9-27-84

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Amitraz (Baam)
N-(2,4-dimethylphenyl)-N-[[(2,4-dimethylphenyl) imino] methyl]-N-methyl methanimidamide. TOX CHEM 374A

TO: Jay Ellenberger, PM #12
Registration Division (TS-767)

THRU: Dave Ritter, Acting Section Head
Review Section #1
Toxicology Branch/HED (TS-769)

FROM: Ray Landolt
Review Section #1
Toxicology Branch/HED (TS-769)

Registrant: Noram Chemical Co.
Letter of February 29, 1984

Petitioner: Noram Chemical Co.
Letter of May 8, 1984

Action Requested:

1. Registration No. 45639-TN (70) Taktic EC, 12.5% for control of ectoparasites on cattle and swine. Review of acute oral, dermal toxicity, dermal and eye irritation studies on this formulation.

2. Petition: 4F2968

To amend 40 CFR 180.287 with permanent tolerances for the combined residues of amitraz and its metabolities containing the 2,4-dimethylaniline moiety in or on the following commodities:

Cattle (fat)	0.1 ppm
Cattle (meat)	0.05 ppm
Cattle (meat by-products)	0.3 ppm
Milk	0.03 ppm
Milk fat	0.3 ppm

Recommendation:

1. The acute toxicity studies support toxicity category III precautionary labeling for this formulation.

2. Toxicology Branch will withhold comment on the safety of those residue levels until the risk assessment on the second oncogenic study is available.

3. The [redacted] needs to be identified and cleared for the requested uses.

Background:

Dietary levels of amitraz fed to CFLP strain of mice for 80 weeks caused a significant increase in the incidence of lymphoreticular tumors in females mice (W. Greear, August 30, 1976). A second mouse oncogenic study was reported (R. Landolt, May 23, 1984) to show an increase in the incidence of hepatocellular tumors in female B6C3F1 mice from feeding dietary levels of amitraz for two years. The second mouse oncogenic study has been referred to the Carcinogen Assessment Group for a risk assessment (John Melone, August 9, 1984).

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Acute Toxicity Studies on Taktic EC, formulation CR 15875 containing 12.5% amitraz.

1. Acute Oral LD_{50} - Rat

FBC Limited No. Tox/83/179-70, Jan. 1984, Acc. No. 252566.

A. Procedure

Ten groups of Sprague-Dawley rats consisting of five groups of six males per group weighing 272-322 grams and five groups of six females per group weighing 214-253 grams were dosed orally at 0, 1100, 1557, 2200, and 3113 mg/kg of the undiluted test material. The rats were observed for mortality and signs of toxicity twice daily for 14 days with body weights recorded initially and on days 8 and 15.

B. Results

1. Observations of the mid dosage levels include: ataxia, reduced activity (except for aggressive and hyperreactive to touch) piloerection, hypothermia, mydriasis, facial soiling, lacrimation and corneal opacity. Deaths were reported between 22 hour and 4 days.

2. Gross necropsy findings include: corneal opacity and vascularisation, hemorrhagic areas on the eyes, stomach distended with fluid and the liver pale with a rounded appearance.

3. Histopathalogical findings of the eyes from animals at the mid and high dosage levels include corneal scarring and minimal keratitis.

C. Conclusions

1. LD_{50} males 2016.9 mg/kg (1477.7-2752.8)
   female 1959.5 mg/kg (1745.8-2199.3).

2. Classification of Data - Guideline

3. Toxicity Category III

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II. Acute Dermal LD_{50} - Rat

FBC Limited No. Tox/83/179-11, Nov. 1983, Acc. No. 252566.

A. Procedure

The undiluted test material (specific gravity of 0.8973 g/ml) was applied to shaven backs of six male (281-319g) and six female (231-253g) Sprague-Dawley rats at a dose level of 2043 mg/kg. The test area was wrapped with aluminium foil and a waterproof plaster. The wrap was removed after 24 hours and the test site washed with soap and water. Animals were observed twice daily for 14 days with body weights recorded on days 1, 8 and 15. Six male and female control rats were similarly treated except for application of the test material.

B. Results

1.

Level Tested mg/kg	Sex	Mortality (day) 1	2	3	4	5	6	7	8	9	10	11	12	13	14
2043	Male	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
2043	Female	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6

2. Observations of both sexes include: reduced activity (except for aggressive and hyperreactive to touch), facial and urogenital soiling, with wrinkling and dryness of the skin.

3. No gross necropsy findings reported.

C. Cnclusions

1. LD_{50} male > 2043 mg/kg (0/6)
   female > 2043 mg/kg (0/6)

2. Classification of Data - Guideline

3. Toxicity Category III

III. Primary eye Irritation - Rabbit

FBC Limited No. Tox/83/179-75, Oct. 1983, Acc. No. 252566.

A. Procedure

The test material (0.1 ml) was placed in the conjunctival sac of six New Zealand White rabbits weighing 2.4-2.7 kg. Eyes were not washed. Observations were made at one hour, then 1, 2, 3, 4 and 7 days. Ocular reactions were graded by the Draize numerical scoring system.

B. Results

Corneal opacity (2/6) with iritis (1/6) and diffuse conjunctival irritation (3/6) and chemosis (5/6) was observed clearing within 4 to 7 days.

C. Conclusion

1. Material was slightly irritating with corneal opacity clearing within 7 days.

2. Classification of Data - Guideline

3. Toxicity Category III

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IV. Primary Dermal Irritation

FBC Limited No. Tox. 83/179-76, Oct. 1983 Acc. No. 252566.

A. Procedure

The test material (0.5 ml) was applied under a 2.5 cm^2 gauze pad over the intact skin of six New Zealand White rabbits. The area was occluded for four hours after which the dressing was removed. The test site was washed and graded for irritation by Draize.

B. Results

Well defined erythema 6/6 and slight edema (6/6) was observed, clearing by day 10 accompanied by desquamation.

C. Conclusion

1. Material was a slight dermal irritant.

2. Classification of Data - Guideline.

3. Toxicity Category - III.

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