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

004921

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: FMC 54800

TO: Mr. George LaRocca, PM 15
Registration Division (TS-767)

FROM: Byron T. Backus *Byron T. Backus*
Toxicology Branch *01-21-86*
HED (TS-769)

THROUGH: Clint Skinner, Ph.D. *Clint Skinner*
Head, Section III *1-22-86*
and
Theodore Farber, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769) *H/WB 2/5/86*

Compound: TALSTAR Registrant: FMC Corp.

Registration #279-3055 Tox. Chem. #463F

Accession # 260178

Project No. 1030

Action:

The Registration Division has requested review and comment on the registrant's response to a previous toxicology review of three studies (21-day dermal application, rabbit; 13-week dog feeding; and rat teratology).

Background:

In a previous Toxicology Branch review (B. Backus, 06/11/85) several studies were classified as supplementary or invalid. The registrant has now responded with additional information and clarifications regarding some of these studies. These include the following:

1. In the 21-day repeated dose dermal toxicity study (no. A83-1041; Feb. 24, 1985) mean liver weights are recalculated, both as originally reported and without "errant values," as are brain weights. In each case there was no statistically significant difference with respect to control values.

[Handwritten initials]

Additionally, it is noted (as part of the cover letter) that the tremors observed in one 100 mg/kg/day animal occurred as a result of the subject losing a collar, and subsequently ingesting some of the test material.

Microscopic evaluation of cross and longitudinal sections of sciatic nerves from control and high-dose (500 mg/kg/day) rabbits failed to reveal any compound-related histomorphologic alterations.

2. With respect to the previously reviewed 13-week sub-chronic oral feeding study in dogs (project 104-217) a letter has been submitted from Hazleton Laboratories America Inc. giving the rationale for calling tremors observed in one male dog as unrelated to treatment, on the basis that they were of the type of slight spontaneous trembling occasionally observed in laboratory dogs. This is a satisfactory explanation.
3. A pilot teratology study conducted in rats has been submitted to demonstrate that 2.0 mg/kg/day is an MTD in this species for this type of study.

Comments and Conclusions:

1. With the information received 10-03-85 the classifications of the previously reviewed rat teratology, 13-week dog feeding and 21-day rabbit dermal studies have been upgraded to the following:

Rat teratology: Core Guideline
13-week dog feeding: Core Minimum
21-day rabbit dermal: Core Minimum

Additionally, the range-finding rat teratology study received 10-03-85 has been classified as Core Supplementary Data.

2. On the basis of the additional information provided in the range-finding teratology study, 2.0 mg/kg/day FMC 54800 is an MTD in the pregnant Sprague-Dawley rat.
3. The NOEL in the 13-week dog feeding study is an NOEL.
4. The NOEL in the 21-day rabbit repeat application dermal study is 100 mg/kg/day.

Data Evaluation Report

Freeman, C., DeProspero, J. R., Madasky, N., and Fletcher, M. J. Pilot Teratology Study in Rats with FMC 54800, Technical. Study No. A83-975. Dated 12-27-83. Study conducted by the FMC Toxicology Laboratory, 76 Fourth St., Somerville, NJ. Received at EPA 10-03-85; in Acc. 260178.

Data Evaluation Report I

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Compound:

FMC 54800, TALSTAR, Biphenthrin, Bifenthrin

Citation:

Freeman, C., DeProspero, J. R., Nadasky, N., and Fletcher, M. J. Pilot Teratology Study in Rats with FMC 54800, Technical. Study No. A83-975. Dated 12-27-83. Study conducted by the FMC Toxicology Laboratory, 76 Fourth St., Somerville, NJ. Received at EPA 10-03-85; in Acc. 260178.

Reviewed by:

Byron T. Backus
Toxicologist

Byron T. Backus
06-21-86

Approved by:

Clint Skinner, Ph.D.
Section Head
Section 3
Toxicology Branch

Core Classification: Supplementary (by itself)

Conclusions:

1. Although the study is classified as supplementary, it establishes 2.0 mg/kg/day of the test material as an MTD in the pregnant Sprague-Dawley rat.
2. With the information contained in this study, the classification of the previously reported (B. Backus, 06-11-85) rat teratology study (study no. A83-091, dated February 24, 1984) has been upgraded to Core Guideline.

Materials:

Sprague-Dawley rats, from Macdonic Farms.

Test material: FMC 54800 Technical, lot no. E2392-105; purity 88.3%.
Composition 98% Cis/2% trans isomer.

Vehicle: Mazola corn oil.

Procedure:

Groups of 10 mated females received either corn oil (vehicle control) or the test material at dosages of 0.5, 1.0, 2.0 or 2.5 mg/kg a day during days 6-15 of gestation. Dosage volume was kept constant at 5.0 ml/kg. From the reporting, it is evident that initially the dosages were 1.0, 2.5, 5.0 and 10.0 mg/kg/day, but on day 8 of the study several rats in the two

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highest dose level groups died. As a result these levels were terminated and replaced with 0. and 2.0 mg/kg/day.

The rats were observed twice daily for mortality and signs of toxicity. Individual body weights were taken on days 0, daily from day 6-15, and then on day 20. Individual food consumption was calculated on a weekly basis.

On day 20 of gestation the rats were sacrificed by CO₂ asphyxiation, their abdomens were opened, and their uteri were exposed. The dams were examined for gross lesions, and their carcasses were discarded. The number and distribution of implantation sites, early and late resorptions, live and dead fetuses, and corpora lutea were recorded. As this was a pilot study, no gross necropsies, soft tissue or skeletal examinations were performed on any of the fetuses.

"Statistical analyses were not performed as a result of the limited number of animals available for evaluation in each group."

Results:

Three rats (out of 10) died at the 2.5 mg/kg/day dose level on days 14-15; one rat which died on day 15 was not pregnant. Additionally, all rats receiving 2.5 mg/kg/day exhibited sporadic tremors; 9/10 rats in the 2.0 mg/kg/day group also had sporadic tremors during the period from day 7 through 18. One of these rats also developed ocular opacity, "became unthrifty and had abdominogenital staining." One rat in the 1.0 mg/kg/day group had unthriftiness, abdominogenital staining and dyspnea between days 14 and 17. There were no evident possible symptoms in the 0.5 mg/kg/day group. One control rat became "unthrifty" and developed rales between days 14 and 17.

Females in the 2.5 mg/kg/day group had somewhat less (roughly 20%) mean food consumption than their controls in the period from day 6-13, although it is doubtful that this was statistically significant. Mean body weight gains appeared somewhat depressed in the 2.5 mg/kg/day group, both for days 6-15 and days 0-20. No evident differences were observed for the lower dose groups with respect to control values.

At least 9/10 of the rats in each group were pregnant. The number of implantations and litter sizes were essentially the same in each of the groups. The mean number of resorptions was similar in the 0, 0.5, 1.0 and 2.0 mg/kg/day groups; for the 2.5 mg/kg/day group it was somewhat higher, but this was attributable to an excessive number of resorptions in a single rat.

Discussion:

The principal finding of this study is that, because of 30% mortality occurring at the 2.5 mg/kg/day dose level, the Sprague-Dawley pregnant rat MTD is established at 2.0 mg/kg/day. It was obviously not the intention of the registrant that this be a definitive rat teratology study, and the lack of fetal evaluations precludes any classification other than Core Supplementary Data for this study.

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