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

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AUG 9 1991

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Kathon 886F Microbicide (EPA Reg. No. 707-130); Commitment to Perform Studies; Clarification of Discrepancies in Test Material Purity

TO: Jim Wilson/John Lee
Product Manager (31)
Registration Division (H7505C)

FROM: Linda L. Taylor, Ph.D. Linda Lee Taylor 8/1/91
Toxicology Branch II, Section II,
Health Effects Division (H7509C)

THRU: K. Clark Swentzel K. Clark Swentzel 8/1/91
Section II Head, Toxicology Branch II
Health Effects Division (H7509C)

and

Marcia van Gemert, Ph.D. Marcia van Gemert 8/1/91
Chief, Toxicology Branch II/HFAS/HED (H7509C)

Registrant:	Rohm & Haas Company
Chemical:	5-chloro-2-methyl-4-isothiazolin-3-one (I) and 2-methyl-4-isothiazolin-3-one (II)
Synonym:	Kathon 886F Microbicide
Project No.:	1-1314
Caswell No.:	195C
Record No.:	not provided; Case#: 282475; Submission#: S396327
Identifying No.:	707-130/282475
MRID No.:	N/A
Action Requested:	Review letter; please return the Jacket 707-166 when review is complete.

Comment: The Registrant's letter (dated April 24, 1991) is in response to the Agency's letter of March 26, 1991 regarding the status of study requirements under the Antimicrobial Data Call-In.

1. Chronic Toxicity/Carcinogenicity Study - The Registrant has committed to submit a 2-year study (species not identified) to support a waiver request for a 90-day study, a request addressed previously by TB II (TB II memo dated 3/19/91). With regard to this study, the Registrant requested a meeting to discuss dose

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selection.

2. Rabbit Developmental Toxicity Study - The Registrant has committed to perform a repeat teratology study in the rabbit and has indicated that since Kathon 886F Microbicide is known to cause a concentration-dependent irritation effect on the gastric mucosa, a modified range of dose levels will be utilized. The estimated time for submission of the study to the Agency is August 1, 1992.

3. Rat Teratology Study - Further clarification regarding the percent of active ingredient utilized in this study was provided, and although no reason can be provided for the submission of an abstract/summary with an inaccurate purity listed for the test material, it can be concluded that the purity of the test material used in the study was 14%. This study can be upgraded to Core Minimum, and it satisfies the guideline requirement (83-3) for a rat developmental toxicity study.

4. Mutagenicity Studies - The Registrant indicated that an in vivo cytogenetic assay and an unscheduled DNA synthesis assay would be submitted to the Agency by May 15, 1991, which would complete their Tier 1 genotoxicity requirements. NOTE: These latter 2 studies have been submitted and were reviewed under HED Project # 1-1292.

DISCUSSION

On several occasions, TB II has requested that the Registrant address the specific discrepancies in composition of Kathon 886F Microbicide used in the various toxicity studies; namely the use of active ingredient (5-chloro-2-methyl-4-isothiazolin-3-one; I) levels greater than the established certified limits (8.6 to 12.1%) and total active ingredient levels above the level considered stable (13.1%). The file containing additional information to explain the differing percentages of a.i. has been reviewed, as requested by the Registrant. Although it does not specifically address the issue of testing a test material whose total % a.i. is above that stated to be stable or that the ratio of the 2 a.i. components [I/II] is greater than 3:1, in all cases the test material characteristics (total % a.i. and % of individual a.i.'s) have been greater than the % specified for this product. Given the fact that the product itself meets the certified limits/specifications, testing with a test material having higher % of a.i. is acceptable as long as the stability of the test material under the experimental conditions is known.

CONCLUSION

The Registrant has committed to perform a 2-year chronic toxicity/carcinogenicity study and a rabbit developmental toxicity study with Kathon 886F Microbicide. A request was made for a meeting to discuss the selection of dose levels to be used in the 2-year study, which TB II will attend (when scheduled). The rat teratology study can be upgraded to Core Minimum.

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