old females

Source: Charles River, Raleigh, NC

Housing: 2/cage

Diet: Lab Diet Certified Rodent Diet #5002 (PMI Nutrition International, St. Louis, MO, *ad libitum*,

Water: Tap water, *ad libitum*

Environmental conditions:
- **Temperature:** 21-23°C
- **Humidity:** 40-70%
- **Air changes:** 10-15/hour
- **Photoperiod:** 12 hrs light/ 12 hrs dark (on at 6 am, off at 6 pm)

Acclimation period: 14 days total and tube acclimation for 4 days before test.

B. STUDY DESIGN

1. In life dates: NA

2. Animal assignment and Treatment: Before administration of test material began, animals were stratified by body weight and then randomly assigned to treatment groups using a computer program designed to increase the probability of uniform group mean weights and standard deviations at the start of the study. Animals placed on study were uniquely identified via sub-cutaneously implanted transponders (BioMedic Data Systems, Seaford, Delaware). Female CD(SD):Crl rats were exposed six consecutive hours to filtered air (control) or a time-weighted average concentration of 35.3 μg/m^3 (2.58 ppb) chlorpyrifos oxon vapors using a flow-past nose-only inhalation exposure system. Rats were sacrificed immediately (0 hr) and 1, 2, 4, 8, or 24 hours after the end of exposure (n=8/exposure group/sacrifice time). Blood and tissues were isolated and processed to determine ChE activity in RBC, plasma, lung, and brain tissue. Oxon

and TCP concentrations were determined in whole blood samples from four rats in each experimental group/sacrifice time.

3. **Concentration selection rationale:** The test concentration was chlorpyrifos oxon at 35.3 $\mu g/m^3$, the intended exposure concentration of the saturated vapor (the highest attainable vapor concentration).

4. **Test material administration:** The test substance was administered as a saturated vapor of chlorpyrifos oxon with air as the vehicle.

5. **Generation of the test atmosphere / chamber description:** The test atmosphere of oxon vapor was generated by passing a preheated stream of filtered compressed air through glassware containing glass beads coated with oxon (based on the J-tube method described by Miller *et al.*, 1980). The glass beads were coated by continuously shaking a melted aliquot of test material in a jar containing approximately 100 mL of 3 mm glass beads until the test material solidified, ensuring homogeneous dispersal. In order to melt the test material and prepare the jar of glass beads, both were heated in a 45°C oven overnight. The volumetric flow of air through the bead bed was held constant at approximately 30 L/min and the temperature of the bead bed was adjusted to achieve the maximum attainable concentration of oxon vapor in the nose-only exposure chamber without the formation of (oxon) aerosol particles while maintaining a chamber exposure atmosphere temperature of 22 ± 3°C. The bead bed temperature was adjusted by heating the air flowing over the oxon-coated beads with a flameless heat torch (FHT-4, Master Appliance Corporation, Racine, Wisconsin). Based on preliminary data of concentration versus temperature, the bead bed was maintained at approximately 31°C during the Phase 2 oxon exposure in order to achieve the maximum attainable vapor concentration of oxon in the nose-only exposure chamber. The generation system was electrically grounded. The saturated vapor concentration represents the maximum vapor concentration of the test material (oxon) with no appreciable concentration of aerosol particles above the ambient concentration measured in the filtered-air control chamber. The control and oxon exposure chamber test atmospheres were monitored for the presence of aerosol particles using a real-time aerosol particle spectrometer (APS; Model 3329, TSI Inc., Shoreview, Minnesota). The control (0 $\mu g/m^3$) chamber was supplied with humidified, filtered compressed air at room temperature.

Test atmosphere concentrations – The concentration of oxon was analytically determined in both the 0 (control) and 35.3 $\mu g/m^3$ oxon vapor exposure chambers during the 6 hour exposure period. Each sample was taken by drawing chamber atmosphere, at a set rate (0.5 liter/minute) using a constant flow air sampling pump through a sampling port located within the animal breathing zone and collecting the vapors on Chromasorb 102 sorbent tubes (SKC Corp., Eighty Four, PA). Samples were desorbed in acetonitrile and then analyzed via liquid chromatography with mass spectrometry detection (LC/MS). The time-weighted average (TWA) exposure concentration of oxon was calculated from the analytically-determined individual oxon sample concentrations. The nominal concentration was calculated based on the amount of test material fed into the generation system and the total chamber airflow. The summary of the test chamber data is listed in Table 1.

Table 1: Test Chamber Summary Data

Chamber	CHAMBER SUMMARY DATA [a] CONTROL	OXON
CHAMBER CONCENTRATION, µg/m³ [b]	0	35.3
RANGE OF CONCENTRATION, µg/m³	0.0 – 0.0	0.18 – 61.33
CHAMBER TEMPERATURE,°C [c]	22.5 ± 0.0	23.5 ± 0.6
RANGE OF CHAMBER TEMPERATURE,°C	21.0 – 22.9	21.6 – 24.0
CHAMBER RELATIVE HUMIDITY, % [c]	32 ± 1.3	19± 3.2
RANGE OF CHAMBER RELATIVE HUMIDITY, %	30 – 34	15 – 26
CHAMBER AIRFLOW, LPM [c]	25 ± 0.0	20 ± 0.0
RANGE OF CHAMBER AIRFLOW, LPM	25 – 25	20 – 20
EXPOSURE ROOM TEMPERATURE,°C [c]	21.4 ± 0.1	22.0 ± 0.3
RANGE OF EXPOSURE ROOM TEMPERATURE,°C	21.3 – 21.5	21.5 – 22.6

[a]Chamber airflow, temperature and relative humidity were measured at approximately half-hour intervals during exposure.
[b]Time Weighted Average for exposure values. The formula for the TWA is [(min1 x conc.1 + min2 x conc.2...)/ 381 minutes] where conc. is the concentration at one time point. Min.x are calculated as the elapsed time between the midpoints of the time intervals between gravimetric samples. Minutes in the denominator (381) are based on 381 minutes of total exposure run time (extended beyond 360 minutes due to incremental (staggered) addition of animals onto exposure chamber).
[c]Mean ± Standard Deviation for exposure means of 13 values/day.

Data taken from page 36 of the study report

Particle size determination – The test composition was a vapor and particles were not the test substance.

6. **Statistics:** Means and standard deviations were calculated for descriptive purposes for chamber concentration (mean only), animal body weights, exposure room temperatures and chamber temperature, humidity, and airflow, ChE activity measured in RBCs, plasma, lung, and brain tissues, and blood levels of oxon, and TCP. Bartlett's test was run on RBC, plasma, lung, and brain cholinesterase data to test for equality of variances at alpha=0.01. The raw data as well as the log, inverse and square root transforms were tested. The lung cholinesterase values at 24 hours had significant Bartlett's test findings for all but the inverse transform thus the inverse transformed data was used in the analysis of variance. Statistical analysis of cholinesterase values for RBCs, plasma, lung, and brain were then conducted using a one-way analysis of variance to determine if doses were statistically different (alpha=0.05) within each time point. If significant at alpha=0.05, a Dunnett's test was used to determine statistical differences from the control group at alpha=0.05.

C. METHODS

1. Observations

a. Cageside observations: A cage-side examination was conducted at least once a day, preferably at the same time each day (usually in the morning). This examination was typically performed with the animals in their cages and was designed to detect significant clinical

abnormalities that were clearly visible upon a limited examination, and to monitor the general health of the animals. The animals were not hand-held for these observations unless deemed necessary. Significant abnormalities that would be observed include, but were not limited to: decreased/increased activity, repetitive behavior, vocalization, incoordination/limping, injury, neuromuscular function (convulsion, fasciculation, tremor, twitches), altered respiration, blue/pale skin and mucous membranes, severe eye injury (rupture), alterations in fecal consistency, and fecal/urinary quantity. All animals were observed for morbidity, mortality, and the availability of feed and water at least twice daily. All animals were observed for exposure-related effects approximately every 30 minutes during the exposure period.

b. Clinical examinations: A hands-on evaluation of skin, fur, mucous membranes, respiration and nervous system function (including tremors, convulsions, diarrhea and animal behavior) was conducted on all animals the day prior to exposure and on the 1, 2, 4, 8, and 24 hours post exposure sacrifice animals once following exposure on test day 1.

2. Body weight: All rats were weighed the day prior to exposure (test day -1). The 1, 2, 4, 8, and 24 hour post-exposure sacrifice animals were also weighed once following exposure on test day 1.

3. Food consumption and food efficiency: Not determined for this acute study focused on ChE inhibition.

4. Ophthalmoscopic examination: Not determined for this acute study focused on ChE inhibition.

5. Hematology and clinical chemistry: Not determined for this acute study focused on ChE inhibition.

a. Hematology

Not determined for this acute study focused on ChE inhibition.

b. Clinical chemistry

Standard clinical chemistry parameters were not determined. For this acute study, it focused on ChE activity in various tissues and pharmacokinetics of oxon and the TCP metabolite. RBC, plasma, lung, and brain samples were shipped on dry ice to WIL Research Laboratories, LLC, Ashland, Ohio for analysis of cholinesterase (ChE) activity using an assay based on a modification of the Ellman reaction (Ellman *et al.*, 1961; Hunter *et al.*, 1997). Blood was analyzed for oxon and TCP in the analytical laboratories of The Dow Chemical Company (Midland, MI) based on validated analytical methods described in Brzak *et al.* (1998), Mattsson *et al.* (2000) and Brzak and Malowinski (2013). Final extracts were analyzed using high performance liquid chromatography separations, electrospray ionization with tandem mass spectrometry detection (HPLC/ESI-MS/MS) operating in the multiple reaction monitoring (MRM) mode, monitoring positive ions.

6. Urinalysis

Not determined for this acute study focused on ChE inhibition.

7. Sacrifice and pathology
Not determined for this acute study focused on ChE inhibition.

8. Functional Oberservational Battery Testing
Not determined for this acute study focused on ChE inhibition.

II. RESULTS

A. OBSERVATIONS

1. Mortality: None

2. Clinical signs of toxicity: No clinical effects were noted during the six-hour exposure or during the post-exposure period

B. BODY WEIGHT AND WEIGHT GAIN: Test day 1 post-exposure mean body weights were decreased 1.4% and 2.2% from test day -1 values for control and oxon exposed rats, respectively. Since similar decreases were observed in both control and oxon exposed rats, these losses are considered not to be adverse and are attributed to stress related to nose-cone confinement. The raw data is listed in Table 2 (obtained from page 39 from the study report).

Table 2: Body Weight Data

DOSE UG/M3		DAYS ON TEST -1	1	GAIN
0	MEAN	214.7	211.9	-3.1&
	S.D.	7.5	9.1	3.6
	N=	48	40	40
35.3	MEAN	213.4	209.1	-4.8&
	S.D.	9.7	9.7	3.6
	N=	48	40	40

& INDICATES NO STATISTICAL COMPARISON OF MEANS.
THERE WERE NO STATISTICAL DIFFERENCES FROM CONTROL AT ALPHA=0.05.

Data obtained from page 39 (raw data) from the study report.

C. FOOD CONSUMPTION

1. Food consumption: Food consumption was not reported in this study.

2. Food efficiency: Food efficiency was not presented in this study.

D. OPHTHALMOSCOPIC EXAMINATION: Not reported in this study.

E. BLOOD ANALYSES: Typical blood results were not reported in this study. However, the blood levels of chlorpyrifos oxon and trichlorophenol (TCP) were monitored.

For chlorpyrifos oxon, the blood levels were below the lower limit of quantitation (LLQ, 0.000353 nmol/g blood) during the time period after exposure, as depicted in the Graph 1. The blood levels of TCP are listed in table 3. For TCP, the blood levels ranged from less than the LLQ (0.0123 nmol/g blood) to 0.0848 nmol/g blood during the time period after exposure. Blood analysis results taken from pages 35 and 49 of the study report.

Graph 1: Oxon and TCP Levels in Blood

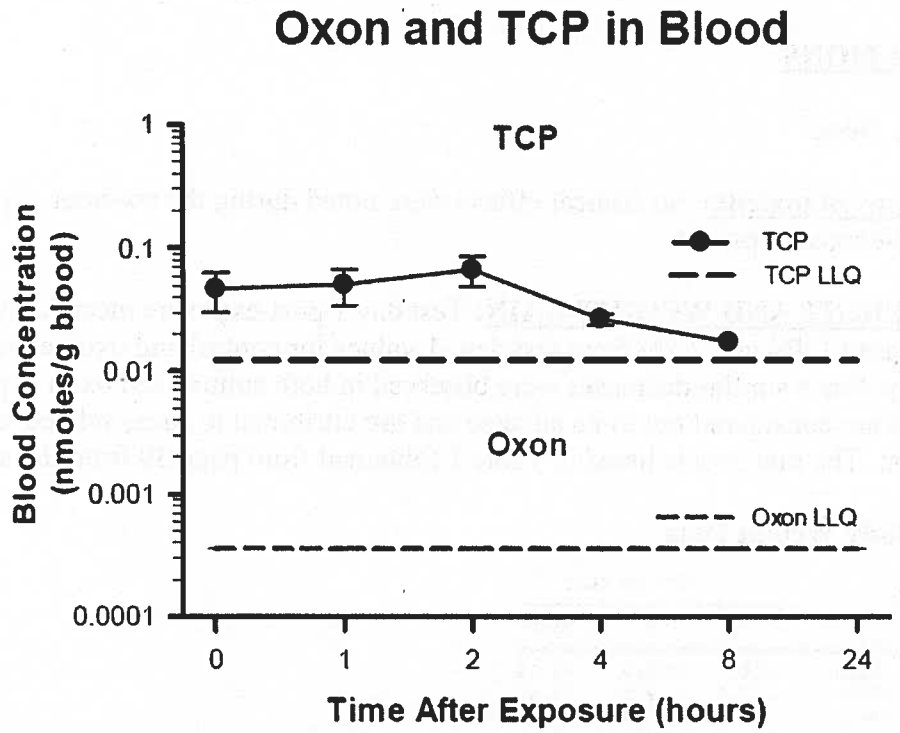


Figure 5. Blood levels of oxon, and TCP measured 0, 1, 2, 4, 8. or 24 hours after 6 hours of exposure to 35.3 µg/m^3 oxon. Values represent the mean concentration of the analyte (nmole/g blood) ± S.D. (n=4/sacrifice time). No oxon ≥ LLQ (0.000353 nmole/g/blood) was detected in any animal at any time point. The LLQ for TCP was 0.0123 nmole/g blood.

Table 3: Blood Analysis for TCP

Blood Levels of TCP in Rats Exposed 6 Hours to 35.3 µg/m^3 Oxon (nmole/g blood)

0 hour		1 hour		2 hour		4 hour		8 hour		24 hour	
Animal	TCP	Animal	TCP	Animal	TCP	Animal	TCP	Animal	TCP	Animal	TCP
2548	6.42E-02	2556	5.89E-02	2564	8.00E-02	2572	2.38E-02	2580	<LLQ	2588	<LLQ
2549	3.63E-02	2557	6.93E-02	2565	5.57E-02	2573	2.56E-02	2581	1.73E-02	2589	<LLQ
2550	2.93E-02	2558	3.34E-02	2566	4.68E-02	2574	3.05E-02	2582	<LLQ	2590	<LLQ
2552	5.69E-02	2560	4.12E-02	2567	8.48E-02	2575	2.66E-02	2583	<LLQ	2591	<LLQ
Mean	4.67E-02		5.07E-02		6.68E-02		2.66E-02		1.73E-02		--
S.D.	1.65E-02		1.64E-02		1.85E-02		2.83E-03		--		--

-- = Not Applicable
LLQ = Lowest Level Quantitated
TCP LLQ = 1.23E-02 nmole/g blood
Oxon LLQ = 3.53E-04 mnole/g blood
All samples from control study animals were <LLQ.
Oxon levels were <LLQ for all study samples.

Results taken from page 35 and 49 of the study report

F. URINALYSIS: Not reported in this study.

G. SACRIFICE AND PATHOLOGY

1. Organ weight: Not reported in this study.

2. Gross pathology: Not reported in this study.

3. Microscopic pathology: Not reported in this study.

H. CHOLINESTERASE RESULTS:

The ChE activity data normalized relative to control values are listed in Graphs 2-5, taken from pages 31-34 of the study report. The raw ChE activity data is listed in Appendix 1.

There were no statistically significant decreases in ChE activity in any tissue monitored. The only statistically significant changes in cholinesterase (ChE) activity were in the RBC and brain, however, increases of ChE activity occurred.

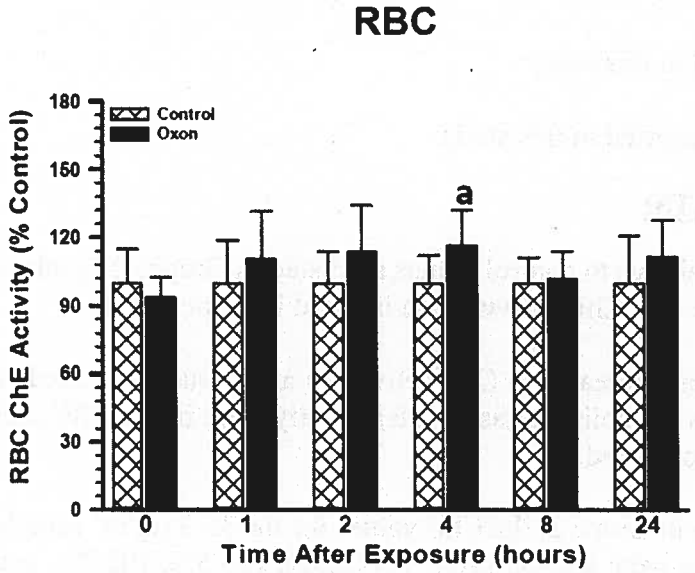
In the red blood cell samples shown in Graph 2, the ChE values for the 35.3 $\mu g/m^3$ samples at 0, 1, 2, 4, 8 and 24 hours after exposure were 93.6%, 110.6%, 113.9%, 116.5%, 102.2%, and 111.9%, respectively, of the 0 $\mu g/m^3$ control group, with none having both statistical significance and an activity decrease greater than 10%. The RBC ChE activity at 4 hours was statistically significant, however it was an increase in activity.

In the plasma samples shown in Graph 3, the ChE values for the 35.3 $\mu g/m^3$ samples at 0, 1, 2, 4, 8 and 24 hours after exposure were 103.0%, 107.5%, 101.5%, 136.7%, 101.0%, and 127.6%, respectively, of the 0 $\mu g/m^3$ control group, with none having statistical significance nor a decrease in ChE activity.

In the lung samples shown in Graph 4, the ChE values for the 35.3 $\mu g/m^3$ samples at 0, 1, 2, 4, 8 and 24 hours after exposure were 93.7%, 108.3%, 118.6%, 109.1%, 101.7% and 91.6%, respectively, of the 0 $\mu g/m^3$ control group, with none having statistical significance nor a decrease in activity greater than 10%.

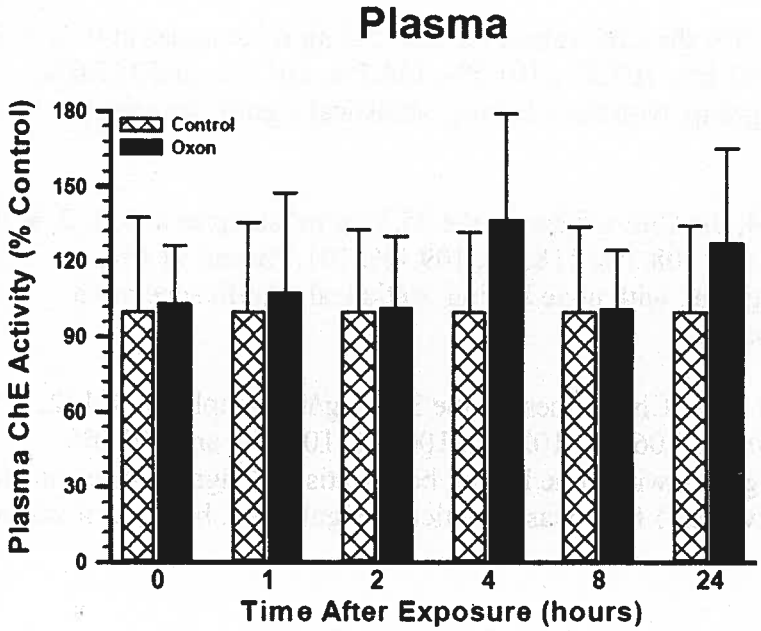
In the brain samples shown in Graph 5, the ChE values for the 35.3 $\mu g/m^3$ samples at 0, 1, 2, 4, 8 and 24 hours after exposure were 100.5%, 106.2%, 102.0%, 100.9%, 101.2%, and 101.0%, respectively, of the 0 $\mu g/m^3$ control group, with none having both statistical significance and an activity decrease. The brain ChE activity at 1 hour was statistically significant, however it was an increase in activity.

Graph 2: RBC ChE Results

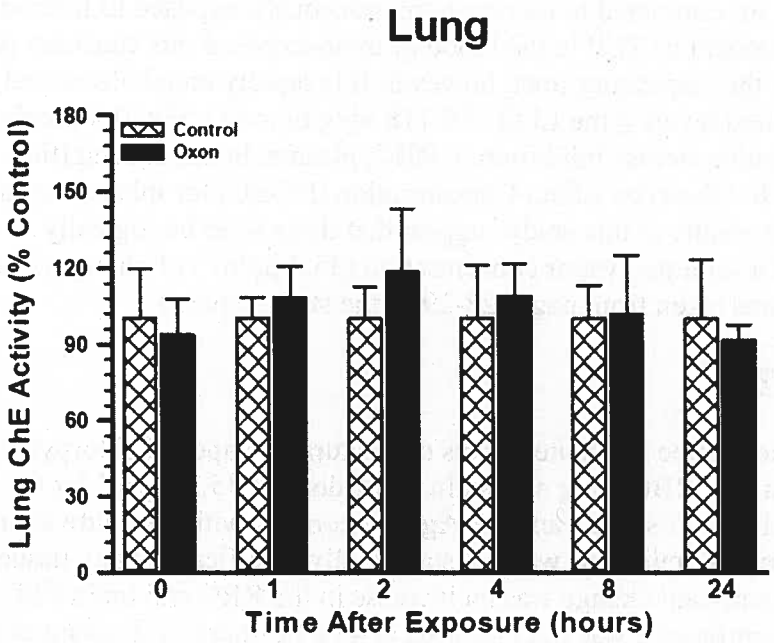


[a] Significantly different than 0 µg/m^3 (control) at the same post-exposure time

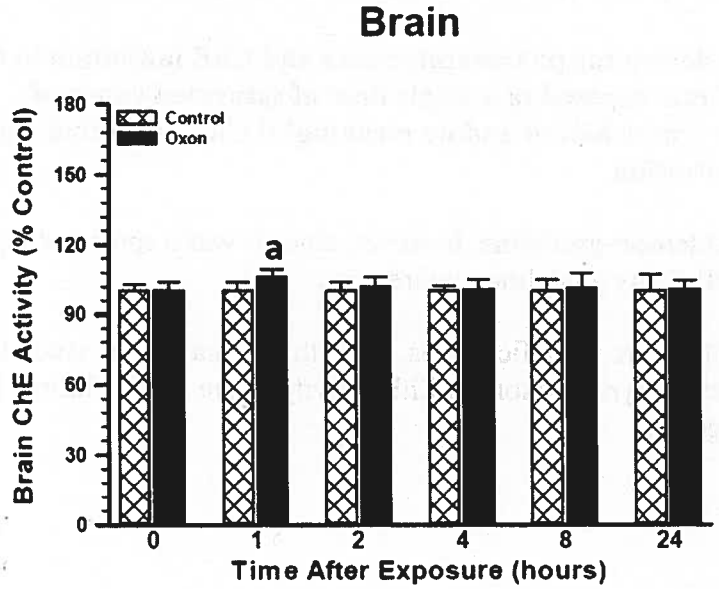
Graph 3: Plasma ChE Results



Graph 4: Lung ChE Results



Graph 5: Brain ChE Results



[a] Significantly different than 0 μg/m^3 (control) at the same post-exposure time

III. DISCUSSION AND CONCLUSIONS

INVESTIGATORS' CONCLUSIONS:

Under the conditions of this study, no clinical signs of toxicity were noted in oxon exposed rats at any time during or after exposure and no inhibition of ChE activity was measured in RBC, plasma, lung, or brain of rats that were nose-only exposed for 6 hours to a saturated vapor concentration of 35.3 μg oxon/m^3 air, compared to rats contemporaneously-exposed to filtered air (0 μg/m3; control). The measurement of TCP in the blood of oxon-exposed rats confirms that inhaled oxon vapor is absorbed by the respiratory tract, however, it is rapidly metabolized and not systemically bioavailable at blood levels ≥ the LLQ of 0.118 ng/g blood (3.53x10-4 nmole/g blood). Based on the absence of cholinesterase inhibition in RBC, plasma, brain, or lung (the portal-of-entry tissue) the 6-hour No Observed Effect Concentration (NOEC) for inhaled oxon vapors is > 35 μg oxon/m^3 air. The results of this study suggest that there is no biologically relevant hazard from inhalation of a saturated vapor concentration (35.3 μg/m^3) of chlorpyrifos oxon. (The investigator's conclusions taken from pages 28-29 of the study report.)

REVIEWER COMMENTS:

The purpose of this study was to determine the acute effects of a saturated vapor of chlorpyrifos oxon on the ChE activity in the plasma, RBC, lung and brain at the dose of 35.3 μg/m^3 for 6 hours on female rats. The study achieved its goals and the Agency concurs with the study author that inhibition of plasma, RBC, lung or brain ChE was not statistically significant in any tissue measured. The only statistically significant change was an increase in the RBC and brain ChE activity although such statistical significance was not observed at 4 or 12 hours. A diagram of the testing apparatus would have provided a more thorough report. The effect of temperature on the oxon concentration was an important point evaluated and presented in the study.

The purpose of the study was to determine pharmacokinetics and ChE inhibition in the RBC, plasma, brain and lung of rats exposed to a single dose of saturated vapor of chlorpyrifos oxon. This purpose was achieved and no meaningful ChE inhibition was observed at the saturated concentration.

This study is classified as **acceptable/non-guideline**, however, since it was a special study, it is acceptable, although it does not fulfill any guideline requirement.

C. STUDY DEFICIENCIES: There are no deficiencies, since this was a special study to test the effects of a saturated vapor of chlorpyrifos oxon on ChE activity in the RBC, plasma, lung and brain. The study achieved its goals.

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Appendix 1: Cholinesterase Activity Raw Data

The data taken from pages 99-103 of the study report.

Table A.1 Plasma, RBC, Lung and Brain Cholinesterase Results

ANALYSIS	GROUP:	FEMALES CONTROL	FEMALES OXON
PLASMA CHE (U/L)			
HOUR 0	MEAN	1984.	2045.
	S.D.	743.1	456.0
	N	7	8
HOUR 1	MEAN	2009.	2160.
	S.D.	717.4	803.8
	N	8	8
HOUR 2	MEAN	2048.	2079.
	S.D.	675.8	584.0
	N	8	8
HOUR 4	MEAN	1599.	2186.
	S.D.	508.6	675.7
	N	8	8
HOUR 8	MEAN	1939.	1958.
	S.D.	658.3	454.7
	N	8	8

ANALYSIS	GROUP:	FEMALES CONTROL	FEMALES OXON
PLASMA CHE (U/L)			
HOUR 24	MEAN	1786.	2279.
	S.D.	611.3	672.6
	N	8	8
RBC CHE (U/L)			
HOUR 0	MEAN	3869.	3622.
	S.D.	572.1	339.4
	N	7	8
HOUR 1	MEAN	3495.	3866.
	S.D.	654.0	729.7
	N	8	8
HOUR 2	MEAN	3424.	3902.
	S.D.	485.1	692.6
	N	8	8
HOUR 4	MEAN	3591.	4182.
	S.D.	431.8	571.2
	N	8	8

ANALYSIS	GROUP:	FEMALES CONTROL	FEMALES OXON
RBC CHE (U/L)			
HOUR 8	MEAN	3362.	3435.
	S.D.	385.0	402.3
	N	8	8
HOUR 24	MEAN	3356.	3757.
	S.D.	699.2	533.4
	N	8	8
BRAIN CHE (U/L)			
HOUR 0	MEAN	50576.	50814.
	S.D.	1454.0	1789.3
	N	8	8
HOUR 1	MEAN	49276.	52347.
	S.D.	1952.7	1506.9
	N	8	8
HOUR 2	MEAN	51538.	52565.
	S.D.	1992.0	2113.1
	N	8	8

ANALYSIS	GROUP:	FEMALES CONTROL	FEMALES OXON
BRAIN CHE (U/L)			
HOUR 4	MEAN	50800.	51236.
	S.D.	1330.1	2218.7
	N	8	8
HOUR 8	MEAN	51961.	52607.
	S.D.	2547.4	3463.3
	N	8	8
HOUR 24	MEAN	49999.	50496.
	S.D.	3486.7	1864.7
	N	8	8
LUNG CHE (U/L)			
HOUR 0	MEAN	3586.	3359.
	S.D.	706.0	516.3
	N	8	8
HOUR 1	MEAN	3169.	3432.
	S.D.	274.1	396.4
	N	8	8

ANALYSIS	GROUP:	FEMALES CONTROL	FEMALES OXON
LUNG CHE (U/L)			
HOUR 2	MEAN	3006.	3566.
	S.D.	387.5	747.6
	N	8	8
HOUR 4	MEAN	2519.	2747.
	S.D.	537.7	319.5
	N	8	8
HOUR 8	MEAN	3042.	3094.
	S.D.	404.7	714.2
	N	8	8
HOUR 24	MEAN	2942.	2694.
	S.D.	695.8	181.7
	N	8	8

U/L = INTERNATIONAL UNIT/LITER

HOUR = HOURS POST-EXPOSURE

Data taken from pages 99-103 of the study report