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HEALTH EFFECTS DIVISION  
SCIENTIFIC DATA REVIEWS  
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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

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OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

JAN 30 1986

MEMORANDUM

SUBJECT: FMC 54800

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

FROM: Byron T. Backus *Byron T. Backus*  
Toxicology Branch *01/28/86*  
HED (TS-769)

THROUGH: Clint Skinner, Ph.D. *ackat 1/28/86*  
Head, Section III *for CS*  
and *HFA W/TS 1/30/86*  
Theodore Farber, Ph.D.  
Chief, Toxicology Branch  
Hazard Evaluation Division (TS-769)

Compound: TALSTAR, Bifenthrin, Biphenthrin, FMC 54800

Registrant: FMC Corp.

Registration #279-3055, 279-3056, 279-3057

Accession # 260700 Tox. Chem. #463F

Project No. 1103

Action:

The Registration Division has requested the review of some data submitted under 6(a)(2) on the subject chemical.

Background:

The registrant has submitted preliminary findings from a mouse chronic feeding & oncogenicity study conducted with FMC 54800. The data indicate a dose-related increased incidence of leiomyosarcomas occurs in the urinary bladders of male mice. Although this increase is statistically significant ( $p < 0.01$  by Fisher's exact test) only at the HDT (600 ppm), there is what appears to be a trend with increasing exposure, and even male mice at the lowest dietary level (50 ppm) of FMC 54800 showed a greater incidence of tumors of this type than did their controls.

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Additionally, there was an increased incidence of combined adenomas and carcinomas of the lung in all the female groups receiving FMC 54800 relative to their controls.

Comments and Recommendations:

1. Before any temporary or permanent tolerances are considered for this active ingredient, it will be necessary for a risk assessment to be done based on the complete data from this study.
2. One of the major concerns at this time is that the increased incidence of leiomyosarcomas in the urinary bladders occurred in all male groups (although the increase was statistically significant only for males at the HDT) receiving FMC 54800, and did so in a dose-related fashion.
3. The incidence data are tentative in that slides from the bladders have not yet been prepared from many of the mice in the 50, 200 and 500 ppm levels.
4. This reviewer tends to agree that the "statistically significant" increased incidence of combined adenomas/carcinomas of the lungs of female mice is probably a result of a lower than normal number of occurrences in controls, particularly as no dose-related trend is evident, and incidences in exposed females are essentially the same as those in males. Submission of historical control data on this point seems to be appropriate.

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Data Evaluation Report

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Compound:

FMC 54800 (Biphenthrin, Bifenthrin, Talstar)

Study type:

Oncogenicity - mouse: 6(a)(2) data

Reviewed by:

Byron T. Backus  
Toxicologist  
Toxicology Branch

*Byron T. Backus  
6/22/80*

Approved by:

Clint Skinner, Ph.D.  
Section Head  
Review Section III  
Toxicology Branch

Core Classification: Supplementary

Toxicity Category: N/A

Background:

This submission (in Acc. 260700) consists of 3 pages summarizing the findings of increased incidences of leiomyosarcomas in bladders of male mice which had received FMC 54800 at doses of 50, 200, 500 and 600 ppm. Some of the incidence values for some of the dose levels must be considered tentative, because slides had not been prepared from bladder tissues of all males.

Additionally, females exposed to FMC 54800 had an increased incidence of combined adenomas/carcinomas of the lungs relative to their control group.

Conclusions:

1. From the data as presented the increased incidence of leiomyosarcomas in the urinary bladders of male mice occurred in all male groups (although the increase was statistically significant only for males at the HDT) receiving FMC 54800. The increased incidence of this type of tumor in these male mice must be considered as an effect of dietary exposure to the test material.
2. The incidence data are tentative in that slides from the bladders have not yet been prepared from many of the mice of the 50, 200 and 500 ppm levels.

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3. This reviewer agrees that the "statistically significant" increased incidence of combined adenomas/carcinomas of the lungs of female mice is probably a result of a lower than normal number of occurrences in controls, particularly as no dose-related trend is evident, and incidences in exposed females are essentially the same as those in males. Submission of historical control data on this point is appropriate.

Discussion:

Basically what are presented in this submission (p. 3) are the following incidence tables:

TABLE 1

Incidence of Leiomyosarcomas in Mouse Urinary Bladder

<u>Group</u>	<u>FMC 54800 Feeding Level (ppm)</u>	<u>Males</u>	<u>Females</u>
1	0	2/48 (4%)	1/49 (2%)
2	50	4/36 (11%)	1/37 (3%)
3	200	4/31 (13%)	2/34 (6%)
4	500	6/42 (14%)	0/26 (0%)
5	600	14/50 (28%) <sup>††</sup>	0/49 (0%)

--- <sup>††</sup>p < 0.01 by Fisher's exact test

TABLE 2

Incidence of Combined Adenomas/Carcinomas in Mouse <sup>Lungs</sup> ~~Urinary Bladder~~

<u>Group</u>	<u>FMC 54800 Feeding Level (ppm)</u>	<u>Males</u>	<u>Females</u>
1	0	25/49 (51%)	14/49 (29%)
2	50	27/50 (54%)	26/50 (52%) <sup>†</sup>
3	200	25/50 (50%)	23/50 (46%)
4	500	18/50 (36%)	19/50 (38%)
5	600	21/50 (42%)	23/49 (47%) <sup>†</sup>

<sup>†</sup> p < 0.05 by Fisher's exact test

Some of the bladder incidence data must be considered tentative, as slides have not been prepared from all animals in the 50, 200 or 500 ppm groups. All males exposed to the FMC 54800 showed an increased incidence in bladder leiomyosarcomas, although only at the HDT (600 ppm) was there a statistically significant increased incidence of this tumor type relative to their controls.

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The dramatic (and statistically significant) increased incidence of leiomyosarcomas of the bladder in male mice at 600 ppm indicate that FMC 54800 must be considered as oncogenic. Another factor is that this is apparently a fairly unusual tumor type.

There is no consistent dose-related trend of increase in the incidence data for the combined adenomas/carcinomas in mouse lungs for females. What appears to have occurred here is that the female control group had a lower than usual incidence of these tumors. This possibility is discussed on p. 2 of the submission.