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

MAR 11 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Aluminum Phosphide - Revised Protocols for the Evaluation of the Mutagenic Potential of Aluminum Phosphide (PH_3 Gas) in the Ames Test and for Chromosomal Aberrations Utilizing Chinese Hamster Ovary [CHO] Cells

TOX Chem No.: 31

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ABK 3/8/88

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Background

In response to EPA comments dated June 25, 1987 (see Toxicology Branch review dated June 17, 1987), Hazleton resubmitted modified protocols for the evaluation of aluminum phosphide in the following assays:

1. Ames Salmonella/microsome reverse mutation assay.

2. Chromosome aberrations in Chinese hamster ovary (CHO) cells.

The initial protocols submitted for review were considered inappropriate because of the volatility of the test material; aluminum reacts readily with moist air and water to produce

gaseous phosphine (PH_3). Accordingly, EPA recommended that the performing laboratory submit additional information that included, but was not limited to, the following:

1. Compound preparation and safe handling procedures.

2. Analytical methods to determine PH_3 concentrations.

3. Treatment conditions.

4. Appropriate direct-acting and S9-activated positive controls.

5. Cell culture preparation for the CHO assay.

Conclusions

1. Ames Salmonella/Microsome Reverse Mutation Assay--Modified Protocol

   EPA assesses that the study director has adequately addressed compound preparation and safe handling procedures. The proposed 20-minute nonactivated and S9-activated exposure of the bacteria in closed chambers may, however, be too short to allow compound interaction with genetic material. Ames plate assays with vapors and gases have generally followed a 48-hour exposure regime; in some instances, liquid suspension assays have employed a 72-hour exposure. Two criteria, therefore, assume paramount importance if the proposed modified assay is to provide adequate evidence that PH_3 was appropriately tested.

   a. The study director must present data demonstrating that during the 20-minute exposure, a sufficient concentration of PH_3 was available and capable of inducing cytotoxic and/or genotoxic events.

   b. The sensitivity of the test system to detect a mutagenic response under the proposed test material conditions must be demonstrated both with and without S9 activation. The study director is, therefore, informed that the use of conventional plate incorporation or preincubation assay positive controls will not be accepted as valid proof of assay sensitivity.

2. Chromosome Aberration in CHO Cells

   The items outlined above for the Salmonella reverse mutation assay apply equally to the CHO assay. As noted

for the Ames test, the length of the CHO cell exposure to the test material, particularly in the nonactivated phase of testing, may be too short. Therefore, the study must fully satisfy the criteria requiring evidence of compound interaction with the target cell and assay sensitivity under test material conditions.

Recommendations

EPA assumes that the specific protocols that are intended for these studies are in a developmental phase; however, when the completed studies are submitted to EPA, they should include raw data and detailed methodology as part of the final report.

The individual data evaluation records are attached.

Attachments