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DATA EVALUATION REPORT

STUDY TYPE: Subchronic Inhalation Range Finder - Rat
TOX. CHEM. NO.: 219AA
P.C. CODE: 059101
MRID NO.: 421449-09
TEST MATERIAL: Chlorpyrifos
SYNONYMS: Pyrinex
STUDY NUMBER: 88-8057
SPONSOR: Makhteshim-Agan (America)
TESTING FACILITY: Bio/dynamics, Inc
Mettlers Road
East Millstone, NJ 08873
TITLE OF REPORT: A Five Day Nose-Only Inhalation Toxicity
Study of Clorpyrifos (Pyrinex) in the Rat
AUTHOR: Paul E. Newton
REPORT ISSUED: 22 December 1988

CONCLUSIONS: Male and female rats were exposed to the test article at either 0 ppb (control) or 23 ppb (0.0034 $\mu\text{g/l}$) for 6 hours/day for five days in a nose-only apparatus. The only significant finding was a significant decrease in RBC cholinesterase activity of female rats in the treatment group. No other signs of toxicity were observed.

$\text{LC}_{50} > 23 \text{ ppb (0.0034 } \mu\text{g/l)}$

Toxicity category I

CLASSIFICATION: core - Supplementary

This is not a guideline study.

MATERIALS AND METHODS:

Test compound: Chlorpyrifos, technical Description: Off-white crystals Batch #: 489205, Purity: 95% Contaminants: list in CBI appendix

Test animals: Species: Rat Strain: Fisher 344 Age: 5 weeks Weight (g): 219 - 233 (males), 144 - 153 (females) Source: Charles River Breeding Laboratories, Inc., Raleigh, NC 27610.

Study design: Two groups of ten rats/group/sex were distributed randomly to control and treatment groups. The exposure lasted 6 hours/day for five days. Rats were observed daily and weighed on days -3 (pretest), 1 and 6.

Test atmosphere generation: The test material vapor was generated using a heated glass fluidized bed apparatus. A supply of dried compressed air was passed through the apparatus at a flow rate of 14 liters/min. The vapor-laden air was passed through the nose-only exposure chamber. Rats were exposed to test article at an average concentration of 23 ppb; the maximum theoretical vapor pressure of the test article at room temperature is 20 ppb. Control animals were exposed to air only. The relative humidity in the nose-only chamber was only 25 to 37% (controls) and 12 to 15 % (treated). These values are significantly lower than the accepted guideline value of 40 to 60%. The temperature in the chamber averaged 22.8 °C for controls and 26.7 °C for treated; guideline temperature is 22 ± 2 °C.

Statistics: Means and standard deviations of animal body weights, chamber temperatures and relative humidities, and chamber air flows were calculated for descriptive purposes.

RESULTS AND DISCUSSION

Although the data presented in the study indicate that equilibrium was established (Table 1), no sampling times were given to verify that equilibrium conditions were maintained throughout the exposure period. The distribution of particle sizes is summarized in Table 2. These data were inadequate to determine if the particle sizes were in compliance with EPA guidelines ($\geq 25\%$ with aerodynamic diameters $\leq 1.0 \mu\text{m}$)

Table 1: Concentration (ppb) of test article in chamber

Run	Chamber Sample			
	1	2	3	4
1	22	30	19	24
2	23	17	22	21
3	21	24	17	21
4	34	21	31	29
5	31	17	17	22

Table 2

<u>Aerodynamic Diameter (μm)</u>	<u>Cumulative Particle Size Distribution</u>
0.77	16%
4.4	84%
< 10	100%
1.5	MMAD

Animals were inspected daily for signs of toxicity, moribundity and mortality. There were no treatment-related changes on either clinical signs or body weights. Plasma cholinesterase activities, measured at the conclusion of the study, were significantly lower in the treated females (Table 3, below)

Table 3: Cholinesterase activities of male and female rats

	<u>Plasma ChE (IU/ml)</u>		<u>RBC ChE (IU/ml)</u>		<u>Brain ChE (IU/g)</u>	
	<u>0 ppb</u>	<u>20 ppb</u>	<u>0 ppb</u>	<u>20 ppb</u>	<u>0 ppb</u>	<u>20 ppb</u>
Male:	6.6	6.8	0.608	0.539	10.7	10.9
Female:	6.8	7.1	1.957	1.118**	10.6	10.6

**, $p < 0.01$

CONCLUSIONS: Male and female rats were exposed to the test article at either 0 ppb (control) or 23 ppb ($0.0034 \mu\text{g/l}$) for 6 hours/day for five days in a nose-only apparatus. The only significant finding was a significant decrease in RBC cholinesterase activity of female rats in the treatment group. No other signs of toxicity were observed.

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