UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

December 15, 1995

MEMORANDUM

Subject: EPA Reg. No.: 64405-1 / Bora Care
64405-3 / Bora-Care Manufacturing Concentrate
64405-4 / Bora-Care IC Injectable Concentrate
64405-5 / RTU Wood Preservative/ Insecticide

From: Ian Blackwell, Biologist IDB 12/15/95
Precautionary Review Section
Registration Support Branch
Registration Division (7505W)

To: Robert Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (7505C)

Applicant: NISUS Corp.
101 Concord ST N.
Knoxville, TN 37919

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.			
	64405-1	64405-3	64405-4	64405-5
Disodium octaborate tetrahydrate	40	40	40	8.5
Inert Ingredient(s):	60	60	60	91.5
Total:	100%	100	100	100.0

BACKGROUND: NISUS Corporation has submitted a complete set of acute toxicity studies in support of "Bora Care", "Bora-Care Manufacturing Concentrate", "Bora-Care IC Injectable Concentrate" and "RTU Wood Preservative/Pesticide". These studies were submitted in response to the Boric Acid RED. The MRID numbers are 419668-01 through 419668-06. Although these studies were conducted in 1990, PRS could not find any evidence that they had been previously reviewed by the Agency.

Registration numbers 64405-1, 64405-3 and 64405-4 were placed into batch #7 of that RED. Reg. no. 64405-5 was registered after the Boric Acid RED was finished. Whereas the three products of batch #7 contain 40% disodium octaborate tetrahydrate, 64405-5 contains only 8.5% of that active ingredient. Although the registrant did not actually request it, PRS assumes that they would like to bridge data from 64405-1 to support 64405-5.

RECOMMENDATIONS:

1. The acute oral toxicity and primary skin irritation studies are classified as acceptable data and are sufficient to support the reregistration of this product.

2. The acute dermal toxicity study is classified as acceptable data and is acceptable to support the reregistration of the product. The study has a deficiency in that the lab covered the test site with a plastic sleeve and not gauze. This single deficiency is reason enough to reject this study. The lab should have covered the test site with gauze and **then** covered the site with an impervious material such as a plastic sleeve. The gauze is used to retain the test material in a position where it is available to be absorbed the skin. Otherwise, there is a likelihood of the test material running into the fur and/or running out of the wrapping itself. Covering the test site with gauze is a standard testing method that is specified in Subdivision F guidelines.

   As the ingredients of this product are not very toxic, and none of the test subjects died, PRS will accept this study. However, the lab should be informed that not covering the test material with gauze is an improper method of conducting the acute dermal toxicity study. In the future, this methodology could lead to the rejection of all studies conducted in this manner.

3. The acute inhalation toxicity study is classified as acceptable data. There are three deficiencies -- two are minor, but one must be addressed:

   a. The particle size was only measured once during the exposure. This flaw is not felt to be substantial in this instance. The test material is a water-soluble liquid which was more than likely well homogenized into the testing solution (50% product and 50% water). The particle concentrations remained relatively consistent during the study -- this supports a belief that the particle atmosphere remained relatively consistent during the study. Under other circumstances, the study could be rejected for this flaw alone.
   b. The MMAD was above the Agency limit of 4.0 microns. However, the MMAD was only 4.09 microns. This is barely out of acceptable range. In addition, it is very possible that

had the lab conducted more than one particle concentration the MMAD would have been acceptable.

c. The lab did not report that the particle concentration was adjusted for a 50:50 dilution. The report gives the impression that the test material did not compensate for the dilution of the test material. However, even if the reported concentration (5.06 mg/L) was not adjusted for dilution, it would still place the product into toxicity category IV.

It should be noted that the product is a thick, viscous liquid and would probably not pose much of a potential for inhalation. Also, the components of the product are not highly toxic. In order for this product to be reconsidered, the lab should report whether the test material concentration was adjusted for the 50:50 dilution in water.

4. The primary eye irritation study is classified as acceptable data and is sufficient to support the reregistration of the product. The study deficiency is that while the lab reported using sodium fluorescein solution to read the eyes of the animals, it did not report the points during the study that the sodium fluorescein was used. That is, was it used in screening, at the final observation, or some other point during the study? This information should be reported in all future primary eye irritation studies.

5. The dermal sensitization study is classified as acceptable data and is sufficient to support this product. The study deficiency is that only 0.2 mL of the test material was used for induction and challenge applications of the test material. According to Buehler, the volume to use is 0.4 mL. The problem with this is that no irritation was obtained from the test material-treated animals. Had the lab used the proper volume of test material, irritation might have been elicited. However, the test material was applied full strength and it does not seem that the animals received such a small dosage of the test material that it would not have brought about sensitization had the potential existed.

6. PRS will allow the registrant to bridge the data from 64405-1 down to support reg. no. 64405-5. Reg. no. 64405-5 is actually a water dilution of reg. no. 64405-5. The toxicity categories for 64405-1 (the studies used to support reg. no. 64405-3) were all toxicity category III and IV. Thus, it is not conceivable that data actually conducted on 64405-5 could result in a change in signal word or other precautionary labeling other than that of the acute dermal toxicity study. Acute dermal toxicity studies for products with the signal word "CAUTION" are seldom placed into toxicity category IV as registrants will usually accept the limit test of category III if they can get it.

The acute toxicity profile for reg. no. 64405-1, 64405-3, 64405-4 and 64405-5 is currently:

acute oral toxicity	IV	acceptable
acute dermal toxicity	III	acceptable
acute inhalation toxicity	IV	acceptable
primary eye irritation	IV	acceptable
primary skin irritation	IV	acceptable
dermal sensitization	nonsensitizer	acceptable

LABELING:

1. The signal word is "CAUTION".

2. The precautionary statements should state:

   "Harmful if absorbed through skin. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling."

3. The statement of practical treatment should state:

   "**If on skin**: Wash with plenty of soap and water. Get medical attention."

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

Product Manager: 25
MRID No.: 419668-01

Reviewer: I. Blackwell
Study Completion Date: 8/1/90
Lab Project ID No.: 90-166-1

Testing Facility : Tox Monitor Laboratories, Inc.
Authors : Michael Kukulinski

Quality Assurance (40 CFR §160.12): included

Test Material: Bora Care, EPA reg. no. 64405-1; "clear liquid"

Species: Sprague-Dawley derived rats
Age: 6-10 weeks
Weight: males = 224-248 grams; females = 221-231 grams
Source: Bio-Lab

Conclusion:

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

Procedure (Deviations from §81-1):

Results:

Dosage (mg/kg)	(Number Killed/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: No abnormalities were observed.

Gross Necropsy: No changes were observed.

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

Product Manager: 25
MRID No.: 419668-02

Reviewer: Ian Blackwell
Study Completion Date: 8/1/90
Lab Project ID No.: 90-166-2

Testing Laboratory: Tox Monitor Laboratories, Inc.
Author: Michael Kukulinski

Quality Assurance (40 CFR §160.12): Included

Test Material: Bora Care; EPA reg. no. 64405-1

Species: New Zealand Albino rabbit
Weight: males = 4.24-4.92 kg; females = 4.02-4.70 kg **Age**: 8-12 weeks
Source: Scientific Small Animal Laboratory

Summary:

1. **LD_{50} (mg/kg)**: **Males** > 2000
   Females > 2000
   Combined > 2000

2. **The estimated LD_{50} is greater than 2000 mg/kg of body weight.**

3. **Tox. Category**: III **Classification**: acceptable

Procedure (Deviation From §81-2):
*The exposure sites were covered with a plastic sleeve and not with gauze.

Results:

Reported Mortality

DOSAGE	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2000 mg/kg	0/5	0/5	0/10

Observations: All animals appeared normal throughout the study.

Gross Necropsy Findings: No changes observed.

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

Product Manager: 25
MRID No.: 419668-03

Reviewer: I. Blackwell
Study Completion Date: 8/8/90
Lab Project ID No.: 90-166-3

Testing Laboratory: Tox Monitor Laboratories, Inc.
Author: Michael Kukulinski

Quality Assurance (40 CFR §160.12): Included

Test Material: Bora Care; EPA reg. no. 64405-1; "clear viscous liquid"
Concentration: 5.06 mg/L (?)

Species: rat
Weight: males = 223-260 g; females = 200-208 g
Age: young adult
Source: Bio-Lab, Inc.

Summary:

1. **LC_{50} (mg/L):** **Males** > 2.53mg/L
   Females > 2.53 mg/L
   Combined > 2.53 mg/L
2. **The estimated LC_{50} is greater than 2.5 mg/L.**
3. **MMAD**: 4.09 microns
4. **Tox. Category**: IV **Classification**: acceptable

Procedure (Deviation From §81-3):
*The particle size was only measured once during the exposure.
*The report did not state that the particle concentration of the test material was adjusted for the 50:50 dilution used to attain a sprayable solution.

Results:

Reported Mortality

Exposure Concentration	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
5.06 mg/L	1/5	0/5	1/10

Chamber Atmosphere		
Dose Level	MMAD	GSD
5.06m mg/L	4.09 um	3.243 um

Chamber Environment	
Chamber Volume	400 L
Airflow	
Temperature	69-71 °F
Relative Humidity	58-91%

Clinical Observations: Hypoactivity, prostration, salivation,

Gross Necropsy Findings: No gross changes were observed.

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

Product Manager: 25
~~MRID No.~~: ~~419668-04~~

Reviewer: Ian Blackwell
~~Study Completion Date~~: 8/1/90
Report No.: 90-166-4

Testing Laboratory: Tox Monitor Laboratories, Inc.
Author(s): Michael Kukulinski

Quality Assurance (40 CFR §160.12): Included

Test Material: Bora-Care; EPA reg. no. 64405-1; "a clear liquid"
Dosage: 0.1 mL

Species: New Zealand White rabbit
Sex: females only
Weight: 2092-2515 grams
Source: Scientific Small Animal Laboratory

Age: 8-10 weeks

Summary:

1. **Toxicity Category**: IV
2. **Classification**: acceptable

Procedure (Deviations From §81-4):
*The report did not state when 2% sodium fluorescein and UV light were used in examinations.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea 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	---	---	---	---
Discharge	4/6	0/6	0/6	0/6	---	---	---	---

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

Product Manager: 25
MRID No.: 419668-05

Reviewer: Ian Blackwell
Study Completion Date: 8/1/90
Report No.: 90-166-5

Testing Laboratory: Tox Monitor Laboratories, Inc.
Author: Michael Kukulinski

Quality Assurance (40 CFR §160.12): Included

Test Material: Bora-Care; EPA reg. no. 64405-1; "clear liquid".
Dosage: 0.5 mL
Species: New Zealand White rabbit
Age: 8-10 weeks old
Sex: male and/or female **Weight**: 2020-2770 kilograms
Source: Scientific Small Animal Laboratory

Summary:

1. **Toxicity Category**: IV
2. **Classification**: acceptable

Procedure (Deviations From §81-5):

Results: One-half hour after test material administration, 4/6 test material-treated animals displayed very slight, erythema and 2/6 displayed very slight edema. No more irritation was seen from 24 hours on to 72 hours at which time the study was ended.

Special Comments: None

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

Product Manager: 25
MRID No.: 419668-06

Reviewer: I. Blackwell
Study Completion Date: 8/3/90
Report No.: 023-001

Testing Laboratory: Biologic Safety Research, Inc.
Author: Michael Kukulinski, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: Bora-Care; EPA reg. no. 64405-1; "clear colored viscous liquid"
Positive Control Material: DNCB

Species: Hartley albino guinea pig
Weight: 224-275 grams
Age: young adult
Sex: males
Source: Harlan Sprague Dawley

Method: Modified Buehler Method

Summary:

1. **This Product is not a dermal sensitizer.**

2. **Classification**: acceptable

Procedure (Deviation From §81-6):
*The volume of test material applied was 0.2 mL.

Procedures: The test material was tested undiluted. The test volume was 0.2 mL in a Hilltop Chamber. The animals were given induction dosages three times a week for three weeks. The first dosage was a 24 hour exposure and the following eight dosages were for 6 hours each. The test animals were scored for irritation 24 hours after each test material application.

Results: No irritation was observed 24 or 48 hours after any of the induction dosages nor after the challenge dose in any of the test material treated animals.

No irritation was observed in any of the positive control animals 24 or 48 hours after induction treatments 1 through 4. After induction #5, 2/6 positive control animals displayed very slight erythema. Through induction treatments 6-10, slight erythema was observed in between 3/6 and 6/6 positive control animals. Following challenge with DNCB, 6/6 positive control animals displayed very slight erythema. No irritation stronger than very slight erythema was displayed in any of the positive control animals during this study.

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ACUTE TOX ONE-LINER

1. PC CODE: 011103

2. CURRENT DATE: December 12, 1995

3. TEST MATERIAL: Disodium octaborate tetrahydrate ... 40%

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat	Core Grade
acute oral toxicity / rat / Tox Monitor Labs / 90-166-1 / 8-8-90	419668-01	LD_{50} (mg/kg) > 5000 for both sexes	IV	A
acute dermal toxicity / rabbit / Tox Monitor Labs / 90-166-2 / 8-1-90	419668-02	LD_{50} (mg/kg) > 2000 for both sexes	III	A
acute inhalation toxicity / rat / Tox Monitor Labs / 90-166-3 / 8-8-90	419668-03	LC_{50} > 2.53 mg/L for both sexes	IV	A
primary eye irritation / rabbit / Tox Monitor Labs / 90-166-4/ 8-1-90	419668-04	Discharge in 4/6 at one hour. No other irritation reported.	IV	A
primary skin irritation / rabbit / Tox Monitor Labs / 90-166-5 / 8-1-90	419668-05	Very slight erythema in 4/6 and very slight edema at one hour.	IV	A
dermal sensitization / guinea pigs / Biologic Safety Research, Inc. / 023-001 / 8-3-90	419668-06	Non-sensitizer	---	A

Core Grade Key:

A = Acceptable
U = Unacceptable
S = Supplementary (upgradeable)