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

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

January 7, 2003

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 69268-3 / H<sub>2</sub>O Orange 120  
DP Barcode: D285388

To: Marshall Swindell, PM 33 / Tony Kish  
Regulatory Management Branch  
Antimicrobials Division (7510C)

From: Ian Blackwell, Biologist  
Efficacy Evaluation Team  
Product Science Branch  
Antimicrobials Division (7510C)

*Ian Blackwell*

Through: Karen Hicks, Team Leader  
Chemistry and Toxicology Team  
Product Science Branch  
Antimicrobials Division (7510C)

*Karen P. Hicks*  
*1/13/03*

Michele E. Wingfield, Chief  
Product Science Branch  
Antimicrobials Division (7510C)

Applicant: Envirox, LLC

FORMULATION FROM LABEL:

Active Ingredient(s):

Hydrogen Peroxide

Other Ingredient(s):

	<u>% by wt.</u>
	1
	99
Total:	<u>100%</u>

**BACKGROUND:** Envirox, LLC, has submitted a set of four acute toxicity/irritation studies to support labeling changes of their product, "H<sub>2</sub>Orange 120 Ready-To-Use". The acute oral toxicity, acute dermal toxicity and primary eye irritation studies were conducted by MB Research Laboratories, Inc. The dermal sensitization study was conducted by Essex Testing Clinic, Inc. No acute inhalation toxicity or primary skin irritation studies were included with this submission. The MRID Numbers are 457465-01 through 457465-04.

These studies were primarily reviewed for CTT/PSB/AD by the EPA contractor, Oak Ridge National Laboratory. PSB/AD scientists performed a secondary review of the data to assure that the studies and reports meet Agency standards.

A cover letter dated 8/22/2002 states that the acute toxicity profile of this product was based upon acute toxicity data derived from other Envirox LLC products, H<sub>2</sub>Orange 112 Super Concentrate and H<sub>2</sub>Orange 117 Concentrate.

A 11/15/00 letter from PM 33 of AD listed the acute toxicity profile of 69268-3 as:

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

**RECOMMENDATIONS:** PSB findings are:

1. The acute oral and acute dermal toxicity studies were conducted according to Agency guidelines. However, these studies are not acceptable due to a problem with the test material identity. The problem is that, while the product this test was submitted to support is H<sub>2</sub>Orange 120, the test material was H<sub>2</sub>Orange<sub>2</sub> 126. The cover letter included with this submission discussed H<sub>2</sub>Orange 120, H<sub>2</sub>Orange 112 Super Concentrate and H<sub>2</sub>Orange 117 Concentrate; however, it does not mention H<sub>2</sub>Orange<sub>2</sub> 126. While the study mentions the percent of active ingredient in H<sub>2</sub>Orange<sub>2</sub> 126, it does not discuss the other 99%+ of ingredients in the test material.

In order to have the status/ acceptability of the acute oral and acute dermal toxicity studies reconsidered, the registrant will have to submit information explaining the similarities and differences between H<sub>2</sub>Orange<sub>2</sub> 126 and H<sub>2</sub>Orange 120. This information is expected to include a CSF of H<sub>2</sub>Orange<sub>2</sub> 126.

2. The primary eye irritation study is acceptable.

3. While the EPA does not recommend the testing of dermal sensitization studies in humans, the submitted dermal sensitization study is acceptable.

The acute toxicity profile for Reg. No. 69268-3 is currently:

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

It is understood that the registrant was hoping for a change in precautionary labeling for this product in that this product label would not be required to display First Aid statements or precautionary labeling. In order to accomplish this, this product would have to be assigned all toxicity category IVs and be a nonsensitizer. However, due to the problems in the reports submitted, this cannot be accomplished at this time. Also, in order to achieve the aforementioned goal, the registrant would have to submit an acute inhalation toxicity study demonstrating that this product should be assigned toxicity category IV for acute inhalation exposure.

LABELING:

No labeling changes are recommended at this time. It is expected that the registrant will resubmit information to change the status of the acute oral and dermal toxicity studies. Revised labeling will be recommended at that time.

DATA EVALUATION RECORD

HYDROGEN PEROXIDE  
(H<sub>2</sub>ORANGE<sub>2</sub> 126)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT  
[OPPTS 870.1100 (§81-1)] OECD 401  
MRID 45746501

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

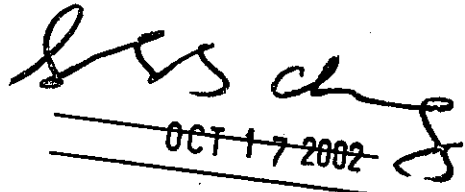
Prepared by  
Toxicology and Hazard Assessment Group  
Life Sciences Division  
Oak Ridge National Laboratory  
Oak Ridge, TN 37831  
Action No. K415


Primary Reviewer:  
Susan Chang, M.S.

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

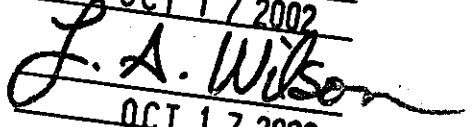
Robert H. Ross, M.S., Group Leader

Quality Assurance:  
Lee Ann Wilson, M.A.

Signature:   
Date: OCT 17 2002

Signature:   
Date: OCT 17 2002

Signature: Robert H. Ross  
Date: OCT 17 2002

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Disclaimer

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

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under  
Contract No. DE-AC05-00OR22725.

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

**Product Manager:** Marshall Swindell  
**MRID No.:** 45746501

**Reviewer:** Susan Chang  
**Study Completion Date:** January 10, 2002

**Report No.:** MB 01-9756.01

**Testing Laboratory:** MB Research Laboratories  
**Author:** Daniel R. Cerven

**GLP Compliance Statement (40 CFR §160.12):** Included

**Test Material:** H<sub>2</sub> Orange<sub>2</sub> 126 (H<sub>2</sub>O<sub>2</sub> = 1.34%), Lot No. 97980; cloudy liquid  
**Dosage:** 5000 mg/kg

**Species:** Wistar rats (5 M and 5 F)

**Weight:** Males: 223-246 g, Females: 220-234 g

**Source:** Ace Animals, Boyertown, PA

**Age:** Approximately 7-11 weeks

**Summary:**

- LD<sub>50</sub> (mg/kg):** Males > 5000 mg/kg  
Females > 5000 mg/kg  
Combined > 5000 mg/kg
- The estimated LD<sub>50</sub> is > 5000 mg/kg.
- Tox. Category:** IV      **Classification:** Acceptable

**Procedure (Deviations from §81-1, 870.1100):** None

**Results:**

Dosage (mg/kg)*	Reported Mortality		
	(Number Deaths/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

**Observations:** All animals survived the study. Eight animals had normal body weight gains, but two females lost weight during the second week. Nine animals appeared normal throughout the study, but one male had alopecia on the left jawline on days 2 through 6.

**Gross Necropsy Findings:** Necropsy results were normal with the exception of one male that had liver abnormalities.

DATA EVALUATION RECORD

HYDROGEN PEROXIDE  
(H<sub>2</sub>ORANGE, 126)

STUDY TYPE: ACUTE DERMAL TOXICITY - RABBIT  
[OPPTS 870.1200 (§81-2)] OECD 402  
MRID 45746502

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

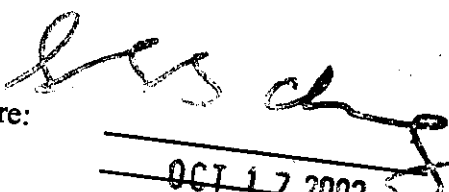
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Oak Ridge National Laboratory  
Oak Ridge, TN 37831  
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Secondary Reviewers:  
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Robert H. Ross, M.S., Group Leader


Quality Assurance:  
Lee Ann Wilson, M.A.

Signature: 

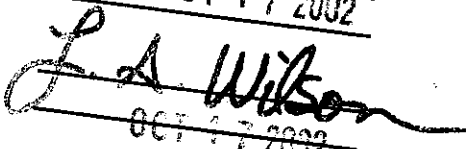
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Contract No. DE-AC05-00OR22725.

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

**Product Manager:** Marshall Swindell  
**MRID No.:** 45746502

**Reviewer:** Susan Chang  
**Study Completion Date:** January 10, 2002

**Report No.:** MB 01-9756.02

**Testing Laboratory:** MB Research Laboratories  
**Author:** Daniel R. Cerven

**GLP Compliance Statement (40 CFR §160.12):** Included

**Test Material:** H<sub>2</sub> Orange<sub>2</sub> 126 (H<sub>2</sub>O<sub>2</sub> = 1.34%), Lot No. 97980; cloudy liquid  
**Dosage:** 5000 mg/kg

**Species:** New Zealand White rabbits (5M and 5F) **Age:** Approximately 13-14 weeks  
**Weight:** Males: 2.0-2.4 kg, Females: 2.0-2.3 kg  
**Source:** Sgarlat's Rabbitry, Harleysville, PA

**Summary:**

- LD<sub>50</sub> (mg/kg):** Males > 5000 mg/kg  
Females > 5000 mg/kg  
Combined > 5000 mg/kg
- The estimated LD<sub>50</sub> is > 5000 mg/kg.
- Tox. Category:** IV **Classification:** Acceptable

**Procedure (Deviation From §81-2, 870.1200):** No deviations were noted.

**Results:**

Dosage (mg/kg)	Reported Mortality		
	(Number Deaths/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

**Observations:** All animals survived the study. Six animals had normal body weight gains, but two males and two females did not gain weight during the second week. All animals appeared normal throughout the study.

**Gross Necropsy Findings:** Necropsy results were normal with the exception of one male that had kidneys with clear fluid filled capsules.



DATA EVALUATION RECORD

HYDROGEN PEROXIDE  
(H<sub>2</sub>ORANGE, 120)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT  
[OPPTS 870.2400 (§81-4)] OECD 405  
MRID 45746503

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

Prepared by  
Toxicology and Hazard Assessment Group  
Life Sciences Division  
Oak Ridge National Laboratory  
Oak Ridge, TN 37831  
Action No. K415

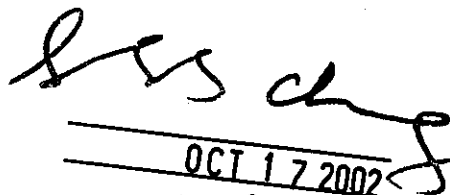
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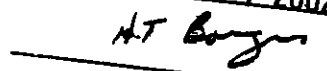
Robert H. Ross, M.S., Group Leader

Quality Assurance:  
Lee Ann Wilson, M.A.

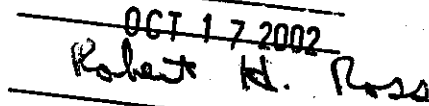
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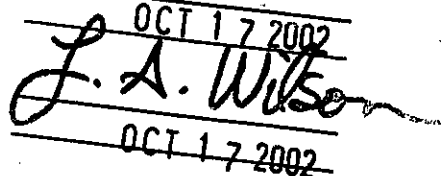
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**DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)**

**Product Manager:** Marshall Swindell  
**MRID No.:** 45746503

**Reviewer:** Susan Chang  
**Study Completion Date:** March 8, 2001

**Report No.:** MB 00-9008.04

**Testing Laboratory:** MB Research Laboratories  
**Author:** Daniel R. Cerven

**GLP Compliance Statement (40 CFR §160.12):** Included

**Test Material:** H<sub>2</sub>Orange<sub>2</sub> 120; colorless liquid  
**Dosage:** 0.1 mL

**Species:** New Zealand White rabbits (3F)  
**Weight:** Females: 2.4-2.9 kg  
**Source:** Sgarlat's Rabbitry, Harvey's lake, PA

**Age:** Approximately 4 months

**Summary:**

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

**Procedure (Deviations From §81-4, 870.2400):** None

**Results:**

Observations	Number "Positive"/Number Tested			
	Hour			
	1	24	48	72
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae	0/3	0/3	0/3	0/3
Redness	0/3	0/3	0/3	0/3
Chemosis	1/3	0/3	0/3	0/3
Discharge	2/3	0/3	0/3	0/3

DATA EVALUATION RECORD

HYDROGEN PEROXIDE  
(H<sub>2</sub>ORANGE, 120)

STUDY TYPE: SKIN SENSITIZATION - HUMAN  
[OPPTS 870.2600 (§81-6)] OECD 406  
MRID 45746504

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

Prepared by  
Toxicology and Hazard Assessment Group  
Life Sciences Division  
Oak Ridge National Laboratory  
Oak Ridge, TN 37831  
Action No. K415

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

Quality Assurance:  
Lee Ann Wilson, M.A.

Signature: \_\_\_\_\_  
Date: \_\_\_\_\_

*Susan Chang*  
OCT 17 2002

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Date: \_\_\_\_\_

*HT Borges*

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OCT 17 2002  
*Robert H. Ross*

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OCT 17 2002  
*J. A. Wilson*  
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Contract No. DE-AC05-00OR22725.

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

**Product Manager:** Marshall Swindell  
**MRID No.:** 45746504  
**Report No.:** ENV-8398

**Reviewer:** Susan Chang  
**Study Completion Date:** December 14, 2001

**Testing Laboratory:** Essex Testing Clinic, Inc., Verona, NJ  
**Author:** Tracey Stavisky

**GLP Compliance Statement (40 CFR §160.12):** The study was conducted in compliance with the Principles of Good Clinical Practice (21 CFR Parts 50, 56, and 312) and the Declaration of Helsinki, and is consistent with 40 CFR 160 Good Laboratory Practice Standard and 40 CFR 26.

**Test Material:** H<sub>2</sub> Orange<sub>2</sub> 120 (ONE); white cloudy liquid  
**Positive Control Material:** None

**Species:** Human (41 males and 184 females)

**Weight:** Not reported

**Source:** Not applicable

**Age:** 18 to 69 years

**Method:** Nine Repeated Insult (semi-occlusive) Patch Test (9-RIPT)

**Summary:**

1. **This product is not a human dermal sensitizer.**
2. **Classification:** Acceptable

**Procedure (Deviation From §81-6, 870.2600):** The study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in Title 21 of the U.S. Code of Federal Regulations (CFR), the Declaration of Helsinki and/or Essex Testing Clinic (ETC) Standard Operating Procedures.

**Procedure:** The test material (approximately 0.2 mL) was applied to the back between the scapulae and waist area adjacent to the spinal midline with a 2x2 cm Webril pad backed by semi-occlusive surgical tape. The procedure was repeated every Monday, Wednesday, and Friday until nine applications had been made. The patch was removed 24 hours after application and scored 24 (prior to Wednesday and Friday applications) or 48 hours (prior to Monday application) later. If a mild dermal response was noted on any subject after induction, an adjacent site was used for the next application. If a mild dermal response occurred again, no further applications were made. After an approximately two week rest period, the subjects who remained in the study were challenged at a naive site. The site was scored 24 and 72 hours after application.

**Results:** Two hundred fourteen subjects completed the induction phase and 212 subjects completed the test procedure. Only one subject had a mild reaction at the application site after induction No. 5. No reaction was noted on any subject after challenge.