

TECHNICAL SUPPORT SECTION TOXICOLOGY REVIEW - I

Disinfectants Branch

IN March 3 92 OUT March 9 92

Reviewed by Alex Arce Date March 9 92

EPA Reg. No. or File Symbol 1965-55

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Date Division Received 12 24 91

Type Product(s): I, D, H, F, N, R, S Industrial Preservative

Data Accession No(s). 43572, 42078, 416205-01, 417737-01

Product Mgr. No. 31, John Lee/ Delaney

Product Name(s) VANCIDE TH

Company Name(s) R. T. Vanderbilt Inc.

Submission Purpose Review of previously submitted data, newly submitted data and latest label

Chemical & Formulation Liquid

Active Ingredient(s):

Hexahydro-1,3,5- triethyl-s-triazone

3
95 %

CONCLUSION The label has to be revised in order that the "Precautionary Statement" follows the requirements as per the results of the submitted Acute Toxicity Data.

COMMENTS : The submitted data is outmoded . ~~However, the submitted data is outmoded and the data required are an acute irritation study, a 28-day repeated dose study, and a 14-day repeated dose study.~~

The Acute Dermal LD50 study although classified as supplementary data do not have to be repeated due to the fact that the product appears to be corrosive while tested for Skin Irritation

COMMENTS : Part of the data in files is outmoded . However, due to the fact that the product is corrosive , The following data is not required
Skin Irritation , Eye Irritation , Dermal Ld50.

The previously submitted Acute Inhalation Toxicity Study has been found to be unacceptable , such data is not required at the present.

Based in conversations with H E D (via J. Wilson) I learned that H E D does not require an Acute Inhalation Toxicity Study.

The product however is volatil and has a "repugnant odor", it appears that the product is an Industrail Preservative for Industrial Use Only. I was informed that the registrant is in the process of conducting a new Acute Inhalation Study

The outmoded unacceptable eye irritation study raises a question .

While the product exhibits corrosive properties via dermal irritation the eye study (Unacceptable) shows that the product is not corrosive to the eye.

BACKGROUND

The product will be used as. Industrial Preservative

RECOMMENDATIONS

The data submitted are adequate to place the product in the following toxicity categories

<u>STUDY</u>	<u>TOXICITY CATEGORY</u>
Acute Oral	<u>Tox Cat 11 (Mrid 43522) and Tox Cat 11 (Mrid 417737-01)</u>
Acute Dermal	<u>Supplementary data New study is not required</u>
Acute Inhalation	<u>Not acceptable</u>
Skin Irritation	<u>Tox Cat 1 CORROSIVE</u>
Eye Irritation	<u>Not acceptable</u>
Dermal Sensitization	<u>Mild (weak) sensitizer</u>

Acute 24 hours dermal ; dilution tests Supplementary data
Other Studies required or recommendations for request of further testing

~~_____~~
~~_____~~
~~_____~~
~~_____~~

CRP STATUS

This product ~~does~~/does not require special packaging

Label The word "POISON" and the SKULL and CROSS BONES has been placed on the label in order to satisfy regulations of the DOT

Revise the label as follows: Under the "Precautionary Statement" delete the phrase "or harmful" , and add "if swallowed, inhaled or absorbed through the skin"; to read , "May be fatal if swallowed , inhaled or absorbed through the skin ".

Under the "Statement of Practical Treatment", delete the phrase "of milk , egg whites , gelatin solution or if these are not available" , to read " If swallowed drink promptly large quantities of water".

Add the sentence " Contact with this product may induce dermal sensitization".

DATA REVIEW

Test Laboratory: Hilltop Research Inc.

Laboratory test identification Number Q-169

Acute Oral LD₅₀ CFR 81.1

Report date: Aug 23 66

MRID No. 43522

Method of Testing: CFR 81-1 Modified

Species: Rats Sex: Male Age: Adult

Levels Tested: 0.0191, 0.0412, 0.0887, 0.191, 0.0412, 0.887 and 4.12 g/k
The s.g. was 0.887

No. Animals/dose: 5 males

Weights: Acceptable

Via: Intubation

Material: Diluted in saline

Observation days: 14

Necropsy: All animals

Procedure

The rats were treated with the material in empty stomachs and observed for signs of toxicity

Results

Signs of Toxicity: Depression, salivation, coma

Mortality: 5/5 at 0.412, 0.887 and 4.12 g/kg, No deaths at other levels

Body weights: The survivors gained

Necropsy: Congestion of the adrenals, kidneys and G I irritation

Conclusion: The Acute Oral LD₅₀ is 0.280 gm/kg or 280 mg/kg

Core Minimum data

Toxicity Category: 11

NOTE: Although only male rats were used and the LD₅₀ was calculated from the all or none deaths response, the study provides sufficient information for a toxicity category classification.

DATA REVIEW

Test Laboratory: Exxon Biomedical Sciences Inc.

Laboratory test identification Number Case Number 3147

Acute Oral LD₅₀ CFR 81.1

Report date: Jan 28-91 MRID No. 417737-01

Method of Testing: CFR 81-1

Species: Rat Sex: Male and female Age: adult

Levels Tested: 150, 300, and 600 mg/kg

No. Animals/dose: 5 m and 5 f

Weights: Acceptable Via: Intubation

Material: Diluted in water Observation days: 14

Necropsy: All animals

Procedure The rats were treated with the material in empty stomachs and observed for signs of toxicity

Results

Signs of Toxicity: oral discharge , dispnea , rales

Mortality: 3/10 at 150, 6/10 at 300, 10/10 at 600. mg/kg

Body weights: The survivors gained weight

Necropsy: distension and discoloration of the GI tract.

Conclusion: The Acute Oral LD₅₀ is 208.83 mg/kg

Core Guidelines data

Toxicity Category: 11

Acute Dermal LD₅₀ CFR 81.2

Laboratory Hill Top Research

Test Number q-169

Report Date: aug 23 66

MRID No. 43522

Method of Testing: CFR 81-2

Species: Rabbits Sex: M and F Age: Adult

Levels Tested: 0.191, 0.412, 0.887 and 1.91 g/kg

No./Animals/dose 2m and 2 f
Via: Occluded patch

Weight: Acceptable

Observation days: 14

Material: Undiluted

Necropsy: Gross nec. in all

Procedure

The material was applied to a previously clipped area in the abdomen, 2 rabbits in each group received the material in abraded areas. A protective wrap was used and the animals were observed for signs of toxicity at intervals

Result

Signs of Toxicity: Shallow respiration at the two largest dose levels

Mortality: 2/4 at 0.412, 3/4 at 0.887 and all at 1.91 g/kg

Body weights: Acceptable

Necropsy: congested lungs and kidneys, adhesions of intestines and peritoneum THE PRODUCT IS CORROSIVE TO THE SKIN

Conclusions: The Acute Dermal LD₅₀ is 0.449 g/kg

Core Supplementary data data

Toxicity Category: Not sufficient information provided

The test does not adhere to CFR 81-2

Primary Skin Irritation

CFR 81.5

Hill Top Research Inc. # Q-169

Patch Test for primary irritation and corrosivity- Rabbits

Report Date: Aug 23 66

MRID No.: 43522

Method of Testing: CFR 81-5

Species: Rabbit

Observation days: 72 hours

No. of animals 6

Material: Undiluted

Dose: 0.5 ml

via: Occluded patch test

Areas: Intact and abraded

Necropsy: No

Procedure

The rabbits were treated with the material in previously clipped areas of the skin and observed for signs of irritation

Results: Severe Irritation was found in all animals

Conclusion: The product is a Severe skin irritant

THE PRODUCT IS CORROSIVE

Core Minimum data

Toxicity Category: 1

Primary Eye Irritation

CFR 81.4

Hill Top Research Inc Test # Q 169

Report Date: Aug 23 66

MRID No.: 43522

Method of Testing CFR 81-4

Species: Rabbit

Observation days: 72 hours

Dose: 0.1ml

Materials: Undiluted

No. of animals: 6

Via: Eye instillation

Areas: One eye

Necropsy: No

Procedure

One eye of each animal was treated with the material and observed for signs of eye irritation

Results: Moderate Corneal opacity iritis Iritis developed 6/6

Conjunctival irritation was moderate in all rabbits

The eyes cleared at : The time in which the eyes cleared is not clearly established , thus the test provides not sufficient info

Core Unacceptable data

Toxicity Category: Not established

The submitted ~~data~~ is incompleted

Acute Inhalation LC50

CFR 31.3

Laboratory Hill Top Research Test Number Q 164

Title " Acute Inhalation Exposure -Rats "

Report Date: 8-23-66

MRID: 43522

Method of Testing: No estated

Measurements: Nominal No Actual Yes

Species: Rat

Sex: Male only

Age: Adult

Chamber size: 29 X 30 cm
glass jar

Levels tested: Not mentioned ; Two
concentration, 55.3 and 2.66 mg/l

No. animals/dose: _____

Temperature Not mentioned

Air Flow Not mentioned

Via: Glass jar exposure

Weight: Acceptable

Observation days: 14 days

Material: Aerosol mist

Necropsy: All animals

Procedure

The rats were exposed to the material in the form of an aerosol, in a glass jar for 1 HOUR. The glass jar was equipped with one source of entry and another for exit for the aerosol. An atomizer was used. The concentration of the material was calculated by substrating the weight of the sample at the end of the exposure (A) from the weight at the beginning (B) and dividing it by the product of the multiplication of the air flow (c), in L/m times the exposure

Results

in minutes (d) as; $\frac{A-B}{c \times d}$ = concentration in mg/l

Signs of toxicity: at 55.3, gasping, depression, cyanotic appearance
at 2.66, depression, salivation

Mortality: at 55.3 10/10, at 2.66 none

Body Weights: Not reported

Necropsy: at 55.3, kidney congestion; at 2.66, no gross path.

Conclusions: The Acute Inhalation LC50 is Not established

Core Not acceptable data (Only males . 1 hour exposure)

Toxicity Category: Incompleted information

Dermal Sensitization

CFR. 81.6

Laboratory Exxon Biomedical Sciences Inc
Toxicology Laboratory

Test No. I D 240822

Report Date: Aug 23 1990

MRID No. 41620501

Other pertaining Info The test used is the Buehler test

Method of Testing: CFR 81-6

Modifications : The Buehler test was modified

Species: G. p No. of applications/week : 3 at in No of weeks : 03 weeks
 Induction Dose: 0.4ml of 5% Area of applic : dorsal induct. Days of Rest 2 weeks
 before Challenge
 Challenge dose: 0.4 ml No. of applic. 1 of 1% Dose: Topical
 Rechallenge , same as challenge
 Areas: dorsal surface Pilot Study : No
 No. of animals used: 10 females Controls: Solvent No Positive : Yes ✓
 Negative : No Naive : Yes ✓
 Material: 5 % w/w Solvent water Irritation: YELL ✓

PROCEDURE

The animals were treated with the material in previously clipped areas of the skin ; 9 application during the induction period and 1 at challenge and rechallenge . Topical application , protected with a wrap. DNCB was used as positive control . An irritation control group received only one application ; 5 females used

Results: Severe erythema and slight edema in all animals at induction. At Challenge , 1 animal showed well defined erythema at 24 hours and slight at At re-challenge 4 animals were positive for erythema

Erythema :	Induction	Control: Pos +++	Neg	Neg	Naive	Not used	Test +++	Challenge 1/10 +
Edema:	Induction	Control Pos +++	Neg	Neg	Naive	Not used	Test Negative	Challenge Negative

Rechallenge 4/10 +
for erythema
dermal sensitizer

Conclusions: The product is a weak

Core Minimum data

Toxicity Category: N/A

Comments