

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

January 28, 1998

MEMORANDUM:

Subject: EPA Reg.No.: 51036-78/Linuron 4L Weed Killer
DP Barcode: D241573
Case No.: 119401

From: Marianne Lewis, Biologist
Product Reregistration Branch
Special Review and Reregistration Division (7508W)

Handwritten signature and date: Marianne Lewis 2/2/98

Handwritten signature and date: Byron T. Baskin 2-FEB-1998

To: Karen Jones, CRM
Product Reregistration Branch
Special Review and Reregistration Division (7508W)

Applicant: Micro-Flo Company
Route 1, Box 190
Sparks, Georgia 31647

FORMULATION FROM EPA Reg.No.51036-78 LABEL:

Table with 2 columns: Ingredient name and % by wt.
Active Ingredient(s): Linuron (3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea) 40.6%
Inert Ingredient(s): 59.4%
Total: 100.0%

BACKGROUND: In the 8 month response to the Linuron RED the registrant has submitted acute toxicology studies in support of the reregistration of their product, EPA Reg.No.51036-78. The MRID numbers are as follows: 155906, 155907, 155908, 155909, 155910, and 155911. The studies were conducted by Cosmopolitan Safety Evaluation, Inc. This product is found in Batch 1 of the Linuron RED. The test material used by Cosmopolitan for the studies was Linuron 4FL. The CSF for EPA Reg.No.51036-78 states the name of the product is Linuron 4L. The registrant was contacted to clarify. Mr. Morris Gaskins, Manager for Registration at Micro-Flo, confirmed that Cosmopolitan Safety Evaluation had made an error in labeling the test material. The material that Cosmopolitan tested was in fact Linuron 4L.

RECOMMENDATIONS: Five of the acute toxicity studies were found to be acceptable, 81-1 through 81-5, and should be used in support the reregistration of EPA Reg.No.51036-78.

The skin sensitization study, 81-6, was unacceptable.

The lab failed to provide adequate information on the positive control used in the skin sensitization study. "Periodically a known sensitizer is tested under the same conditions. All known sensitizers used have shown as strong positives."(Study 1331F, 8/85) The study conducted on the positive control used in the lab should have been submitted with the skin sensitization study.

The classification of the skin sensitization study can be upgraded to acceptable, provided the cited positive control study (Reference Notebook #51407-1312F) is adequate and it was conducted within 6 months of Study #1331F.

The acute toxicity profile for EPA Reg.No.51036-78 is currently:

Acute Oral	III	Acceptable
Acute Dermal	III	Acceptable
Acute Inhalation	III	Acceptable
Primary Eye	IV	Acceptable
Primary Dermal	IV	Acceptable
Skin Sensitization	--	Unacceptable

This label information does not include the skin sensitization data.

LABELING:

ID #: 051036-00078 LINURON 4L WEED KILLER

CHILD RESISTANT PACKAGING REQUIRED

AGRICULTURAL USE REQUIREMENTS:

DIRECTIONS FOR USE:

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, wear: coveralls over long-sleeved shirt and long pants, socks and chemical resistant footwear and waterproof gloves.

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

Harmful if swallowed or absorbed through skin or inhaled. Avoid contact with eyes, skin or clothing. Avoid breathing spray mist. Wear long-sleeved shirt and long pants, socks and shoes and waterproof gloves. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. If person is unconscious, do not give anything by mouth and do not induce vomiting.

OR

IF SWALLOWED: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger, or if available by administering syrup of ipecac. If person is unconscious, do not give anything by mouth and do not induce vomiting.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

IF INHALED: Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

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

Product Manager: Jim Tompkins, 25
MRID No.: 00155906

Reviewer: Marianne Lewis
Study Completion Date: 11/9/85
Report No.: 1331A

Testing Facility: Cosmopolitan Safety Evaluation, Inc.
Author: G. Rosenfeld

Quality Assurance (40 CFR §160.12): Included

Test Material: Linuron 4L, thick beige liquid, EPA Reg.No.51036-78

Species: Sprague-Dawley derived albino rats

Age: young adult

Weight: males = 240-340 g; females = 200-300 g

Source: not stated

Conclusion:

1. **LD₅₀ (mg/kg):** Males : 3540 (2395-5232) mg/kg
Females: 3247 (1719-6133) mg/kg
Combined: 3407 (2419-4798) mg/kg
2. **Tox. Category:** III **Classification:** Acceptable

Procedure (Deviations from §81-1):

Results:

Dosage (mg/kg)	Number Deaths/Number Tested		
	Males	Females	Combined
1256	0/5	1/5	1/10
2506	1/5	2/5	3/10
5000	4/5	3/5	7/10

Observations: Clinical signs included decreased activity and ataxia, prostration was observed especially in animals which died. Other signs were chromodacryorrhea/ chromorrhinnorrea, and perineal staining. Most fatalities occurred days 1-3. Survivors were normal in appearance and behavior from day 5 to the end of the study on day 14.

Gross Necropsy: In animals that survived to the end of the study all organs and tissues examined appeared normal. In the animals that died abnormalities included: congestion of alimentary tract and mottling of liver. In some animals which died at 5000 mg/kg renal pallor was observed.

DATA REVIEW FOR ACUTE DERMAL TOXICITY (§81-2, 870.1100)

Product Manager: Jim Tompkins, 25
MRID No.: 00155907

Reviewer: Marianne Lewis
Study Completion Date: 9/11/85
Report No.: 1331B

Testing Laboratory: Cosmopolitan Safety Evaluation, Inc.
Author: G. Rosenfeld

Quality Assurance (40 CFR § 160.12): Included

Test Material: Linuron 4L, thick beige liquid, EPA Reg.No.51036-78
Species: New Zealand White Rabbit
Weight: combined 2.5-3.5 kg
Age: young adult
Source: none stated

Summary:

- LD₅₀ (mg/kg):** Males = >2000 mg/kg
Females = >2000 mg/kg
Combined = >2000 mg/kg
- Tox. Category:** III **Classification:** Acceptable

Procedure (Deviations From §81-2):

Results:

DOSAGE (mg/kg)	Reported Mortality (number deaths/number tested)		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: "Mild irritation" noted when wraps were removed; by 72 hours there was only very slight erythema which was gone by day 7.

Gross Necropsy Findings: Nothing unusual noted.

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

Product Manager: Jim Tompkins, 25
MRID No.: 00155908

Reviewer: Marianne Lewis
Study Completion Date: 11/13/85
Report No.: 1331C

Testing Laboratory: Cosmopolitan Safety Evaluation, Inc.
Author: G. Rosenfeld

Quality Assurance (40 CFR §160.12): Included

Test Material: Linuron 4L, thick beige liquid, EPA Reg.No.51036-78
Concentration: 50% w/w in distilled water

Species: Sprague-Dawley derived rats
Weight: males = 240-340 g, females = 200-300 g
Age: young adult
Source: not stated

Summary:

1. LC_{50} (mg/L): Combined > 1.7 mg/L (gravimetrically determined)
2. MMAD: 0.8 microns at 1.25 hours, GSD = 7.1 microns;
1.6 microns at 3 hours, GSD = 6.7 microns
3. Tox. Category: III Classification: Acceptable

Procedure (Deviation From §81-3):

Results: Reported Mortality

Exposure Concentration	(Number Deaths/Number Tested)		
	Males	Females	Combined
1.7 mg/L	0/5	0/5	0/10

Chamber Atmosphere				
Dose Level	MMAD*	GSD*	% particles < 2.5 μ *	% particles < 7 μ *
1.7 mg/L	1.6 μ m	6.7 μ m	50.7	68.2

*At 2 hours 55 minutes.

Chamber Environment	Dose levels
	1.7 mg/L
Chamber Volume	47.4 liters
Airflow	10 Lpm
Temperature (°F)	68-74
Relative Humidity (%)	72-74

The lab conducting the study compared the nominal concentration(10.3 mg diluted test article/L) and the actual concentration used indicating a dosing efficiency of approximately 33% in the chamber. The report states that this dosing efficiency indicated the instability of the aerosol as the atmosphere approached saturation due to the frequency of particle collision. Within the chamber the atmosphere was very cloudy and there was precipitation on the walls and floor of the chamber. It was concluded that the actual concentration was the maximal attainable concentration.

Clinical Observations: Muzzle fur was wet during the 4th hour of exposure and immediately after exposure. Animals exposed to the test material remained normal in appearance and behavior during exposure and throughout the study.

Gross Necropsy Findings: Nothing unusual noted.

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

Product Manager: Jim Tompkins, 25
MRID No.: 00155909

Reviewer: Marianne Lewis
Study Completion Date: 7/20/85
Report No.: 1331D

Testing Laboratory: Cosmopolitan Safety Evaluation, Inc.
Author: G. Rosenfeld

Quality Assurance (40 CFR §160.12): Included

Test Material: Linuron 4L, thick beige liquid, EPA Reg.No.51036-78

Dosage: 0.1 ml
Species: albino rabbits
Sex: not stated
Weight: 2.0-3.5 kg
Age: young adult
Source: not stated

Summary:

- 1. Toxicity Category:** IV
- 2. Classification:** Acceptable

Procedure (Deviations From §81-4):

Results:

OBSERVATIONS	(number "positive"/number tested)			
	Hours			
	1	24	48	72
Corneal Opacity	0/6	0/6	0/6	0/6
Iris	0/6	0/6	0/6	0/6
Conjunctivae				
Redness	0/6	0/6	0/6	0/6
Chemosis	0/6	0/6	0/6	0/6

One hour after application there was slight conjunctival redness in 6/6 and very slight chemosis in 2/6. By 24 hours all irritation had cleared.

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

Product Manager: Jim Tompkins, 25
MRID No.: 00155910

Reviewer: Marianne Lewis
Study Completion Date: 8/19/85
Report No.: 1331E

Testing Laboratory: Cosmopolitan Safety Evaluation, Inc.
Author: G. Rosenfeld

Quality Assurance (40 CFR §160.12): Included

Test Material: Linuron 4L, thick beige liquid, EPA Reg.No.51036-78

Dosage: 0.5 ml
Species: New Zealand Albino Rabbit
Age: young adult
Sex: not stated
Weight: 2.0-3.5 kg
Source: not given

Summary:

- 1. Toxicity Category:** IV
- 2. Classification:** Acceptable

Procedure (Deviations From §81-5):

Results:

OBSERVATIONS	(number "positive"/number tested)			
	minutes	hours		
	30-60	24	48	72
erythema & eschar formation	6/6	4/6	2/6	0/6
edema	2/6	0/6	0/6	0/6

The maximum score for erythema and/or edema observed in this study was 1. All sites were normal by 72 hours.

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

Product Manager: Jim Tompkins, 25
MRID No.: 0155911

Reviewer: Marianne Lewis
Study Completion Date: 9/13/85
Report No.: 1331F

Testing Laboratory: Cosmopolitan Safety Evaluation, Inc.
Author: G. Rosenfeld

Quality Assurance (40 CFR §160.12): Included

Test Material: Linuron 4L, thick beige liquid, EPA Reg.No.51036-78

Positive Control Material: p-phenylenediamine (complete report not received)

Species: albino guinea pigs
Weight: 300-500 g
Age: young adult
Source: Summit View Farm

Method: Buehler

Summary:

1. **Classification:** Unacceptable (potential to be upgraded; see below)

Procedure (Deviation From §81-6):

- positive control study mentioned was not submitted with this study

Procedure: The test animals were induced with 0.5 ml of undiluted test material once per week for three weeks. Two weeks after the last induction dose, the test material-induced animals were challenged with 0.5 ml at the original induction site and a virgin site on the opposite side of the animals. The animals were scored 24 and 48 hours after the challenge application.

According to the study report, a known sensitizer is periodically tested under the same conditions. However, the results from the positive control (p-phenylenediamine as a 2.0% w/w concentration in saline) are presented only in summary form, with no additional information as to the individual scores.

Results: The maximum score for erythema at 24 or 48 hours following any of the induction exposures was 1; all scores for edema were 0. The same results (at both the previously used and virgin sites) were observed following challenge.

There is no indication then that Linuron 4L is a dermal sensitizer. However, before the Agency can accept this finding (and upgrade it to acceptable), the report for the positive

control study (Reference Notebook #51407-1312F) must be reviewed to determine if this study was adequate and if it was conducted within the ± 6 months time frame of this study (#1331F).

ACUTE TOX ONE-LINER

1. PC CODE: 035506
2. CURRENT DATE: February 2, 1998
3. TEST MATERIAL: Linuron 4L Weed Killer, EPA Reg.No.51036-78, Linuron: 40.6%

Study/Species/ Lab/Study#/Date	MRID #	Results	Tox. Cat.	Core Grade
acute oral toxicity/rat/ Cosmopolitan Safety Eval., Inc./1331A/11-9-85	00155906	LD ₅₀ males = 3540 mg/kg females = 3247 mg/kg combined = 3407 mg/kg	III	A
acute dermal toxicity/rabbit/ Cosmopolitan Safety Eval., Inc./1331B/9-11-85	00155907	LD ₅₀ > 2000 mg/kg	III	A
acute inhalation toxicity/rat/ Cosmopolitan Safety Eval., Inc./1331C/11-13-85	00155908	LC ₅₀ combined = > 1.7 mg/L	III	A
primary eye irritation/rabbit/ Cosmopolitan Safety Eval., Inc./1331D/7-20-85	00155909	In all 6 rabbits there was slight conjunctival redness & in 2/6 very slight chemosis. By 24 hours all symptoms cleared.	IV	A
primary dermal irritation/ rabbit/Cosmopolitan Safety Eval.,Inc./1331E/8-19-85	00155910	All 6 rabbits exhibited slight erythema & 2/6 had slight edema in the first 60 minutes. The edema subsided, the erythema remained very slight & all completely cleared by 72 hours.	IV	A
skin sensitization/rabbit/ Cosmopolitan Safety Eval., Inc./1331F/9-13-85	00155911	No indication that this is a dermal sensitizer, but need to see positive control study results before this study can be classified as acceptable.	--	U

Core Grade Key:

- A = Acceptable
- S = Supplementary (upgradeable)
- U = Unacceptable
- V = self-Validated