



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

CASWELL FILE

007687

JAN 23 1990

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OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: ARSENIC ACID - ACUTE INHALATION TOXICITY STUDY

TO: E. FERIS
PRODUCT MANAGER (74)
REGISTRATION DIVISION (H7505C)

FROM: LINDA L. TAYLOR, PH.D. *Linda Lee Taylor* 1/14/90
TOXICOLOGY BRANCH II, SECTION II
HEALTH EFFECTS DIVISION (H7509C)

THRU: K. CLARK SWENTZEL *K. Clark Swentzel* 1/17/90
SECTION II HEAD, TOXICOLOGY BRANCH II
HEALTH EFFECTS DIVISION (H7509C)

AND

MARCIA VAN GEMERT, PH.D. *Marcia Van Gemert* 1/18/90
CHIEF, TOXICOLOGY BRANCH/HFAS/HED (H7509C)

REGISTRANT: PENNWALT CORPORATION
CHEMICAL: ARSENIC ACID
SYNONYM: ARSENIC ACID AS DESICCANT L-10
PROJECT: 0-0232
CASWELL No.: 56
RECORD No.: 255117
IDENTIFYING No.: 4581-231
MRID No.: 404639-02
ACTION REQUESTED: PLEASE REVIEW DATA.

COMMENT: IN RESPONSE TO THE EPA REGISTRATION STANDARD FOR NON-WOOD PRESERVING USES OF ARSENIC ACID (DATED SEPTEMBER 10, 1986), AN ACUTE INHALATION STUDY WAS SUBMITTED. THIS WAS RECEIVED IN TB II ON NOVEMBER 29, 1989. THE STUDY HAS BEEN REVIEWED AND THE DER IS ATTACHED.

UNDER THE CONDITIONS OF THIS STUDY, THE LC50 FOR ARSENIC ACID (75%) WAS DETERMINED TO BE 0.794 MG/L FOR MALE MICE, 1.153 MG/L FOR FEMALE MICE, AND 1.040 MG/L FOR THE COMBINED SEXES (ANALYTICAL EXPOSURE CONCENTRATIONS). THIS STUDY IS CLASSIFIED AS CORE: SUPPLEMENTARY, PENDING SUBMISSION OF DATA TO SHOW THAT THE MEDIAN DIAMETER OF TEST MATERIAL PARTICLES WAS IN THE "RESPIRABLE RANGE" FOR THE MOUSE (AROUND ONE MICROMETER) AND THAT AT LEAST 25% OF THE PARTICLE DISTRIBUTION USED WAS IN THE SUBMICRON RANGE (AS PER EPA GUIDELINES).

REVIEWED BY: LINDA L. TAYLOR, PH.D.
 Tox. BRANCH II, SECTION II (H7509C)
 SECONDARY REVIEWER: K. CLARK SWENTZEL
 HEAD SECTION II, Tox. BRANCH II (H7509C)

Linda Taylor 1/16/90

K. Clark Swentzel 1/17/90

DATA EVALUATION REPORT

STUDY TYPE: ACUTE INHALATION LD50 - MICE

TOX CHEM NO: 56

ACCESSION NO.: 404639-02

TEST MATERIAL: ARSENIC ACID

SYNONYMS: ARSENIC ACID AS DESICCANT L-10

STUDY NUMBER: HLA 153-136

SPONSOR: PENNWALT CORPORATION, PUYALLUP, WASHINGTON

TESTING FACILITY: HAZLETON LABORATORIES AMERICA, INC.

TITLE OF REPORT: ACUTE INHALATION TOXICITY STUDY WITH ARSENIC ACID IN THE MOUSE

AUTHORS: JAMES B. TERRILL, PH.D.

REPORT ISSUED: DECEMBER 30, 1987

QUALITY ASSURANCE: A QUALITY ASSURANCE STATEMENT WAS PROVIDED.

CONCLUSIONS: UNDER THE CONDITIONS OF THIS STUDY, THE LC₅₀ FOR ARSENIC ACID (75%) WAS DETERMINED TO BE 0.794 MG/L FOR MALE MICE, 1.153 MG/L FOR FEMALE MICE, AND 1.040 MG/L FOR THE COMBINED SEXES.

CLASSIFICATION: CORE: SUPPLEMENTARY, PENDING SUBMISSION OF DATA TO SHOW THAT THE MEDIAN DIAMETER OF TEST MATERIAL PARTICLES WAS APPROXIMATELY 1 MICROMETER AND THAT AT LEAST 25% OF THE PARTICLE DISTRIBUTION USED WAS IN THE SUBMICRIN RANGE. THIS STUDY DOES NOT SATISFY THE GUIDELINE REQUIREMENTS (81.3) FOR AN ACUTE INHALATION STUDY (SEE ABOVE).

TOXICITY CATEGORY: II

A. MATERIALS:

1. TEST COMPOUND: ARSENIC ACID
 BATCH #: 8619 (2 SHIPMENTS)
 DESCRIPTION: GREEN LIQUID
 PURITY: 75%

THE TEST MATERIAL WAS ATOMIZED (SEE PAGES 12-14, ATTACHED) AND PRESENTED TO THE ANIMALS AS AN AEROSOL. THE CONCENTRATIONS OF TEST MATERIAL IN THE EXPOSURE CHAMBERS WERE DETERMINED GRAVIMETRICALLY AT LEAST HOURLY DURING THE STUDY; THE FRACTION SOLIDS OF THE ARSENIC ACID FORMULATION WERE DETERMINED GRAVIMETRICALLY AND FOUND TO BE 0.77.

THE PARTICLE SIZE DISTRIBUTION OF THE ARSENIC ACID AEROSOL WAS DETERMINED USING AN ANDERSEN MODEL 2000 CASCADE IMPACTOR.

2. TEST ANIMALS:

SPECIES: MOUSE

STRAIN: CD-1

AGE: 5-6 WEEKS

WEIGHT: MALES: 25.6-30.7; FEMALES: 21.8-27.8

SOURCE: CHARLES RIVER LABORATORIES, INC., PORTAGE, MI

3. STATISTICAL PROCEDURES: THE ESTIMATION OF LC₅₀ AND ANALYSIS OF PARTICLE SIZE DISTRIBUTION DATA ARE DESCRIBED ON PAGE 16 OF THE REPORT (COPY ATTACHED).

STUDY DESIGN: FIVE MALE AND 5 FEMALE MICE WERE EXPOSED TO A TARGET CONCENTRATION OF TEST MATERIAL OF 5 MG/L BY A SINGLE 4-HOUR WHOLE BODY INHALATION EXPOSURE. NO CONTROLS WERE UTILIZED. BECAUSE OF HIGH MORTALITY, TWO ADDITIONAL GROUPS WERE TESTED AT TARGET CONCENTRATIONS OF EITHER 0.5 MG/L OR 1 MG/L ARSENIC ACID. THERE WAS A RANDOM ASSIGNMENT OF THE ANIMALS TO THE GROUPS BY WEIGHT. FOOD (PURINA CERTIFIED LABORATORY CHOW® #5002) AND WATER WERE PROVIDED AD LIBITUM, EXCEPT DURING THE 4-HOUR EXPOSURE PERIOD. ANIMALS WERE MONITORED HOURLY DURING EXPOSURE FOR MORTALITY AND ANY GROSS SIGNS OF TOXICITY, AND WERE OBSERVED TWICE DAILY FOLLOWING TREATMENT FOR 14 DAYS. DETAILED PHYSICAL EXAMINATIONS WERE PERFORMED PRIOR TO EXPOSURE, 30 MINUTES POST-EXPOSURE, AT 60 MINUTES POST-EXPOSURE, AND DAILY UNTIL TERMINATION. BODY WEIGHTS WERE MEASURED PRIOR TO STUDY INITIATION, ON DAYS 8 AND 15, AND AT DEATH/SACRIFICE. ALL ANIMALS WERE SUBJECTED TO NECROPSY, WHICH CONSISTED OF A GROSS EXAMINATION OF THE EXTERNAL SURFACE AS WELL AS THE CRANIAL, THORACIC AND ABDOMINAL CAVITIES, AND THEIR ORGANS/TISSUES.

RESULTS: THE MEAN ANALYTICAL AND NOMINAL EXPOSURE CONCENTRATIONS ARE LISTED BELOW. THE AUTHOR ATTRIBUTED THE DIFFERENCES TO SEDIMENTATION AND/OR IMPACTION OF THE AEROSOL DROPLETS IN THE EXPOSURE CHAMBER. GOOD UNIFORMITY OF DISTRIBUTION WAS REPORTED BETWEEN SAMPLES TAKEN AT THE TOP OF THE CHAMBER AND AT THE NORMAL SAMPLE PORT. PARTICLE SIZE DISTRIBUTION MEASUREMENTS INDICATE THAT THE AEROSOL WAS WITHIN THE RESPIRABLE SIZE RANGE OF THE MOUSE (LESS THAN 10 MICRONS, ACCORDING TO THE STUDY AUTHOR).

DEATHS OCCURRED AS FOLLOWS:

| GROUP TARGET CONCENTRATION (MG/L) | EXPOSURE CONCENTRATIONS | | DEATHS | |
|---|-------------------------|-------------------|--------|---------|
| | ANALYTICAL (MG/L) | NOMINAL (MG/L) | MALES | FEMALES |
| 5 | 2.41 | 206.7 | 4/5 | 4/5 |
| 0.5 | 0.57 | 24.9 | 0/5 | 0/5 |
| 1 | 1.01 | 49.1 | 5/5 | 4/5 |

ONLY ONE ANIMAL/SEX IN THE FIRST GROUP (5 MG/L) SURVIVED TO TERMINATION. BODY WEIGHT OF EACH SURVIVOR WAS DECREASED FROM THE PRE-STUDY VALUE ON DAY 8 BUT GREATER THAN PRE-STUDY VALUE ON DAY 15. IN THE 1 MG/L GROUP, THE ONE SURVIVING FEMALE SHOWED INCREASED BODY WEIGHT AT DAY 15 COMPARED TO ITS PRE-STUDY VALUE. FOR THE 0.5 MG/L GROUP, ONE ANIMAL/SEX DISPLAYED A NET DECREASE IN BODY WEIGHT OVER THE STUDY DURATION; ALL OTHER ANIMALS DISPLAYED AN OVERALL INCREASE.

SURVIVORS IN THE TWO HIGHEST DOSE LEVELS EXHIBITED RESPIRATORY DISTRESS, INCREASED SECRETORY RESPONSES AND SIGNS OF POOR CONDITION. THE LOWEST DOSE ANIMALS WERE GENERALLY UNREMARKABLE, WITH ONLY SQUINTED EYES BEING REPORTED. OTHER CLINICAL SIGNS OBSERVED INCLUDE LANGUID BEHAVIOR†, DYSPNEA†, POLYPNEA†, SALIVATION†, PROSTRATION, TREMORS, LACRIMATION†, WHEEZING†, AND ROUGH HAIRCOAT (ONLY SIGNS FOUND AT LOWEST DOSE).

APPARENT COMPOUND RESIDUE ON THE FUR WAS REPORTED, AND SEVERAL ANIMALS WERE REPORTED AS NOT BEING VISIBLE DURING THE EXPOSURE PERIOD DUE TO THE LEVEL OF AEROSOL IN THE CHAMBER.

AT NECROPSY, MACROSCOPIC FINDINGS INCLUDED THE FOLLOWING: DARKENED NASAL TURBINATES AND LUNG, FAILURE OF THE LUNG TO COLLAPSE, MOTTLED LUNG, DARK AREA OF THE STOMACH, FLUID IN THE UTERUS, AND DISTENDED UTERUS. ONLY THE RESPIRATORY FINDINGS WERE CONSIDERED TREATMENT-RELATED. NOTE: THE GROSS PATHOLOGY INCIDENCE SUMMARY (TABLE 4) IS MARKED DRAFT, BUT IS INCLUDED IN THE FINAL REPORT.

MACROSCOPIC FINDING

LUNG - DARK - 4/SEX GROUP 3*, 2/SEX IN GROUP 1
FAILURE TO COLLAPSE - 3 MALES/1 FEMALE IN GROUP 3, 3/SEX IN GROUP 1
MOTTLED - 1 MALE IN GROUP 3, 3/SEX IN GROUP 1
NASAL TURBINATES - DARK - 2/SEX IN GROUP 3, 2 MALES/1 FEMALE IN GROUP 1
STOMACH - DARK AREA - 1 MALE IN GROUP 1
UTERUS - DISTENDED - 1 FEMALE IN GROUP 2
LUMEN, FLUID - 1 FEMALE IN GROUP 2

*GROUP 1 - TARGET CONCENTRATION OF 5 MG/L
GROUP 2 - TARGET CONCENTRATION OF 0.5 MG/L
GROUP 3 - TARGET CONCENTRATION OF 1.0 MG/L

UNDER THE CONDITIONS OF THIS STUDY, THE LC50 FOR ARSENIC ACID (75%) WAS DETERMINED TO BE AS FOLLOWS.

| | ANALYTICAL (MG/L) | 95% CONFIDENCE LIMITS | NOMINAL (MG/L) | 95% CONFIDENCE LIMITS |
|------------|----------------------|--------------------------|-------------------|--------------------------|
| MALES | 0.794 | 0.548-1.149 | 39.2 | 23.2-60.3 |
| FEMALES | 1.153 | 0.410-1.897 | 37.4 | 19.9-86.4 |
| BOTH SEXES | 1.040 | 0.512-1.567 | 41.4 | 27.4-55.9 |

CONCLUSION: LC50 FOR ARSENIC ACID IN MICE WAS FOUND TO BE 0.794 MG/L FOR MALES AND 1.153 MG/L FOR FEMALES (BASED ON ANALYTICAL EXPOSURE CONCENTRATIONS). THE VALUE FOR BOTH SEXES COMBINED WAS REPORTED AS 1.040 MG/L. THIS STUDY IS CLASSIFIED AS CORE: SUPPLEMENTARY, PENDING SUBMISSION OF DATA TO SHOW THAT THE MEDIAN DIAMETER OF TEST MATERIAL PARTICLES WAS IN THE "RESPIRABLE RANGE" FOR THE MOUSE (AROUND ONE MICROMETER) AND THAT AT LEAST 25% OF THE PARTICLE DISTRIBUTION USED WAS IN THE SUBMICRON RANGE (AS PER EPA GUIDELINES).

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Page _____ is not included in this copy.

Pages 5 through 8 are not included.

The material not included contains the following type of information:

- Identity of product inert ingredients.
 - Identity of product impurities.
 - Description of the product manufacturing process.
 - Description of quality control procedures.
 - Identity of the source of product ingredients.
 - Sales or other commercial/financial information.
 - A draft product label.
 - The product confidential statement of formula.
 - Information about a pending registration action.
 - FIFRA registration data.
 - The document is a duplicate of page(s) _____.
 - The document is not responsive to the request.
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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Tox Chem No. _____ ARSENIC ACID

FILE LAST UPDATED _____

CURRENT DATE 1/16/90

EPA
Accession
No. _____

RESULTS:
LD50, LC50, PIS, NOEL, LEL

TOX
CATEGORY

CORE GRADE/
Doc. No. _____

ACUTE INHALATION
SPECIES: MOUSE
HAZLETON LAB, Inc.
HLA 153-136; 12/31/87

ARSENIC
ACID
75%

4046390-02

UNDER THE CONDITIONS OF THE STUDY,
THE LC50 (INHALATION) IN MICE IS
0.794 MG/L IN MALES, 1.153 MG/L IN
FEMALES, & 1.040 MG/L COMBINED
(ANALYTICAL EXPOSURE CONCENTRATIONS)
**NOTE: SUBMISSION OF DATA REGARDING
% OF PARTICLE DISTRIBUTION IN THE
"RESPIRABLE RANGE" FOR MOUSE IS
REQUIRED TO UPGRADE THIS STUDY.**

II

SUPPLEMENTARY