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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: February 21, 1979

SUBJECT: EPA No.: 100-EUP-AE, MILOCEP Herbicide (Metolachlor-Propazine Prepack). Caswell#188DD and #184

FROM: John Doherty John Doherty Branch 3/6/79
Toxicology Branch, HED (TS-769)

TO: W. Garner
Product Manager#23

Action Requested: An EUP is requested to test this product on sorghum grown for grain. The proposed program would limit treatment to 50 acres of sorghum grown for grain. 34 gallons of MILOCEP will be shipped, representing 113.22 lbs of metolachlor and 56.44 lbs of propazine. The states involved include Arkansas (2), Colorado (2), Kansas (8), Missouri (3), Nebraska (8), New Mexico (3), North Carolina (1), Oklahoma (3) and Texas (20). The number in ( ) is the number of acres. The total treated acreage represents about 0.0003623% of the total grain sorghum acreage. The duration of this EUP is scheduled for March 1, 1979 to March 1, 1980.

Product: MILOCEP Herbicide

Active Ingredients: Metolachlor: (2-chloro-N-(2-ethyl-6-methyl-phenyl) -N-(2-methoxy-1-methylethyl) acetamide ------ 36.3%

Propazine: 2-chloro-4,6-bis (isopropylamino)-s-triazine ---------- 18.7%

Inerts ---------- 45.0%
100%

Inert ingredient name deleted.

The inerts have been cleared under 180.1001, except for [redacted]

40 CFR 180.243 has set tolerances for propazine in/on sorghum grain, forage, and fodder at 0.25 ppm.

40 CFR 180.368 has set permanent tolerances for Metochlor only on corn grain (exc. pop) at 0.1 ppm.

P.P.8G2019 has been approved and has set temporary tolerances for metolachlor and its metabolites in/on sorghum forage and fodder at 1 ppm and sorghum grain at 0.3 ppm. Also in eggs, meat, and milk fat and meat byproducts of cattle, goats, hogs, horses, poultry and sheep at 0.02 ppm. This temporary tolerance has been extended to April, 1980 (Dr. E. Wilson, personal communication, 2/6/79).

Conclusion:

1. Attaflow will have to be identified and cleared.

2. Provided that CHEMISTRY BRANCH decides that use as directed will not result in residues in excess of set tolerances, TOXICOLOGY BRANCH has no further objection to granting this EUP.

Acute Toxicity of MILOCEP

		Toxicity Category	Core Categorization
Acute Oral (rats) LD_{50}	3,868 mg/kg	III	Minimum
Acute Dermal (rabbit) LD_{50}	>5.0 gm/kg	III	"
Eye Irritation	Opacity not reversed	I	"
Skin Irritation	Slight	III	"
Inhalation LC_{50}	>20.8 mg/Li	IV	"

This product must be labelled DANGER and the proper precautionary information for an eye irritant must be included.

Review of Acute Studies with MILOCEP.

1. Acute Oral Toxicity (LD_{50}) Study in Rats.

International Research and Development Corporation Study No. 382-043, October 17, 1978.

Test Material (a creamy beige substance, identified as CGA-24705/G-30028 5L (3.3/1.7)-A, and considered to be MILOCEP 5L) was administered to 6 groups of 10 rats (5M and 5F) by gavage. The rats were fasted prior to dosage. Dose levels of 1,574; 2,314; 3,401; 5,000; 7,350; and 10,805 mg/kg. were tested. Sprague-Dawley rats were used.

The LD_{50}'s were:

Males: 4,811 (3,771-6,139) mg/kg.
Females: 2,944 (2,185-3,965) mg/kg.
Combined: 3,868 (3,142-4,761) mg/kg.

Pharmacological signs included hypoactivity, ataxia at the higher doses. Gross necropsy revealed internal congestion. Most of the animals that died, died within one day following administration.

This test is CORE MINIMUM.

2. Acute Dermal Toxicity Study in the Albino Rabbit.

International Research and Development Corporation Study No. 382-044, October 17, 1978.

Two groups of 8 rabbits (4M and 4F) were prepared for treatment. The hair was removed from the backs of all rabbits and 2 male and 2 female were further abraded. The test material was applied to one group at the dosage level of 5000 mg/kg (MILOCEP) and held in place for 24 hours following application.

None of the rabbits died in either of the test or control groups. The treated animals appeared normal throughout the 14 day study period. None of the treated rabbits showed definite signs of poisoning when necropsied.

Dermal Irritation was also evaluated for this test chemical. Slight to moderate degrees of irritation were reported.

This test is CORE MINIMUM (upgraded from Supplementary). Although only a single dose was applied, toxicity category III can be assigned without debate for more toxic classification.

3. Primary Eye Irritation Study in the Albino Rabbit.

International Research and Development Corporation 382-045, October 17, 1978.

4 male and 5 female New Zealand White rabbits were used in this study. 0.1 ml of test material (MILOCEP) was placed into the cupped conjunctival sac of the right eye of each rabbit and the eyes were held shut for 1 second. Three of the rabbits were washed with distilled water 30 seconds following test material instillation.

Corneal opacity that was not reversed in 7 days developed in the rabbits that were not washed with distilled water.

This test is CORE MINIMUM. The product is CORROSIVE and the signal word must be DANGER.

4. Primary Skin Irritation Study in the Albino Rabbit.

International Research and Development Corporation 382-046, October 17, 1976.

3 male and 3 female New Zealand White rabbits, from H.A.R.E., Hewitt, New Jersey) were prepared for the study by removing 20-30% of the body hair and further abrading the surface. 0.5 ml of the test material (MILOCEP) was applied to each site on the back of the rabbit under a 1 inch square of gauze and held in place for 24 hours.

A primary irritation score of 2.0 was determined. At 72 hours only slight irritation persisted.

This test is CORE MINIMUM.

5. Acute Inhalation Toxicity Study in Rats.

International Research and Development Corporation 382-047, November 3, 1978.

5M and 5F Charles River CD rats were exposed to vapors of MILOCEP. The rats (in individual cages) were placed in a 160 liter cubical, stainless steel and glass chamber. The vapors were generated by metering the liquid with a FMI lab pump into a positive pressure atomizer. The concentration of the compound (20.8 mg/l) in the chamber atmosphere was calculated from the ratio of the rate of liquid dissemination (1556.6 mg/min) to the rate of chamber airflow (75 l/min). The particle size was determined using an 8 stage Fractionating Sampler (Andersen). The samples of the atmosphere were also taken 4 times during the 4 hour exposure period.

Results:

No rats died during the exposure period and gross necropsy of the survivors revealed no gross lesions. All rats appeared normal on day 1 post exposure and throughout the 14 day observation period.

Particle size determinations revealed that 70% of the particles were 7 micrometers or smaller.

The concentration is stated as being 20.8 $\frac{mg}{l}$ but the actual results of analysing the chamber are not reported.

This test is CORE MINIMUM (upgraded from Supplementary). Although no LC_{50} was determined it can be safety concluded that the product is category III or IV and not category II.

TOX/HED:th:RD Initial EBUDD:12-26-78

2/26/79 RD 3/6/79