UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

07/13/99

MEMORANDUM

Subject: D255210
BST Protectant Concentrate C15, Product No. 70871-G

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

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

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

To: Velma Noble, Product Manager, Team 31
Tracy Lantz, Team Reviewer, Team 31
Regulatory Management Branch I
Antimicrobials Division (7510C)

BACKGROUND

The applicant, BioShield Technologies, Inc., has submitted (through its agent) a primary eye irritation study, MRID No. 447899-01. The study was submitted in support of product registration for BST Protectant Concentrate C15, EPA File Symbol 70871-G. The active ingredient in the product is 3-(trimethoxysilyl) propyldimethyloctadecyl ammonium chloride (EPA code 107401), at 1.5% of the formulation by weight.

In support of the acute inhalation toxicity data requirement, BioShield has cited MRID 411578-03. For primary dermal irritation and, BioShield has cited MRID 403852-01. Acute oral toxicity Category IV and acute dermal toxicity Category III were previously established for the product (refer to 1/13/98 EPA letter and its 1/13/98 review memo attachment).

DISCUSSION AND RECOMMENDATION

Acute Inhalation Toxicity. BioShield previously cited MRID 411578-03 (submitted in the past for EPA Reg. No. 64881-2, prior to its being transferred from Reg. No. 34292-2). In a 1/13/98 ESSB review for the subject product, the study was called unacceptable based on a cursory review, because the number and spacing of the dose concentrations were not adequate for the calculation of an LC_{50}. A Health Effects Division (HED) full review dated 1/5/90 called the study Supplementary (unacceptable but upgradable) and requested submittal of the purity of the test material and submittal of a rationale for the low test doses used. In a "Phase Four Review" dated 12/3/92 (from the reregistration file for Case No. 3148), it is noted that the registrant subsequently supplied information by Fax that allowed the study to be upgraded to Minimum. The study used two doses, 0.35 and 0.45 mg/L. There were no deaths at either dose. Although the 1/5/90 review placed the test material in Category II, the 0.45 mg/L dose is so close to the Category III boundary dose of 0.50 mg/L[1] that the test material most likely would have turned out to be in the Category III range had the study been conducted with a complete range of doses. Therefore, since the active ingredient was 72% (w/w) in the product tested, this argues in favor of assigning Category III to the subject product 70871-G, which contains the active ingredient at only 1.5% (w/w). The two products appear reasonably similar otherwise.

Primary Eye Irritation. The submitted study on the subject product is acceptable and places the test substance in Category III. The test substance is substantially similar (and appears identical) to the subject product. The ESSB review of the study is attached to this memorandum.

Primary Dermal Irritation. As pointed out in the 1/13/98 ESSB review, the subject product 70871-G would appear similar to the product for which the cited study was submitted in the past (EPA Reg. No. 64881-2), except that the subject product is far less concentrated in terms of the active ingredient. Because the cited study indicates Category III, the subject product can also be assigned to Category III.

Dermal Sensitization. The cited study, MRID No. 421974-01, was cited in the applicant's previous submission. (It appears that the study was initially submitted in the past for EPA Reg. No. 64881-1 or -2; purity of active ingredient was 72%.) The study had been submitted as 'generic' data in the reregistration process. In the 1/13/98 ESSB review for the subject product (70871-G), based on a cursory review, the study was said to appear acceptable and could be bridged to support the subject product on a tentative basis. A formal review was (and still is) pending in the reregistration process. Since that time, a 2/7/92 Agency review was found which calls the study acceptable with a non-sensitizing response. In the unlikely

---

[1] Category III begins at LC_{50} > 0.50 mg/L

event that the pending reregistration review disagrees with the 2/7/92 review, a resulting requirement will be given under the reregistration program.

The current acute toxicity regulatory profile for BST Protectant Concentrate C15 is summarized in the table below.

Data Requirement	Means of Support	Tox. Category for 70871-G
Acute Oral Toxicity	previously cited study (MRID 403852-01)	IV
Acute Dermal Toxicity	previously cited study (MRID 403852-01)	III
Acute Inhalation Tox.	cited study (MRID 411578-03)	III
Primary Eye Irritation	submitted study (MRID 447899-01)	III
Primary Dermal Irritation	previously cited study (MRID 403852-01)	III
Dermal Sensitization	previously cited study (MRID 421974-01)	Non-sensitizer

PRODUCT LABELING

Based on the above acute toxicity profile, the required human-hazard and first-aid label statements in accordance with the *Label Review Manual* are given below.

Signal Word: CAUTION

Precautionary statements to appear under the heading HAZARDS TO HUMANS AND DOMESTIC ANIMALS:

CAUTION. Causes moderate eye irritation. Avoid contact with eyes, skin or clothing. Harmful if inhaled or absorbed through skin. Avoid breathing vapor or spray mist. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

Instructions to appear under the heading STATEMENT OF PRACTICAL TREATMENT (or FIRST AID):

IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

IF INHALED: Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention if irritation persists.

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

Reviewer: W. Powell
Product No.: 70871-G
DP Barcode: D255210
MRID No.: 447899-01
Study No.: 4841-98
Report Date: 01/21/99 (study completion date)
Author: Janice O. Kuhn

Conclusion:
Toxicity Category: III
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included
Deficiencies: None noted

Testing Facility: Stillmeadow, Inc. (12852 Park One Drive, Sugar Land, TX 77478-2521)

Test Material: AM500, Lot # B039830A-2 (Dilute to 1.5% a.i. from 5% a.i.), a yellow gel; 5.04% total quaternary ammonium chloride; dilution material was deionized water. (BioShield's 3/18/99 Transmittal Document calls it a "1.5% dilution of BioShield product AM500.")

Test Animal: Rabbit, albino, New Zealand White; 3 per sex
Age: 13 to 16 weeks
Weight: Males 2300-2400 g; females 2000-3050 g
Source: Ray Nichols Rabbitry - Lumberton, TX

Test Method: 0.1 mL of the diluted test material was instilled into the conjunctival sac of one eye of each of three rabbits per sex that were pre-screened for eye abnormalities. The eyelids were held together for 1 second. The other eye was untreated and served as a control. All treated eyes were washed with de-ionized water following the 24-hour observation. Ocular reactions were recorded at approximately 1, 24, 48, and 72 hours and 7 and 10 days after dosing, and graded in accordance with the Draize scale and EPA guidelines. Fluorescein ophthalmic solution was employed at the 24-hour observation. Where corneal staining resulted, this solution was re-applied at each consecutive observation time until retention of staining no longer occurred.

Results and Discussion:

The numbers of animals showing 'positive' irritation response at each observation time are indicated in the following table.

Table: Eye Irritation Responses

Areas observed	Number of 'positive'* irritation scores (Draize criteria) per number of animals tested					
	1 Hour	24 Hrs	48 Hrs	72 Hrs	7 Days	10 Days
Cornea: Opacity	1/6	0/6	0/6	0/6	0/6	0/6
Iris	0/6	0/6	0/6	0/6	0/6	0/6
Conjunctivae: Redness	6/6	6/6	6/6	0/6	0/6	0/6
Chemosis	0/6	0/6	0/6	0/6	0/6	0/6

*'Positive' as defined by EPA guidelines.

Severity of corneal opacity was limited to grade 1 on the Draize/EPA scale, this occurring in 1/6 animals, at the 1-hour observation only. No 'positive' iridal involvement was observed in the study. 'Positive' conjunctival involvement was limited to grade 2 redness in 1/6 animals, at the 1-, 24-, and 48-hour observations.

The data indicate Category III for primary eye irritation (i.e., corneal involvement or 'positive' eye irritation effects, clearing in 7 days or less).