1-8-92

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

JAN 8 1992

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Kathon 886 MW Microbiocide: Rebuttal of Agency's Review of Chromosome Aberration Study

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

FROM: Linda L. Taylor, Ph.D. Linda Lee Taylor 1/2/92
Toxicology Branch II, Section II,
Health Effects Division (H7509C)

THRU: K. Clark Swentzel K. Clark Swentzel 1/2/92
Section II Head, Toxicology Branch II
Health Effects Division (H7509C)

and

Marcia van Gemert, Ph.D. concurrence 1/7/92
Chief, Toxicology Branch II/HFAS/HED (H7509C)

Registrant: Rohm & Haas Company
Chemical: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one
Synonym: Kathon 886 MW Microbiocide
Project No.: 2-0205
Caswell No.: 195C
Record No.: none; Case: 022081; Submission: S405297
DP Barcode: D170043
Identifying No.: 000707-00130
MRID No.: relates to 418755-01
Action Requested: Please review rebuttal of the chromosomal aberration study.

Comment: The Registrant has submitted a rebuttal of the Agency's review of the chromosomal aberration study (DER dated 7/29/91) on Kathon 886 MW Microbiocide. It was concluded by TB II that the study did not meet Agency guideline requirements since less than 50% of the high-dose females survived to study termination and none of the high-dose animals were scored for the induction of chromosome aberration.

The Registrant contends that the rejection of the study is inappropriate based on the following:

1) The criteria for selecting the highest dose for the Chromosome Aberration Study (CAS): If possible, the highest dose level in the range-finding study that results in no deaths and/or up to a 10% loss of body weight or clinical symptoms of toxicity is selected as the highest dose in the CAS. TB II notes that, since the lowest dose (45 mg/kg) tested in the range-finding study resulted in the deaths of 50% of the males and females, there was insufficient information with which to determine a dose where no deaths would occur. The dose chosen for the CAS was 40 mg/kg.

2) In the CAS, 3 out of 7 males and 2 out of 7 females at the highest dose level displayed clinical symptoms of sickness at 24 hours post-treatment, and at 48 hours 2 of the males and 4 of the females died. Additionally, 3 of 5 males and 3 of 5 females in the additional 40 mg/kg group used for body-weight and clinical signs measurements died. Since, according to the protocol criteria, this dose was too toxic, the Registrant selected the next lower dose (20 mg/kg) as the highest dose for the study. The Registrant concludes that, since there was no dose between 20 and 40 mg/kg for scoring, the selection was appropriate. Additionally, from their experience, a chemical need not be tested at such a highly toxic dose to determine its genotoxicity.

TB II reiterates that all of the high-dose males and females scheduled for the 6- and 24-hour sacrifices survived to these times but were not scored, and those surviving to the 48-hour sacrifice also were not scored. It is acknowledged that severely toxic dose levels are not required for testing for chromosome aberration; however, the animals surviving to the 6- and 24-hour sacrifices did not display any clinical signs of toxicity. If the 40 mg/kg group had been scored at the 6- and 24-hour sacrifices, arguments regarding toxicity could have been used to interpret the results.

CONCLUSION

The arguments presented by the Registrant do not alter TB II's conclusions regarding the study.

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