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

EPA Petition or EUP No. None

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	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 . [redacted]

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

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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

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

Acute 24 hours dermal ; dilution tests Supplementary data

Other Studies required or recomendations for request of further testing

[redacted]

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 absorved through the skin"; to read , "May be fatal if swallowed , inhaled or absorved 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 LD_{50} 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 Toxcity: Depression , salivation, coma

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

Body weihgts: The survivors gained

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

Conclusion: The Acute Oral LD_{50} is 0.280 gm/kg or 280 mg/kg

Core Minimum **data**

Toxicity Category: II

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 classifi...

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DATA REVIEW

Test Laboratory: Exxon Biomedical Sciences Inc.

Laboratory test identification Number Case Number 3147

Acute Oral LD_{50} 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 Toxcity: oral discharge , dispnea , rales

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

Body weihgts: The survivors gained weight

Necropsy: distension and discoloration of the GI tract.

Conclusion: The Acute Oral LD_{50} is 208.83 mg/kg

Core Guidelines data

Toxicity Category: 11

Acute Dermal LD_{50} 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 respitation at the two largest dose leve

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 LD_{50} is 0.449 g/kg

Core Supplementary data **data**

Toxicity Category: Not sufficient information provided

The test does not adheres 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: o.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: Undilited

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 LC_{50} CFR 81.3

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 cancentration, 55.3 and 2.66 mg/1 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 matrial in the form of an aerosol , in a glass jar for 1 HOUR . The glass jar was equiped 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 beguining (B) and dividing it by the product of the multiplication of the air flow (c) , in L/m times the exposure in minutes (d) as; $\frac{A-B}{c \times d}$ = concentration in mg/1

Results

Signs of toxicity: at 55.3 , gasping,depression,cynotic appearence 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 LC_{50} is Not established

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

Toxicity Category: Incompleted information

Acute Dermal LD_{50} CFR 81.2

Title : Acute 24 hour dermal studies of Vancide Th dilutions

Laboratory : Duquesne University Test Number None

This is an unsolicited data

Report Date: April 23 1970 MRID No. 42078

Method of Testing: Method Development

Species: Rabbits Sex: M and F Age: adult

Levels Tested: 1000 and 10,000 ppm No./animals/dose 5 m and 5 f

Via: Occluded aptch

Weight: Acceptable Observation days: 14

Material: Diluted Necropsy: All animals

Procedure

2 male and 2 female rabbits were treated with the material in previously clipped areas of the skin ; one male and one female were used as control; per dose level .
The animals were obsrved for signs of toxicity and dermal irritation

Result

Signs of Toxicity: Mild dermal irritation

Mortality: None . NOTE - In the Acute Dermal Ld50 study deaths occured at the 0.412 g/kg.All animals died at 1,91 g/kg

Body weights: Most animals gained weight

Necropsy: ~~Examined kidneys and kidneys of the intestines of the exposed~~ No signs of toxicity

Conclusions: The Acute Dermal LD_{50} is N/a

Core Supplementary data **data**

Toxicity Category: N/A

This test is doubtfull. The results conflict with the observations arrived in the Acute dermal Ld 50 study

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

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

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

Conclusions: The product is a weak dermal sensitizer

Core Minimum data

Toxicity Category: N/A

Comments