9.3.98

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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

Acute Tox Review

September 3, 1998

MEMORANDUM

Subject: EPA Reg. No.: 045087-AR
DP Barcode: D245998
Case No: 062130

From: Eugenia McAndrew, Biologist
Technical Review Branch
Registration Division (7505C)

To: Daniel Peacock, PM Team 04
Insecticide/Rodenticide Branch
Registration Division (7505C)

Applicant: Zema Corporation
P.O. Box 12803
Research Triangle Park, NC 27709

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
44102	Methyl Nonyl Ketone	12%
21901	Oil of Citronella	6%
	Inert Ingredient(s):	82%
	Total:	100%

BACKGROUND: The registrant has submitted a 6-pack of acute toxicity studies which were performed on an earlier formulation dated 8/11/97. The revised formula dated 2/4/98 contains a small increase in the active ingredient methyl nonyl ketone from 11.54 % by weight to 12.0% by weight. This amount, however, is still within the certified upper limit stated in the earlier formula.

RECOMMENDATIONS: Five of the six studies were reviewed and found to be acceptable. The sixth, the acute inhalation toxicity study, could not be performed because according to the Study Director, results of the trials "indicate that the physical properties of Reppers Grain Repellent, Lot #158161, prevented aerosolization even for short periods of time." Based on the results of this feasibilty study, the Guideline 81-3 Acute Inhalation LC_{50} is waived.

The acute toxicity profile for EPA Reg. No. 045087-AR is as follows:

acute oral toxicity	IV	Acceptable
acute dermal toxicity	IV	Acceptable
acute inhalation toxicity	--	Waived
primary eye irritation	III	Acceptable
primary skin irritation	III	Acceptable
dermal sensitization	No	Acceptable

LABELING: Date: 09/03/98 LABEL REVIEW SYSTEM

ID #: 045087-00061 REPPERS REPELLENT GRAINS

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

Causes moderate eye irritation. Avoid contact with eyes, skin or clothing. Wear long-sleeved shirt and long pants, socks and shoes and waterproof gloves. Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF ON SKIN: Wash with plenty of soap and water. Get medical attention, if irritation persists.

IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

NOTE TO PHYSICIAN:

The proposed label should contain a Note to Physicians. Some suggested types of information include the following:

- technical information on symptomatology;
- use of supportive treatments to maintain life functions;
- medicine that will counteract the specific physiological effects of the pesticide;
- company telephone number to specific medical personnel who can provide specialized medical advice.

DATA EVALUATION REPORT

REPPERS GRAIN REPELLENT

STUDY TYPES: ACUTE ORAL TOXICITY - RAT (81-1)
ACUTE DERMAL TOXICITY - RAT (81-2)
DUST GENERATION FEASIBILITY STUDY
PRIMARY EYE IRRITATION - RABBIT (81-4)
PRIMARY DERMAL IRRITATION - RABBIT (81-5)
DERMAL SENSITIZATION - GUINEA PIG (81-6)

SUMMARY: ACUTE TOXICITY ONE-LINERS (81-1, 81-2, 81-4 through 81-6)

Prepared for

Registration Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
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Oak Ridge, TN 37831

Primary Reviewer:
Susan Chang, M.S. Signature: _____
Date: _____

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.),Ph.D., D.A.B.T.
Signature: _____
Date: _____

Robert H. Ross, M.S., Group Leader Signature: _____
Date: _____

Quality Assurance:
LeeAnn Wilson, M.A. Signature: _____
Date: _____

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1, 870.1100)

Product Manager: PM 04
MRID No.: 44352804

Reviewer: Susan Chang
Study Completion Date: July 25, 1997
Study No.: 5217

Testing Facility: Product Safety Labs
Author: Wnorowski, G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Reppers Grain Reppellent (11.54% Methyl nonyl ketone); Lot 158161; light yellow-brown grains
Species: Rats; Albino, Sprague-Dawley
Age: Young adult
Weight: Males: 225-256 g; Females: 189-215 g
Source: Ace Animals, Inc., Boyertown, PA

Conclusion:

1. **LD_{50} (mg/kg):**
   Males: > 5000 mg/kg
   Females: > 5000 mg/kg
   Combined: > 5000 mg/kg
2. **The estimated LD_{50} is** > 5000 mg/kg
3. **Tox. Category:** IV **Classification:** Acceptable

Procedure (Deviations from §81-1): None

Results:

Dosage (mg/kg)[a]	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

[a]administered as 13% w/w suspension in a 1% solution of CMC in distilled water by gavage

Observations: One male rat had a hunched posture, one female had facial staining, and one female showed irregular respiration on the day of test material administration. All other rats were active and healthy and all rats had normal body weight gains.

Gross Necropsy: Gross necropsy findings were generally unremarkable. All rats had slightly or moderately red lungs due to CO_2 inhalation euthanasia.

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: PM 04
MRID No.: 44352805

Reviewer: Susan Chang
Study Completion Date: July 25, 1997
Study No.: 5288

Testing Facility: Product Safety Labs
Author: Wnorowski, G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Reppers Grain Reppellent (11.54% Methyl nonyl ketone); Lot 158161; light yellow-brown grains
Species: Rats; Albino, Sprague-Dawley
Age: Young adult
Weight: Males: 211-231 g; Females: 203-222 g
Source: Ace Animals, Inc., Boyertown, PA

Dermal LD_{50} Testing:

Conclusion:

1. **LD_{50} (mg/kg):**
   Males: > 5000 mg/kg
   Females: > 5000 mg/kg
   Combined: > 5000 mg/kg
2. **The estimated LD_{50} is** > 5000 mg/kg
3. **Tox. Category:** IV **Classification:** Acceptable

Procedure (Deviations from §81-2): None

Results:

Dosage (mg/kg)[a]	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

[a]The test material was ground to a powder and moistened to achieve a dry paste by preparing an 80% w/w mixture in distilled water.

Observations: No animals died during the study. No clinical abnormalities were observed. All animals had normal body weight gains.

Gross Necropsy: Gross necropsy findings were generally unremarkable. All rats had slightly red lungs due to CO_2 inhalation euthanasia.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3, 870.1300)

Product Manager: PM 04
MRID No.: 44352806

Reviewer: Susan Chang
Study Completion Date: July 25, 1997
Study No.: 5290

Testing Facility: Product Safety Labs
Author: Wnorowski, G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Reppers Grain Reppellent (11.54% Methyl nonyl ketone); Lot 158161; light yellow-brown grains

Conclusion: " Due to the nature of the test substance, it could not be aerosolized successfully. The grinding and/or generation process caused the material to release an oily liquid which obstructed the cutting blade and dust outlet assembly of the dust generator. Efforts to correct this problem, including the use of various grinding equipment and generation procedures, were unsuccessful. In every case, attempts at aerosol generation failed to produce an atmosphere."

This is an acute inhalation - dust generation feasibility study. Since the test material could not be aerosolized successfully, the EPA guidelines for acute inhalation testing could not be satisfied. Based on the results of this feasibility study, the Guideline 81-3 Acute Inhalation LD_{50} is waived.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: PM 04
MRID No.: 44352807

Reviewer: Susan Chang
Study Completion Date: July 25, 1997
Study No.: 5287

Testing Facility: Product Safety Labs
Author: Wnorowski, G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Reppers Grain Reppellent (11.54% Methyl nonyl ketone); Lot 158161; light yellow-brown grains
Dosage: 0.1 mL (approximately 0.03-0.04 g)
Species: Rabbits; Albino, New Zealand White
Age: Adult
Weight: Not reported
Source: Davidson's Mill Farm, South Brunswick, NJ

Conclusion:
1. **Toxicity Category:** III
2. **Classification:** Acceptable

Procedure (Deviations from §81-4): Weights of animals not reported. However, this is a minor deviation not affecting the outcome of the study.

Observations	Number "positive"/number tested				
	Hours				Days
	1	24	48	72	4
	Unwashed eyes				
Corneal Opacity	0/6	4/6	2/6	0/6	0/6
Iritis	0/6	2/6	0/6	0/6	0/6
Conjunctivae:					
Redness	5/6	6/6	1/6	0/6	0/6
Chemosis	0/6	3/6	0/6	0/6	0/6
Discharge	6/6	4/6	0/6	0/6	0/6

Summary: Within 24 hours after test material instillation, 4/6 rabbits exhibited corneal opacity that cleared by 72 hours. Iritis was seen on 2/6 rabbits at 24 hours that cleared by 48 hours. Conjunctival redness was noted on 5/6 rabbits one hour after test material instillation that resolved by 72 hours. Conjunctival chemosis was noted on 3/6 rabbits at 24 hours that resolved by 48 hours. Conjunctival discharge was noted on all six rabbits at one hour that resolved by 48 hours. The highest average ocular irritation index was 15.3, recorded 24 hours after test material instillation. This classifies the test material as a mild irritant.

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (§81-5, 870.2500)

Product Manager: PM 04
MRID No.: 44352808

Reviewer: Susan Chang
Study Completion Date: July 25, 1997
Study No.: 5218

Testing Facility: Product Safety Labs
Author: Wnorowski, G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Reppers Grain Reppellent (11.54% Methyl nonyl ketone); Lot 158161; light yellow-brown grains
Dosage: 0.5 g dry weight basis (The test material was ground to a powder and moistened to achieve a dry paste by preparing an 80% w/w mixture in distilled water.)
Species: Rabbits; Albino, New Zealand White
Age: Adult
Weight: Not reported
Source: Davidson's Mill Farm, South Brunswick, NJ

Conclusion:
1. **Toxicity Category:** III
2. **Classification:** Acceptable

Procedure (Deviations from §81-5): None

Results: PDIS = 2.4 (Moderate irritant). One hour after patch removal, very slight erythema and well defined erythema were noted on 3/6 and 3/6 rabbits, respectively. Very slight edema and slight edema were noted on 4/6 and 2/6 rabbits, respectively. By 24 hours, very slight erythema on one rabbit, well defined erythema on five rabbits, very slight edema on four rabbits, and slight edema on one rabbit were observed. The erythema persisted on all rabbits through 72 hours. All irritation cleared by day 7; however, desquamation was present at dose site on five rabbits.

Special Comments: None

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: PM 04
MRID No.: 44352809

Reviewer: Susan Chang
Study Completion Date: July 28, 1997
Study No.: 5289

Testing Facility: Product Safety Labs
Author: Wnorowski, G.

Quality Assurance (40 CFR §160.12): Included

Test Material: Reppers Grain Reppellent (11.54% Methyl nonyl ketone); Lot 158161; light yellow-brown grains
Positive Control Material: 1-Chloro-2,4-dinitrobenzene (DNCB)
Species: Guinea pigs; Albino, Hartley
Age: Young adult
Weight: Males: 276-371 g
Source: Davidson's Mill Farm, South Brunswick, NJ
Method: Buehler

Conclusion:

1. **There is no indication that this product is a dermal sensitizer.**
2. **Classification:** Acceptable

Procedure (Deviations from §81-6): 1. The Guidelines suggest that the guinea pigs "should be at least 300 grams, preferably 350-450 grams." Two of the guinea pigs in the study weighed 276 g and 298 g. However, this minor deviation should not affect the outcome of the study. 2. Guideline 870.2600 recommends a minimum of 20 animals in a treatment group and 10 in controls. However, TRB has concluded that the number of animals used in the study is adequate to determine the dermal sensitization potential of this compound.

Procedure: For the induction phase, 0.4 g of a 75% w/w mixture of the ground test material in distilled water was applied under occlusion for six hours once each week for three weeks. Guinea pigs were left untreated for thirteen days before primary challenge. The animals were challenged with 75% w/w mixture of the ground test material in distilled water under occlusion at naive sites for 6 hours. A naive control group was treated with 75% w/w mixture of the ground test material in distilled water at challenge only. The positive control group animals were induced with 0.4 mL of 0.08% DNCB in 80% aqueous ethanol and challenged with 0.04% w/w DNCB in acetone. A naive positive control group was challenged with 0.04% w/w DNCB in acetone at challenge. Reactions were scored 24 and 48 hours post exposure.

Results: Very faint erythema was noted on 9/10 animals after the first, second, or third induction. Very faint erythema were noted on 3/10 test animals and 2/5 control animals following challenge. The DNCB positive control and naive control animals responded appropriately.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D245998
2. **PC CODE:** 44102, 21901
3. **CURRENT DATE:** September 3, 1998
4. **TEST MATERIAL:** Reppers Grain Reppellent [a, b, c] (11.54% Methyl nonyl ketone); Lot 158161; light yellow-brown grains

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity rat/Product Safety Labs, 5217/7-25-97	44352804	LD_{50} > 5000 mg/kg (males, females, combined)	IV	A
Acute dermal toxicity rat/Product Safety Labs, 5288/7-25-97	44352805	LD_{50} > 5000 mg/kg (males, females, combined)	IV	A
Acute inhalation toxicity rat/Product Safety Labs, 5290/7-25-97	44352806	Not a toxicity study		
Primary eye irritation rabbit/Product Safety Labs, 5287/7-25-97	44352807	Mild irritant; corneal opacity on 4/6 rabbits at 24 hours that cleared by 72 hours; iritis on 2/6 rabbits at 24 hours that cleared by 48 hours; conjunctival redness on 5/6 rabbits one hour after test material instillation that resolved by 72 hours; conjunctival chemosis on 3/6 rabbits at 24 hours that resolved by 48 hours; conjunctival discharge on all six rabbits at one hour that resolved by 48 hours. The highest average ocular irritation index was 15.3, recorded 24 hours after test material instillation.	III	A
Primary dermal irritation rabbit/Product Safety Labs, 5218/7-25-97	44352808	Moderate irritant; very slight erythema and well defined erythema on 3/6 and 3/6 rabbits, respectively, at 1 hour; very slight edema and slight edema on 4/6 and 2/6 rabbits, respectively, at 1 hour; very slight erythema on one rabbit, well defined erythema on five rabbits, very slight edema on four rabbits, and slight edema on one rabbit by 24 hours; erythema persisted on all rabbits through 48 and 72 hours and all irritation cleared by day 7, however, desquamation was present at dose site on five rabbits.	III	A
Dermal sensitization guinea pig/Product Safety Labs, 5289/7-28-97	44352809	Not a sensitizer	--	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated**

[a]Acute oral toxicity study - administered as 13% w/w suspension in a 1% solution of CMC in distilled water by gavage

[b]Acute dermal toxicity and primary dermal irritation studies - The test material was ground to a powder and moistened to achieve a dry paste by preparing an 80% w/w mixture in distilled water.

[c]Dermal sensitization study - 75% w/w mixture of the ground test material in distilled water.