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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: EPA ID No. 080801-000100 Ametryn Technical, Acute 4-hr Inhalation
Toxicity Study in Rats (81-3)

Tox. Chem. No. 431
Submission No. S425764

DP Barcode No. D182836
PC Code No. 129099

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2/25/93

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Marion Copley
2/25/93

CONCLUSION

The inhalation toxicity demonstrated by ~~NTN 33893~~ ^{Ametryn} is low, with a Toxicity Category of IV. The study is core classified as: acceptable for regulatory purposes ~~for the technical~~

ACTION REQUESTED

Toxicology Branch I has been requested to review the data submitted and determine Toxicity Category and compliance with Guideline #81-3. (*DER attached*)

DISCUSSION

None.

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Reviewed by: Myron S. Ottley, Ph.D. *M. S. Ottley* 2/25/93
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DATA EVALUATION REPORT

STUDY TYPE: Inhalation -- Rat (81-3)
TOX. CHEM. NO.: 431
PC NUMBER: 080801
MRID NO.: 424709-02
TEST MATERIAL: Ametryn Technical
SYNONYMS: None
STUDY NUMBER: 8988-92
SPONSOR: Ciba-Geigy Corp., Greensboro, NC
TESTING FACILITY: Stillmeadow, Inc., Sugar Land, Texas
TITLE OF REPORT: Acute Inhalation Toxicity Study in Rats
AUTHOR(S): Mark S. Holbert, B.S.
REPORT ISSUED: July 7, 1992

CONCLUSIONS
LC₅₀ > 5.03 mg/L
Toxicity Category: IV

Classification: Acceptable. This study satisfies the guideline requirements for an inhalation study in the rat (81-3) *on the technical*

MATERIALS

1. Test Compound: Ametryn Technical; Description: Fine White Powder; I.D. No: FL-921297 ARS-19327; Batch No. GP-920505; Purity: 97.7%; Stability: through 5/26/94 (22 months beyond study completion date).
2. Test Animals: Species & Strain: Rat, HSD:(SD); Weight when tested: Males

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(238-270 g), Females (229-245g); Source: Harlan Sprague Dawley, Inc., Houston, TX.

3. **Environment:** Animals were housed individually in stainless steel, wire-bottom, suspended cages. Temperature: not reported. Humidity: not reported. Photoperiod: not reported. Food: Purina Formulab Chow #5001, available *ad libitum*. Water: Tap, available *ad libitum*.

METHODS

Aerosol Generation

The aerosol was generated by a Venturi Aspirator which aspirated the test material from a motorized revolving disc delivery system coupled to the aspirator, then elutriated the resulting aerosol through a baffling chamber. The Concentrated aerosol was then diluted with filtered air and drawn into the exposure chamber. Air flow into the chamber was maintained through the use of a calibrated critical orifice, at a rate of 22 air changes per hour. Air flow was recorded at 30-minute intervals during the exposure period, and was sufficient to ensure an oxygen content of at least 19% of the exposure atmosphere. Temperature and humidity were recorded at 30-minute intervals during the exposure period from a Taylor wet-bulb/dry-bulb hygrometer located in the exposure chamber. Test substance concentration in the breathing zone was determined gravimetrically at least once per hour. Particle size was determined twice during each exposure, using an Andersen cascade impactor, at a rate of 22 L/min. for a duration of 0.75 - 4.0 minutes. The mass median aerodynamic diameter and percentage of the mass of the particles under 1.1μ was calculated from these data.

Exposure

Groups of five male and five female rats were exposed in a single 4-hour exposure to concentrations of 0.547 mg/L or 5.03 mg/L of aerosol. Animals were observed for signs of toxicity or mortality frequently on the day of exposure, and at least once/day thereafter for 14 more days.

RESULTS

Clinical Signs

No treatment-related deaths occurred. Clinical signs observed were piloerection, decreased activity, nasal discharge, lacrimation, polyuria, salivation, and polyuria. As Tables 1 and 2 show, these signs were observed in virtually all animals, at both dose levels (the exception is polyuria, observed in high-dose animals only). All clinical signs had cleared by day 3 post treatment.

TABLE 1. CLINICAL SIGNS OBSERVED FOLLOWING 4-HR INHALATION EXPOSURE TO AMETRYN TECHNICAL AT 0.547 MG/L								
Reaction and Severity	HOURS					DAYS		
	0.5	1.0	2.5	4.5	6.0	1	2	3
Males								
Piloerection (v - m)	1	1	1	5	5	5	5	0
Activity Decrease (v - m)	1	1	1	5	5	3	0	0
Ptosis (s - e)	1	1	1	0	0	0	0	0
Nasal Discharge (v - s)	1	1	1	5	5	2	0	0
Lacrimation (v)	0	0	1	5	0	0	0	0
Polyuria (v)	0	0	0	5	5	0	0	0
Salivation (v)	0	0	0	5	0	0	0	0
Females								
Piloerection (v - m)	1	1	1	5	5	5	5	0
Activity Decrease (v - m)	1	1	1	5	5	0	0	0
Ptosis (s - e)	1	1	1	0	0	0	0	0
Nasal Discharge (v - s)	1	1	1	5	5	0	0	0
Lacrimation (v)	0	0	1	5	0	0	0	0
Polyuria (v)	0	0	0	5	5	0	0	0
Salivation (v)	0	0	0	5	0	0	0	0

v = very slight; s = slight; m = moderate; e = extreme

TABLE 2. CLINICAL SIGNS OBSERVED FOLLOWING 4-HR INHALATION EXPOSURE TO AMETRYN TECHNICAL AT 5.03 MG/L					
Reaction and Severity	HOURS		DAYS		
	4.5	6.0	1	2	3
Males					
Piloerection (v - m)	5	5	5	5	0
Activity Decrease (v - s)	5	5	5	0	0
Nasal Discharge (v - s)	5	5	5	0	0
Lacrimation (v)	5	5	0	0	0
Polyuria (s)	5	5	0	0	0
Salivation (s)	5	5	0	0	0
Females					
Piloerection (v - m)	5	5	5	5	0
Activity Decrease (v - m)	5	5	5	1	0
Nasal Discharge (v - s)	5	5	5	0	0
Lacrimation (v)	5	5	0	0	0
Polyuria (v - m)	5	5	5	0	0
Salivation (s)	5	5	0	0	0

v = very slight; s = slight; m = moderate; e = extreme

Body Weight

No treatment-related changes in body weight or body weight gain were observed.

Gross Pathology

No treatment-related findings were made.

Particle Size (Table 3)**TABLE 3. AEROSOL PARTICLE SIZES AS MEASURED DURING THE 4 HR EXPOSURE**

Mean Concentration (nominal)	Mass Median Aerodynamic Diameter		Geometric Standard Deviation		% Particles < 1.1 μ	
	1 ½ hr Distrib.	3 ¼ hr Distrib.	1 ½ hr Distrib.	3 ¼ hr Distrib.	1 ½ hr Distrib.	3 ¼ hr Distrib.
0.547 mg/L (1.86)	2.872	3.190	1.933	2.184	10.2	10.6
5.03 mg/L (28.3)	3.200	3.495	2.298	2.134	11.1	8.57

The submitter stated that due to the nature of the test compound, it was not possible to bring the MMAD within guideline limits.

DISCUSSION

Ametryn Technical aerosol appeared to be non-toxic to rats at the inhalation exposure levels tested. The LD_{50} is greater than 5.03 mg/L with a Tox. Category of IV.

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