3-2-99

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Subject: D247619
Intersmooth 365 Ecoloflex SPC Antifouling, Product No. 2693-RII

From: Wallace Powell, Biologist
Efficacy and Science Support Branch
Antimicrobials Division (7510W)

Thru: Karen P. Hicks, Team Leader
Chemistry/Toxicology Team
Efficacy and Science Support Branch
Antimicrobials Division (7510W)

Michele E. Wingfield, Chief
Efficacy and Science Support Branch
Antimicrobials Division (7510W)

To: Marshall Swindell, Product Manager, Team 33
Karen Leavy-Munk, Team Reviewer, Team 33
Regulatory Management Branch I
Antimicrobials Division (7510W)

BACKGROUND

The applicant, Courtaulds Coatings, Inc., has submitted studies for acute oral toxicity, acute dermal toxicity, acute inhalation toxicity, primary eye irritation, primary dermal irritation (three studies), and dermal sensitization, to support registration of an antifouling paint product (EPA File Symbol 2693-RII). The studies were initially reviewed for Efficacy and Science Support Branch (ESSB) by Oak Ridge National Laboratory. The reviews are attached to this memorandum and may have been edited by ESSB staff. The primary eye irritation study was submitted in support of a waiver request and did not receive an MRID number.

RECOMMENDATION

Test Materials:

It is the reviewer's understanding, based on a conversation with John Pazdera of Courtaulds Coatings, that the formulation tested in the acute oral, acute dermal, and acute inhalation toxicity studies, the dermal sensitization study, and in the MRID 445872-04 dermal irritation study in the rabbit, is the formulation presented on the submitted sheet that is identified by the headings "COURTAULDS COATINGS" and "COMMERCIAL IN CONFIDENCE." The sheet calls the formulation "Intersmooth 360 Ecoloflex" and shows its composition. The applicant's resubmission should include a statement to verify that these things are true.

Additionally, the dermal irritation study with MRID No. 445872-05 was conducted on the 'overspray' of an aerosolized version of the above Intersmooth 360 Ecoloflex. It is also the reviewer's understanding that the formulation discussed in the submitted eye irritation waiver request is also presented on the above "COURTAULDS COATINGS" sheet and is identified as "VC17M - YBA762/YBA674."

The subject product contains a [redacted] at [redacted]% of the formulation. This component is not listed in the composition of the above test materials. The applicant's resubmission should include identification of the chemical identity or chemical composition of the [redacted]

§81-1, Acute Oral Toxicity:

In the submitted study, 2/5 males and 3/5 females died at a dose of 2000 mg/kg. Based on the study results, the product cannot be placed in a Toxicity Category. The study is unacceptable. Three doses are the minimum for determination of an LD_{50}, though two doses are sometimes sufficient to bracket the LD_{50} into a specific Toxicity Category range.

It is preferable for a study to be conducted on the product formulation itself rather than on a substitute test material such as the "Intersmooth 360 Ecoloflex" in the submitted study. If an acceptable acute oral study using the "Intersmooth 360 Ecoloflex" were to indicate Category III or IV, it would most likely be accepted in support of the subject product, which is not expected to be more hazardous than "Intersmooth 360 Ecoloflex." If, however, a study were to indicate Category I or II, the study would most likely be rejected because the Category might represent a significant overstatement of the 'actual' hazard level.

§81-2, Acute Dermal Toxicity: The submitted study indicates Toxicity Category III or IV based on the limit test; Category III (i.e., 2000 mg/kg < LD_{50} ≤ 5000 mg/kg) is being assigned for regulatory purposes. The study is acceptable. The subject product is not expected to be more hazardous than the test material ("Intersmooth 360 Ecoloflex"), which contains far more [redacted] than the subject product, and contains two other solvents, each at [redacted]% of the formulation, which are not contained in the subject product. Therefore, the 'actual' acute dermal toxicity for the subject product is not be expected to be worse than Category III.

§81-3, Acute Inhalation Toxicity: The submitted study indicates Toxicity Category IV. The study is acceptable. The subject product is not expected to be more hazardous than the test material ("Intersmooth 360 Ecoloflex"). However, in view of the fact that the test material was not the product itself, Category III is assigned rather than IV so that the label will not be without a statement alerting the user to the possibility of a hazard.

§81-4, Primary Eye Irritation:

No Toxicity Category can be assigned. A study is required for the subject product formulation.

The waiver request was accompanied by a low-volume eye test (LVET) report (which did not received an MRID number). It appears that some LVET's can be suitable substitutes for the usual Draize test. However, in comparing the subject product (2693-RII) with the LVET test material (VC17M - YBA762/YBA674), the formulations are too different for the test to be accepted in support of the subject product. One reason is that [redacted] is [redacted]% of the test material and only [redacted]% of subject product. Concentrated [redacted] may be a severe irritant. To assign eye irritation Category I to the subject product might represent a significant overstatement of the 'actual' hazard level.

The submitted dermal irritation study cannot be used in support of assigning an eye irritation Toxicity Category. The dermal irritation study indicates Category I, with corrosiveness, for the test material (Intersmooth 360 Ecoloflex). If the results were Category III or IV, then the subject product could be assigned Category III for eye irritation on the assumption that the subject product is not more hazardous than the test material. However, with the Category I result for the dermal irritation test material, to take this Category I and apply it to the subject product might represent a significant overstatement of the 'actual' hazard. Likewise, to assume Category I for eye irritation for the test material might also represent a significant overstatement of the 'actual' hazard level.

§81-5, Primary Dermal Irritation: No Toxicity Category can be assigned. A study is required for the subject product formulation.

Three studies were submitted: MRID 445872-04 (dermal irritation in the rabbit, test article was the paint itself), MRID 445872-05 (dermal irritation in the rabbit, test article was paint overspray), and MRID 445872-08 (dermal irritation in humans).

MRID 445872-04: study acceptable per se, with Toxicity Category I result for the test material ("Intersmooth 360 Ecoloflex"). However, the test material and the subject product do not appear similar enough to assume that they share the same Toxicity Category. To assign Category I to the subject product might represent a significant overstatement of the 'actual' hazard level.

MRID 445872-05: study acceptable per se, with Toxicity Category IV result. The study represents normal in-use dermal conditions for exposure to the product. However, because the

requirement applies to the product as-sold, and worse dermal exposure cannot be ruled out, Category IV is not assigned to the product.

MRID 445872-08: As indicated in the attached Data Evaluation Report, "This study is considered unacceptable (nonguideline). Problems in the selection of individuals for study participation, dosing, amount of test substance applied and the scoring system preclude the use of this study in considering the dermal effects induced by the test substance."

§81-6, Dermal Sensitization: Non-sensitizing. The submitted study is acceptable.

The acute toxicity regulatory profile for the subject product is summarized in the following table.

Acute Effect	Study MRID No.	Status / Toxicity Category Assigned
Acute Oral Toxicity	445872-02*	Study unacceptable
Acute Dermal Toxicity	445872-03*	III
Acute Inhalation Toxicity	445872-06*	III
Primary Eye Irritation	waiver request and low-volume eye test (no MRID)	Test material unacceptable
Primary Dermal Irritation	445872-04*: dermal irritation - rabbit - test article was the paint. 445872-05: dermal irritation - rabbit - test article was paint overspray. 445872-08: dermal irritation - human	MRID 445872-04: Category I result but test material unacceptable. MRID 445872-05: Category IV result but only reflects normal in-use conditions. MRID 445872-08: Study unacceptable
Dermal Sensitization	445872-07*	Non-sensitizing

* Applicant's resubmission should include a statement to verify the composition of the test material, as explained above in the first paragraph under the "**Test Materials**" heading. Applicant should also identify the chemical identity of the [redacted] in the subject product formulation.

PRODUCT LABELING

Determination of the required precautionary and practical treatment label statements cannot be completed until the remaining acute toxicity data requirements have been met.

DATA EVALUATION REPORT

ECOLOFLEX PAINT

STUDY TYPE: ACUTE ORAL TOXICITY – RATS

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2800 Crystal Drive
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 98-170

Primary Reviewer:
H. T. Borges, Ph.D., MT(ASCP), D.A.B.T

Secondary Reviewers:
Cheryl B. Bast, Ph.D., D.A.B.T

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

Quality Assurance:
LeeAnn Wilson, M.A.

Signature: H.T. Borges
Date: _____

Signature: Cheryl B Bast
Date: _____

Signature: Robert H Ross
Date: _____

Signature: L. A. Wilson
Date: _____

Disclaimer

This Data Evaluation Report may have been altered by the Antimicrobials Division subsequent to signing by Oak Ridge National Laboratory personnel.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

EPA Reviewer: Wallace Powell _____, Date _____
EPA Work Assignment Manager: Peter Thompson, Ph.D._____, Date _____
Antimicrobials Division (7510W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity – Rats
OPPTS 870.1100 [§81-1]

DP BARCODE: D247619
CASE: 062406

SUBMISSION CODE: S545496
TOX. CHEM. NO.: 025601

TEST MATERIAL: Ecoloflex Paint

CITATION: MacBeth, D. and S.W. Ogilvie. (1994) Ecoloflex paint; Acute oral toxicity (Limit) test in rats. Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 554474, Report No. 9976 (EPA), January 11, 1994. MRID 44587202. Unpublished.

SPONSOR: Courtaulds Coatings (Holdings) Ltd., Stoneygate Lane, Felling, Gateshead, Tyne & Wear, NE 10 OJY

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44587202), groups of fasted, 6-8 week old Sprague-Dawley rats (5/sex) were given a single oral dose of Ecoloflex Paint (42.69% cuprous oxide, 3.18% zinc 2-pyridinethiol 1-oxide, a.i.) (Batch #: Z0474) at a dose of 2000 mg/kg and observed for 14 days. The study was conducted as a Limit Test.

Within 48 hours of treatment, all surviving rats developed piloerection, a hunched appearance, and a red discharge from the eyes and nose. The piloerection and hunched appearance persisted until day 13 in surviving males and day 14 in females. Two male and three female rats died or were killed *in extremis* during the study. Three of the five surviving animals lost weight during the first week of the study but recovered their initial body weight and gained weight during the second week. No treatment-related effects were found at necropsy in surviving animals. The stomach and/or intestines of animals that died during the study were distended with gas or contained a green or dark liquid.

The oral LD_{50} for males rats is > 2000 mg/kg and is < 2000 mg/kg for female rats. Based on the study results, Ecoloflex Paint cannot be placed in a Toxicity Category.

This acute oral study is classified as unacceptable and does not satisfy the guideline requirement for an Acute Oral Study (81-1) in the rat. The study was conducted as a Limit Test, but only a single dose of 2000 mg/kg rather than 5000 mg/kg was used. Since a second and lower dose was not used, the LD_{50} for female rats cannot be determined. In addition, the male rat oral LD_{50} cannot be further delineated other than to state that it exceeds 2000 mg/kg.

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COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:

Ecoloflex Paint SP500 Blue
Description: blue liquid
Lot/Batch #: Z0474
Purity: not applicable
CAS #: not reported
Specific Gravity: 1.4

2 Vehicle: not reported

3. Test animals

Species: rat
Strain: Sprague-Dawley
Age and/or weight at dosing: 6-8 weeks; males 170-191 g; females 137-152 g
Source: Harlan Olac Limited, Shaw's Farm, Blackthorn, Bicester, OX6 OTP
Acclimation period: 9 days
Diet: Rat and Mouse No. 1 Maintenance Diet, Special Diets Services Limited, ad libitum
Water: tap water, ad libitum
Housing: by sex in polypropylene cages with mesh floors
Environmental conditions:
Temperature: 20-21°C
Average Humidity: 58%
Air changes: 15-20/hour
Photoperiod: 12-hour light/dark

B. STUDY DESIGN and METHODS

1. In life dates

Start: 09/16/93; end: 09/30/93

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2. Animal assignment and treatment

Animals were assigned to the test groups noted in Table 1. Following an overnight fast, rats were given a single gavage dose of test material. The vehicle used for dosing and the dosing volume were not reported. The animals were weighed prior to treatment and on study days 7 and 14. Survivors were sacrificed 14 days later. All animals were necropsied.

TABLE 1. Dose, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
2000	2/5	3/5	5/10

3. Statistics

Calculation of an LD_{50} was not done.

II. RESULTS AND DISCUSSION

A. MORTALITY

Mortality is given in Table 1. One male rat on day one, one male rat on day 3, and one female rat on day 4 were killed *in extremis*. Two other female rats were found dead on day 4.

An oral LD_{50} for Ecoloflex Paint was not calculated. The male rat oral LD_{50} is > 2000 mg/kg while the female LD_{50} is < 2000 mg/kg.

B. CLINICAL OBSERVATIONS

Four hours after treatment, all rats had blue-stained coats and one male and all females had increased salivation. Within 48 hours of treatment, all surviving rats developed pilo-erection, a hunched appearance, and a red discharge from the eyes and nose. The pilo-erection and hunched appearance persisted until day 13 in surviving males and day 14 in females.

C. BODY WEIGHT

Two surviving male and two surviving female rats lost weight during the first week of the study. All surviving rats recovered their initial body weight and gained weight during the second week.

D. NECROPSY

No treatment-related effects were found in animals that survived the study. One female rat that died on day four had autolyzed but no abnormalities were identified. The stomach

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or intestines of the other two female rats contained dark contents. The stomach of one male rat killed *in extremis* on day one contained a green liquid while the stomach and intestines of the other male rat were distended with gas. No other abnormalities were identified.

E. DEFICIENCIES

According to the author, the study was conducted as a Limit Test in accordance with OECD and EPA guidelines. However, only a single 2000 mg/kg oral dose was used while both OECD and EPA guidelines call for a 5000 mg/kg dose for a Limit Test. In addition, 3/5 female rats died or were killed *in extremis* during the study which would give an LD_{50} of <2000 mg/kg. Since a second and lower dose was not used, the LD_{50} for female rats cannot be determined. In addition, the male rat oral LD_{50} cannot be further delineated other than to state it exceeds 2000 mg/kg. Therefore, the study is unacceptable and cannot be upgraded.

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DATA EVALUATION REPORT

ECOLOFLEX PAINT

STUDY TYPE: ACUTE DERMAL TOXICITY - RAT

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2800 Crystal Drive
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Biomedical and Environmental Information Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 98-170

Primary Reviewer:
H. T. Borges, Ph.D., MT(ASCP), D.A.B.T

Secondary Reviewers:
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Robert H. Ross, M.S., Group Leader

Quality Assurance:
LeeAnn Wilson, M.A.

Signature: H T Borges
Date: AUG 2 5 1998

Signature: Cheryl B Bast
Date: AUG 2 5 1998

Signature: Robert H Ross
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Signature: L. A. Wilson
Date: AUG 2 5 1998

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Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464

EPA Reviewer: Wallace Powell _____, Date _____
EPA Work Assignment Manager: Peter Thompson, Ph.D._____, Date _____
Antimicrobials Division (7510W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rat
OPPTS 870.1200 [§81-2]

DP BARCODE: D247619
CASE: 062406

SUBMISSION CODE: S545496
TOX. CHEM. NO.: 025601

TEST MATERIAL: Ecoloflex Paint

CITATION MacBeth, D. and S.W. Ogilvie. (1994) Ecoloflex paint; Acute dermal toxicity (Limit) test in rats. Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 554474, Report No. 9977 (EPA), January 11, 1994. MRID 44587203. Unpublished.

SPONSOR: Courtaulds Coatings (Holdings) Ltd., Stoneygate Lane, Felling, Gateshead, Tyne & Wear, NE 10 OJY

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44587203), groups of young adult Sprague Dawley rats (5/sex) were given a single dermal dose of 2000 mg/kg Ecoloflex Paint (42.69% cuprous oxide, 3.18% zinc 2-pyridinethiol 1-oxide, a.i.) (Batch # Z0474) and observed for 11 days. The study was conducted as a Limit Test.

None of the animals died during the study. Hardened skin developed at the application site on all animals that progressed to form large scabs by day 8. Because of the scab formation, the study was terminated on day 11. The test material did not affect the body weight of male rats, but 4/5 female rats lost weight which they did not recover by study termination. Other than the scab formation, no treatment-related effects were noted at necropsy.

Based on the study results, the dermal LD_{50} of Ecoloflex Paint to male, female, and male and female Sprague Dawley rats is > 2000 mg/kg. This places the test material in Toxicity Category III.

This acute dermal toxicity study is classified as acceptable and satisfies the guideline requirements for an acute dermal toxicity study (81-2) in the rat. Although the study was terminated on day 11 rather than day 14, this would not affect the study results.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Ecoloflex Paint SP500 Blue

Description: blue liquid
Lot/Batch #: Z0474
Purity: not applicable
CAS #: not reported
Specific Gravity: 1.4

2 Vehicle: not reported

3. Test animals

Species: rat
Strain: Sprague-Dawley
Age and/or weight at dosing: 8-10 weeks; males 252-283 g; females 230-246 g
Source: Harlan Olac Limited, Shaw's Farm, Blackthorn, Bicester, OX6 OTP
Acclimation period: 9 days
Diet: Rat and Mouse No. 1 Maintenance Diet, Special Diets Services Limited, ad libitum
Water: tap water, ad libitum
Housing: by sex in polypropylene cages with mesh floors
Environmental conditions:
Temperature: 20-21 °C
Average Humidity: 58%
Air changes: 15-20/hour
Photoperiod: 12-hour light/dark

B. STUDY DESIGN AND METHODS

1 In life dates

Start: 09/16/93, end: 09/27/93

2. Animal assignment and treatment

Animals were assigned to the test groups noted in Table 1. Before treatment, an area equivalent to approximately 10% of the total body area was shaved on the back of each rat. The test material, applied evenly onto a gauze pad moistened with distilled water, was applied to the shaved area. The trunk of the rat was then wrapped with non-irritating occlusive tape. Twenty-four hours later, the dressing was removed and the skin wiped with a damp tissue to remove excess test material. The rats were observed for clinical signs of toxicity and mortality frequently on the day of dosing and

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daily thereafter for the duration of the 11-day study. At the end of the study, the survivors were sacrificed and necropsied. Body weights were recorded immediately before treatment and on study days 7 and 11.

TABLE 1. Doses, mortality/animals treated			
Dose (mg/kg)	**Males**	**Females**	**Combined**
2000	0/5	0/5	0/10

3. Statistics - Calculation of a dermal LD_{50} was not required.

II. RESULTS AND DISCUSSION

A. MORTALITY

As shown in Table 1, none of the animals died during the study. Therefore, the dermal LD_{50} of Ecoloflex Paint for male, female, and male and female Sprague Dawley rats >2000 mg/kg.

B. CLINICAL OBSERVATIONS

One female rat had a red ocular discharge on day two. Hard brown skin at the application site became apparent on day 2 for male rats and day 4 for female rats. This condition progressed for both sexes of animals to form large scabs by day 8 that remained until study termination. The study was terminated on day 11 because of the scab formation. No other remarkable clinical observations were recorded.

C. BODY WEIGHT

Treatment with the test material had no effect on the body weight of male rats and one female rat. Four female rats lost weight during the first week of treatment which they did not recover by study termination.

D. NECROPSY

Other than the dark red scabs present at the application site of all animals, no treatment-related effects were noted.

E. DEFICIENCIES

The study was terminated on day 11 rather than day 14. In all probability, this would not affect the study results.

DATA EVALUATION REPORT

ECOLOFLEX PAINT

STUDY TYPE: ACUTE INHALATION TOXICITY – RATS

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2800 Crystal Drive
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Biomedical and Environmental Information Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 98-170

Primary Reviewer:
H. T. Borges, Ph.D., MT(ASCP), D.A.B.T

H T Borges
Signature: _____
Date: AUG 2 5 1998

Secondary Reviewers:
Cheryl B. Bast, Ph.D., D.A.B.T

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Date: AUG 2 5 1998

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

Robert H Ross
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Date: AUG 2 5 1998

Quality Assurance:
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L. A. Wilson
Signature: _____
Date: AUG 2 5 1998

Disclaimer

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Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464

EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____

EPA Reviewer: Wallace Powell _____, Date _____
EPA Work Assignment Manager: Peter Thompson, Ph.D._____, Date _____
Antimicrobials Division (7510W)

DATA EVALUATION RECORD

STUDY TYPE: Acute Inhalation Toxicity - Rats
OPPTS 870.1300 [§81-3]

DP BARCODE: D247619
CASE: 062406

SUBMISSION CODE: S545496
TOX. CHEM. NO.: 025601

TEST MATERIAL: Ecoloflex Paint

CITATION: Walker, S.A. (1994) Ecoloflex paint; Acute inhalation toxicity study in rats. Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 653671, Report No. 10157 (EPA), December 12, 1994. MRID 44587206. Unpublished.

SPONSOR: Courtaulds Coatings (Holdings) Ltd., Stoneygate Lane, Felling, Gateshead, Tyne & Wear, NE 10 OJY

EXECUTIVE SUMMARY: In an acute inhalation limit toxicity study (MRID 44587206), groups of young adult Sprague-Dawley rats (5/sex) were exposed by inhalation (nose-only) for four hours to Ecoloflex Paint (42.69% cuprous oxide, 3.18% zinc 2-pyridinethiol 1-oxide, a.i.) (Batch # Z0682) at a concentration of 5.89 mg/L and observed for 14 days.

No mortality occurred. During exposure, all rats appeared to have shallow breathing and immediately after exposure had a hunched appearance and test material on their coats. Four female rats had slight red staining around the head on study day 1. No other remarkable clinical observations were made for the remainder of the study. Several male and female rats either lost or failed to gain weight two days after treatment. By the third day, all rats had gained weight and no other effects on body weight were noted. At necropsy, the lungs of 3/5 male and 5/5 female rats were pale and the heart and lungs of 2/5 male and 3/5 female rats were surrounded by a large amount of fat. No other remarkable treatment-related effects were noted.

The Ecoloflex Paint inhalation LC_{50} for male and female Sprague Dawley rats is > 5.89 mg/L. This places the test material in TOXICITY CATEGORY IV.

This acute inhalation study is classified as acceptable and does satisfy the guideline requirement for an Acute Inhalation Study (81-3) in the rat even though the MMAD was 4.49. The reviewer feels this MMAD is likely the best that can be achieved with the test material formulation. In addition, approximately 43% of the test material particles had an aerodynamic diameter < 4.0 μm.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material: Ecoloflex Paint SP500 Blue

   Description: supplied in aerosol cans
   Lot/Batch #: Z0682
   Purity: not applicable
   CAS #: not reported

2 Vehicle: not reported

3. Test animals

   Species: rat
   Strain: Sprague-Dawley
   Age and/or weight at dosing: 6-7 weeks; males 233-248 g; females 183-212 g
   Source: Charles River (UK) Limited, Manston Road, Margate, Kent, England
   Acclimation period: 9 days
   Diet: Rat and Mouse No. 1 Diet SQC Expanded, Special Diets Services Limited, ad libitum
   Water: tap water, ad libitum
   Housing: by sex in polypropylene cages with mesh floors
   Environmental conditions:
   Temperature: 20 ± 2°C
   Average Humidity: 55 ± 10%
   Air changes: 15-20/hour
   Photoperiod: 12-hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

   Start: 12/21/93; end: 01/05/94

2. Exposure conditions

   Temperature and humidity were recorded at 30 minute intervals during the four-hour nose-only exposure. Particle size was determined twice, however, the first sample was collected for an extended time invalidating the results. Exposure concentration was determined gravimetrically at 15 minute intervals throughout the exposure period.

3. Animal assignment and treatment

Animals were assigned to the test groups noted in Table 1. Rats were exposed to Ecoloflex Paint for 4 hours and observed daily for 14 days. The animals were weighed before exposure and on study days 2, 3, 4, 7, 10, and 14. Survivors were sacrificed and a necropsy done at study end.

TABLE 1. Concentrations, exposure conditions, mortality/animals treated

Nominal Conc. (mg/L)	Gravimetric Conc. (mg/L)	MMAD (μm)	GSD (μm)	Average Temp. (°C)	Average Humidity (%)	Males	Females	Combined
59.6	5.89	4.49[a]	1.52[a]	21.2	36	0/5	0/5	0/10

[a]Calculated by reviewer

4. Generation of the test atmosphere and description of the chamber

The animals were exposed nose-only in an aluminum exposure chamber that had an internal volume of approximately 45 L. The test material was used as supplied by spraying the well-mixed aerosol into the open orifice at the top of the exposure chamber at 5 minute intervals. Airflow through the chamber was approximately 15 L/min.

Test atmosphere concentration was gravimetrically measured at 15 minute intervals throughout exposure. Because of the volatile nature of the test material aerosol, however, the nominal concentration was calculated by dividing the total weight of material used by the total airflow through the chamber. The nominal concentration was adjusted to reflect the 35.5% concentration of test material in the aerosol mixture.

Particle size determination was determined twice during exposure using a Marple Cascade Impactor, Model No. 296.

5. Statistics

An LC_{50} was not calculated

II. RESULTS AND DISCUSSION

A. MORTALITY

Given in Table 1. None of the animals died during the study.

The Ecoloflex Paint LC_{50} for male and female Sprague Dawley rats is >5.89 mg/L

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B. CLINICAL OBSERVATIONS

During exposure all animals exhibited shallow breathing. Upon removal from the chamber all rats had compound on the face and a hunched appearance. Four female rats had slight red staining around the head on study day 1. Clinical observations for the remainder of the study were unremarkable.

C. BODY WEIGHT

Several male and female rats either lost or failed to gain weight two days after treatment. By day 3, all rats had regained their initial body weight and no further treatment-related effects were observed.

D. NECROPSY

The lungs of 3/5 male and 5/5 female rats were pale and the heart and lungs of 2/5 male and 3/5 female rats were surrounded by a large amount of fat. No other remarkable treatment-related effects were noted.

E. DEFICIENCIES

Although the MMAD of this study was > 4 μm, approximately 43% of the aerosol particles had a diameter <4.0 μm. Considering the physical nature of the test material, this is probably the best that could be achieved.

DATA EVALUATION REPORT

ECOLOFLEX PAINT

STUDY TYPE: PRIMARY DERMAL IRRITATION - RABBIT

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2800 Crystal Drive
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 98-170

Primary Reviewer:
H. T. Borges, Ph.D., MT(ASCP), D.A.B.T

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Date: AUG 25 1998

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Disclaimer

This Data Evaluation Report may have been altered by the Antimicrobials Division subsequent to signing by Oak Ridge National Laboratory personnel.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464

EPA Reviewer: Wallace Powell _____, Date _____
EPA Work Assignment Manager: Peter Thompson, Ph.D._____, Date _____
Antimicrobials Division (7510W)

DATA EVALUATION RECORD

STUDY TYPE: Primary Dermal Irritation - Rabbit
OPPTS 870.2500 [§81-5]

DP BARCODE: D247619
CASE: 062406

SUBMISSION CODE: S545496
TOX. CHEM. NO.: 025601

TEST MATERIAL: Ecoloflex Paint

CITATION: MacBeth, D. and S.W. Ogilvie. (1994) Ecoloflex paint; Acute dermal irritation test in rabbits. Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 554474, Report No. 9978 (EPA), January 11, 1994. MRID 44587204. Unpublished.

SPONSOR: Courtaulds Coatings (Holdings) Ltd., Stoneygate Lane, Felling, Gateshead, Tyne & Wear, NE 10 OJY

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 44587204), 0.5 mL of Ecoloflex Paint (42.69% cuprous oxide, 3.18% zinc 2-pyridinethiol 1-oxide, a.i.) (Batch #Z0474) was applied to a 6 cm^2 area on the shaved back of one New Zealand white rabbit. The treatment area was covered with a gauze pad held in place with tape that in turn was overwrapped with an Elastoplast Bandage. Four hours later, the bandage, tape, and gauze pads were removed and the application site wiped with a acetone to remove excess material. The site was scored for erythema and edema 1, 24, 48, and 72 hours after removal of the patch according to the Draize method.

Severe erythema and moderate edema developed at the application site within one hour of patch removal and persisted through 48 hours. At 72 hours after patch removal, the severe erythema and slight edema were still present and the application site had become necrotic. Because of the severity of the reactions, the study was terminated.

In this study, Ecoloflex Paint was a severe irritant to the skin of a New Zealand white rabbit and is placed in TOXICITY CATEGORY I.

Although only one rabbit was used for the study, it is classified as acceptable and satisfies the guideline requirement for a primary dermal irritation study (81-5) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Ecoloflex Paint SP500 Blue

Description: blue liquid
Lot/Batch #: Z0474
Purity: not applicable
CAS #: not reported
Specific Gravity: 1.4

2 Vehicle: not reported

3. Test animals

Species: rabbit
Strain: New Zealand white
Age and/or weight at dosing: young adult; male 2.56 kg
Source: Interfauna (UK) Ltd., Manston Road, Margate, Kent
Acclimation period: 12 days
Diet: Standard Rabbit Diet, Special Diets Services Limited, ad libitum
Water: tap water, ad libitum
Housing: individually in aluminum cage
Environmental conditions:
Temperature: 20-21°C
Average Humidity: 45%
Air changes: 15-20/hour
Photoperiod: 12-hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start 09/28/93; end 10/01/93

2. Animal assignment and treatment

Before treatment, sufficient hair over the dorsal-lumbar region of one male rabbit was shaved to provide a treatment site of approximately 6 cm^2. The test material, 0.5 mL, was applied to a patch which in turn was applied to the intact skin. The patch was then covered with Micropore tape and the trunk loosely bound with an Elastoplast bandage. Four hours later, the bandage, tape, and patch were removed and the site wiped with acetone to remove excess test material. The site was scored for erythema and edema 1, 24, 48, and 72 hours after removal of the patch according to the Draize method.

II. RESULTS AND DISCUSSION

A. Severe erythema (score = 4) and moderate edema (score = 3) developed at the application site within one hour of patch removal and persisted through 48 hours. By 72 hours after patch removal, severe erythema and slight edema (score = 1) were still present and the application site had become necrotic. Because of the severity and duration of the dermal reaction, the study was terminated and no further animals were tested. The results of the study classify Ecoloflex Paint as a severe irritant and place the test material in Toxicity Category I.

B. DEFICIENCIES

Although only one instead of the required three animals was used for the study, due to the anticipated and actual results, the study is acceptable.

DATA EVALUATION REPORT

ECOLOFLEX PAINT

STUDY TYPE: DERMAL IRRITATION - RABBIT

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2800 Crystal Drive
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Prepared by

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Life Sciences Division
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EPA Reviewer: Wallace Powell _____, Date _____
EPA Work Assignment Manager: Peter Thompson, Ph.D._____, Date _____
Antimicrobials Division (7510W)

DATA EVALUATION RECORD

STUDY TYPE: Dermal Irritation - Rabbit

DP BARCODE: D247619
CASE: 062406

SUBMISSION CODE: S545496
TOX. CHEM. NO.: 025601

TEST MATERIAL: Ecolofelx XGP Paint

CITATION: Kieran, P.C. (1997) Intersmooth 360 Ecoloflex; Dermal irritation test in rabbits. Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 657461, Report No. 15236, December 16, 1997. MRID 44587205. Unpublished.

SPONSOR: Courtaulds Coatings (Holdings) Ltd., Stoneygate Lane, Felling, Gateshead, Tyne & Wear, NE 10 OJY

EXECUTIVE SUMMARY: A dermal irritation study (MRID 44587205) was conducted to supplement an earlier dermal irritation study (MRID 44587204) of Ecoloflex Paint that showed the test material to be a severe irritant to the skin of New Zealand white rabbits. The study was conducted to assess the dermal toxicity of the test material in a setting created to simulate normal application conditions. Pads containing oversprayed paint, 0.071-0.096 g/4.5 cm^2, were applied to the shaved back of three rabbits. Four hours later, the pads were removed and the site evaluated for dermal irritation for the next 96 hours.

No dermal irritation or clinical signs of toxicity were observed during the study period.

In this study, Ecoloflex Paint was not an irritant to the skin of New Zealand white rabbits when applied in a manner to mimic actual exposure conditions.

This study is classified as an acceptable nonguideline study of the irritant properties of Ecoloflex Paint to the skin of New Zealand white rabbits.

COMPLIANCE: The study was conducted under GLP conditions according to guideline OECD No. 404, Guideline for Testing of Chemicals, adopted 17 July 1992. EEC Commission Directive, 92/69/EEC, 31 July 1992.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Ecoloflex XGP 11 GP Paint

Composition:

Name	Concentration Range (%)
[redacted]	
Zinc pyridinethione	2.5-10.0
Copper(I) oxide	25.0-50.0

Description: plum colored liquid
Lot/Batch #: G0625

2 Vehicle: not reported

3. Test animals

Species: rabbit
Strain: New Zealand white
Age and/or weight at dosing: young adult; male 2.29-2.43 kg
Source: Harlan (UK) Limited, Shaws Farm, Blackthorn, Bicester, Oxford, England
Acclimation period: 9 days
Diet: Standard Rabbit Diet, Special Diets Services Limited, ad libitum; supplemental cabbage and hay
Water: tap water, ad libitum
Housing: individually in aluminum cages
Environmental conditions:
Temperature: 20 ± 3°C
Average Humidity: 30-70%
Air changes: 15-20/hour
Photoperiod: 12-hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start 06/06/97; end 06/10/97

2. Study rationale and design

The normal use of the test material is as a paint that dries shortly after contact. However, an earlier study (MRID 44587204) showed the test material to be a severe irritant to the skin of New Zealand white rabbits when applied as a liquid. The

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INERT INGREDIENT INFORMATION IS NOT INCLUDED

present study was done to mimic expected exposure scenarios and investigate the dermal irritation of aerosolized test material to rabbits following a single four hour exposure to substrate pads coated with collected overspray paint.

Information for setting the dose was derived from data taken during a human operator exposure study conducted in 1995. On the basis of this study, a dose of 0.078 g dry paint/4500 mm^2 of rabbit skin was selected. The dose represents a "worst case scenario" since in normal application, the operator is wearing protective equipment, including gloves. In order to simulate actual exposure conditions, the study was conducted outdoors on a warm dry day suitable for application of the paint under normal circumstances.

3. Animal treatment

Sufficient hair over the dorsal-lumbar region of three male rabbits was shaved to provide a treatment site of approximately 4.5 cm^2. The animals were then taken outdoors near the spray paint test site. The preweighed test pads (Unisorb tray paper) were arranged horizontally to collect overspray paint from the target site. Within 60 seconds of having collected sufficient sample, the pad was weighed and applied to the shaved site of the animals. It was then secured in place with an occlusive support bandage and the animals returned to the care facility. Four hours later, the pads were removed and the animals observed 1, 24, 48, 72, and 96 hours later for clinical signs of toxicity and evidence of dermal irritation.

II. RESULTS AND DISCUSSION

A. The weight of overspray collected on the three pads ranged from 0.071 to 0.096 g/4500 mm^2 and equated to an average exposure concentration of 31-40 mg/kg. Following removal of overspray pads from the rabbits, no erythema, edema, or clinical signs of toxicity were observed throughout the 96-hour observation period. The reviewer feels this study accurately reflects the dermal exposure hazards from Ecoloflex Paint that would be experienced by a well-protected human applicator.

B. DEFICIENCIES

None identified.

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DATA EVALUATION REPORT

ECOLOFLEX PAINT

STUDY TYPE: DERMAL IRRITATION - HUMAN

Prepared for

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EPA Work Assignment Manager: Peter Thompson, Ph.D._____, Date _____
Antimicrobials Division (7510W)

DATA EVALUATION RECORD

STUDY TYPE: Dermal Irritation - Human

DP BARCODE: D247619
CASE: 062406

SUBMISSION CODE: S545496
TOX. CHEM. NO.: 025601

TEST MATERIAL: Ecolofelx XGP Paint

CITATION: Pazdera, J. (1998) Human skin irritation study - Ecoloflex Paint. Nippon Paint & Marine Coatings, Ltd., Osaka 531, Japan. Study No. not reported, June 5, 1998. MRID 44587208. Unpublished.

SPONSOR: Courtaulds Coatings (Holdings) Ltd., Stoneygate Lane, Felling, Gateshead, Tyne & Wear, NE 10 OJY

EXECUTIVE SUMMARY: A human dermal irritation study (MRID 44587208) was conducted to determine the potential dermal irritation of the Ecoloflex polymers and Ecoloflex Paint to skin. In addition, the effects to human skin of another type of paint were studied. No single causative agent for inducing dermal irritation was identified.

This study is considered unacceptable (nonguideline). Problems in the selection of individuals for study participation, dosing, amount of test substance applied and the scoring system preclude the use of this study in considering the dermal effects induced by the test substance.

COMPLIANCE: The study was does not comply with the conditions of 40 CFR 160.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test samples

The test samples used for exposure are shown in Table 1. The composition of Ecoloflex 600 (M) Paint (Sample f) and Hisol 900 Paint (Sample g) are shown in Table 2.

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Table 1. Human Exposure Test Samples[a]										
Sample	a	b	c	d	e	f	g	h	i	j
Composition	100%[b] Ecoloflex Polymer	100% Ecoloflex Polymer	100% Ecoloflex Polymer	100% Ecoloflex Polymer	100% Tributyltin Polymer	Ecoloflex 600(M) Paint	Hisol 900 Paint	Solvent Control	Solvent Control	Solid Ecoloflex Polymer
	21.4% MIBK[c]	13.7% MIBK	13.7% MIBK	13.7% MIBK	12.0% MIBK			4.4% MIBK	100% Xylene	
	31.4% Xylene	25.6% Xylene	32.2% Xylene	16.6% Xylene	24.4% Xylene			22.6% Xylene		
		15.6% n-Butyl Alcohol	6.9% Butyl Cellosolve	15.6% n-Butyl Alcohol				5.0% n-Butyl Alcohol		
				6.9% Butyl Cellosolve				2.2% Butyl Cellosolve		

[a]Data from Page 7 of MRID 44587208
[b]All samples were diluted with a constant volume of acetone except for Sample j which was used dry.
[c]Not further identified but assumed to be Methyl Isobutyl Ketone

Table 2. Composition of Ecoloflex 600(M) and Hisol 900 Paints			
Ecoloflex 600 (M) Paint		Hisol 900 Paint	
Chemical	Conc. (% w/w)	Chemical	Conc. (% w/w)
Zinc Pyrithione	4.29	Zineb	4.76
Copper Oxide	40.11	Cuprous Oxide	14.51
[redacted]		Tributyltin Oxide	0.55
		Tributyltin Methacrylate	17.32
		[redacted]	

From MRID 44587208, page 8

2. Test subjects

At least nine males between the ages of 23 and 58 were used for the two studies. No further information on the test subjects was supplied. From the ages of subjects in the study, it appears that some males were used for both phases of the study while others participated in one or the other.

B. STUDY DESIGN AND METHODS

1. In life dates

Not reported

2. Study rationale and design

The study was designed to investigate the potential dermal irritation of Ecoloflex polymer and Ecoloflex Paint applied to human skin. Two methods of exposure were used; the first used filter paper (5 mm) and the second cotton cloth (7 mm). According to the study author, all test samples (Table 1) were diluted with an equal volume of acetone before use (except for Sample j which was left dry) however, the amount used was not reported. The study was designed in the following manner: Samples a, b, c, and d were used to investigate the effects of Ecoloflex polymer in combination with various solvents; Sample e was used as a polymer comparison to Sample a; Sample f and g were Ecoloflex and Hisol 900 paints (Table 2); Samples h and i were solvent controls; and Sample j was dried Ecoloflex polymer.

For both methods, the filter paper or cloth were immersed in the sample, removed, allowed to dry for 10 seconds and applied to the inside surface of the upper arm of each test subject. The application site was then overlain with "surgical sticking plaster." It was not reported whether the samples were applied individually, all at once, or whether the two studies were done concurrently or consecutively.

Study 1: Three hours after application, the arm was unwrapped, the filter paper removed, and the application site washed with soap and water. The site was assessed for erythema, eczema, urtication, and swelling 6, 15, and 24 hours after patch removal.

Study 2: Thirty minutes after application, the arm was unwrapped, the cotton patch removed, and the application site washed with soap and water. The site was assessed for erythema, eczema, urtication, and swelling 1, 6, 15, and 24 hours after patch removal.

The scoring system used for evaluating erythema, eczema, urtication, and swelling was not provided. In addition, the scoring system did not evaluate the degree of irritation at the site.

II. RESULTS AND DISCUSSION

A. **Study 1**: One male developed erythema at the application site within 6 hours of patch removal that persisted through 24 hours when tested with Samples b and f (Table 3). (Page 7 of MRID 44587208 indicates a positive erythema reading on this same male and negative readings for all other subjects and treatment groups recorded immediately following removal of the filter paper. The study protocol states that readings would be taken at 6, 15, and 24 hours after patch removal. It cannot be determined whether these readings were typographical errors, whether they were taken immediately, or whether the readings were taken one hour after patch removal as the protocol for Study 2 states. For completeness, these reading are included in Table 3.) No other test subjects developed a dermal response during Study 1. (It should be noted that responses of eight individuals were presented although the study protocol states nine individuals would be used.).

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Study 2. The following discussion of the incidence of erythema following treatment with the test materials proceeds in the order of Samples a-j. Within one hour of patch removal, one individual developed erythema in response to Samples c and d that cleared by the 6-hour observation (Table 3). This same individual developed erythema in response to Sample g (Hisol 900 paint) that persisted through the 24-hour observation. A second individual developed erythema within one hour of patch removal in response to Sample c, as well as to Sample g; both persisting through the 15-hour observation before clearing. This same individual also developed erythema which was present through the 24-hour observation in response to Ecoloflex Paint (Sample f). One other individual developed erythema within one hour of patch removal in response to Sample d. This same individual developed erythema within one hour of patch removal in response to both Ecoloflex and Hisol 900 paints (Samples f and g, respectively) that persisted throughout the observation period. Within one hour of patch removal, one individual developed erythema in response to Samples e, f, and g. The erythema due to Samples e and f cleared by 6 hours while that of Sample g persisted through the 24-hour observation period. Three other individuals also developed erythema to Sample f (Ecoloflex Paint) within one hour of patch removal. For one of the three, the erythema induced by Sample f, as well as by Sample g, cleared by the 6-hour observation. The erythema induced by Sample f on the other two individuals persisted through the 24-hour observation. One of these two also developed erythema in response to Samples g and i that persisted through the 24-hour observation. The final two individuals developed erythema in response to Sample g (Hisol 900 paint) that persisted through the 24-hour observation. One of these two individuals also developed a response to Sample i that persisted through the 6-hour observation.

Incidences of eczema, urtication, or swelling were not reported. Based on the study results, no consistent causative agent for inducing dermal irritation was identified.

Table 3. Incidence of Erythema Following Exposure to Various Test Samples

Sample	a				b				c				d				e				f				g				h				i				j			
Time (hrs)	1	6	15	24	1	6	15	24	1	6	15	24	1	6	15	24	1	6	15	24	1	6	15	24	1	6	15	24	1	6	15	24	1	6	15	24	1	6	15	24
Study 1[b]	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Study 2[c]	0	0	0	0	0	0	0	0	2	1	1	0	2	0	0	0	1	0	0	0	6	4	4	4	8	7	7	6	0	0	0	0	2	2	1	1	ND			

[a]Adapted from page 7 of MRID 44587208
[b]N=8
[c]N=9

B. DEFICIENCIES

This study is classified as unacceptable (nonguideline) because of several deficiencies that preclude its usefulness in determining the human irritation potential of Ecoloflex Paint. First, the selection of individuals included in the study was not described. It cannot be determined from the study description if any of the individuals had been previously been exposed to any of the samples tested. It is possible that the subjects used for the study were employees of Nippon Paint & Marine Coatings, Ltd. It is also possible that the

subjects were dock workers who had previously been exposed to various components of the samples used. Regardless, it is impossible to determine from the study results if any of the positive results were due to prior sensitization to some of the chemicals used. Finally, it cannot be determined from the study how many individuals participated in both studies and how many individuals participated in one or the other.

Secondly, the method of dosing was not adequately described. The study report states that the filter paper was 5 mm and the cotton cloth was 7 mm. It is not clear if the 5 mm and 7 mm measurements are length measurements and therefore the patches had an area of approximately 25 and 49 mm^2 , or if the total surface area was 5 and 7 mm^2, respectively. In addition, the amount of acetone used to dilute the samples was not reported and the approximate volume of sample on the patch is not known. Therefore, it can not be determined what the final concentration of the sample constituents were or the dose volume.

Third, it cannot be determined whether the studies were done consecutively or concurrently. If they were done consecutively, it is not know what effects the time interval between the studies had or whether exposure to the samples during Study 1 influenced the effects observed during Study 2.

Finally, the scoring system used for evaluating irritation was not adequately reported. While the subjects were supposedly evaluated for erythema, edema, urticaria, and swelling, the degree to which these occurred was not reported. For example, was the erythema observed equivalent to a Draize score of 1, 2, or 3.

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DATA EVALUATION REPORT

ECOLOFLEX PAINT

STUDY TYPE: DERMAL SENSITIZATION – GUINEA PIG

Prepared for

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U.S. Environmental Protection Agency
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Prepared by

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ECOLOFLEX PAINT **Dermal Sensitization Study (81-6)**

EPA Reviewer: Wallace Powell _____, Date _____
EPA Work Assignment Manager: Peter Thompson, Ph.D._____, Date _____
Antimicrobials Division (7510W)

DATA EVALUATION RECORD

STUDY TYPE Dermal Sensitization - Guinea Pig
OPPTS 870.2600 [§81-6]

DP BARCODE: D247619
CASE: 062406

SUBMISSION CODE: S545496
TOX. CHEM. NO.: 025601

TEST MATERIAL: Ecoloflex Paint

CITATION: MacBeth, D. and S.W. Ogilvie. (1994) Ecoloflex paint; Buehler sensitisation (sic) test in guinea pigs. Inveresk Research International, Tranent, EH33 2NE, Scotland. IRI Project No. 554474, Report No. 9979 (EPA), January 11, 1994. MRID 44587207. Unpublished.

SPONSOR: Courtaulds Coatings (Holdings) Ltd., Stoneygate Lane, Felling, Gateshead, Tyne & Wear, NE 10 OJY

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44587207) with Ecoloflex Paint (42.69% cuprous oxide, 3.18% zinc 2-pyridinethiol 1-oxide, a.i.) (Batch # Z0474), young adult female Hartley-Albino guinea pigs (20/sex) were tested using the method of Buehler.

By the time of the third induction all animals induced with the test material developed moderate to severe irritation at the application site. Following challenge with the test material at a naive site, none of the animals developed a dermal response. Appropriate results were obtained with the positive control DNCB in a study conducted approximately four months earlier. In this study, Ecoloflex Paint was not a dermal sensitizer.

This study is classified as acceptable and does satisfy the guideline requirement for a dermal sensitization study (81-6) in the guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Ecoloflex Paint SP500 Blue

Description: blue liquid
Lot/Batch #: Z0474
Purity: not applicable
CAS #: not reported

2. Vehicle and positive control

Acetone, 2,4-Dinitro-chlorobenzene (DNCB)

3. Test animals

Species: guinea pig
Strain: Hartley-Albino
Age and weight at start of treatment: young adult, females 459-576 g
Source: David Hall Limited, Darley Oaks, Newchurch, Burton-on-Trent, Staffordshire
Acclimation period: ≥ 16 days
Diet: FD1, Special Diets Services, 1 Stepfield, Witham, Essex, ad libitum
Water: tap water, ad libitum
Environmental conditions:
Temperature: 20-21 °C
Humidity: 63%
Photoperiod: 12 hour light/dark
Air Changes: 15-20/hour

B. STUDY DESIGN AND METHODS

1. In life dates

Start: 09/03/93 end: 10/11/93

2. Animal assignment and treatment

Before the start of the definitive study, an irritation screen was done with eight female guinea pigs. Based on the results of this study, 100% test material was used for induction and 25% test material was used for challenge.

The definitive study was conducted according to the Buehler method with two groups of guinea pigs. One group of twenty female guinea pigs served as the test animals while another group of twenty female guinea pigs served as the

naive controls. Once a week for three weeks, a Webril pad wetted with 0.5 mL test material was applied for 6 hours to the shaved back of each test guinea pig. The patch was secured by wrapping the whole trunk with Blenderm tape. At the end of induction, the patch was removed and the site cleansed with acetone. The naive control animals were treated similarly with the exception the test material was replaced with acetone. One week after the last induction, all test and control animals were challenged with 25% test material in acetone applied to the shaved left flank for six hours. A positive control was not run concurrently, however such a study was conducted approximately four months earlier in a manner similar to that described above. During the course of that study, the animals were induced with 0.8% DNCB in ethanol and challenged with 0.4% and 0.2% DNCB in ethanol.

II. RESULTS AND DISCUSSION

A. INDUCTION REACTIONS AND DURATION

Slight erythema (score = 1) was noted on 2/20 animals following the first induction; slight to moderate erythema (score = 1 or 2) on 19/20 animals following the second induction; and moderate to severe erythema (score = 2 or 3) was noted on all animals following the third induction.

B. CHALLENGE REACTIONS AND DURATION

None of the test or naive control animals developed dermal irritation at the challenge site 24 or 48 hours after test material application. In this study, Ecoloflex Paint was not a dermal sensitizing agent.

C. POSITIVE CONTROL

Following challenge with 0.2% DNCB in ethanol, all guinea pigs developed slight to moderate erythema.

D. DEFICIENCIES

None identified