9-10-90

PHASE FOUR REVIEW

(NOTE: This only contains additions and changes from the phase 2 response)

Pesticide: Octhilinone — Chem.#/Case#: 099901/ 2475
Transmitted to HED on 8/17/90
Tox. Chem.#: 613C
Sponsor: Rohm and Haas
CRM: Frank Rubis — Phone #: 308-8184

Branch: Toxicology I, Section II — Reviewer: M. Morrow D.V.M. MSM 8/31/90
Completed: _____ — Concurrence: [signature] 9/10/90

Response by Guideline

Guideline #: 81-1 — Description: Acute oral/rat
MRID #: 414825-02, Study # 86R178
Discussion/ Recommendation: Based on a preliminary assessment, the study was conducted using a 46.7% formulation. This concentration can not be substituted for the technical concentration.

Guideline #: 81-3 — Description: Acute inh/ rat
MRID: 414825-03, Study #: 85R-203
Discussion/ Recommendation: Based on a cursory review, this study is not acceptable at this time, but may be upgraded by the submission of an additional study. In their cover letter, the sponsor states that a subchronic 90 day inhalation study has been filed to support the waiver for the technical grade active ingredient; however, this report is not included with the other reports filed in phase 3.X

Guideline #: 81-5 — Description: 1° Derm. Irr/ rabbit
MRID # 414825-04, Study #: 84R-0189
Discussion/ Recommendation: This study is tentatively acceptable. The technical form of the active ingredient was substituted with a 46.7% solution and the application site was examined through day 7. Animals were not observed for the entire day of dosing, but rather at intervals immediately following dosing, at 4 hours post dosing and 1 hour after the patch was removed. Additionally, animals were observed by the investigator at 1, 2, 4, 48 and 72 hours and on day 7. Technicians conducted daily observations for mortality. These deviations from the guidelines should not affect the outcome of the study. Furthermore it was demonstrated that the 46.7% solution is corrosive which leads to a waiver of 81-2 (acute dermal toxicity) and 81-4 (primary eye irritation). A DER will be completed at a later date.

X 2/15/91 Per Marion Copley, marks 81-3 reserved pending submission + review of the subchronic 90-day inhalation study (85-4).

13C

Guideline #: 81-6 Description: Dermal sens./Guinea pig
a.) MRID #: 414825-05, Study #: 83R-143
b.) MRID #: 414825-06, Study #: 85R-019
c.) MRID #: 414825-07, Study #: 85R-025

Discussion/ Recommendation: Three sensitization studies have submitted. A cursory review reveals that study (b) is tentatively acceptable. The other two studies failed to include a positive control and are therefore unacceptable. A DER will be completed at a later date.

Guideline #: 82-3 Description: Repeat dose dermal tox.(90d)
Discussion/ Recommendation: The sponsor indicated that this study would be submitted in phase 3; however, it has been omitted. No reference is made to this study in the cover letter of May 9, 1990. A request should be made for this study.

Guideline #: 82-4 Description: 90 day inh./ rat
MRID #: not available, Study#: 87R-013
Discussion/ Recommendation: In their cover letter, the sponsor has identified this study as being a part of the submission; however, it has not been included (i.e. sent to HED). This study was to be used to support the waiver request for the acute inhalation study on the TGAI. A request should be made to RD for this study.

Guideline #: 83-3(a) Description: Teratology/ rat
MRID #: 414825-08, Study#: 87RC-0009
Discussion/ Recommendation: Based on a cursory review of the information provided, the study is tentatively acceptable for review. The sponsor has used the ~~47.6%~~ 43% active ingredient formulation and conducted a full analysis of the homogeneity, stability and concentration in the developmental toxicity study conducted in rabbits (83-3b). A DER will be completed at a later date. The use of the 43%~~47.6%~~ formulation in lieu of the technical would not necessitate repeating the study.

Guideline #: 83-3(b) Description: Develop. Tox/ rabbit
MRID #: 414825-09, Study #: 87R-019
Discussion/Recommendation: Based on a preliminary assessment, the study is tentatively acceptable for review. A DER will be conducted at a later date. The study used a 46.3% formulation but this would not be serious enough to invalidate the study.

Guideline #: 84-2 Description: Salm. typhim. gene mut. assay
MRID #: 414825-10, Study #: 88R-203

Discussion/ Recommendation: Based on a cursory assessment, the study is tentatively acceptable for review. A DER will be conducted at a later date.