



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

OCT 22 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Thiram, Reply to Registration Standard, Review
of Acute Toxicity Studies

TO: Henry Jacoby, PM-21
Registration Division (TS-767)

FROM: Robert P. Zendzian PhD, Acting head
Review Section IV
Toxicology Branch
HED (TS-769)

10/8/85
WPA 10/22/85

THROUGH: Theodore M. Farber PhD, Chief
Toxicology Branch

Compound Thiram

Tox Chem #856

Registration #45728-1

Registrant UCB

Accession #259250

Tox Project #617

Action requested

Review the following studies submitted in response to
the Thiram Registration Standard;

1) Evaluation of the acute dermal toxicity of TMTD in
the rabbit, M.H. Thouin, 's-Hertogenbosch, NOTOX 0113/211,
June 1985

2) Assessment of eye irritation by TMTD technical in
the rabbit, D.E. Mulder, 's-Hertogenbosch, NOTOX 0113/174,
June 1985

3) Assessment of primary skin irritation by TMTD technical
in the rabbit, P.J.J.M. Weterings, 's-Hertogenbosch, NOTOX
0113/173, June 1985

Conclusions

1) Acute dermal toxicity

Core classification Minimum

Tox catagory acute toxicity III
 dermal irritation IV

Summary

LD₅₀ >2000mg/kg in male and female rabbits. Irritation seen at 2000 mg/kg but disappeared by 7-days post dose.

2) Eye irritation.

Core classification Guideline

Tox catagory II

Summary

The test material produced conjunctival irritation for a period of 7 days. The treated eyes were normal at 15 days.

3) Primary skin irritation.

Core classification Guideline

Tox catagory IV

Summary

Mild erythrema in 1/5 animals cleared by 48 hours.

Data Evaluation Report

Compound Tetramethylthiuram disulfide (Thiram)

Citation Evaluation of the acute dermal toxicity of TMTD in the rabbit, M.H. Thouin, 's-Hertogenbosch, NOTOX 0113/211, June 1985

Reviewed by  10/21/85
Robert P. Zendzian PhD
Pharmacologist

Core classification Minimum

Tox catagory acute toxicity III
dermal irritation IV

Summary

LD₅₀ >2000mg/kg in male and female rabbits. Irritation seen at 2000 mg/kg but disappeared by 7-days post dose.

Materials

Tetramethylthiuram disulfide, TMTD technical
Batch # P53/02-85, 98.8% pure.

Young adult New Zealand White rabbits (spf-quality, randomly bred) Broekman Institute, Someren, The Netherlands

Methods

Five males and five females were given a single dose of 2000 mg/kg. One day prior to dosing the fur was clipped from the back of the test animals. The dose was applied as a paste to surgical gauze fixed to aluminium foil and applied to the mid-dorsal area for 24-hours. The bandage was removed and the remaining material washed from the application site. Animals were observed for 14 days following treatment then sacrificed and necropsied.

Results

No signs of toxicity were observed during the study. The application site "generally showed slight erythema. Some areas revealed well-defined and moderate erythema. By the end of the first week these irritations had disappeared from all animals.". Individual animal observations were not presented. No treatment-related abnormalities were observed at necropsy.

Data Evaluation Report

Compound Tetramethylthiuram disulfide (Thiram)

Citation Assesment of primary skin irritation by TMTD technical in the rabbit, P.J.J.M. Weterings, 's-Hertogenbosch, NOTOX 0113/173, June 1985

Reviewed by  Robert P. Zendzian PhD
Pharmacologist

10/51/85

Core classification Guideline

Tox catagory IV

Summary

Mild erythrema in 1/5 animals cleared by 48 hours.

Materials

Tetramethylthiuram disulfide, TMTD technical
Batch # P53/02-85, 98.8% pure.

Adult female New Zealand White rabbits from Broekman Instituut, Someren, The Netherlands

Methods

Fur was shaved from the application site 24 hours before dosing. A dose of 5000 mg was moistened with 0.5ml distilled water, applied to a 6 cm² patch of Metalline wound dressing and applied to the left flank of each of six test animals. The same dressing without test material was applied to the right flank. After 4 hours the test and control materials were removed and the application site washed. The application site was scored at 30-60 minutes and 24, 48 and 72 hours after dosing.

Results

Mild erythema was observed on one animal at one and 24 hours after dosing. The site was normal at 58 and 72 hours. The remaining five animals remained normal. No systemic toxicity reported.

Data Evaluation Report

Compound Tetramethylthiuram disulfide (Thiram)

Citation Assesment of eye irritation by TMTD technical in the rabbit, D.E. Mulder, 's-Hertogenbosch, NOTOX 0113/174, June 1985

Reviewed by  10/21/85
Robert P. Zendzian PhD
Pharmacologist

Core classification Guideline

Tox catagory II

Summary

The test material produced conjunctival irritation for a period of 7 days. The treated eyes were normal at 15 days.

Materials

Tetramethylthiuram disulfide, TMTD technical
Batch # P53/02-85, 98.8% pure.

Adult female New Zealand White rabbits from Cpb/TNO Zeist, The Netherlands

Methods

Thirty milligrams of the test material was placed in the conjunctival sac of the left eye of each of six rabbits. Eyes were examined at 1, 24, 48 and 72 hours and 7 and 15 days after dosing. At 24 hours fluorescein staining was used to detect corneal injury.

Results

Conjunctival swelling and redness was observed within one hour of dosing which regressed but had not disappeared over a period of 7 days. Effects on the blood vessels of the iris were observed in two of the six animals. The treated eyes were normal at 15 days. No evidence of corneal damage was reported.