US EPA ARCHIVE DOCUMENT

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

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

11/MAR/1999
MEMORANDUM

Subject: EPA Reg. No.: 1812-UEN Boa Herbicide
DP Barcode: D251641
Case No: 064471
PC Code: 061601

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

To: Vickie Walters, PM Team 25
Herbicide Branch
Registration Division (7505C)

Applicant: Griffin L.L.C.
P.O.Box 1847
Valdosta, Georgia 31603-1847

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
061601	Paraquat dichloride (1,1-dimethyl-4,4-bipyridinium dichloride)	37
	Inert Ingredient(s):	63
	Total:	100%

ACTION REQUESTED: PM requests review of acute toxicity data for file symbol 1812-UEN, a product known as Boa Herbicide.

BACKGROUND: Griffin L.L.C. has submitted a 6-pack of acute toxicity studies to support registration of file symbol 1812-UEN, a new product known as Boa Herbicide. The MRID # are 446532-02 through -07. The studies were conducted at Product Safety Labs, East Brunswick, New Jersey. The studies were summarized by an Agency contractor and then evaluated and revised by TRB.

RECOMMENDATIONS: The six studies were reviewed and five are classified as acceptable.

The guinea pig sensitization is classified as supplementary because it was aborted before the challenge phase. The test article was highly toxic and several animals died during the induction phase. A screening test should have been conducted in order to select a proper (minimally toxic) dose for the study. However, it is noted that at 24 hours following the second induction treatment, 8/10 animals showed "severe" erythema, while the maximum reaction noted following the first induction treatment was "very faint" erythema, suggesting development of a dermal sensitization response. In lieu of an acceptable study demonstrating otherwise, we will accept labeling for this formulation indicating that it is a potential dermal sensitizer. The acute toxicity profile for File Symbol No. 1812-UEN is then as follows:

acute oral toxicity	II	acceptable
acute dermal toxicity	III	acceptable
acute inhalation toxicity	I	acceptable
primary eye irritation	II	acceptable
primary skin irritation	III	acceptable
dermal sensitization	Positive	supplementary

LABELING: The following precautionary and first aid statements are required according to the Label Review System. The proposed label submitted does contain the required statements with a few exceptions. In the first aid statement for IF INHALED the required statement "If not breathing give artificial respiration, preferably mouth-to-mouth" is missing. Also, in the NOTE TO PHYSICIAN the statement "Probable mucosal damage may contraindicate the use of gastric lavage" is missing. Also, the label does have the precautionary statement " May cause allergic skin reaction" but the statement is incomplete. The complete statement reads: " Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals."

Date: 03/11/99 LABEL REVIEW SYSTEM

ID #: 001812-00420 Boa Herbicide

RESTRICTED USE CLASSIFICATION RECOMMENDED:

Due to acute inhalation toxicity category.

The PM Team should decide if restricted use classification is necessary or if alternative labeling will allay the requirement for restricted use classification.

2

SIGNAL WORD: DANGER PELIGRO

POISON SKULL and CROSSBONES symbol

PRECAUTIONARY STATEMENTS:

Fatal If inhaled. May be fatal if swallowed. Causes substantial but temporary eye injury. Harmful if absorbed through skin. Do not get in eyes or on clothing. Avoid contact with skin. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Do not breathe spray mist. For handling activities, use a NIOSH respirator with an organic vapor (OV) cartridge or canister with any N, P, R, or HE prefilter. Wear long-sleeved shirt and long pants, socks and shoes, goggles or face shield and chemical resistant gloves (such as Nitrile, Butyl, Neoprene, and/or Barrier Laminate).

USER SAFETY RECOMMENDATIONS:

Wash hands before chewing gum, using tobacco or using the toilet. 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, 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.

IF IN EYES: Hold eyelids open and flush with steady, gentle stream of water for 15 minutes. Get medical attention.

NOTE TO PHYSICIAN:

Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician." The following statements are suggested types of information that may be included, if applicable:

- 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.

The following "Note to Physician" statement is required for the subject product:

NOTE TO PHYSICIAN: Probable mucosal damage may contraindicate the use of gastric lavage.

#45534

DP BARCODE: D251640

CASE: 064471
SUBMISSION: S552747

DATA PACKAGE RECORD
BEAN SHEET

DATE: 12/14/98

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REGISTRATION ACTION: 166 RESB NEW PRO-OC-MIN CHG
RANKING : 10 POINTS ()
CHEMICALS: 061601 Paraquat dichloride 37.0000%

ID#: 001812-UEN Boa Herbicide
COMPANY: 001812 GRIFFIN L.L.C.
PRODUCT MANAGER: 25 JIM TOMPKINS 703-305-5697 ROOM: CM2 239
PM TEAM REVIEWER: VICKIE WALTERS 703-305-5704 ROOM: CM2 233
RECEIVED DATE: 12/10/98 DUE OUT DATE: 06/18/99

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 251640 EXPEDITE: N DATE SENT: 12/14/98 DATE RET.: / /
CHEMICAL: 061601 Paraquat dichloride
DP TYPE: 001 Submission Related Data Package
CSF: Y LABEL: Y

ASSIGNED TO	DATE IN	DATE OUT
DIV : RD	/ /	/ /
BRAN: TRB	/ /	/ /
SECT: CHEM	/ /	/ /
REVR : S. Mitchell	12/15/98	1/19/99
CONTR:	/ /	/ /

ADMIN DUE DATE: ~~05/13/99~~
NEGOT DATE: 3/14/99
PROJ DATE: / /

* * * DATA REVIEW INSTRUCTIONS * * *

Please review enclosed product chemistry data to determine if formulation is acceptable and similar to 10182-280. MRIDs enclosed are 44653201,44658601. Information on technical routed concurrently under 1812-UEU.

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL

5

DATA EVALUATION REPORT

BOA

STUDY TYPES: ACUTE ORAL TOXICITY - RAT (81-1)
ACUTE DERMAL TOXICITY - RAT (81-2)
ACUTE INHALATION TOXICITY - RAT (81-3)
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 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
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831

Primary Reviewer:
Susan Chang, M.S.

Signature: Robert H. Ross
Susan S. Chang
Date: FEB 17 1999

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

Signature: H.T. Borges
Date: FEB 17 1999

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: FEB 17 1999

Quality Assurance:
Eric Lewis, M.S.

Signature: Eric B. Lewis
Date: FEB 17 1999

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: 25
MRID No.: 44653202

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6078

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

Quality Assurance (40 CFR §160.12): Included

Test Material: BOA (GX-575, 36.1% Paraquat dichloride 0.05% Emetic); Lot/Batch No. 378-83E; pH 5; blue green liquid
Species: Rats; Albino, Sprague-Dawley derived
Age: Young adult
Weight (fasted): Males: 222-282 g; Females: 160-228 g
Source: Ace Animals, Inc., Boyertown, PA

Conclusion:

1. **LD_{50} (mg/kg):**
   Males: > 300 mg/kg and < 600 mg/kg
   Females: = 292 mg/kg (95% C.L. 239-371 mg/kg)[a]
   Combined: = 315 mg/kg [b]
2. **The estimated LD_{50} is** 292 mg/kg
3. **Tox. Category:** II **Classification:** Acceptable

[a] LD_{50} calculated by Moving Angle Average Method
[b] LD_{50} estimated graphically

Procedure (Deviations from §81-1): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
150	0/5	0/5	0/10
300	0/5	3/5	3/10
600	5/5	5/5	10/10

Observations: Three females in the mid-dose group died on days 5, 7, or 13. Eight rats in the high-dose group died in the first week of study and two rats died on day 11. Prior to death, the decedents had nasal discharge, facial staining, hunched posture, hypoactivity, piloerection, irregular respiration, reduced food intake, reduced fecal volume, soft feces, anogenital staining, and/or appeared emaciated. The two surviving females in the mid-dose group had piloerection, reduced food intake, reduced fecal volume, and/or soft feces, but recovered by day 9. All other surviving rats appeared active and healthy. All surviving rats had normal body weight gains.

Gross Necropsy: The decedents had discolored livers and lungs, red/black/yellow intestines, or green/black/red/yellow gastrointestinal tracts. Pink fluid was present in the abdomen of one male decedent in the high-dose group. Gross necropsy findings were generally unremarkable in the surviving rats.

7

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

Product Manager: 25
MRID No.: 44653203

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6079

Testing Facility: Product Safety Labs
Author: Moore, G.E.

Quality Assurance (40 CFR §160.12): Included

Test Material: BOA (GX-575, ~36.1% Paraquat dichloride, ~0.05% Emetic); Lot/Batch No. 378-83E; pH 5; blue green liquid
Species: Rats; Albino, Sprague-Dawley derived
Age: Young adult
Weight: Males: 244-277 g; Females: 209-226 g
Source: Ace Animals, Inc., Boyertown, PA

Dermal LD_{50} Testing:

Conclusion:

1. **LD_{50} (mg/kg):**
   Males: > 2000 mg/kg
   Females: > 2000 mg/kg
   Combined: > 2000 mg/kg
2. **The estimated LD_{50} is** > 2000 mg/kg
3. **Tox. Category:** III **Classification:** Acceptable

Procedure (Deviations from §81-2): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: No animals died during the study. No clinical abnormalities were observed. Erythema/ edema were present at all dose sites. Superficial eschar was present at dose site of one male and eschar was present at dose sites of 4/5 females. All animals had normal body weight gains.

Gross Necropsy: Gross necropsy findings were generally unremarkable.

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

Product Manager: 25
MRID No.: 44653204

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6080

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

Quality Assurance (40 CFR §160.12): Included

Test Material: BOA (GX-575, ~36.1% Paraquat dichloride, ~0.05% Emetic, Lot/Batch No. 378-83E; pH 5; blue green liquid
Species: Rats; Albino, Sprague-Dawley derived
Age: Young adult
Weight: Males: 261-286 g; Females: 201-230 g
Source: Ace Animals, Inc., Boyertown, PA

Conclusion:

1. **LC_{50} (mg/L):**
   Males: < 0.054 mg/L
   Females: < 0.054 mg/L
   Combined: < 0.054 mg/L
2. **The estimated LC_{50} is** < 0.054 mg/L
3. **Tox. Category:** I **Classification**: Acceptable

Procedure (Deviations from §81-3): None

Exposure Concentration mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
0.054	5/5	5/5	10/10

Clinical Observations: All males and four females died within three days of exposure. One female died on day 10. The test material was on the fur of all rats. Ocular discharge, hunched posture, and/or hypoactivity were noted on all rats during exposure. The clinical signs persisted on all rats upon chamber removal and in addition, some of the rats developed irregular respiration, dyspnea, and/or reduced fecal volume. The female that died on day 10 also exhibited reduced food consumption and alopecia around the eyes prior to death.

Gross Necropsy Findings: Gross necropsy findings included discoloration of the lungs, liver, and intestines; edema of the lungs; and/or rigor mortis. The female that died on day 10 also had an empty stomach.

Chamber Atmosphere		
Grav. Conc.	MMAD	GSD
0.054 mg/L	3.0 μm	1.70-1.75

Other Information: Approximately 82% of particles had an aerodynamic diameter $\leq$3.3 μm.

Chamber Environment [a]	
Chamber Volume	150 L
Airflow	45.7 LPM
Temperature	72-73°F
Relative Humidity	52-60%

[a] Whole body

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

Product Manager: 25
MRID No.: 44653205

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6081

Testing Facility: Product Safety Labs
Author: Moore, G.E.

Quality Assurance (40 CFR §160.12): Included

Test Material: BOA (GX-575, ~37.0% Paraquat dichloride, ~0.05% Fmetic) Lot/Batch No. 378-83E; pH 5; blue green liquid
Dosage: 0.1 mL (undiluted)
Species: Rabbits; Albino, New Zealand White
Age: Adult
Source: Davidson's Mill Farm, South Brunswick, NJ

Conclusion:
1. **Toxicity Category:** II (Moderate irritant)
2. **Classification**: Acceptable

Procedure (Deviations from §81-4): None

Observations	Number "positive"/number tested									
	Hours				Days					
	1	24	48	72	4	7	10	14	17	21
	Unwashed eyes									
Corneal Opacity	0/6	0/6	0/6	0/6	0/6	1/6	2/6	2/6	1/6	0/6
Iritis	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
Conjunctivae:										
Redness*	3/6	1/6	2/6	1/6	1/6	1/6	1/6	1/6	0/6	0/6
Chemosis*	0/6	2/6	1/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6
Discharge*	2/6	2/6	6/6	6/6	6/6	6/6	3/6	3/6	1/6	1/6

* Score of 2 or more required to be considered positive.

Summary: All rabbits had soft stools or diarrhea, decreased fecal volume and/or clear oral discharge between days 2 and 9. No iritis was noted throughout the study. Corneal opacity was first noted on one rabbit on day 7 and on another rabbit on day 10 that resolved by day 17 and day 14, respectively. 3/6 rabbits were positive for conjunctival redness one hour after test material instillation with resolution by day 17. Conjunctival chemosis noted on two rabbits at 24 hours resolved by 72 hours. 6/6 rabbits were positive for conjunctival discharge (score 3) at 48 hours persisting on 6/6 (score 2 and 3) through day 7. The discharge gradually improved but one rabbit remained positive through the end of the study at day 21.

11

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

Product Manager: 25
MRID No.: 44653206

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6082

Testing Facility: Product Safety Labs
Author: Moore, G.E.

Quality Assurance (40 CFR §160.12): Included

Test Material: BOA (GX-575, ~36.1% Paraquat dichlorid -0.05% Emetic Lot/Batch No. 378-83E; pH 5; blue green liquid
Dosage: 0.5 mL
Species: Rabbits; Albino, New Zealand White
Age: Adult
Source: Davidson's Mill Farm, South Brunswick, NJ

Conclusion:

1. **Toxicity Category:** III (Moderate irritant)
2. **Classification**: Acceptable

Procedure (Deviations from §81-5): None

Results: PDIS = 2.04 (Moderate irritant). One hour after patch removal, very slight erythema was noted on 4/6 rabbits. By 24 hours, very slight to well defined erythema and very slight edema were noted on all rabbits. At 72 hours, 3/6 rabbits showed well defined erythema, 3/6 showed very slight erythema and 3/6 very slight edema. Very slight erythema persisted on 3/6 rabbits and very slight edema on 1/6 rabbits through day 14 (the end of the study.) Hyperkeratosis was present at 3/6 test sites on day 10 persisting through day 14 at one site. Desquamation was present at 2/6 test sites on day 14.

12

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

Product Manager: 25
MRID No.: 44653207

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6083

Testing Facility: Product Safety Labs
Author: Moore, G.E.

Quality Assurance (40 CFR §160.12): Included

Test Material: BOA (GX-575, ~37.0% Paraquat dichloride, 0.05% Emetic) Lot/Batch No. 378-83E; pH 5; blue green liquid
Positive Control Material: None
Species: Guinea pigs; Albino, Hartley
Age: Young adult
Weight: Not reported
Source: Davidson's Mill Farm, South Brunswick, NJ
Method: Buehler

Conclusions:

1. Due to mortality in 7/10 animals following the second induction, the study was terminated prior to challenge.
2. The study is classified as supplementary. However, it is noted that 8/10 animals showed "severe" erythema at 24 hours following the second induction treatment, whereas the maximum reaction observed following the first induction treatment was only "very faint" erythema (observed in 3/10). In lieu of acceptable data demonstrating otherwise, this formulation must be labeled as a potential dermal sensitizer.

Procedure (Deviations from §81-6): Due to the dermal toxicity of the test material on guinea pigs, the study was terminated after the second induction.

Procedure: For the induction phase, 0.4 mL of the undiluted test material was applied under occlusion for six hours once each week for two weeks. Reactions were scored 24 and 48 hours post exposure.

Results: Very faint usually non-confluent erythema was noted on 3/10 and 2/10 animals 24 and 48 hours, respectively, after the first induction. Moderate and severe erythema were noted on 1/10 and 8/10 animals 24 hours after the second induction. Seven of ten guinea pigs died within 48 hours of the second induction. Subsequently, the sponsor authorized the termination of the study. Discoloration of the lungs, livers, and intestines, and/or edema of the lungs were found in the decedents at necropsy. Two decedents also had clear pink fluid in the gall bladder.

Comments: This severe effect on the guinea pigs was not seen on the rats or rabbits.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D251641
2. **PC CODE:** 061601
3. **CURRENT DATE:** 11/MAR/1999
4. **TEST MATERIAL:** BOA (36.1 - 37.0% Paraquat dichloride, ~0.05% Emetic); Lot/Batch No. 378-83E; blue green liquid

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity rat/Product Safety Labs, 6078/8-11-98	44653202	LD_{50} = 292 mg/kg (females), > 300 and < 600 mg/kg (males), = 315 mg/kg (combined)	II	A
Acute dermal toxicity rat/Product Safety Labs, 6079/8-11-98	44653203	LD_{50} > 2000 mg/kg (males, females, combined)	III	A
Acute inhalation toxicity rat/Product Safety Labs, 6080/8-11-98	44653204	LC_{50} < 0.054 mg/L (males, females, combined)	I	A
Primary eye irritation rabbit/Product Safety Labs, 6081/8-11-98	44653205	No iritis observed; corneal opacity on 2/6 rabbits by day 10 resolving by day 21; conjunctival irritation on all rabbits by 48 hours with resolution on 5/6 rabbits by day 17. Discharge persisted on one rabbit through day 21, the end of the study.	II	A
Primary dermal irritation rabbit/Product Safety Labs, 6082/8-11-98	44653206	Moderate irritant; by 24 hours, 6/6 rabbits with very slight to well-defined erythema and very slight edema; at 72 hours 6/6 still positive for very slight to well-defined erythema and 3/6 positive for very slight edema; very slight erythema still present on 3/6 at end of study and very slight edema present on 1/6.	III	A
Dermal sensitization guinea pig/Product Safety Labs, 6083/8-11-98	44653207	Not evaluated for sensitization due to dermal toxicity, 7/10 animals died following the second induction. However, severe erythema was noted in 8/10 animals at 24 hours following the second induction treatment, whereas the greatest irritation seen at 24 hours following the first induction treatment was "very faint" erythema suggesting some dermal sensitization potential. In lieu of an acceptable study demonstrating otherwise, this formulation should be labeled as a dermal sensitizer.	--	s

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