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

NOV 24 1992

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MEMORANDUM

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

Subject: Triethylhexahydro-s-triazine (Vancide TH).
DP Barcode D181155 Submission 422779 MRID 424061-01

To: Virginia Dietrich PM # 53 Tox Chem 481B
Accelerated Reregistration Branch
Special Review and Reregistration Division H7508W

From: Joycelyn E. Stewart, Ph.D., Pharmacologist,
Section 2, Toxicology Branch I
Health Effects Division H7509C

Thru: Melba S. Morrow, D.V.M., Acting Section head,
Section 2, Toxicology Branch I
Health Effects Division H7509C

Registrant: R.T. Vanderbilt Co, Inc.
Norwalk, Ct. 06856

Action Requested: Review acute inhalation study in rats in support of reregistration of Vancide TH as an antimicrobial agent.

Conclusion:

The data presented demonstrate an acute inhalation LC50 of 251 mg/m^3 with 95% confidence intervals of 249-253 mg/m^3 for male rats and inhalation LC50 of 260 mg/m^3 with 95% confidence intervals of 233-290 mg/m^3 for female rats. The combined LC50 for both sexes was calculated to be 254 mg/m^3 with confidence intervals of 212-305 mg/m^3. LC_{50}'s were calculated using actual chamber concentrations.

Classification: Acceptable
Toxicity CAtegory: II

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Reviewed by: Joycelyn E. Stewart, Ph.D. 10/29/92
Section II, Tox. Branch I (H7509C)
Secondary Reviewer: Melba Morrow, D.V.M. 10/29/92
Section II, Tox. Branch I (H7509C)

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DATA EVALUATION REPORT

STUDY TYPE: Acute Inhalation

TOX. CHEM. No.: 481B

MRID No.: 424061-01

GUIDELINE #: 81-3

TEST MATERIAL: Triethylhexahydro-s-triazine

SYNONYMS: Tris-Nitro

STUDY NUMBERS: 140816

SPONSOR: R.T. Vanderbilt Co.
Norwalk, Ct.

TESTING FACILITY: Exxon Biomedical Sciences, Inc.
East Millstone, N.J.

TITLE OF REPORT: Vancide TH: Acute Inhalation Toxicity Study in Rats

AUTHORS: F.T. Whitman, D.J. Letinski, and R.D. Phillips.

REPORT ISSUED: 7/2/92

CONCLUSIONS: The data presented demonstrate an inhalation LC 50 of 251 mg/m^3 for male rats with 95% confidence intervals of 249-253 mg/m^3 and inhalation LC50 of 260 mg/m^3 for female rats with 95% confidence intervals of 233-290 mg/m^3. The combined LC_{50} for both sexes was calculated to be 254 mg/m^3 with confidence intervals of 212 to 305 mg/m^3. LC_{50}'s were calculated using actual chamber concentrations.

CLASSIFICATION: Acceptable
TOX. CATERGORY: II

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MATERIALS: Vancide TH, a.i. 96.06%, Lot No. OM -324, a colorless liquid, was the test chemical. Crl: CDBR Sprague-Dawley rats obtained from Charles River Laboratories, Stone Ridge, New York were the test animals. They were 6-7 weeks old, 160-398 grams at study initiation. After acclimation to the laboratory environment, the rats were assigned to dosage groups as follows:

GROUP	NOM CONC (MG/M^3)	ACT CONC	M	F
1	17425	7308	5	5
2	5249	1967	5	5
3	705	282	5	5
4	159	Undetermined		
5	134	114	5	5
6	157	140	5	5
7	195	174	5	5
8	257	240	5	5
9	311	295	5	5
10	273	254	5	-
11	276	270	-	5

METHODS: Groups of animals were exposed head only in 150 L stainless steel inhalation chambers for four hours. The test material was delivered to the chamber via a Sage syringe pump through an air atomizing nozzle (1/8" JSS spraying Systems) to which compressed air was added. The resulting aerosol/vapor mixture was introduced into the chamber through a diffuser/premixer. The exposure chamber was operated under slight negative pressure at an airflow rate of 38.0 L/min, with an equilibration time (T99) 0f 18.2 minutes. The airflow was regulated by a transvector jet supplied with compressed air and measured by a calibrated flow-limiting device. Nominal chamber concentrations were determined by weighing the reservoir containing the test material before and after exposure and dividing the net weight loss by the total volume of air passing through the chamber during the exposure. Actual chamber concentrations > 300 mg/m^3 were determined by drawing a known volume of chamber air through a glass midget impinger containing 20 ml of a 50/50 mixture of methanol and 7.0 pH buffered reverse osmosis water, followed by HPLC analysis. For the lower concentrations, actual chamber concentrations were determined by an infra-red monitor, measured against a calibration curve. Chamber concentrations were measured hourly during exposure. During the exposure period, chamber tempearture and relative humidity were monitored continuously and recorded at thirty minute intervals. Temperatures ranged from 68-75° F and relative humidity 40-70%. During exposure of the Group 1 animals, gravimetric filter samples were drawn from four different sites within the chamber to determine homogeneity of the aerosol distribution.

Animals were monitored every 15 minutes for the first hour after being placed in the chamber, then hourly thereafter. Detailed individual observations were recorded pre-exposure, immediately

after removal from the chamber, and daily for fourteen days post-exposure. Body weights were recorded for all animals on days 0, 7, and 14 of exposure. At study tearmination, all surviving animals were sacrificed and necropsied.

Particle sizes were measured with a Sierra Model 210 Cascade Impactor. Preweighed glass fiber filters were used to collect the aerosol on each stage. The change in weight for each filter was measured and the cumulative percent of the sample collected was calculated. The 15.9%, 50% and 84.1% particle sizes (equivalent aerodynamic diameter), the geometric standard deviation, the estimated percent of the aerosol less than or equal to 1, 10, and 15 microns in size were calculated.

QUALITY ASSURANCE: Signed and dated quality assurance statements were included in the submission.

STATISTICAL ANALYSIS; Means and standard deviations were calculated for exposure and animal data. The median lethal concentrations was calculated using the Litchfield -Wilkinson technique.

RESULTS: No Group I, Group 2 or Group 3 animals survived the inhalation exposure. All animals in these groups were observed gasping and salivating during the exposures. Group 4 was declared invalid due to a malfunction in the generation equipment. Of the remaining groups survival was as follows:

GROUP	CONC (MG/M^3)	SURVIVAL M	F
5	114	4	5
6	140	5	5
7	174	4	5
8	240	4	5
9	295	0	1
10	254	2	-
11	270	-	2

The following clinical signs were observed in all animals during exposure: labored breathing, gasping, nasal discharge, ocular irritation and salivation. These symptoms increased with chamber concentration. Post exposure, toxicity was manifested by reddened and/or swollen eyelids, nasal discharge, soft stools, anogenital staining, and decreased activity. Most of the surviving animals appeared to recover and were free of abnormalities by day 14 post exposure. All surviving animals gained weight.

Only three concentrations, 7308 mg/m^3, 1967 mg/m^3, and 282 mg/m^3 generated enough aerosol to determine particle sizes. The other concentrations existed in vapor phase. Particle sizes ranged from 1.4 to 4.2 microns, with geometric standard deviations of 2.0 to 5.0. The percent of the aerosol less than or equal to 1, 10, and 15 microns was 2%, 90% and 97% for Group 1, 11% 78% and

87% for Group 2, and 41%, 89% and 93% for Group 3, respectively. Both animals which died during exposure and those which survived to study termination showed lung and liver discoloration at necropsy.

DISCUSSION:

The study was adequately performed and described. None of the protocol deviations were significant enough to adversely affect the outcome of the study. The data presented supports the investigators' calculation of the acute inhalation LC_{50}. The study is classified Acceptable and satisfies the Guideline requirement for 81-3. Based on the acute inhalation LC 50 of 254 mg/m^3 (combined) with confidence intervals of 212 to 305 mg/m^3, the toxicology category is II.

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