Acute Inhal

EPA No.: 68D80056
DYNAMAC No.: 343-A
TASK No.: 3-43A
July 15, 1991

DATA EVALUATION RECORD

PHOSPHINE (AIP)

Acute Inhalation Toxicity Study in Rats

STUDY IDENTIFICATION: Newton, P. E. An acute inhalation toxicity study of phosphine (PH_3) in the rat. (Unpublished study No. 87-8029, performed by Bio/dynamics Inc., East Millstone, NJ, for the Metal Phosphide Task Force; dated September 5, 1989.) MRID No. 413770-01.

APPROVED BY:

Robert J. Weir, Ph.D.
Program Manager
Dynamac Corporation

Signature: William L. McLellan Jr.

Date: July 15, 1991

1. CHEMICAL: Phosphine (PH_3).

2. TEST MATERIAL: 1.06% phosphine in N_2.

3. STUDY/ACTION TYPE: Acute inhalation toxicity study in rats.

4. STUDY IDENTIFICATION: Newton, P. E. An acute inhalation toxicity study of phosgine (PH_3) in the rat. (Unpublished study No. 87-8029, performed by Bio/dynamics Inc., East Millstone, NJ, for the Metal Phosphide Task Force; dated September 5, 1989.) MRID No. 413770-01.

5. REVIEWED BY:

William L. McLellan, Ph.D. Signature: William L McLellan
Principal Reviewer
Dynamac Corporation Date: July 15, 1991

Margaret E. Brower, Ph.D. Signature: Margaret Brower
Independent Reviewer
Dynamac Corporation Date: July 15, 1991

6. APPROVED BY:

Nicolas P. Hajjar, Ph.D. Signature: Nicolas P. Hajjar
Department Manager
Dynamac Corporation Date: 7/15/91

Stanley Gross, Ph.D. Signature: Stanley Gross
EPA Reviewer, Section II
Toxicology Branch I Date: 4/14/92
(H-7509C)

~~Marion P. Copley, D.V.M.~~, Signature: Joycelyn Stewart
~~D.A.B.T.~~ JOYCELYN STEWART
EPA Section Head, Section II Date: 4/14/92
Toxicology Branch I
(H-7509C)

7. CONCLUSIONS:

Core Classification: CORE Supplementary.

The LC_{50} was not established, since no mortality occurred at the highest exposure level. In addition, an effect level was not established. Phosphine caused no toxic effects other than secretory responses as mucoid nasal discharge.

Toxicity Category: Not established.

8. SUMMARY: Groups of 15 male and 15 female Fischer 344 rats (Charles River Breeding Laboratories, Inc., Kingston, NY) having mean weights of 198 g (males) or 145 g (females) were exposed to phosphine for 6 hours at levels of 0, 2.5, 5.0, or 10 ppm (0, 2.4 ± 0.9, 4.9 ± 1.8, or 11 ± 2.4 ppm, mean analyzed values of samples at four intervals). Each animal was individually caged during exposure in a 1000-L glass and stainless steel exposure chamber and received no food or water. The chamber had an airflow rate of 200 L/min (complete air changes every 5 minutes), and the 99% equilibrium time was 23 minutes. The temperature and relative humidity ranges during exposure were 63-75°F and 45-63%, respectively. All animals were observed prior to exposure, at 15-minute intervals during exposure, and 30 minutes following completion of exposure when the rats were removed from the chambers. Five rats/sex/group were sacrificed at the end of exposure, and 10/sex/group were retained for 15 days. Detailed observations of survivors were performed weekly; body weights were recorded pre-exposure, on day 8, and just prior to sacrifice (day 15). All rats were subjected to a gross necropsy, and brain, heart, kidneys, liver, and lungs were fixed and examined histologically.

All animals survived the exposure. Physical observations during exposure included red or mucoid nasal discharge in some rats in all treated groups; these findings were not present at 7 or 14 days after exposure. There were no adverse effects on body weights, although there were sporadic increases in weight in exposed groups.

No gross findings related to exposure were seen at day 1 or day 14. No histologic findings of importance were observed in the groups sacrificed on the day of exposure. Minimal hyperplasia of the lungs was seen in one low-level male and two mid-level males. Minimal focal alveolitis was observed in one control female, and minimal hyperplasia of the lung was seen in another control female. No lesions of the lungs were seen in any exposed males. Focal mineralization of the kidneys was seen in several females, but there was no difference in incidence between groups (4/5 for controls and 3/5, 3/5, and 4/5 in females exposed at 2.4, 4.9 or 11 ppm). Histologic examination

was not performed on the rats sacrificed 2 weeks after exposure.

9. REVIEWERS' COMMENTS AND QUALITY ASSURANCE MEASURES: The study was adequately conducted and reported. Exposure levels were close to target, and chamber temperature and humidity values were all within an acceptable range. A subchronic inhalation toxicity study (MRID No. 413770-02), found that exposure to 10 ppm phosphine for 6 hours/day caused 40% mortality in Fischer 344 rats on the third exposure. A higher dose should have been tested in the single exposure study. However, it is expected that the dose-response curve for mortality will have an extremely sharp slope; therefore, close spacing of doses will be needed to establish an LD_{50}.

   A Quality Assurance statement was signed and dated June 22, 1989.

10. CBI APPENDIX: Materials and Methods (pp 8-16).

Phosphine

Page _____ is not included in this copy.

Pages _5_ through _14_ are not included in this copy.

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