7.29.88

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

JUL 29 1988

MEMORANDUM

SUBJECT: EPA File Symbol 773-LL
Clinafarm EC

FROM: Mary L. Waller
Precautionary Review Section
Fungicide-Herbicide Branch
Registration Division (TS-767C)

TO: Lois A. Rossi, PM 21
Fungicide-Herbicide Branch
Registration Division (TS-767C)

APPLICANT: Pitman-Moore, Inc.
ATTN: Regulatory Affairs
P.O. Box 344
Washington Crossing, NJ 08560

ACTIVE INGREDIENT:

Imazalil: 1-(2-(2,4-dichlorophenyl)-2-(2-propenyloxy)ethyl)-1H-imidazole	13.76%
INERT INGREDIENTS:	86.24%

BACKGROUND:

The registrant has cited an acute oral, acute dermal, primary eye irritation and primary skin irritation study conducted on 773-EUP-2 and reviewed by HED on 11-20-85. The registrant has also questioned the FHB/PRS review of 3-11-88. The registrant has also cited an acute inhalation toxicity study (acc. no. 258173) and a dermal sensitization study (acc. no. 072250) in support of 773-LL. The method of support was not indicated.

RECOMMENDATIONS:

RSB/PRS findings are:

1. The primary eye irritation study conducted by Janseen Pharmaceutica, experiment number 1675 of 5-12-83 which was submitted in support of 773-LL was correctly found unacceptable and was classified as supplementary data. The registrant should be informed that this was not the same study submitted in support of 773-EUP-2. This study was experiment number 1291 conducted on 6-30-83 by Janseen Pharmaceutica.

2. The data submitted in support of 773-EUP-2 and reviewed by HED on 11-20-85 can be used to support 773-LL. The HED review classified the studies as core minimum data and assigned the following categories: acute oral (category III), acute dermal (category III), primary eye irritation (category I) and primary skin irritation study (category IV).

3. The acute inhalation toxicity study and dermal sensitization study were found unacceptable and were classified as supplementary. In addition, the product tested (R23979) is not considered substantially similar to 773-LL. Therefore, the registrant must submit another acute inhalation toxicity study and dermal sensitization study conducted on 773-LL.

   These studies were classified as supplementary for the following reasons:

   a. Acute Inhalation Toxicity Study

      It is not clearly specified whether the actual or nominal concentration was reported. The characterization of the particle size of the test atmosphere is not specific enough. Results of each atmosphere sample analysed by UV spectrophotometry should have been identified.

   b. Dermal Sensitization Study

      The test was identified as the Optimization Test; however, the methods used differ from the Optimization Test methods as identified by T. Maurer. FCA was not used in 2nd and 3rd week of induction phase, no positive control group treated, and second epidermal challenge was not performed.

4. The signal word is "DANGER" based on the primary eye irritation study.

LABELING:

1. Revise Statements of Practical Treatment as follows:

> **IF IN EYES:** Flush with plenty of water. Call a physician.
>
> **IF SWALLOWED:** Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person.
>
> **IF ON SKIN:** Wash with plenty of soap and water. Get medical attention.
>
> **IF INHALED:** Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth to mouth. Get medical attention.

2. Revise precautionary statements as follows:

> Causes irreversible eye damage. Harmful or fatal if swallowed. Harmful if absorbed through skin. Do not get in eyes or on clothing. Avoid contact with skin. Wear goggles, face shield or safety glasses. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse.

REVIEW:

(1) Acute Inhalation Toxicity Study: Central Institute For Food and Research; Report no. 4806; Data accession no. 258173; 10-75.

PROCEDURE:

Five male and five female Sprague-Dawley rats were exposed for 4 hours in a 1.5 m^3 stainless steel/glass exposure chamber to a fine mist generated from the test material. The highest concentration was 16 g/m^3. Animals were observed for 14 days and necropsied at study conclusion.

RESULTS:

No deaths occurred. Animals exhibited immobility and slight stupor during exposure. No abnormalities were noted at necropsy.

STUDY CLASSIFICATION:

Supplementary - See comments under Recommendation.

(2) Dermal Sensitization Study: Optimization Test; Janseen Pharmaceutica Research Laboratories; Exp. 965; Data accession number 072250; 8-27-80.

PROCEDURE:

Two groups of twenty Pirbright guinea pigs were clipped free of hair from the trunk to the flank. During the induction phase, the test group was administered an initial intradermal injection of 0.05 ml of 68% w/w dilution of test material in arachid oil. The control group was administered an intradermal injection of 0.05 ml of arachid oil. Beginning two days later, each group was administered intradermal injections of 0.1 ml three times weekly on alternate days for three weeks. Five of the injections were administered in the left anterior flank and five in the right flank. Each injection was made at a new site. Two weeks after the last injection, each group was challenged with 0.1 ml of the respective material. Skin reaction volume was calculated for each animal at 24 hours after each treatment. Threshold value for each animal was calculated after the first four injections.

RESULTS:

Reaction volume after each treatment and threshold value for each animal in both the test and control group was zero. Reaction volume at challenge for both groups was zero.

STUDY CLASSIFICATION:

Supplementary - See comments under Recommendation.