1-9-89

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

JAN 9 1989

SUBJECT: EPA File Symbol 773-LL
Clinafarm EC 15%

FROM: Mary L. Waller Mary Waller 1/9/89 E 1/9/89
Precautionary Review Section
Registration Support Branch
Registration Division (TS-767)

TO: Larry Schnaubelt, Acting PM 21
Fungicide-Herbicide Branch
Registration Division (TS-767)

APPLICANT: Pitman-Moore, Inc.
Attn: Regulatory Affairs & QA
P.O. BOX 207
Terre Haute, IN 47808 08560

773-LL

Active Ingredient:
Imazalil: 1-(2-(2,4-dichlorophenyl)-2-(2-propenyloxy) ethyl)-1H-imidazole 13.76%
Inert Ingredients: 86.24%

BACKGROUND:

The applicant has submitted a protocol for an acute inhalation toxicity study and a protocol for a dermal sensitization study. These protocols were discussed with Mr. Robert S. Baldwin of Pitman-Moore, Inc. in a telephone conversation on 1/5/88.

RECOMMENDATION:

RSB finds the protocols acceptable with the following revisions and/or clarifications.

The protocol for the acute inhalation toxicity study should state the following:

1. List the starting date and completion dates rather than proposed starting and completion dates.

2. Females selected for the study will be nulliparous and nonpregnant.

3. Test animals will not exceed 5% of the volume of the test chamber.

4. If a solvent or vehicle is used, it will not elicit important toxic effects itself or substantially alter the chemical or toxicological properties of the test substance.

5. Appropriate additional time will be allowed for chamber equallibrium prior to exposure of animals.

6. Actual concentrations of the test material will be determined from chamber atmosphere samples taken from the breathing zone of the animals.

7. Particle size analysis will be conducted frequently enough during test animals' exposure to adequately characterize the aerosols to which the animals are exposed.

8. If the particle size of the test material, as provided by the sponsor, is such that respirable particles cannot be generated during the study, then the test material particles will be reduced in size to increase respirability.

Ideally, the median diameter usually used in rodent studies is around 1.0 micrometer with geometric standard deviations of approximately 2.5 or less. For additional discussion, see the attached excerpt from the Hazard Evaluation Division's Standard Evaluation Procedure for Inhalation Toxicity Testing.

The protocol for the dermal sensitization study should be revised to include the following points as clarified by Mr. Baldwin and other requested revisions:

1. Mr. Baldwin stated that the test method which will be used is a modification of the Buehler method.

2. The protocol should list starting and completion dates rather than proposed starting and completion dates.

3. Mr. Baldwin stated that the first negative control group which will be treated with 0.9% NaCl will be challenged twice, first challenge will use 0.9% NaCl and the second challenge will use all the materials as specified in the protocol. He also stated that the 0.9% NaCl will serve as the vehicle in which the test material (product as formulated) will be dissolved.

4. The protocol identifies a second negative control group which will be induced with the vehicle. Mr. Baldwin stated that the term "vehicle" in this case, refers to the finished product less the active ingredient. I have informed him that for our purposes this group is unnecessary but if Pitman-Moore wishes to include this group for their information I have no objections to this.

5. Preliminary skin test should be conducted to determine the concentration producing minimal irritation (concentration for induction) and the maximum nonirritating concentration (concentration for challenge). If the company has data on the formulated product which identifies these concentrations, then inclusion of of this data with the final report will be sufficient.

6. The exposure period should be 6 hours. After exposure, the patch or cotton gauze should be removed and the test site washed with warm water.

7. The protocol should specify that the final report will include individual induction scores for each animal after each induction treatment and individual challenge scores for each animal. The protocol should also state that the final report will provide initial and terminal body weights for each animal.

8. The protocol should specify that the study will be conducted in accordance with the specific GLP (Good Laboratory Practice Standards as outlined in 40 CFR Part 160) in addition, to any other in-house GLP which the laboratory may be using.

9. The protocol states that it may be changed as the study progresses. It should be noted that significant changes, if deemed by the Agency to adversely affect the quality of the data, may result in rejection of the particular study.