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-UEU
DP Barcodes: D251644
Case No: 064400
PC Code: 061601

From: Masih Hashim, Toxicologist MH
Technical Review Branch
Registration Division (7505C)

Bryan T. Bond 3/11/99

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

Applicant: Griffin Corporation
P O Box1847
Valdosta, GA 31603-1847

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Paraquat dichloride	43.5
Inert Ingredients	56.5
Total:	100.0

BACKGROUND: Griffin Corporation has submitted a set of six toxicity studies to support the registration of its product Griffin Boa Concentrate, File Symbol # 1812-UEU. These studies were conducted at the Product Safety Laboratory, East Brunswick, NJ with the MRID Nos. 447026-06 through 11. An Agency contractor summarized all the studies, then they were revised and evaluated by TRB.

RECOMMENDATIONS: Each of the six studies (except sensitization) is acceptable in accordance with the Sub-Division F guidelines.

The guinea pig sensitization study was 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, 5/10 animals showed severe erythema, while the maximum reaction noted following the first induction treatment was "moderate" 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 EPA Reg. No. 1812-UEU 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	IV	acceptable
dermal sensitization	Positive	supplementary

LABELING: The following is the precautionary labeling for this product, as obtained from the Label Review System:

Date: 03/11/99 LABEL REVIEW SYSTEM

ID #: 001812-00424 Griffin Boa Concentrate

SIGNAL WORD: DANGER

POISON SKULL and CROSSBONES symbol

PRECAUTIONARY STATEMENTS:

Fatal If inhaled. May be fatal if swallowed. Causes substantial but temprary eye injury. Harmful if absorbed through skin. Do not get in eyes or on clothing. Avoid contact with skin. Do not breathe spray mist. Wear goggles or face shield. For handling activities, use a NIOSH respirator with an organic vapor (OV) cartridge or canister with any N, P, R, or HE prefilter. Prolonged or frequently repeated skin contact may cause allergic reaction in some individuals.

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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.

The following statement should appear under the heading USER SAFETY RECOMMENDATIONS:

Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet. Remove contaminated clothing and wash clothing before reuse.

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

Product Manager: 25
MRID No.: 44702606

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6097

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

Quality Assurance (40 CFR §160.12): Included

Test Material: Paraquat dichloride technical (GX-574, 48.6% Paraquat dichloride); Lot/Batch No. 97-4-2; opaque brown, semi-viscous liquid
Species: Rats; Albino, Sprague-Dawley derived
Age: Young adult
Weight (fasted): Males: 202-276 g; Females: 160-204 g
Source: Ace Animals, Inc., Boyertown, PA

Conclusion:

1. **LD_{50} (mg/kg)[a]:**
   Males: = 292 mg/kg (95% C.L. 239-371 mg/kg)
   Females: = 276 mg/kg (95% C.L. 230-341 mg/kg)
   Combined: = 284 mg/kg (95% C.L. 248-331 mg/kg)
2. **The estimated LD_{50} is** 276 mg/kg
3. **Tox. Category:** II **Classification:** Acceptable

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

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	3/5	4/5	7/10
600	5/5	5/5	10/10

Observations: Three males and four females in the mid-dose group died on days 2, 4, or 5 . All rats in the high-dose group died on days 2, 3, or 4. Two rats in the low-dose group developed piloerection and/or soft feces on days 1 and 5. Two surviving rats in the mid-dose group exhibited hunched posture and/or reduced fecal volume but recovered by day 5. Prior to death, the decedents had ocular discharge, facial staining, hunched posture, hypoactivity, piloerection, irregular respiration, reduced fecal volume, soft feces, anogenital staining, and/or diarrhea. All surviving rats had normal body weight gains.

Gross Necropsy: The decedents in the high-dose group had discolored lungs, liver, and gastrointestinal tract and/or gaseous distention of the stomach.

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

Product Manager: 25
MRID No.: 44702607

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6098

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

Quality Assurance (40 CFR §160.12): Included

Test Material: Paraquat dichloride technical (GX-574, 48.6% Paraquat dichloride); Lot/Batch No. 97-4-2; opaque brown, semi-viscous liquid
Species: Rats; Albino, Sprague-Dawley derived
Age: Young adult
Weight: Males: 282-312 g; Females: 190-223 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, and/or eschar were present at the site of test material application. 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.: 44702608

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6099

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

Quality Assurance (40 CFR §160.12): Included

Test Material: Paraquat dichloride technical (GX-574, 48.6% Paraquat dichloride); Lot/Batch No. 97-4-2; opaque brown, semi-viscous liquid
Species: Rats; Albino, Sprague-Dawley derived
Age: Young adult
Weight: Males: 257-290 g; Females: 185-208 g
Source: Ace Animals, Inc., Boyertown, PA

Conclusion:

1. **LC_{50} (mg/L):**
   Males: < 0.05 mg/L
   Females: < 0.05 mg/L
   Combined: < 0.05 mg/L
2. **The estimated LC_{50} is** < 0.05 mg/L
3. **Tox. Category:** Classification: Acceptable

Procedure (Deviations from §81-3): None

Exposure Concentration mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
0.05	5/5	5/5	10/10

Clinical Observations: One male and two females died within three days of exposure. All other rats died during the second week. All rats had irregular respiration and hypoactivity during exposure. The clinical signs persisted on all rats upon chamber removal at which time some of the rats developed irregular respiration, dyspnea, moist or dry rales, red ocular discharge, facial staining, piloerection, reduced food consumption, and/or reduced fecal volume prior to death.

Gross Necropsy Findings: Gross necropsy findings included discoloration of the lungs, liver, and intestines; edema of the lungs; and/or gaseous distention of the gastrointestinal tract. The testicles of two males also appeared discolored.

Chamber Atmosphere		
Grav. Conc.	MMAD	GSD
0.05 mg/L	3.3 μm	1.62-2.25

Other Information: Approximately 70% of particles had an aerodynamic diameter ≤3.3 μm.

Chamber Environment [a]	
Chamber Volume	150 L
Airflow	34.9 LPM
Temperature	67-74°F
Relative Humidity	39-47%

[a] Whole body

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

Product Manager: 25
MRID No.: 44702609

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6100

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

Quality Assurance (40 CFR §160.12): Included

Test Material: Paraquat dichloride technical (GX-574, 48.6% Paraquat dichloride); Lot/Batch No. 97-4-2; opaque brown, semi-viscous liquid
Dosage: 0.1 mL (undiluted)
Species: Rabbits; Albino, New Zealand White
Age: Adult
Weight: Not reported
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	0/6	0/6	0/6	0/6	0/6
Iritis	0/6	0/6	1/6	1/6	1/6	1/6	1/6	1/6	0/6	0/6
Conjunctivae:										
Redness	3/6	3/6	6/6	5/6	5/6	4/6	0/6	0/6	0/6	0/6
Chemosis	0/6	1/6	1/6	1/6	1/6	1/6	0/6	0/6	0/6	0/6
Discharge	0/6	5/6	6/6	6/6	6/6	6/6	5/6	3/6	1/6	0/6

Summary: All rabbits had decreased fecal volume and/or oral discharge, between days 2 and 9. No corneal opacity was noted throughout the study. One rabbit had iritis at 48 hours through day 14. Conjunctival redness (score 2) was noted on 3/6 rabbits at one hour after test material instillation that persisted through day 7 with resolution by day 10. Conjunctival redness was noted on 1/6 rabbits at 24 hours and 2/6 rabbits at 48 hours that resolved by 72 hours and day 10, respectively. Conjunctival chemosis (score 2) was noted on one rabbit at 24 hours with resolution by 48 hours and on another rabbit at 48 hours with resolution by day 10. Conjunctival

discharge (score 2) on 5/6 rabbits at 24 hours intensified to score 3 by 48 hours through days 4 or 14 before resolving by day 21. Conjunctival discharge (score 2) was noted on 1/6 rabbits from 48 hours through day 14. The highest average ocular irritation index was 12.8 recorded 48 hours after initiation. This classifies the test material as a moderate irritant.

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

Product Manager: 25
MRID No.: 44702610

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6101

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

Quality Assurance (40 CFR §160.12): Included

Test Material: Paraquat dichloride technical (GX-574, 48.6% Paraquat dichloride); Lot/Batch No. 97-4-2; opaque brown, semi-viscous liquid
Dosage: 0.5 mL
Species: Rabbits; Albino, New Zealand White
Age: Adult
Weight: Not reported
Source: Davidson's Mill Farm, South Brunswick, NJ

Conclusion:

1. **Toxicity Category:** IV (Moderate irritant)
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, that persisted through 72 hours. By day 7, very slight erythema was noted on all rabbits that resolved on 1/6 and 5/6 rabbits by days 10 and 14, respectively. Very slight edema and slight edema were noted on 5/6 and 1/6 rabbits at one hour, respectively. Edema cleared on 1/6, 1/6, 2/6, and 2/6 rabbits by 24 hours and days 7, 10, and 14, respectively. Desquamation was present on one rabbit at days 7 and 10 and another rabbit at day 14.

Special Comments: None

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

Product Manager: 25
MRID No.: 44702611

Reviewer: Susan Chang
Study Completion Date: August 11, 1998
Study No.: 6102

Testing Facility: Product Safety Labs
Author: Wnorowski, G.
Quality Assurance (40 CFR §160.12): Included
Test Material: Paraquat dichloride technical (GX-574, 48.6% Paraquat dichloride); Lot/Batch No. 97-4-2; opaque brown, semi-viscous 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 5/10 animals showed "severe" erythema at 24 hours following the second induction treatment, whereas the maximum reaction observed following the first induction treatment was only "moderate" 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, faint confluent erythema, and moderate erythema were noted on 1/10, 6/10, and 3/10 animals 24 hours, respectively, after the first induction. Very faint usually non-confluent erythema, faint confluent erythema, and moderate erythema were noted on 2/10, 5/10, and 3/10 animals, respectively, 48 hours after the first induction. Moderate and severe erythema were noted on 1/10 and 5/10 animals 24 hours after the second induction. Moderate erythema was noted on one animal and severe erythema was noted on another animal at 48 hours following the second induction. One animal died prior to the second induction and 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, gaseous detention of the gastrointestinal tract, and/or edema of the lungs were found in the decedents at necropsy. One decedent 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. Page 9 was missing in the study report, instead it contained page 9 of study Number 6079 (MRID 44653203).

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ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D251644
2. **PC CODE:** 061601
3. **CURRENT DATE:** February 9, 1999
4. **TEST MATERIAL:** Paraquat dichloride technical (48.6% Paraquat dichloride); Lot/Batch No. 97-4-2; opaque brown, semi-viscous liquid

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/Product Safety Labs, 6097/8-11-98	44702606	LD_{50} = 292 mg/kg (males), 276 mg/kg (females), 284 mg/kg (combined)	II	A
Acute dermal toxicity/rat/Product Safety Labs, 6098/8-11-98	44702607	LD_{50} > 2000 mg/kg (males, females, combined)	III	A
Acute inhalation toxicity/rat/ Product Safety Labs, 6099/8-11-98	44702608	LC_{50} < 0.05 mg/L (males, females, combined)	I	A
Primary eye irritation rabbit/Product Safety Labs, 6100/8-11-98	44702609	Moderate irritant; no corneal opacity on any rabbits; iritis on 1/6 rabbits at 48 hours thru day 10; conjunctival redness in 6/6 rabbits by 48 hours with resolution by day 10; conjunctival chemosis on one rabbit at 24 hours with resolution by 48 hours and on one rabbit at 48 hours with resolution by day 10; conjunctival discharge on 5/6 rabbits at 24 hours with resolution by day 21. The highest average ocular irritation index was 12.8 recorded 48 hours after initiation. This classifies the test material as a moderate irritant.	II	A
Primary dermal irritation rabbit/Product Safety Labs, 6101/8-11-98	44702610	Moderate irritant; very slight erythema and well defined erythema on 3/6 and 3/6 rabbits, respectively, at one hour that persisted through 72 hours; very slight erythema on all rabbits by day 7 that resolved on 1/6 and 5/6 rabbits by days 10 and 14, respectively; very slight edema and slight edema on 5/6 and 1/6 rabbits at one hour, respectively; edema cleared on 1/6, 1/6, 2/6, and 2/6 rabbits by 24 hours and days 7, 10, and 14; desquamation present on one rabbit at days 7 and 10 and another rabbit at day 14, respectively.	IV	A
Dermal sensitization guinea pig/Product Safety Labs, 6102/8-11-98	44702611	Not evaluated for sensitization due to dermal toxicity, 1/10 and 7/10 animals died prior to and following the second induction, respectiviely. However, severe erythema was noted in 5/10 animals at 24 hours following the second induction treatment, whereas the greatest irritation seen at 24 hours following the first induction treatment was "moderate" erythema (observed in 3/10 animals), 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**