UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Caswell 63

DATE: December 8, 1978

SUBJECT: State registration for Missouri (24C) of a flowable herbicide formulation containing proprehlor and atrazine in a 3:1 ratio

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Atrazine /Review #22/
12.8.78/ 6 pages
Releasable

Registration No. MO 780017

Registrant: Monsanto Agricultural Product Company
For Missouri State Board of Agriculture

Action requested: Registration of a flowable formulation of propachlor and atrazine to be used for preemergent weed control in grain sorghum

Recommendation: The registration of a flowable formulation of atrazine propachlor for use in Missouri is toxicologically supported by the data submitted with this application.

The statement on the label "may be fatal by skin absorption" is not supported by the dermal toxicity data presented and may be deleted.

Discussion: This state registration constitutes a change in percent of active ingredients and the physical form of the mixture to be applied. A wettable powder (WP) mixture of atrazine and propachlor is registered, EPA No. 524-286, for preemergent weed control in grain sorghum. The 3:1 ratio of active ingredients and use pattern has not changed. Propachlor WP formulations have a use history among growers and applicators of causing an itching irritation upon skin and inhalation exposure to dust. The registrant purposes to register a flowable formulation of atrazine and propachlor to minimize the undersirable irritation reported during handling of the dry formulations of propachlor. A comparison of the irritation data on these two formulations shows the flowable formulation to be approximately twice as irritationg as the wettable powder to the skin of experimental animals in standard Primary dermal Irritation Studies.

Tolerances: The following tolerances are established:
Atrazine in petition 7F0525, 40 CFR 180.220
0.25 p.p.m. sorghum grain
15.0 p.p.m. sorghum forage

Propachlor is petition 6F0479, 40CFR 180.211
0.25 ppm sorghum grain
3.0 ppm sorghum forage

Summary of the acute toxicity submitted with this registration

Flowable formulation of atrazine and propachlor

Study	Species	Sex	Results	Toxicity Category
Oral	Rat	Male/female	LD 50 3800 mg/kg (3270-4410)	III
Dermal	Rabbit	Male/female	LD 50 > 5010 mg/kg	III
Inhalation	Rat	Male	LC 50 > 9.5 mg/l	III
Eye Irritation (unwashed)	Rabbit	Slight to moderate erythema and corneal dullness reversible at 7 days.		III
Dermal Irritation	Rabbit	Moderate to marked erythema. Primary irritation score 6.0		II

Wettable powder formulation of atrazine and propachlor

Study	Species	Sex	Results	Toxicity Category
Oral	Rat	Male/Female	LD 50 1620 mg/kg (1460-1800)	III
Dermal	Rabbit	Male/female	LD 50 > 3160 and < 5010 mg/kg	III
Eye Irritation (unwashed)	Rabbit	Moderate to severe erythema reversible within 7 days. No corneal involvement		II
Dermal Irritation	Rabbit	Primary Irritation score 3.3		III

Propachlor dust

Study	Species	Sex	Results	Toxicity Category
Inhalation	Rat	Male/female	LC 50 > 4.13 mg/l	III

Toxicity data submitted on:

Flowable mixture of atrazine and propachlor by Younger Labortories

Acute rat oral LD 50

Method: Single oral doses were administered undiluted to five Sprague-Dawley rats per level for six dosage levels. Sexes were combined in all six dosage levels. The animals were observed for 14 days.

Results: Combined male and female LD 50 3800 mg/kg (3270-4410) slope 7.9

Toxicity category III

Observations: Weight loss, weakness, salivation. Death within 7 days. The results of gross autopsy were hemorrhagic lungs, areas of liver discoloration and acute gastrointestinal inflammations.

Data evaluation: Supplementary Study
Deficiency of this study: (1) LD 50 value not reported for separate sexes.
(2) No indication of fasting prior to administration of the test material.

Acute rabbit dermal LD 50

Method: The undiluted test material was applied dermally to one to four albino rabbits per level for three dosage levels. Sexes were combined in all three dosage levels. The animals were exposed for 24 hours and observed for 14 days.

Results: Combined male and female LD 50 > 5010 mg/kg

Toxicity Category III

Observations: Severe defatting effect. Skin did not slough off in 14 days. Weight loss, weakness and death reported within 2 to 4 days. The results of gross autopsy were hemorrhagic areas of the lungs liver discoloration, enlarged gall bladder and gastrointestinal inflammation.

Data evaluation: Supplementary Study
Deficiency of this study: (1) Not enough animals per level
(2) Animals not abraded

Acute rat inhalation LC 50

Method: Six male Sprague-Dawley albino rats were exposed to 9.5 mg/l of the undiluted formulation for six hours. The animals were observed for 14 days.

Results: No signs of toxicity or gross pathology observed. All animals survived the six hour exposure.

LC 50> 9.5 mg/l
Toxicity Category III

Data Evaluation: Core minimum data

Eye Irritation

Method: The undiluted material in the volume of 0.1 ml was applied to the eye or six albino rabbits. Animals were observed for 7 days.

Results; Slight to moderate erythema, congested iris, slight edema, copious discharge and corneal dullness were reported within 24 hours observation. All eyes were cleared and normal within 5 to 7 days of exposure.

Toxicity Category III

Data evaluation: Core minimum data
Deficiency of this study: Did not include both wash and unwashed eyes.

Dermal Irritation

Method: A volume of 0.5 ml of the undiluted material was applied dermally to six albino rabbits. The animals were exposed for 24 hours and observed for 14 days.

Results: Primary skin irritation score 6.0 moderate to marked erythema and edema was reported within 72 hours and clearning by the 7 th day. A defatting effect was reported with skin sloughing off in 10 to 14 days. No injury in depth reported.

Toxicity category II

Data evaluation: Core guidelines

Toxicity data submitted on:

Wettable powder formulations of atrazine and propachlor

Acute rat oral LD 50- Younger Laboratories

Method: Single oral doses of aqueous suspension were administered to five Sprague-Dawley rats per level of five dosage levels. Sexes were combined in all five dosage levels. The animals were observed for 7 days.

Results: Combined male and female LD 50 1620 mg/kg (1460-1800)

Toxicity Category III

Observations: include reduced appetite, weakness and death within twelve hours to three days. The results of gross autopsy were hemorrhagic lungs and slight liver discoloration.

Data evaluation: Supplementary Study
Deficiency of this study (1) LD 50 values not reported for separate sexes
(2) No indication of fasting prior to administration of the test material.

Acute rabbit dermal LD 50- Younger Laboratories

Method: An aqueous suspension was applied to the clipped intact skin of one to two albino rabbits per level for five dosage levels. The treated areas were occluded for 24 hours. Sexes were combined in the determination of the LD 50 value. The animals were observed for 14 days.

Results: Combined male and female LD 50 > 3160 mg/kg/but ~~weight~~ < 5010 mg/kg

Toxicity category III

Observations: include reduced appetite, weakness, collapse and death within two days. Gross autopsy findings were lung hyperemia and slight liver discoloration.

Data evaluation: Supplementary study
Deficiency of this study (1) Not enough animals per level
(2) Animals not abraded.

Eye irritation- Younger Laboratories

Method: A finely ground sample of 100 mg was placed in the conjunctival sac of the right eye of two albino male and one female rabbits. The eyes were rinsed after 24 hours and observed for 7 days.

Results: Moderate to severe erythema, slight edema and copious dischange was reported within 48 hours. No corneal involvement reported. Normal readings were reported within 7 days.

Toxicity Category II

Data Evaluation: Supplementary Study
Deficiency of this study (1) Need three more animals for this study

Dermal Irritation- Younger Laboratories

Method: A finely ground sample of 500 mg was moistened with water and applied to the clipped intact skin of two male and one female rabbit under a patch one inch square. The patches were held in place with adhesive tape and wrapped with plastic. The animals were exposed for 24 hours and observed for 7 days for irritation.

Results: Slight erythema and edema was reported at 48 hours, with clearing within 5 days. Primary irritation score 3.3.

Toxicity category III

Data evaluation: Supplementary study
Deficiency of this study (1) Need three additional animals
(2) Need application to abraded skin.

Toxicity data submitted on: Propachlor Dust

Acute rat inhalation- Bio-test Laboratories

Method: Five male and five female Charles River Rats received a single 6 hour exposure to 4.13 mg/l of propachlor dust and were observed for 14 days. Under conditions of this study 4.13 mg/l was the maximal attainable concentration. Seventy-six percent of the dust particles were less than 10 microns diameter.

Results: Two of the ten animals exposed died within 24 hours. The following signs were observed within 5 to 60 minutes and lasting for the duration of the exposure period: hyperactivity, ptosis, dyspnea, lacrimation and salivation. No gross pathological changes were reported in the survivors or the two animals that died during the study.

LC 50 > 4.13 mg/l
Toxicity category III

Data evaluation: Supplementary Study
Deficiency of this study (1) Submitted for comparison in the principle irritant. Not relevant to this registration.

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