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

009623

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

JUN 23 1992

MEMORANDUM

SUBJECT: ID. No. 065359-EUP-R, Experimental Use Permit For Ecobrite 3 (Boric Acid) on Green Wood.

Tox. Chem. No.: 109
(cross ref: 108, 331A)
Project No.: 2-1732
Record No. : S413973

FROM: Melba S. Morrow, D.V.M. MSM 6/25/92
Review Section II, Toxicology Branch I
Health Effects Division (H7509C)

TO: Susan Lewis, PM 21
Registration Division (H7505C).

THRU: Joycelyn E. Stewart, Ph.D. 6/25/92
Acting Section Head, Review Section II KTS 7/25/92
Toxicology Branch I
Health Effects Division (H7509C)

Sponsor: Canadian Forest Products, Ltd.

CONCLUSIONS:

The toxicology data filed for Ecobrite 3 which contains 2% boric acid, 2% sodium borate and 2% didecyl dimethyl ammonium chloride as active ingredients, supports the request for an experimental use permit. Additionally, based on the results of the acute studies, the product appears to be appropriately labeled. The sponsor should be advised that applicable data (based on exposure) on the active ingredients will be required for full registration.

ACTION REQUESTED:

The sponsor has requested an experimental use permit for the use of Ecobrite 3 to prevent the growth of fungal spores and mold mycelium on green lumber. The sponsor proposes that the product will be used for one year and that the test material will be applied year round except when ambient temperatures fall below freezing.

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The product would be used only in Washington and Alabama and it is estimated that approximately 240,000 board feet of lumber will be treated. This would involve a total of 21,825 pounds of the product with 85% of the estimated total weight being from water.

The data supporting this EUP are attached. Additionally, a Toxicology Profile for boric acid is also attached.

Copies of the DERs are attached for your reference.

REQUIREMENTS (CFR 158.135): Updated: July 9, 1992

Technical: Boric Acid

	Required	Satisfied
81-1 Acute Oral Toxicity	Y	Y
81-2 Acute Dermal Toxicity	Y	Y
81-3 Acute Inhalation Toxicity	Y	W
81-4 Primary Eye Irritation	Y	Y
81-5 Primary Dermal Irritation	Y	Y
81-6 Dermal Sensitization	Y	N
81-7 Acute Delayed Neurotox.(hen)	N	-
82-1 Subchronic Oral (rodent)*	Y	N
82-1 Subchronic Oral (nonrodent)	Y	N
82-2 21-Day Dermal	Y	N
82-3 90-Day Dermal	N	-
82-4 90-Day Inhalation	N	-
82-5 90-Day Neurotoxicity (hen)	N	-
82-5 90-Day Neurotoxicity (mammal)	N	-
83-1 Chronic Toxicity (rodent)**	N	N
83-1 Chronic Toxicity (nonrodent) **	N	N
83-2 Oncogenicity (2 species)	N	N
83-3 Teratogenicity (2 species)	Y	Y
83-4 Reproduction	Y	Y
83-5 Chronic/Oncogenicity	N	N
84-2 Mutagenicity - Gene Mutation	Y	N
84-2 Mutagenicity - Struct. Chrom. Aber.	Y	N
84-2 Mutagenicity - Other Genotoxic Effect	Y	N
85-1 General Metabolism	N	N
85-2 Dermal Penetration	N	N
86-1 Domestic Animal Safety	N	-

Formulation

A. Ecobrite (2%)

81-1 Acute Oral Toxicity	Y	Y
81-2 Acute Dermal Toxicity	Y	Y
81-3 Acute Inhalation Toxicity	Y	Y
81-4 Primary Eye Irritation	Y	Y
81-5 Primary Dermal Irritation	Y	Y
81-6 Dermal Sensitization	Y	Y
81-7 Acute Delayed Neurotox.(hen)	N	-

Y - Yes; N - No; Not available in HED files, W - Waived
* - study may be satisfied by rat chronic/onco
** - chronic studies may be required as tiered data
Mutagenicity studies are currently under review.

TOXICOLOGY PROFILE: Updated: July 9,1992

STUDY;CLASSIFICATION; CATEGORY;STUDY #;DATE	RESULTS
Technical	
81-1 Acute Oral LD_{50}-Rat; Cat. IV, Guideline DBH4; 12/19/85	LD_{50} = 5280 mg/kg (males) 5830 mg/kg (females)
81-2 Acute Dermal LD_{50}-Rabbit Cat III, Guideline 82-0280-21, 3/15/82	LD_{50} > 2 g/kg
81-3 Acute Inhalation -Rat Waived 2/28/89	Requirement waived
81-4 1^0 Eye Irritation - Rabbit Cat III, guideline S-152A; 5/16/68	irritation up to day 4
81-5 1^0 Dermal Irritation - Rabbit Cat. IV, Guideline 82-0280-21; 3/15/82	Dermal irritation reversible within 72 hrs in 1/6 rabbits
83-3 Developmental Tox.-mouse Minimum Mi88-Bort, 8/11/89	mat. NOEL < 0.1% (248 mg/kg/d) Mat. LOEL = 0.1% renal/tubular regeneration Dev. NOEL = 0.1% Dev. LOEL = 0.2% Increased resorptions, decreased body weight
83-3 Developmental Tox. -Rabbit Guideline Rb 90 BORA; 10/30/91	Mat. NOEL = 125 mg/kg/d Mat. LOEL = 250 mg/kg based on vaginal bleeding, decreased weight gain and increased rel. kidney weight DEV. NOEL = 125 mg/kg/d Dev. LOEL = 250 mg/kg/d based on incr. resorptions, incr. post impl. loss and incr. fetuses w/ventricular-septal defects

83-4 2 Generation Repro. - Mice Minimum NTP/NIEHS 90-105 4/13/90	Parental NOEL = 1000 ppm Par. LOEL = 4500 ppm Repro. NOEL = 1000 ppm Repro. LOEL = 4000 ppm based on decreased fertility and pup weights and increased days between litters

FORMULATION(S)
A. Ecobrite (2% a.i.)

81-1 Acute Oral Toxicity -Rat Tox. Cat. IV, Acceptable	LD_{50} > 5000 mg/kg
81-2 Acute Dermal Toxicity - Rabbit Tox. Cat. IV, Acceptable	LD_{50} > 2000 mg/kg
81-3 Acute Inhalation - Rat Tox. Cat. II, Acceptable	LC_{50} = 1.6 mg/L
81-4 Primary Eye Irritation- Rabbit Tox. Cat.III, Acceptable	eye irritant
81-5 Primary Dermal Irrit. - Rabbit Tox. Cat.II, Acceptable	dermal irritant
81-6 Dermal Sens. - Guinea pig Acceptable	Not a sensitizer

DATA GAPS IN HED FILES: For the technical product, the following data gaps have been identified:

81-6 Dermal Sensitization
82-1 Subchronic Oral
82-2 21 Day Dermal

These data gaps will not affect this request for an Experimental Use Permit for the 2% boric acid product. Additionally, one oncogenicity study from NTP and studies to satisfy the mutagenicity requirements are currently under review. The oncogenicity study appears to be negative.

ACTION TAKEN TO REMOVE DATA GAPS AND OBTAIN ADDITIONAL INFORMATION: The registrant should be notified that these data gaps exist.

REFERENCE DOSE (RfD): An RfD has not been established for this compound.

PENDING REGULATORY ACTIONS: Tox Branch is unaware of any pending regulatory action for this compound.

TOXICOLOGIC ISSUES: The product has been associated with decreases in sperm concentration and motility when administered to mice at dietary concentrations of 9000 ppm. At this same dose, no litters were produced. These results were obtained in a 2 generation reproduction study.

When administered at a dose of 250 mg/kg/day to rabbits in a developmental toxicity study, the compound was associated with an increase in the number of resorptions, an increase in the post-implantation loss and an increase in the number of fetuses with ventricular-septal defects. In maternal animals receiving the same dose, there was an increase in the incidence of vaginal bleeding.

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Reviewed by: Melba S. Morrow, D.V.M. 6/16/92
Section II, Tox. Branch I (H7509C)
Secondary Reviewer: Joycelyn E. Stewart, Ph.D.
Section II, Tox. Branch I (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Dermal Sensitization - Guinea Pigs

GUIDELINE #: 81-6

TOX. CHEM. #: 109

MRID #: 420326-07

TEST MATERIAL: Antistain Solution ($C_{10}B_2A_2Q_2$)

SYNONYMS: Ecobrite 3 (material contains 2% boric acid, 2% sodium borate and 2% didecyl dimethyl ammonium chloride as active ingredients and 94% inert ingredients)

STUDY NUMBERS: 616-005

SPONSOR: Canadian Forestry Products, Ltd.
Vancouver, B.C.

TESTING FACILITY: International Research and Development Corp.
Mattawan, Michigan

TITLE OF REPORT: Dermal Sensitization Study in Hartley Guinea Pigs (Buelher)

AUTHORS: J.R. Myer

REPORT ISSUED: 12/15/89

CONCLUSIONS: The test material was not a sensitizer when administered to albino guinea pigs.

CLASSIFICATION: Acceptable
TOX. CATEGORY: N/A

MATERIALS:

The test material was Antistain Solution and the test animals were Hartley Guinea pigs, approximately 1.5 months at the start of the study and weighing 301 to 426 grams.

METHODS:

Screening studies were conducted to determine the concentration of test material that would be used in the main sensitization study. Screening procedures involved the administration of 0.4

mL of test material in deionized water to the shaved left flank areas of eaach animal. Concentrations used for screening were 5, 10, 25 or 50%. During this phase, animals were challenged with 0.4 mL of the test material at concentrations of 10, 15, 20 or 25%. At both sensitization and challenge, the test material was held in contact with the skin by dermal patches that remained in place for 6 hours for each period. Approximately 19 to 20 hours after exposure, the treated areas and adjacent sites were depilated with Nair. Sites were scored for irritation at 3 to 4 hours post depilation and at 48 hours following exposure.

Based on the results from the screening phase, a 25% concentration was selected for induction and a 20% solution was selected for challenge since it represented the highest dose at which no dermal irritation was observed.

Prior to administering the induction doses, the left shoulder of each animal was clipped to remove fur. A total of 0.4 mL of a 25% concentration was applied to a Webril pad and placed on the clipped ar a. The patch was occluded and wrapped and held in contact with the skin for 6 hours. One week after the first induction, a second induction dose was administered using the same procedure. The second induction dose was followed by a third induction dose on day 15.

Ten guinea pigs served as negative controls and remained untreated during the induction phase.

Two weeks following the final induction, all animals (treated and controls) were challenged with 0.4 mL of tne test material in a 20% concentration. Prior to dosing, hair was removed from the left flank. Material was administered and animals were bandaged in the same manner that was used during the induction phase. Test material remained in contact with the skin for 6 hours, after which, all patches were removed.

Animals were observed twice daily and body weights were recorded prior to induction and at the termination of the study. Test sites were compared to the surrounding skin and were graded for erythema and edema using the following scale:

0 = no skin reactions
± = slight erythema
1 = slight, confluent or moderate erythema
2 = moderate erythema
3 = severe erythema

No positive controls were used in this study.

QUALITY ASSURANCE:

A statement of compliance with GLPs and a Quality Assurance

statement were included in the submission.

RESULTS:

All guinea pigs survived the study and no changes in body weights were reported. None of the animals had reactions as indicated by erythema scores. Both incidence (number of animals with scores greater than 1 divided by the number of animals tested) and average severity scores were 0 at both the 24 and 48 hour assessments. It was concluded that the test article was not a sensitizing agent when administered to albino guinea pigs.

DISCUSSION:

Although positive control animals were not used in the study, the study is acceptable and satisfies the requirement for a dermal sensitization study. (81-6).

009623

Reviewed by: Melba S. Morrow, D.V.M.
Section II, Tox. Branch I (H7509C)
Secondary Reviewer: Joycelyn E. Stewart, Ph.D.
Section II, Tox. Branch I (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute Dermal- Rabbits

GUIDELINE #: 81-2

TOX. CHEM. #: 109

MRID #: 420326-04

TEST MATERIAL: Antistain solution

SYNONYMS: Ecobrite 3 (contains 2% boric acid, 2%sodium borate and 2% didecyldimethyl ammonium chloride as active ingredients and 94% inert ingredients)

STUDY NUMBERS: 616-002

SPONSOR: Canadian Forest Products, Ltd.
Vancouver, B.C.

TESTING FACILITY: IRDC
Mattawan, Michigan

TITLE OF REPORT: Acute Dermal Toxicity Study in Rabbits

AUTHORS: J.R. Myers

REPORT ISSUED: November 28, 1989

CONCLUSIONS: Based on the results of this study, the dermal LD50 was greater than 2000 mg/kg when administered to New Zealand White rabbits.

CLASSIFICATION: Acceptable
TOX. CATEGORY: IV

MATERIALS:

Antistain solution ($C_{10}B_2A_2Q_2$), administered dermally at a rate of 2000 mg/kg, was the test material and five male and five female New Zealand White rabbits weighing from 3.2 to 3.9 kg were the test animals.

METHODS:

Prior to the administration of the test material, the hair was clipped on the dorsum affecting approximately 15% of the body

surface area of the animals. Test material was applied and covered the entire clipped area. The animals were wrapped with gauze bandages and the bandages were secured with tape. Collars were applied to prevent disruption of the test site. Wraps were held in place for approximately 24 hours, afterwhich, all bandages were removed and the test site was washed with tap water.

Animals were observed for clinical signs of toxicity and mortality at 1, 2.5 and 4 hours following the removal of the bandages. Thereafter, animals were observed for mortality twice daily and for clinical signs of toxiocity once daily up to day 13.

QUALITY ASSURANCE:

A statement of compliance with Good Laboratory Practices (6/29/90) and a Quality Assurance Statement (5/30/90) were included in the submission.

RESULTS:

No deaths were reported. Clinically, soft stool was observed in one female on day 3 of the study but this was not considered treatment related. Weight loss was reported in one male and one female during the first week of the study; however, these animals gained weight during the second week of the study.

On necropsy, the only abnormalities reported were desquamation and coriaceousness at the application site.

DISCUSSION:

Based on the results of this study, the dermal LD_{50} is greater than 2000 mg/kg. The study meets the criteria for an acute dermal toxicity study as set forth in 81-2 of the Subdivision F Guidelines and the chemical meets the requirements for Tox Category IV.

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Reviewed by: Melba S. Morrow, D.V.M.
Section II, Tox. Branch I (H7509C)
Secondary Reviewer: Joycelyn E. Stewart, Ph.D. 6/15/94
Section II, Tox. Branch I (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute Oral Toxicity- Rat

GUIDELINE #: 81-1

TOX. CHEM. #: 109

MRID #: 420326-03

TEST MATERIAL: Antistain Solution $C_{10}B_2A_2Q_2$

SYNONYMS: Ecobrite 3 (material contains 2% boric acid, 2% sodium borate and 2% didecyl dimethyl ammonium chloride as active ingredients and 94% inert ingredients)

STUDY NUMBERS: 616-001

SPONSOR: Canadian Forest Products, Ltd.
Vancouver, B.C.

TESTING FACILITY: International Research and Development Corp.
Mattawan, Michigan

TITLE OF REPORT: Acute Oral Toxicity Study in Rats

AUTHORS: J.R. Myers

REPORT ISSUED: November 28, 1991

CONCLUSIONS: Based on the results of this study, the LD_{50} of the test compound was greater than 5000 mg/kg.

CLASSIFICATION: Acceptable
TOX. CATEGORY: IV

MATERIALS:

The test material was antistain solution which has the chemical formula of $C_{10}B_2A_2Q_2$. Five male and 5 female Crl:CDBR rats, approximately 9 weeks of age at the start of the study were the test animals. Male rats weighed from 257 to 275 grams and females weighed from 178 to 186 grams at dosing.

METHODS:

Animals were individually housed, identified and quarantined for 14 days prior to the start of the study. Rats were maintained in

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an environment wh[illegible] allowed for a 12 hour light/dark cycle. Food and water wer[illegible]ovided ad libitum except during the 18 hours prior to dos[illegible]n and 3 to 4 hours post-dosing.

The test material was administered to the ten animals at a limit dose of 5000 mg/kg via oral gavage. Animals were observed for mortality and clinical signs of toxicity at 1, 2.5 and 4 hours following the administration of the test material. Up to day 13, animals were monitored once daily for mortality and twice daily for clinical signs of toxicity. Body weights were recorded prior to dosing, on day 8 and at study termination on day 15. Complete necropsies were conducted on all animals.

QUALITY ASSURANCE:

A statement of compliance with GLPs (dated 6/29/90) and a Quality Assurance Statement (dated 5/30/90) were included in the submission.

RESULTS:

No deaths and no changes in body weight were reported. Clinical observations included ptosis and soft stools in 3 males at 2.5 and 4 hours and absent or decreased defecation in 4/5 females. At necropsy, two males had erosions in the non- glandular mucosa of the stomach. These animals also had adhesions of the stomach to the spleen and diaphragm. These gross findings were probably related to the administration of the test material.

DISCUSSION:

The LD_{50} of the test material was determined to be greater than 5000 mg/kg. The study satisfies the criteria for an acute oral toxicity study as set forth in the Subdivision F Guidelines (81-1). The compound meets the requirements for Tox Category IV.

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Reviewed by: Melba S. Morrow, D.V.M. MSM 6/19/92
Section II, Tox. Branch I (H7509C)
Secondary Reviewer: Joycelyn E. Stewart, Ph.D. JES 6/25/92
Section II, Tox. Branch I (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute Inhalation

GUIDELINE #: 81-3

TOX. CHEM. #: 109

MRID #: 422123-02

TEST MATERIAL: Antistain solution

SYNONYMS: Ecobrite 3 (Test material contains 2% boric acid, 2% sodium, 2% didecyl dimethyl ammonium chloride and 94% inert ingredients)

STUDY NUMBERS: 616-006

SPONSOR: Canadian Forestry Products
Vancouver, B.C.

TESTING FACILITY: IRDC
Mattawan, Michigan

TITLE OF REPORT: Acute Inhalation Toxicity Evaluation in Rats

AUTHORS: C.E. Ulrich

REPORT ISSUED: 3/23/90

CONCLUSIONS:

Under the conditions of this study, the LC_{50} of Antistain Solution was 1.6 mg/L with a 95% confidence limit of 1.34 to 1.80 mg/L. The LC_{50} was calculated using a dose -mortality curve. In addition, following exposure, labored breathing and lethargy were observed and body weights were lower than expected for all groups. At necropsy, congestion, focal and diffuse red areas and edema were present in the lungs with the exception of animals in groups I, VII and IX.

CLASSIFICATION: Acceptable.
TOX. CATEGORY: II

MATERIALS:

Approximately 7.5 liters of Antistain Solution was obtained for this study. The test animals were male and female Sprague Dawley rats, between 45 and 55 days of age at the time of exposure.

METHODS:

After completing a 14 day acclimation period, the test animals were assigned to groups that received the following concentrations of the test material:

Group #	Actual Conc. (mg/L)	Nominal Conc. (mg/L)
I	2.6	19
II	3.8	19
V	2.7	19
VI	1.8	16
VII	1.1	14
IX	1.2	26

Group numbers were not consecutive because the study was aborted in three groups due to technical difficulties that were not discussed in the report.

Each group was exposed to the test material atmosphere for 4 hours. A 54 liter glass top exposure chamber was used and the temperature, relative humidity and chamber airflow were recorded at 30 minute intervals. During exposure, the oxygen levels in the exposure atmosphere ranged from 19.6 to 20.1%

Aerosol atmospheres were generated by metering the test material into a pneumatic atomizer mounted in a 4 liter glass atomization chamber. The chamber was operated by compressed air which was metered into the atomization chamber. A cyclone was placed between the atomization chamber and the exposure chamber to reduce the size of the aerosol particles entering the exposure unit. The cyclone was discontinued after it was used for Group I because the maximum concentration that could be obtained with its use was 2.7 mg/L and it was possible that the LC_{50} could exceed this value.

The nominal concentration of the test material was calculated by dividing the amount of the test material used during the experiment by the total volume of air passing through the chamber. Actual exposure concentrations were determined gravimetrically and were expressed as equivalentt aerodynamic diameters and geometric standard deviations. Gravimetric determination of exposure concentrations involved collecting chamber samples on pre-weighed glass fiber filters, heating the filters and comparing the results to a standard curve to obtain a net weight. The net weight was then divided by the sample volume

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to yield the actual chamber concentration. Standard curves were prepared with spiked material.

The particle sizes were determined using an Anderson 8 Stage Cascade Impactor. The percent of particles with aerodynamic diameters less than the cut-off percentages for individual stages of the impactor were derived and plotted by computer.

Animals were weighed prior to the start of the study and at 7 and 14 days. All animals dying prior to the designated weighing intervals were weighed when they were found. Animals were observed for clinical signs of toxicity at hourly intervals during exposure and following removal from the chamber. Observations were conducted once daily for mortality and once daily for toxic signs during the 14 day post exposure period.

Animals were sacrificed by exsanguination following an intraperitoneal injection of Sodium pentobarbital. Lungs and major thoracic and abdominal organs were examined for gross abnormalities. LC_{50} values were calculated using a dose - mortality curve.

QUALITY ASSURANCE:

Statements of Quality Assurance (3/22/90) and Compliance with GLPs (6/29/90) were included in the submission.

RESULTS:

The actual concentrations in the test groups ranged from 1.1 to 3.8 mg/L. Particle sizes ranged from 1.7 to 2.8 micrometers for the six treatment groups, with no relationship between the concentration of the test material in the chamber and the particle size.

The mortality was highest (10/10) in Group II which received 3.8 mg/L of the test material. In Group I, the mortality was 1/10 at concentrations of 2.6 mg/L and in Group V, the mortality was 9/10 at 2.7 mg/L. It was determined that in Group I, the particle size was smaller and the temperature of the test material was lower than that recorded for the other groups. The relative humidity in the chamber was also greater than 100% for Group I. These factors may have been responsible for the dramatic differences in mortality at 2.6 mg/L and 2.7 mg/L. (See Table I for information on group mortality, mean particle size and actual chamber concentrations).

The LC_{50} was determined to be 1.6 mg/L with a 95% confidence level of 1.34 to 1.80 mg/L. Most of the deaths occured during the first hour of exposure. Labored breathing and lethargy were observed most frequently during and following exposure. (See

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Table II for information on clinical signs and mortality).

Body weight gains were lower than expected for all groups, with weight loss being reported for surviving animals in groups II, V, VI and VII. At necropsy, congestion, focal and diffuse red areas and edema were present in the lungs of most of the animals. No visible lesions were found in the lungs of any of the animals in groups I, VII and IX.

DISCUSSION:

In 4/6 groups, the relative humidity in the exposure chambers exceeded 80%. This may have led to condensation of the test material in the chambers which would in turn alter the amount of the test material that was respirable. Conceivably, the LC_{50} could have been lower than that which was calculated if optimal test conditions were present in these groups.

In groups VII and IX, the relative humidity was within an acceptable range and mortality was 2/10 and 0/10, respectively. The highest concentration for these two groups was 1.2 mg/L (Group VII). Based on this, the assumption can be made that the LC_{50} would not have been lower than 1.2 mg/L and the chemical would not meet the criteria for a lower Tox Category.

The study is acceptable. The chemical meets the requirements for Tox Category II.

TABLE I
Concentration, Particle Size and Mortality

Group =	Actual Conc. (mg/L)	Part. Size (mcm)	Mortality
I	2.6	1.7	1/10
II	3.8	3.2	10/10
V	2.7	2.8	9/10
VI	1.8	1.8	9/10
VII	1.1	2.0	2/10
IX	1.2	2.4	0/10

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TABLE II
Clinical Observations During First Hour of Exposure

Males Clinical Observations	GROUP I	II	V	VI	VII	IX
Labored Breathing	5/5	5/5	5/5	5/5	5/5	5/5
Lethargy	0/5	1/5	0/5	0/5	0/5	0/5
Death	0/5	3/5	4/5	3/5	0/5	0/5
post-exposure mortality	---	2/5	1/5	2/5	1/5	0/5
Females Clinical Observations						
Labored Breathing	4/5	5/5	5/5	5/5	5/5	5/5
Lethargy	1/5	0/5	0/5	0/5	0/5	0/5
Death	0/5	3/5	1/5	2/5	0/5	0/5
Post-exposure mortality	1/5	2/5	3/5	2/5	1/5	0/5

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Reviewed by: Melba S. Morrow, D.V.M. 6/19/92
Section II, Tox. Branch I (H7509C)
Secondary Reviewer: Joycelyn E. Stewart, Ph.D. 6/25/92
Section II, Tox. Branch I (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Primary Eye Irritation- rabbits

GUIDELINE #: 81-4

TOX. CHEM. #: 109

MRID #: 420326-05

TEST MATERIAL: Antistain Solution ($C_{10}B_2A_2Q_2$)

SYNONYMS: Ecobrite 3 (contains 2% Boric acid, 2% sodium borate and 2% didecyl dimethyl ammonium chloride as active ingredients and 94% inert ingredients)

STUDY NUMBERS: 616-004

SPONSOR: Canadian Forest Products, Ltd.
Vancouver, B.C.

TESTING FACILITY: IRDC
Mattawan, Michigan

TITLE OF REPORT: Eye Irritation Study in Rabbits

AUTHORS: J.R. Myers

REPORT ISSUED: November, 1989

CONCLUSIONS:

Based on the results of this study, antistain solution was associated with severe eye irritation, swelling and ocular discharge. Swelling and discharge subsided at 72 hours in all but one of the affected animals; however, redness persisted up to day 7 in five of the six test animals. The compound was not reported to affect the iris or the cornea.

CLASSIFICATION: Acceptable
TOX. CATEGORY: III

MATERIALS:

Undiluted Antistain Solution ($C_{10}B_2A_2Q_2$) was the test material and six New Zealand white rabbits were the test animals. Rabbits weighed from 3.4 to 3.9 kg and were approximately 5 months of age at the start of the study.

METHODS:

A total of 0.1 ml of the test material was instilled in the right conjunctival sac of each rabbit and the lids were held together. The left eye served as an untreated control.

The treated eye was examined and scored according to the method described by Draize. Eyes were examined for irritation at 1, 24, 48, 72 and 96 hours post-instillation and on days 7 and 14. Sodium flourescein was used to determine the degree of corneal damage at 72 hours, 7 and 14 days.

QUALITY ASSURANCE: A statement of Quality Assurance dated 5/30/90 and a statement of compliance with Good Laboratory Practices dated 6/29/90 was included in the submission.

RESULTS:

Conjunctival irritation was observed in all animals and consisted of severe redness, swelling and discharge. These signs were apparent from 1 to 48 hours following the instillation of the test material. At 72 hours, all swelling and discharge had subsided in all rabbits except one. In this animal, redness persisted until day 14. In all of the remaining animals, redness was present up to day 7.

No effects on the cornea or iris were reported.

DISCUSSION:

Based on the results of this study, the test material meets the criteria for classification in Tox. Category III. The study is acceptable and satisfies the requirement for primary ocular irritation as set forth in Subdivision F Guidelines (81-4).

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Reviewed by: Melba S. Morrow, D.V.M. 6/14/92
Section II, Tox. Branch I (H7509C)
Secondary Reviewer: Joycelyn E. Stewart, Ph.D.
Section II, Tox. Branch I (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Primary Dermal Irritation -Rabbits

GUIDELINE #: 81-5

TOX. CHEM. #: 109

MRID #: 420326-06

TEST MATERIAL: Antistain Solution $C_{10}B_2A_2Q_2$

SYNONYMS: Contains 2% boric acid, 2% sodium borate and 2% didecyl dimethyl ammonium chloride as active ingredients and 94% inert ingredients.

STUDY NUMBERS: 616-003

SPONSOR: Canadian Forest Products
Vancouver, B.C.

TESTING FACILITY: International Research and Development Corp
Mattawan, Michigan

TITLE OF REPORT: Primary Dermal Irritation Test in Rabbits

AUTHORS: J.R. Myers

REPORT ISSUED: 12/15/89

CONCLUSIONS: Based on the results of this study the chemical caused moderate to severe dermal irritation up to and beyond 72 hours. The compound was also associated with blanching, desquamation and coriaceousness. Edema persisted in one animal up to day 14 and erythema persisted in all animals up to day 21.

CLASSIFICATION: Acceptable
TOX. CATEGORY: II

MATERIALS: Antistain solution was applied undiluted. The test animals were 3M and 3F young adult, New Zealand white rabbits, weighing from 3.6 to 4.1 kg. At the start of the study, the animals were approximately 5 months of age.

METHODS: The upper backs of each animal were clipped to remove hair prior to the administration of the test material. A total of 0.5 mL of undiluted test material was applied to the intact skin and held in contact by a gauze square. The patch was

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secured with tape and the trunks of each animal were wrapped with gauze. Animals were fitted with collars to prevent disruption of the test site. Material was kept in contact with the skin for a 4 hour period, after which, bandages were removed and the test sites were washed.

Animals were evaluated for dermal irritation (erythema and edema) based on the methods used by Draize. (see Table I for Draize Scoring System). Dermal observations were conducted at 30 to 60 minutes after bandages were removed, at 24, 48 and 72 hours and on days 7, 14, 21 and 28. Body weights were recorded prior to dosing, on days 3 and 14 and at the end of the study on day 28.

QUALITY ASSURANCE:

A statement of Quality Assurance (5/30/90) and a statement of compliance with GLPs (6/29/90) were both included in the submission.

RESULTS:

Blanching was observed in one male and in one female, desquamation was present in all 6 rabbits and coriaceousness was present in one female. Edema was present in 3/6 animals and persisted in one animal up to day 14. Erythema was observed in all animals and persisted in all affected animals up to day 21. By day 28, no erythema or edema were observed and all animals were considered to be normal.

Weight loss was reported in one female on day 3 of the study; however, weight gain was reported when this animal was weighed on days 14 and 28. At these weighing intervals, the reported body weight was comparable to that of the other two females. No adverse effects were reported on the body weights of males.

DISCUSSION:

Based on the results of this study, the topical administration of the test material was associated with erythema, edema, blanching, desquamation and coriaceousness of the skin of New Zealand White rabbits. The test material resulted in moderate to severe irritation beyond 72 hours and meets the criteria for Tox Category II based on these results. The study satisfies the requirements for a primary dermal irritation study in accordance with Subdivision F Guidelines (81-4).