

US EPA ARCHIVE DOCUMENT

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JAN 4 1990



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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WASHINGTON, DC 20460

JAN 4 1990

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: CHLORPYRIFOS (PYRINEX): Makhteshim-Agan (America) Inc.; Rat Inhalation Study, Agency Reply to Registrant's Response; Toxicology Requirements for "Crack and Crevice" Application.

Tox. Chemical No.: 219AA
HED Project No.: 9-2003
MRID No.: 409084-01 (Inhalation Study)

FROM: Alan C. Levy, Ph. D., Toxicologist *Alan C. Levy 12/11/89*
Review Section I, Toxicology Branch II (HFAS)
Health Effects Division (H7509C)

TO: Dennis H. Edwards, Jr. PM # 12
Registration Division (H7505C)

THROUGH: Yiannakis M. Ioannou, Ph. D., Section Head *Y. Ioannou 12/11/89*
Review Section I, Toxicology Branch II (HFAS)
Health Effects Division (H7509C)

and

Marcia van Gemert, Ph. D., Branch Chief *M. van Gemert 12/18/89*
Toxicology Branch II (HFAS)
Health Effects Division (H7509C)

Registrant: Makhteshim-Agan (America) Inc.
New York, NY

Action Requested: Reply to the Registrant's response regarding the thirteen week nose-only inhalation toxicity study of Chlorpyrifos Technical (Pyrinex) in the rat. Comment on the requirement of chronic toxicity studies for "crack and crevice" application.

RECOMMENDATION

1. Registrant's Response Regarding Inhalation Study:

A. Vapor versus Aerosol

Agency Request - The Registrant had submitted the study

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with the test article being administered as a vapor. The study was rejected because the test article was not administered as an aerosol.

Registrant's Response - A letter from A. Eimanis of Makhteshim-Agan (America) Inc. to Dennis H. Edwards, Jr. of EPA, 8/16/89 (a copy is attached) explained the reasons for the use of vapor versus aerosol.

Agency's Reply - The Registrant's Response was reviewed by the Health Effects Division (HED). [A copy of comments by Stanley B. Gross, 10/16/89, is attached.] HED concluded that the inhalation rat study with administration of the test article as a vapor would be acceptable.

B. Inconsistencies in Number of Rats that Died Accidentally/Were Killed at Termination/Died Spontaneously

Agency's Request - Within the report, there were inconsistencies regarding the cause of death of a number of the rats. The Registrant was requested to comment on these.

Registrant's Response - The letter referred to above (Eimanis to Edwards, 8/16/89, copy attached) explains the inconsistencies.

Agency's Reply - The Registrant's explanation is accepted.

AGENCY RECOMMENDATION: The inhalation rat study should be upgraded from Core Supplementary to Core Minimum (satisfies data requirements).

2. Requirement of Chronic Toxicity Studies for "Crack and Crevice" Application

The Health Effects Division (HED) feels that the chronic dog, chronic rat, oncogenic rat, oncogenic mouse, reproduction rat, and rat metabolism studies are not necessary in support of the registration of a chemical for "crack and crevice" application unless exposure data and data from subchronic studies necessitate the requirement of such studies.

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CONSULTATION NOTE.

SUBJECT: Chlorpyrifos Technical: Makhteshim-Agan Pyrinex,
EPA #11678-UL: Subchronic inhalation toxicity study.
MRID No. 40908401. Caswell No. 219AA.

TO: Yiannakis M. Ioannou, PhD
Toxicology Branch (H7509C)

FROM: Stanley B. Gross, PhD
Toxicology Branch (H7509C)

cc: Marion Copley, (Tox)
Dennis Edwards (RD)

Makhteshim-Agan (America) Inc. submitted a subchronic inhalation toxicity study using technical Pyrinex (chlorpyrifos) in its vapor form. The study was rejected by Toxicology Branch (July 13, 1989 memorandum by Alan Levy to Dennis Edwards) because it was not tested as an aerosol. An aerosol study would simulate applicator exposure while a vapor study would simulate reentry exposure. It was not clear from the previous submission which exposure was of concern. The label provided was for reformulating the technical material only.

In talking to the company (phone call to Dr. Elliott Gordon, 10/12/89), Dr. Gordon said the company was following the requirements specified by Stephen Saunders in his memo of August 18, 1986 to Larry Schnaubelt. Dennis Edwards noted to me that the Saunderson's requirements were those required for Dow's Dursban as a termiticide (non-food indoor domestic use); however, Pyrinex is to be applied as a crack and crevice spray (undated note by Dennis Edwards to Tox Reviewer).

Recommendations.

1) A subchronic inhalation study Pyrinex is not required based on a crack and crevice application UNLESS there are volatile and persistent inerts in the end-use product. A CSF for an end-use product was not provided.

2) If the company plans to use Pyrinex as a termiticide, as noted by Dennis Edwards' note, an inhalation test using a vapor form would be in order. However, we may need an exposure assessment for the end-use application (indoor home exposures) depending on the inerts, etc.)

clpyrfs.cns SBG 10/16/1989

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