PM 51

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

JUL 22 1998

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: FERBAM (ferric dimethyl dithiocarbamate)---Tox. Data Submitted Under MRID Nos. 40561501, 40561502, 40561503, 40561504, and 40561505.

P.C. CODE: 034801 (458)
SUBMISSION: S488177
I.D. #: 034801-045728 D.P. BARCODE: D233973

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch II
Health Effects Division (7509C)

THRU: Stephen C. Dapson, Ph.D.
Branch Senior Scientist
Toxicology Branch II
Health Effects Division (7509C)

TO: Karen Whitby, Ph.D., Chief
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

and

Kathleen Depukat/Ron Kendall, PM51
Special Review and Reregistration Division (7508W)

Registrant: UCB Chemicals, Norfolk VA

Request: Review and evaluate the following acute toxicity studies, performed on FERBAM Technical by NOTOX C.V. 'sHertogenbosch (The Netherlands):

(81-1) Evaluation of the acute oral toxicity of FERBAM TECHNICAL in the rat, NOTOX Study 0740/930, dated December 09, 1987. Unpublished. MRID 40561501.

(81-2) Evaluation of the acute dermal toxicity of FERBAM TECHNICAL in the rabbit, NOTOX Study 0740/931, dated December 08, 1987. Unpublished. MRID 40561502.

(81-4) Assessment of primary eye irritation/corrosion by FERBAM TECHNICAL in the rabbit, NOTOX Study 0740/933, dated December 04, 1987. Unpublished. MRID 40561503.

(81-5) Assessment of primary skin irritation/corrosion by FERBAM TECHNICAL in the rabbit, NOTOX Study 0740/932, dated November 20, 1987. Unpublished. MRID 40561505.

(81-6) Assessment of the skin sensitization potential of FERBAM TECHNICAL in the guinea pig (Split Adjuvant Test), NOTOX Study 0740/934, dated December 11, 1987. Unpublished. MRID 40561504

TB CONCLUSIONS: (Detailed reviews are attached)

(GDLN)	STUDY (MRID)	REPORTED RESULTS	TOX. CAT.	TB EVALUATION
(81-1)	Acute oral (40561501)	LD50 (males/females) > 5000 mg/kg	IV	ACCEPTABLE
(81-2)	Acute dermal (40561502)	LD50 (males/females) > 4000 mg/kg	III	ACCEPTABLE
(81-4)	Primary eye irritation (40561503)	PIS (24 hrs.) = 6.3 PIS (7 days) = 0.7	III	ACCEPTABLE*
(81-5)	Primary dermal irritation (40561505)	PII = 0.02	IV	ACCEPTABLE
(81-6)	Skin sensitization (40561504)	Weak sensitizer	-	ACCEPTABLE*
* Previously reviewed; DER in HED Doc. No. 012151 (stamp-dated January 28, 1997)				

Attachments: DERs for MRIDs 40561501 (81-1), 40561502 (81-2), and 40561505 (81-5) only.

FERBAM

Acute Oral Study (81-1)

EPA Reviewer: Irving Mauer, Ph.D
Toxicology Branch II (7509C)
Date: 06-18-98

EPA Secondary Reviewer:
Toxicology Branch (7509C)
Date: 7/22/98

DATA EVALUATION RECORD

012689

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS 870.1100 [81-1]

DP BARCODE: D233973
P.C. CODE: 034801
SUBMISSION CODE: S488177
TOX. CHEM. NO.: 458

TEST MATERIAL (PURITY): Ferbam technical (91.8% a.i.)

SYNONYMS: Ferric dimethyl dithiocarbamate

CITATION: Ir.J.B.J. Reijnders (1987) Evaluation of the acute oral toxicity of FERBAM TECHNICAL in the rat, performed by NOTOX C.V., 'sHertogenbosch (The Netherlands), Study Report No. 0740/930, dated December 09, 1987. MRID 40561501. Unpublished.

SPONSOR: UCB Chemicals, Norfolk VA

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 40561501), one group of Wistar rats (5 males, 5 females) were given a single oral dose of 5000 mg/kg test material (the limit dose), and observed for 14 days.

One female died four days after dosing (only an enlarged liver was seen at necropsy); all other rats survived the period of observation. Initial signs of toxicity (lethargy, piloerection, dacryorrhea, diarrhea, and mild emaciation) were no longer observed by Day 9.

Since only one animal died, the LD50 value for both males and females exceeds 5000 mg/kg.

This acute oral study is classified ACCEPTABLE; the test substance is assigned TOXICITY CATEGORY IV for acute oral toxicity. This study satisfies the guideline requirement for an acute oral study (81-1) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and Flagging statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Ferbam technical
   Description: Black powder
   Lot/Batch #: G3699
   Purity: 91.8% a.i.
   CAS #: 14484-64-1

   Verification of concentration/homogeneity as necessary: [Not provided]

2. Vehicle and/or positive control: 1% Aqueous methyl cellulose.

3. Test animals: Species: Rat
   Strain: Wistar SPF
   Age and/or weight at dosing: 8 weeks/males - 224 g (mean); females - 175 g (mean).
   Source: Charles River, Sulzfeld (DRG)
   Acclimation period: 5 days
   Diet: ad libitum
   Water: ad libitum
   Housing: Singly, in polycarbonate cages.
   Environmental conditions:
   Temperature: 20-22° C
   Humidity: 50-70%
   Air changes: [Not provided]
   Photoperiod: 12 hrs. light, 12 hrs. dark.

B. STUDY DESIGN AND METHODS:

1. In life dates: Start: 11/25/87. End: 12/09/87.

2. Animal assignment and treatment: Animals (5 males/5 females) were assigned to one test group as noted in the table below. Following an overnight fast, rats were given a single dose of 5000 mg/kg by gavage, then observed daily for 14 days; animals were weighed weekly. Survivors were sacrificed and a necropsy was performed on all animals.

TABLE 1. Doses, Mortality/Animals Treated

Dose (mg/kg)	Males	Females	Combined
5000	0/5	1/5	1/10

3. Statistics: An oral LD50 was not calculated, since only one animal died at the limit dose.

II. RESULTS AND DISCUSSION

A. MORTALITY is given in the table above. One female died four days after dosing; all other animals survived the period of observation (14 days).

The oral LD50 for both males and females is greater than 5000 mg/kg.

B. CLINICAL OBSERVATIONS: Lethargy, piloerection, dacryorrhea, diarrhea and emaciation lasting up to 9 days; no signs after that (Final Report Table 1).

C. BODY WEIGHT: Body weight loss for the female which died on study; less or no change in survivors during first week post-dose (Final Report Table 2).

D. NECROPSY: No abnormalities macroscopically in any animal, except for enlarged liver in female that died on post-dose Day 4.

E. DEFICIENCIES: [None]

EPA Reviewer: Irving Mauer, Ph.D. Date: 06-18-98
Toxicology Branch II (7509C)
EPA Secondary Reviewer: Date: 7/22/98
Toxicology Branch (7509C)

DATA EVALUATION RECORD

012689

STUDY TYPE: Acute Dermal toxicity - Rabbit
OPPTS 870.1200 [81-2]

DP BARCODE: D233973 SUBMISSION CODE: S488177
P.C.CODE: 034801 TOX. CHEM. NO.: 458

TEST MATERIAL (PURITY): Ferbam Technical (91.8% a.i.)

SYNONYMS: Ferric dimethyl dithiocarbamate

CITATION: Ir.J.B.J. Reijnders (1987). Evaluation of the acute dermal toxicity of FERBAM TECHNICAL in the rabbit, performed by NOTOX C.V., 'sHertogenboch (The Netherlands), Study Report No. 0740/931, dated December 08, 1987. Unpublished. MRID 40561502.

SPONSOR: UCB Chemicals, Norfolk VA

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 40561502), one group of NZW rabbits (5 males/5 females) was dermally treated with a single dose of test article at 4000 mg/kg for 24 hours, and observed daily for 14 days, as well as weighed weekly. All survivors were necropsied after the 14-day observation period.

No mortalities occurred during the observation period. Treated skin revealed slight erythema and edema which disappeared by the end of the first week. Third eyelid irritation was observed in 6 animals. All animals showed body weight gain during the observation period. Minor macroscopic lesions were noted in some animals.

Dermal LD50 males > 4000 mg/kg; females > 4000 mg/kg.

This acute dermal study is classified as ACCEPTABLE and the test substance assigned TOXICITY CATEGORY III for dermal toxicity. It satisfies the guideline requirement for an acute dermal study (81-2) in rabbits.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data confidentiality, and Flagging statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Ferbam Technical

   Description: Black powder
   Lot/Batch #: G3699
   Purity: 91.8% a.i.
   CAS #: 14484-64-1
   Verification of concentration/homogeneity as necessary: [Not provided]

2. Vehicle and/or positive control: 1% Aqueous methyl cellulose

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age and mean weight at dosing: 9-10 weeks: males = 2.1 kg; females = 2.2 kg
   Source: Broekman Institute, Someren (The Netherlands)
   Acclimation Period: 5 days Diet: LK-01, ad libitum. Water: ad libitum.
   Housing: Singly in metal cages.
   Environmental conditions: Temperature, 20-21° C
   Humidity, 55-65%;
   Air changes, [Not provided]
   Photoperiod, 12 hrs. light/ 12 hrs. dark

B. STUDY DESIGN AND METHODS:

1. In life dates: Start, 11/19/87; end, 12/8/87.

2. Animal assignment and treatment. Rabbits (5 males/5 females) were assigned to one test group, as noted in the table below. Animals were administered a single dose of 4000 mg/kg Ferbam dermally, spread on surgical gauze and affixed to clipped areas, which were bandaged. Twenty-four hours later, all dressings were removed, and animals observed daily for 14 days, as well as being weighed weekly. Survivors were sacrificed and a necropsy performed on all animals.

Dose (mg/kg)	Males	Females	Combined
4000	0/5	0/5	0/10

3. Statistics. The dermal LD50 was not calculated, since there were no deaths.

II. RESULTS AND DISCUSSION:

A. MORTALITY is given in the table above. There were no mortalities.

The dermal LD50 for males and females is greater than 4000 mg/kg.

B. CLINICAL OBSERVATIONS: Closed 3rd eyelid (red, swollen) was observed in 6 animals (Final Report Table 1). Treated skin surfaces revealed slight erythema and edema, which disappeared by the end of Week 1 (Final Report Table 2).

C. BODY WEIGHT: All animals gained weight during the study period (Final Report Table 3).

D. NECROPSY: The following macroscopic abnormalities were noted in some animals: localized dark red areas in the lungs; enlarged spleen; accessory splenic tissue in the pancreas; dilated ileum; some petechiae in the dorsa-lateral muscles.

EPA Reviewer: Irving Mauer, Ph.D Date: 06-18-98
Toxicology Branch II (7509C)
EPA Secondary Reviewer:
Toxicology Branch (7509C) Stephen C. Dapson Date: 7/22/98

DATA EVALUATION RECORD

012689

STUDY TYPE: Primary Dermal Irritation - Rabbit
OPPTS 870.2500 [81-5]

DP BARCODE: D233973 SUBMISSION CODE: S488177
P.C. CODE: 034801 TOX. CHEM. NO.: 458

TEST MATERIAL (PURITY): Ferbam Technical (91.8% a.i.)

SYNONYMS: Ferric dimethyl dithiocarbamate

CITATION: P.J.J.M. Weterings and P.A.M. Daamen (1987). Assessment of primary skin irritation/corrosion by FERBAM TECHNICAL in the rabbit, performed by NOTOX C.V., s'Hertogenbosch (The Netherlands). Study Report 0740/932, dated November 20, 1987. MRID 40561505. Unpublished.

SPONSOR: UCB Chemicals, Norfolk VA

EXECUTIVE SUMMARY: In a study of potential primary dermal irritation (MRID 40561505), 0.5 grams test article, slightly moistened (with water), was applied (over an area of 10 cm^2) to the clipped flanks of six NZW rabbits, and removed four hours later. Any resulting dermal effects were monitored for 72 hour after removal of dressings, and scored by the method of Draize et al. (1944).

Only very slight-to-slight erythema was observed in only one animal 60 minutes after removal of dressings, but disappeared by 24 hours.

PII = 0.02. No systemic effects were noted.
FERBAM TECHNICAL is TOXICITY CATEGORY IV

This primary dermal irritation study is ACCEPTABLE, and satisfies the FIFRA Test Guideline for a primary dermal irritation study (81-5) in the rabbit for this formulation of FERBAM.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and Flagging statements were provided.

012689

I. MATERIALS AND METHODS

A. MATERIALS:

1. Description: Ferbam technical
Description: Black powder
Lot/Batch #: G3699
Purity: 91.8% a.i.
CAS #: 14484-64-1

Verification of concentration/homogeneity as necessary: [Not provided]

2. Vehicle: 0.5 mL deionized water (DW).

3. Test animals: Species: Lagomorph

Strain: New Zealand White (2M:4F)
Age and weight at treatment: 10 weeks: M = 2186-2190 g; F = 2248-2427 g.
Source: Broekman Institute, Somers (The Netherlands)
Acclimation period: 7 days
Housing: Individually in plastic cages
Diet: Hope Farms diet (Woerden)
Water: Modified Tap Water
Environmental Conditions: Temperature, 20-21° C.
Humidity, 60-70%.
Photoperiod, 12 hrs. light/ 12 hours dark.

B. STUDY DESIGN AND METHODS: 0.5 grams of test material, moistened with 0.5 mL water, was spread on a 6 cm^2 gauze patch mounted on permeable tape, and applied to the left flank of each animal, the right flank being covered with a similar patch but without test substance. All animals were then wrapped in flexible bandages. Coverings were removed 4 hours later, and test areas scored at 60 minutes, as well as at 24, 48 and 72 hours (by method of Draize et al, 1944).

II. RESULTS AND DISCUSSION: Only one animal (M3216) showed any reaction, very slight erythema 60 minutes after bandage removal, which disappeared by 24 hours (Report Table 1).

The investigators concluded that Ferbam technical is lightly irritating to the skin of rabbits, if at all (since the reaction disappears one day later). The calculated primary irritating index (PII) is 0.02 (0.13/6, Report Table 1).

III. REVIEWER'S DISCUSSION/CONCLUSIONS: The reviewer agrees with the investigators' conclusions that FERBAM TECHNICAL is minimally irritating in this study. TOXICITY CATEGORY assigned is IV.

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R167926

Chemical Name: Ferbam

PC Code: 034801
HED File Code: 61400 SRRD DERs
Memo Date: 7/22/1998
File ID: TX0012689
Accession #: 000-00-8012

HED Records Reference Center
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