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_2Orange 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)

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

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

Applicant: Envirox, LLC

FORMULATION FROM LABEL:

	% by wt.
Active Ingredient(s):	
Hydrogen Peroxide	1
Other Ingredient(s):	99
Total:	100%

1
11

BACKGROUND: Envirox, LLC, has submitted a set of four acute toxicity / irritation studies to support labeling changes of their product, "H_2Orange 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_2Orange 112 Super Concentrate and H_2Orange 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	IV	acceptable
primary skin irritation	?	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_2Orange 120, the test material was H_2Orange$_2$ 126. The cover letter included with this submission discussed H_2Orange 120, H_2Orange 112 Super Concentrate and H_2Orange 117 Concentrate; however, it does not mention H_2Orange$_2$ 126. While the study mentions the percent of active ingredient in H_2Orange$_2$ 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_2Orange$_2$ 126 and H_2Orange 120. This information is expected to include a CSF of H_2Orange$_2$ 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	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
($H_2ORANGE_2$ 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.

Signature:
Date: OCT 17 2002

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

Signature:
Date: OCT 17 2002

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

Signature:
Date: OCT 17 2002

Quality Assurance:
Lee Ann Wilson, M.A.

Signature:
Date: OCT 17 2002

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_2 Orange$_2$ 126 (H_2O_2 = 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 **Age**: Approximately 7-11 weeks
Source: Ace Animals, Boyertown, PA

Summary:

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

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

Results:

Dosage (mg/kg)[a]	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
($H_2ORANGE_2$ 126)

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

Prepared for
Antimicrobials Division
Office of Pesticide Programs
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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_2 Orange$_2$ 126 (H_2O_2 = 1.34%), Lot No. 97980; cloudy liquid
Dosage: 5000 mg/kg

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

Summary:

1. **LD_{50} (mg/kg)**: **Males** > 5000 mg/kg
   Females > 5000 mg/kg
   Combined > 5000 mg/kg
2. **The estimated LD_{50} is** > 5000 mg/kg.
3. **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
($H_2ORANGE_2$ 120)

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

Prepared for
Antimicrobials Division
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Prepared by
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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: $H_2Orange_2$ 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				
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
($H_2ORANGE_2$ 120)

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

Prepared for
Antimicrobials Division
Office of Pesticide Programs
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Prepared by
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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_2 Orange$_2$ 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 2×2 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.