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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

February 27, 2006

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 64881-A/ Aegis 444-02 RTU

DP Barcode: D324457

To: Velma Noble, PM 31/ Jacqueline Campbell-McFarlane
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)

2/28/06

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

Applicant: Aegis Environmental Management, Inc.

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
3-(trimethoxysilyl) propyldimethyloctadecyl ammonium chloride	0.84
Other Ingredient(s):	99.16
Total:	100%

I BACKGROUND: Aegis Environmental Management, Inc., has submitted a complete set of six acute toxicity studies to support the registration of their product, "Aegis 444-02 RTU Antimicrobial". The studies were conducted by Stillmeadow, Inc.

There is an issue in that, while the product is named "Aegis 444-02 RTU Antimicrobial", the test material is named AEGIS Exp-201. The registrant's consultant, ChemReg International LLC, informs us (via email) that they are indeed the same product.

II RECOMMENDATIONS: PSB findings are:

1 Each of the six submitted studies is acceptable.

The acute toxicity profile for File Symbol 64881-A is currently:

Study	MRID Number	Toxicity Category	Acceptability
acute oral toxicity	466938-03	IV	Acceptable
acute dermal toxicity	466938-04	IV	Acceptable
acute inhalation toxicity	466938-07	IV	Acceptable
primary eye irritation	466938-08	IV	Acceptable
primary skin irritation	466938-05	IV	Acceptable
dermal sensitization	466938-06	Nonsensitizer	Acceptable

III LABELING:

No precautionary labeling is required for this product. The label does not require a Signal Word, Precautionary Statements, or, First Aid statements (also known as Statements of Practical treatment). However, the registrants may choose to utilize toxicity category III labeling statements if they choose to do so.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (OPPTS 870.1100)
(UP AND DOWN PROCEDURE)

Product Manager: 31 **Reviewer:** Ian Blackwell
MRID No.: 466938-03 **Study Completion Date:** July 13, 2005
Report No.: 8989-05

Testing Laboratory: STILLMEADOW, Inc.
Author: Janice O. Kuhn, Ph.D., DABT

Quality Assurance (40 CFR §160.12): A Quality Assurance statement was included. A statement of Good Laboratory Practice (GLP) compliance also was included stating that the study was conducted in compliance with:

- U.S. EPA FIFRA 40 CFR Part 160 with exception of Sec. 160.31 (d), and 160.105 (b) (e) stability information was not provided in a Certificate of Analysis
- U.S. EPA TSCA 40 CFR Part 792 with exception of Sec. 792.31 (d), and 792.105 (b) (e) stability information was not provided in a Certificate of Analysis
- OECD Principles of GLP, Annex 2, C(98)17 with exception of Sec. 6.2 (4) stability information was not provided in a Certificate of Analysis
- Japan Ministry of Agriculture, Forestry & Fisheries, Notification No. 11-Nousan-6283, Director-General of Agricultural Prod. Bureau with exception of Art. 12.7 stability information was not provided in a Certificate of Analysis

Test Material: AEGIS Exp-201; Alternative name: RTU; 2% / Lot # N0325 / Clear liquid

Dosage: Limit Test: 5,000 mg/kg (administered as received)

Species:	3 Sprague-Dawley albino rats	
Sex:	Female; nulliparous and non-pregnant	
Age:	Young adult; Approximately 8 weeks	
Weight:	169 - 170 g (fasted weight on dosing day)	
Source:	Texas Animal Specialties, Humble, TX	
Housing:	Temperature Range set to:	22 ± 3 °C
	Relative Humidity set to:	30 - 70 %
	Photoperiod set to:	12-hour light/dark cycle

Acclimation: 5 days

Conclusion:

1. **LD_{50} (mg/kg):** Females > 5,000 mg/kg

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

Procedure (Deviations from 870.1100):

- The laboratory claims that there were no deviations from the protocol that affected the quality or outcome of the study.
- Changes in body weights were recorded, but not calculated.

Results:

Limit Test - Reported Mortality

Dosing Sequence	Animal No.	Dose Level (mg/kg)	Result
1	111-F	5,000	O
2	112-F		O
3	113-F		O

O - Survived

Observations: There was no mortality during the study. All animals appeared normal for the duration of the study. Body weight gain was unaffected by the administration of the test substance.

Gross Necropsy Findings: The gross necropsy conducted at termination of the study revealed no observable abnormalities.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (OPPTS 870.1200)
(LIMIT TEST)

Product Manager: 31
MRID No.: 466938-04
Reviewer: Ian Blackwell
Study Completion Date: July 13, 2005
Report No.: 8990-05

Testing Laboratory: STILLMEADOW, Inc.
Author: Janice O. Kuhn, Ph.D., DABT

Quality Assurance (40 CFR §160.12): A Quality Assurance statement was included. A statement of Good Laboratory Practice (GLP) compliance also was included stating that the study was conducted in compliance with:

- U.S. EPA FIFRA 40 CFR Part 160 with exception of Sec. 160.31 (d), and 160.105 (b) (e) stability information was not provided in a Certificate of Analysis
- U.S. EPA TSCA 40 CFR Part 792 with exception of Sec. 792.31 (d), and 792.105 (b) (e) stability information was not provided in a Certificate of Analysis
- OECD Principles of GLP, Annex 2, C(98)17 with exception of Sec. 6.2 (4) stability information was not provided in a Certificate of Analysis
- Japan Ministry of Agriculture, Forestry & Fisheries, Notification No. 11-Nousan-6283, Director-General of Agricultural Prod. Bureau with exception of Art. 12.7 stability information was not provided in a Certificate of Analysis

Test Material: AEGIS Exp-201; Alternative name: RTU; 2% / Lot # N0325 / Clear liquid

Species: New Zealand White; Albino rabbit
Sex: 5 / sex; females were nulliparous and nonpregnant
Age: Approximately 12 weeks
Weight : Males: 2.350 - 3.200 kg
Females: 2.300 - 3.000 kg
Source: Nichols Rabbitry Inc., Lumberton, TX
Housing: Temperature Range set to: 20 ± 3 °C
Relative Humidity set to: 30 - 70 %
Photoperiod set to: 12-hour light / 12-hour dark cycle
Acclimation: 5 days

Summary:

1. **LD_{50} (mg/kg):** Males > 5,050 mg/kg
   Females > 5,050 mg/kg
   Combined > 5,050 mg/kg

2. **The estimated LD_{50} is** > 5,050 mg/kg

3. **Toxicity Category:** IV **Classification:** Acceptable

Procedure (Deviations From 870.1200):

- The laboratory claims that there were no deviations from the protocol that affected the quality of the outcome of the study.
- The method of randomization in assigning animals to test groups was not indicated.
- Changes in body weights were recorded, but not calculated.

Results: No mortality occurred during the study.

Reported Mortality

DOSAGE (mg/kg)	DEATHS / number tested		
	Males	Females	Total
5050	0 / 5	0 / 5	0 / 10

Observations: All animals appeared normal for the duration of the study. There were no signs of dermal irritation in any animals at any time during the study. Body weight gain was somewhat affected by the administration of the test substance. One male lost weight between Days 0 and 7, and three females lost weight between Days 7 and 14.

Gross necropsy findings: The gross necropsy conducted at termination of the study revealed no observable abnormalities.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (OPPTS 870.1300)
(NOSE-ONLY EXPOSURE - LIMIT TEST)

Product Manager: 31 **Reviewer**: Ian Blackwell
MRID No.: 466938-07 **Study Completion Date**: July 13, 2005
Report No.: 8991-05

Testing Laboratory: STILLMEADOW, Inc.
Author: Lori Carter, B.A.

Quality Assurance (40 CFR §160.12): A Quality Assurance statement was included. A statement of Good Laboratory Practice (GLP) compliance also was included stating that the study was conducted in compliance with:

- U.S. EPA FIFRA 40 CFR Part 160 with exception of Sec. 160.31 (d), and 160.105 (b) (e) stability information was not provided in a Certificate of Analysis
- U.S. EPA TSCA 40 CFR Part 792 with exception of Sec. 792.31 (d), and 792.105 (b) (e) stability information was not provided in a Certificate of Analysis
- OECD Principles of GLP, Annex 2, C(98)17 with exception of Sec. 6.2 (4) stability information was not provided in a Certificate of Analysis
- Japan Ministry of Agriculture, Forestry & Fisheries, Notification No. 11-Nousan-6283, Director-General of Agricultural Prod. Bureau with exception of Art. 12.7 stability information was not provided in a Certificate of Analysis

Test Material: AEGIS Exp-201 / Lot # N0325 / clear liquid

Species:	10 Sprague-Dawley albino rats	
Sex:	5 males and 5 females (nulliparous and non-pregnant)	
Age:	Young adult (Approximately 8 weeks)	
Weight:	Males:	260 - 288 grams
	Females:	178 - 205 grams
Housing:	Temperature Range set to:	22 ± 3 °C
	Relative Humidity set to:	30 - 70 %
	Photoperiod set to:	12-hour light/dark cycle
Acclimation:	5 days	
Source:	Texas Animal Specialities, Humble, TX	

Concentration:

Group	Analytical Exposure Concentration (mg/L)	Nominal Concentration (mg/L)
I	2.21	2.50

Summary:

1. **LC_{50} (mg/L) 4-hr exposure:** Male rats > 2.21 mg/L
   Female rats > 2.21 mg/L
   Combined >2.21 mg/L

2. **The estimated 4-hr LC_{50} in rats is > 2.21 mg/L**

3. **Average MMAD**: 1.8 µm

4. **Toxicity Category**: IV **Classification**: Acceptable

Procedure (Deviation From 870.1300):

- The laboratory states that there were no deviations from the protocol that affected the quality or outcome of the study.
- The method of randomization of assigning animals to the test group was not documented.
- The laboratory does not state whether animals were acclimated to the test chamber conditions.
- Only one MMAD was determined for the three trial assays. Thus, it is unclear as to whether pretest measurements of MMAD values were within 10 percent of each other. The guidelines suggest that three to four measurements should be taken if pretest measurements are not within 10 percent of each other, and two measurements during the exposure should be sufficient if measurements are within 10 percent of each other. The MMAD values during the exposure of the animals to the test substance were not within 10 percent of each other, and only two measurements were taken.

Results:

Reported Mortality

Exposure Concentration (mg/L)	Number of deaths / number tested		
	Males	Females	Combined
2.21	0 / 5	0 / 5	0 / 10

Chamber Atmosphere

Exposure conc. (mg/L)	Sample	MMAD (µm)	GSD (µm)	% Particles at Effective Cutoff Diameter (µm) (Cumulative)							
				>17.4	>10.4	> 4.2	> 2.5	> 1.6	> 0.9	> 0.5	> 0.3
2.21	1	1.6	5.6	100.0	100.0	75.0	50.0	50.0	50.0	12.5	12.5
	2	2.0	5.1	95.0	95.0	95.0	45.0	25.0	25.0	25.0	5.0

Chamber Environment During Exposure

Exposure Level (mg/L)	**2.21**
Chamber Volume (L)	500
Airflow (Lpm)	184
Temperature (°C)	23
Relative Humidity (%)	65

Clinical Observations: There was no mortality during the study. Body weight gain was unaffected by the administration of the test substance. Prominent in-life observations included activity decrease and piloerection in both sexes, and red crust around the eyes in males. Animals were asymptomatic by Day 3.

Gross Necropsy Findings: The gross necropsy conducted on each animal at termination of the study revealed no observable abnormalities.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING
(OPPTS 870.2400)

Product Manager: 31
MRID No.: 466938-08

Reviewer: Ian Blackwell
Study Completion Date: July 13, 2005
Report No.: 8992-05

Testing Laboratory: STILLMEADOW, Inc.
Author: Janice O. Kuhn, Ph.D., DABT

Quality Assurance (40 CFR §160.12): A Quality Assurance statement was included. A statement of Good Laboratory Practice (GLP) compliance also was included stating that the study was conducted in compliance with:

- U.S. EPA FIFRA 40 CFR Part 160 with exception of Sec. 160.31 (d), and 160.105 (b) (e) stability information was not provided in a Certificate of Analysis
- U.S. EPA TSCA 40 CFR Part 792 with exception of Sec. 792.31 (d), and 792.105 (b) (e) stability information was not provided in a Certificate of Analysis
- OECD Principles of GLP, Annex 2, C(98)17 with exception of Sec. 6.2 (4) stability information was not provided in a Certificate of Analysis
- Japan Ministry of Agriculture, Forestry & Fisheries, Notification No. 11-Nousan-6283, Director-General of Agricultural Prod. Bureau with exception of Art. 12.7 stability information was not provided in a Certificate of Analysis

Test Material: AEGIS Exp-201; Alternate name: RTU; 2% / Lot # N0325 / Clear liquid

Dosage: 0.1 mL - undiluted
Species: New Zealand White; Albino rabbits
Sex: 1 Male; 2 Females
Age: Approximately 12 weeks
Source: Nichols Rabbitry Inc., Lumberton, TX
Housing: Temperature Range set to: 20 ± 3 °C
Relative Humidity set to: 30 - 70 %
Photoperiod set to: 12-hour light / 12-hour dark cycle
Acclimation: 5 days

Summary:

1. **Toxicity Category:** IV

2. **Classification:** Acceptable

Procedure (Deviations From 870.2400):

- The laboratory states that there were no deviations from the protocol that affected the quality or outcome of the study. No deviations were noted by the study reviewer.

Results:

Based on the maximum average irritation score of 10.7, the test substance AEGIS Exp-201 is rated minimally irritating. Since all "positive" effects had cleared by 24 hours, the test substance is assigned to Toxicity Category IV. No irritation was observed in any eyes at 72 hours.

Incidence of Irritation

Time Post	Corneal	Iritis	Conjunctivitis
1 hour	0 / 3	2 / 3	0 / 3
24 hours	0 / 3	0 / 3	0 / 3
48 hours	0 / 3	0 / 3	0 / 3
72 hours	0 / 3	0 / 3	0 / 3

Individual Ocular Irritation Scores

Observations	Rabbit No.: 8620-M				Rabbit No.: 8619-F				Rabbit No.: 8621-F			
	Hours				Hours				Hours			
	1	24	48	72	1	24	48	72	1	24	48	72
I. Corneal	+	+	+	0	+	+	0	0	+	+	0	0
II. Iritis	0	0	0	0	1	0	0	0	1	0	0	0
III.												
A. Redness	1	1	1	0	1	1	1	0	1	1	1	0
B. Chemosis	1	0	0	0	1	1	1	0	1	0	0	0
C. Discharge	1	0	0	0	3	1	1	0	1	0	0	0

M - Male; F - Female;

+ - slight dulling of normal luster

DATA REVIEW FOR DERMAL IRRITATION TESTING (OPPTS 870.2500)

Product Manager: 31
MRID No.: 466938-05
Reviewer: Ian Blackwell
Study Completion Date: July 13, 2005
Report No.: 8993-05

Testing Laboratory: STILLMEADOW, Inc.
Author: Janice O. Kuhn, Ph.D., DABT

Quality Assurance (40 CFR §160.12): A Quality Assurance statement was included. A statement of Good Laboratory Practice (GLP) compliance also was included stating that the study was conducted in compliance with:

- U.S. EPA FIFRA 40 CFR Part 160 with exception of Sec. 160.31 (d), and 160.105 (b) (e) stability information was not provided in a Certificate of Analysis
- U.S. EPA TSCA 40 CFR Part 792 with exception of Sec. 792.31 (d), and 792.105 (b) (e) stability information was not provided in a Certificate of Analysis
- OECD Principles of GLP, Annex 2, C(98)17 with exception of Sec. 6.2 (4) stability information was not provided in a Certificate of Analysis
- Japan Ministry of Agriculture, Forestry & Fisheries, Notification No. 11-Nousan-6283, Director-General of Agricultural Prod. Bureau with exception of Art. 12.7 stability information was not provided in a Certificate of Analysis

Test Material: AEGIS Exp-201; Alternative name: RTU; 2% / Lot # N0325 / Clear liquid

Dosage: 0.5 mL - undiluted

Species: New Zealand White; Albino rabbits
Sex: 2 Males; 1 Females
Age: Approximately 12 weeks
Source: Nichols Rabbitry Inc., Lumberton, TX
Housing: Temperature Range set to: 20 ± 3 °C
Humidity Range set to: 30 - 70 %
Photoperiod set to: 12-hour light / 12-hour dark cycle
Acclimation: 5 days

Summary:

1. **Toxicity Category:** IV

2. **Classification:** Acceptable

Procedure (Deviations From 870.2500):

- The laboratory claims that there were no deviations from the protocol that affected the quality or outcome of the study. No protocol deviations were noted by the study reviewer.

Results: Erythema and edema were not observed at any time throughout the study. No other signs of irritation were observed during the study.

Incidence of Irritation

Time after Patch Removal	Erythema	Edema
1 Hour	0 / 3	0 / 3
24 Hours	0 / 3	0 / 3
48 Hours	0 / 3	0 / 3
72 Hours	0 / 3	0 / 3

DATA REVIEW FOR SKIN SENSITIZATION TESTING (OPPTS 870.2600)
(MODIFIED BUEHLER METHOD)

Product Manager: 31
MRID No.: 466938-06
Reviewer: Ian Blackwell
Study Completion Date: July 13, 2005
Report No.: 8994-05

Testing Laboratory: STILLMEADOW, Inc.
Author: Janice O. Kuhn, Ph.D., DABT

Quality Assurance (40 CFR §160.12): A Quality Assurance statement was included. A statement of Good Laboratory Practice (GLP) compliance also was included stating that the study was conducted in compliance with:

- U.S. EPA FIFRA 40 CFR Part 160 with exception of Sec. 160.31 (d), and 160.105 (b) (e) stability information was not provided in a Certificate of Analysis
- U.S. EPA TSCA 40 CFR Part 792 with exception of Sec. 792.31 (d), and 792.105 (b) (e) stability information was not provided in a Certificate of Analysis
- OECD Principles of GLP, Annex 2, C(98)17 with exception of Sec. 6.2 (4) stability information was not provided in a Certificate of Analysis
- Japan Ministry of Agriculture, Forestry & Fisheries, Notification No. 11-Nousan-6283, Director-General of Agricultural Prod. Bureau with exception of Art. 12.7 stability information was not provided in a Certificate of Analysis

Test Material: AEGIS Exp-201; Alternative name: RTU; 2% / Lot # N0325 / Clear liquid
Positive Control Material: 1-Chloro-2,4-dinitrobenzene (DNCB) (Historical data - completed April 1, 2005)

Species: 34 Hartley-Albino guinea pigs
Sex: 2 males and 2 females (Range-finding)
15 males and 15 females (Definitive)
Age: Approximately 5 weeks (young adult)
Weight: Males: 385 - 441 grams
Females: 350 - 455 grams
Source: Charles River Laboratories, Wilmington, MA
Housing: Temperature Range set to: 20 ± 3 °C
Relative Humidity set to: 30 - 70 %
Photoperiod set to: 12-hour light/dark cycle
Acclimation: 5 days

Method: Modified Buehler method

Summary:

1. **Based on these findings and on the evaluation system used, AEGIS Exp-201 is not considered to be a contact sensitizer.**
   Note: Study evaluated erythema only

2. **Classification**: Acceptable

Procedure (Deviation From 870.2600):

- The laboratory states that there were no deviations from the protocol that affected the quality or outcome of the study.
- The laboratory does not state whether female animals were nulliparous and nonpregnant.
- Only erythema was graded, and not edema.

Procedure:

Preliminary Irritation: Two male and two female albino guinea pigs were selected for irritation screening to determine both the maximum dose producing no more than moderate irritation, and the maximum non-irritating dose. Concentrations tested in the screening were 100% (undiluted), and 75%, 50% and 25% v/v dilutions in deionized water, with each animal receiving 0.4 mL of each concentration at different test sites.

Induction Phase: On the day prior to each treatment, the animals were prepared by clipping the back of the trunk free of hair to expose a longitudinal area at least 8 x 10 cm on each animal. Based on the results of the irritation screening, the test substance was administered by application of 0.4 mL of the undiluted test substance. For each induction treatment, Group II animals (test group - 10/sex) were treated by introducing the test substance beneath a 4 ply, 2.5 x 2.5 cm surgical gauze patch. Each gauze patch was placed laterally from the midline of the back on the left front quadrant of the exposure area and secured with a strip of non-irritating adhesive tape. A strip of clear polyethylene film was placed over the patch and securely taped. Each animal was then placed in a restrainer for approximately six hours. At the end of the exposure period, the animals were removed from the restrainers, the wrappings and patches were removed, and the animals were returned to their cages. Group II animals were treated once weekly for three weeks with 0.4 mL of the undiluted test substance. Induction treatments were on Days 1, 8 and 15. The same treatment regimen and test site location was used for all three induction treatments. Group I animals (naive control group - 5/sex) remained untreated during the induction phase of the study. Observations for skin reactions at each test site were made approximately 24 hours after each treatment and approximately 48 hours after the first induction treatment.

Challenge Phase: After a two-week rest period, all animals (Groups I an II) were each challenged at a virgin test site with an application of 0.4 mL of the undiluted test substance. The challenge treatment was on Day 29. The dose was applied in a manner identical to the induction treatments, except the test site was placed laterally on the right rear quadrant of the exposure area. Observations for skin reactions were made approximately 24 hours and 48 hours after the challenge treatment.

Results:
Based on the results of this study, the laboratory states that the test substance did not elicit a sensitizing reaction in guinea pigs.

	Sensitization Response Indices (Erythema)			
	Incidence of Positive Response[1]		Average Scores	
	Hours		Hours	
	24	48	24	48
Test Animals	0 / 20	0 / 20	0.0	0.0
Naive Control Animals	0/ 10	0 / 10	0.0	0.0