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

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JUL 13 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Tetrahydro-3,5-dimethyl-2H-1,3,5-thiadiazine-2-thione (Dazomet): Review of Acute Toxicity Data Submitted by the Registrant.

Caswell No: 840
DP Barcode: D178986
Submission: S418933
MRID Nos: 423288-01; 423288-02

FROM: Timothy F. McMahon, Ph.D., Toxicologist 6/26/92
Review Section I, Toxicology Branch II
Health Effects Division (H7509C)

TO: Betty Crompton / PM 51
Special Review and Reregistration Division (H7508W)

THRU: Yiannakis M. Ioannou, Ph.D., Section Head 7/1/92
Review Section I, Toxicology Branch II
Health Effects Division (H7509C)

and

Marcia Van Gemert, Ph.D., Branch Chief
Toxicology Branch II
Health Effects Division (H7509C)

Registrant: BASF Corporation

Action Requested: Review of the following Toxicology studies with Dazomet:

§ 81-2 Acute Dermal Toxicity in Rats
§ 81-5 Primary Dermal Irritation in Rabbits

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Data Summary / Conclusions:

MRID # 423288-02

Title of Report: Study on the Acute Dermal Toxicity of Dazomet Technical in Rats

Conclusions: Under the conditions of this study, the acute dermal LD_{50} of Dazomet technical was > 2000 mg/kg in male and female rats.

Toxicity Category III

Core Classification: minimum

This study fulfills the requirements (81-2) for an acute dermal toxicity study in rats.

MRID # 423288-01

Title of Report: Primary Skin Irritation / Corrosion Study with Dazomet in the Rabbit

Conclusions: Under the conditions of this study, Dazomet technical was non-irritating to the skin of male rabbits.

Toxicity Category IV

Core Classification: minimum

This study fulfills the requirements (81-5) for a primary dermal irritation study in rabbits.

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Reviewed by: Timothy F. McMahon, Ph.D. 4/9/92
Section I, Toxicology Branch II (H/509C)
Secondary Reviewer: Yiannakis M. Ioannou, Ph.D. 7/1/92
Head, Section I, Toxicology Branch II (H7509C)

Data Evaluation Report

Study type: Acute dermal-rats (81-2)

Tox. Chem. No.: 840
Submission: S418933
DP Barcode: D178986

MRID number: 423288-02

Test material: tetrahydro-3,5-dimethyl-2H-1,3,5-thiadiazine-2-thione

Synonyms: Dazomet

Study number: 11AO111/911011

Testing Facility: BASF Aktiengesellschaft
D-W6700 Ludwigshafen, Germany

Sponsor: BASF Corporation
Agricultural Products, Research Triangle Park, N.C.

Title of report: Study on the Acute Dermal Toxicity of Dazomet Technical in Rats

Author(s): Dr. Kirsch

Study completed: April 14, 1992

Conclusions:
Under the conditions of this study, the acute dermal LD_{50} of Dazomet technical was > 2000 mg/kg in male and female rats.

Toxicity Category III

Core Classification: minimum

This study fulfills the requirements (81-2) for an acute dermal toxicity study in rats.

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I. MATERIALS

A. Test Material: Dazomet technical; description: white-grey crystalline powder; purity: 101.4% a.i.; lot # 540194.

B. Test Animals: Male and female Wistar rats. Source: Dr. K. Thomae GmbH, D-W7950 Biberach, FRG. Age: young adult; Weight (on day of dosing): males: 265-274g; females, 227-243g.

II. METHODS

Five male and 5 female rats were selected for use in this study. Rats were given KLIBA-LABORDIAT 343 and tap water *ad libitum*. Rats were housed individually in stainless steel wire mesh cages, type DK-III. Temperature and humidity were in the range of 20-24 ^{o}C and 30-70% , respectively. A 12 hour light/dark cycle was used. An acclimation period of at least one week was allowed prior to dosing.

At least 15 hours prior to dosing, the fur of each rat was clipped from the dorsal and dorso-lateral parts of the trunk to create an area appproximately 50 cm^2. The following day, a dose of 2000 mg/kg dazomet technical (in a 0.5% suspension of Tylose CB 30,000) was applied in a volume of 4 ml/kg to the shaved area. The application site was then covered with a porous dressing and allowed to remain on for 24 hours. Following the 24 hour exposure, all dressings and tape were removed, and the exposure site rinsed with warm water to remove residual test article. Each animal was observed for signs of clinical toxicity several times on the day of dosing, and once daily thereafter up to study termination (day 14 post-dosing). A check for mortality was performed twice daily except weekends and holidays, when observations were made once a day. Body weights were recorded on study days 0 and weekly thereafter.

On the last day of the observation period (day 14), surviving rats were killed by carbon dioxide asphyxia and gross necropsy was performed.

III. RESULTS

No systemic or local effects from application of 2000 mg/kg dazomet technical were noted in male or female rats. Slight but insignificant weight loss was observed in female rats over the course of the study. No mortality was recorded for either male or female rats. No abnormal pathology was reported.

IV. CONCLUSIONS

Under the conditions of this study, the acute dermal LD_{50} of Dazomet technical was > 2000 mg/kg in male and female rats.

Toxicity Category III

V. CORE CLASSIFICATION

minimum

This study fulfills the requirements (81-2) for an acute dermal toxicity study in rats.

Reviewed by: Timothy F. McMahon, Ph.D. 9/11/92
Section I, Toxicology Branch II (H7509C)
Secondary Reviewer: Yiannakis M. Ioannou, Ph.D. 9/11/92
Head, Section I, Toxicology Branch II (H7509C)

Data Evaluation Report

Study type: Primary dermal-rabbits (81-5)

Tox. Chem. No.: 840
Submission: S418933
DP Barcode: D178986

MRID number: 423288-01

Test material: tetrahydro-3,5-dimethyl-2H-1,3,5-thiadiazine-2-thione

Synonyms: Dazomet

Study number: 14H0111/919012

Testing Facility: RCC NOTOX B.V.
The Netherlands

Sponsor: BASF Aktiengesellschaft
D-W6700 Ludwigshafen, Germany

Title of report: Primary Skin Irritation/Corrosion Study with Dazomet in the Rabbit

Author(s): Ir. W.R. Pels Rijcken

Study completed: April 28, 1992

Conclusions:

Under the conditions of this study, Dazomet technical was non-irritating to the skin of male rabbits.

Toxicity Category IV

Core Classification: minimum

This study fulfills the requirements (81-5) for a primary dermal irritation study in rabbits.

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I. MATERIALS

A. Test Material: Dazomet: purity: 98.5% a.i.; description: white grey solid
batch # 540194

B. Test Animals: Male New Zealand White Rabbits ; Source: Broekman Institute, Someren, The Netherlands. These rabbits were apparently selected from in house rabbits "not previously used," according to the registrant (page 12 of the report). Age: approximately 12 weeks at the start of treatment. Weight: 2000-2238g.

II. METHODS

Six male rabbits were selected for use in this study. Rabbits were given approximately 100g of food per day (LKK-20, Hope Farms, The Netherlands) and tap water *ad libitum*. Rabbits were housed individually in "cages with perforated floors and equipped with an automatic drinking system" (page 13 of the report). Temperature and humidity were stated as "optimal conditions considered as being a temperature of 21 ^{o}C and relative humidity of 55%." Rabbits were acclimated to the lab environment for at least 5 days prior to start of the study. It was not stated how the three male and three female rabbits were selected for use.

Approximately 24 hours prior to application of the test material, hair was clipped from the dorsal area of the trunk of each rabbit, exposing an area of approximately 10 x 15 cm. The shaved skin area was physically examined prior to test article administration to ensure the use of only normal skin.

On test day 1, 0.5g amount of test material was moistened and then immediately applied to the test site using a Scotchpak-non-woven patch (2 x 3 cm). This patch was mounted on Micropore (3M) tape. The dressing was wrapped around the abdomen and secured with an elastic bandage (Coban, 3M). The contralateral flank was treated in a similar manner, but without test substance or vehicle. Duration of exposure to test material was 4 hours. **Note:** On page 14 of the report, it is noted that dazomet has a limited stability in water (= 0.6 hr).

Four hours after application of test material, the wrap and dressing were removed, and remaining test substance removed using a tissue moistened with tap water and subsequently a dry tissue.

The degree of erythema and edema was assessed at intervals of approximately 50 minutes, 24 hours, 48 hours, and 72 hours following treatment. Observations for clinical toxicity and mortality were performed daily. Body weight was recorded on the day of test article application only.

A numerical scoring system (attached) was used to grade skin lesions. A primary irritation index was calculated by combining the average skin scores for erythema and edema after 24 and 72 hours.

III. RESULTS

At 50 minutes following removal of the dressing, very slight erythema was observed in 4 of 6 rabbits. No sign of edema was present at this time point. At all subsequent time intervals, there were no reported signs of edema or erythema in any rabbit.

IV. CONCLUSIONS

Under the conditions of this study, Dazomet technical was non-irritating to the skin of male rabbits.

Toxicity Category IV

V. CORE CLASSIFICATION

minimum

This study fulfills the requirements (81-5) for a primary dermal irritation study in rabbits.