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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Methyl isothiocyanate (MITC): Review of Interim Risk Assessment for MITC by the Department of Pesticide Regulation, State of California.

PCCODE
Shaugnessey: 039003

Submission: N/A

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Registrant: N/A

Action Requested: Review and comment on the interim risk assessment conducted for MITC by the Department of Pesticide Regulation, State of California.



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Summary:

Toxicology Branch II received a request from the Chemical Coordination Branch to comment on a recently conducted interim risk assessment for MITC, an environmental decomposition product of metam sodium (June 9, 1994 document from Larry L. Nelson, Chief, Medical Toxicology Branch to Ronald J. Oshima, Assistant Director, California Department of Environmental Protection). The interim risk assessment included summaries of the available Toxicology data on MITC. These data included both submitted studies as well as literature reports.

Of all the studies reported, the study demonstrating toxic effects at the lowest exposure concentrations of MITC was a study conducted by Nesterova in 1969 (Hygiene and Sanitation USSR 34: 191-196 [translation of Gig. Sanit. 34: 33-37]), in which cats were exposed to MITC vapors by the application of carbathion (metam) to a flask containing wetted soil, which was then placed in either a dynamic inhalation chamber or a vacuum dessicator. Concentrations of MITC were varied by altering the rate of air supply to the chamber, varying the amount of metam added to the soil, or heating the flask containing the test chemical. In this preparation, cats were found to show acute toxic effects (irritation of ocular mucosae) at 0.1-0.3 mg/m³, corresponding to doses of approximately 7 µg/kg. Repeated exposure to 0.1 mg/m³ for four hours per day for four months resulted in no apparent toxic effects. Thus, the apparent NOEL in this study was 3 µg/kg. The LEL and NOEL from this study are considerably lower than those observed in any other acute toxicity study conducted with MITC.

In another study, human volunteers were exposed to MITC vapor through the use of squeeze bottles. Various concentrations of MITC were used, and exposure was for 5 seconds. The eye irritation threshold from this study was reported to be approximately 200 ppm. Normalization of values to a four hour exposure period (equal to that of the cat study) would produce an irritation threshold of 70 ppb (compared to 35 ppb for the NOEL and 70 ppb for the LEL in the cat study).

As stated in the interim risk assessment document (page 12), "The most obvious area of uncertainty in this risk assessment is the reliability of the animal toxicity data for MITC." Although the study by Nesterova was considered old, it was also considered the most thorough investigation of the toxicity of MITC for acute and subchronic effects, and was the best available information for use in MITC risk assessment. With regard to the human data, the document noted the uncertainty inherent in extrapolating a 5-second human exposure to a 4-hour estimate, but stated that it was considered for interim risk assessment purposes "only because reliable data on longer exposures was not available."

Conclusions:

Toxicology Branch II agrees with the California viewpoint that the animal and human toxicity data add considerable uncertainty to the risk assessment of MITC. However, the use of an older Russian study as well as the normalization of 5-second human exposures to a four hour time period do not present a credible database for risk assessment of MITC. In addition, the current EPA database for MITC is incomplete, and no toxicology endpoints can be identified at this time for use in risk assessment of MITC. It is the conclusion of Toxicology Branch II that the existing cat and human toxicology data as presented in the interim risk assessment document by the California Department of Pesticide Regulation cannot be scientifically defended and therefore should not be relied upon for risk assessment of MITC. The use of a developmental toxicity NOEL of 3 mg/kg/day for metam sodium in this assessment may not be relevant and may actually underestimate risk, based on the suspected higher toxicity of MITC vs metam sodium.