BL-907
TXR-3150

003150

DATE: January 7, 1982

867EF, 101, 896H

SUBJECT: EPA File Symbol 10250-EUP-E
Hempel's Antifouling Nautic (1)

EPA File Symbol 10250-RU
Hempel's Antifouling Nautic (2)

EPA File Symbol 10250-RG
Hempel's Antifouling Nautic (3)

FROM: Deloris F. Graham DFG 1/12/82
FEB/TSS

TO: Richard Mountfort 1/12/82
Product Manager (23)

Applicant: Hempel's Marine Paints, Inc.
Foot of Currie Avenue
Wallington, NJ 07057

#7687 — (1) Active Ingredients:

Tributyltin methacrylate	12.40
Tributyltin oxide	1.05
Triphenyltin fluoride	7.79
Inert Ingredients	78.76

#7680 — (2) Active Ingredients:

Tributyltin methacrylate	13.00
Tributyltin oxide	0.95
Triphenyltin fluoride	7.60
Inert Ingredients	78.45

#7697 — (3) Active Ingredients:

Tributyltin methacrylate	9.80
Tributyltin oxide	1.33
Triphenyltin fluoride	1.71
Cuprous oxide	37.05
Inert Ingredients	50.11

Background:

Submitted Acute Oral, Acute Dermal, Acute Inhalation, Eye Irritation, and Primary Dermal Irritation studies on series 7680. Studies conducted by Bio/dynamics, Inc. Data under accession numbers: 246312, 246317, 246311, 246314, 246319, 246320. Acute Oral, Acute Dermal, Eye Irritation, and Primary Dermal Irritation studies submitted for the following series 7687, 7690, and 7697. Studies conducted by Bio/dynamics, Inc. Data under accession numbers: 246318, 246315, 246316, 246313 for series 7687; 246306, 246305, 246303, 246304 for series 7690; 246310, 246309, 246308, 246307 for series 7697. Data on series ~~Number~~ 7680 and 7697 are on EPA File # 10250-EU and series 7690 and 7697 are on EPA File # 10250-RG.

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Recommendations:

(1) FHB/TSS finds these studies acceptable to support an Experimental Use Permit and conditional registration of products under EPA File Symbols 10250-RU and 10250-RG.

(2) The appropriate signal word is DANGER.

Label:

(1) The precautionary statements must be revised as follows:

"Corrosive causes irreversible eye damage and corrosive to skin. Wear protective clothing such as gloves, long-sleeved cotton shirt, long pants and hat. Wear goggles or face shield and rubber gloves when handling. Do not breathe vapor or spray mist. When spraying paint, if a face shield is not worn, wear a mask or pesticide respirator jointly approved by the Mining Enforcement and Safety Administration and by the National Institute for Occupational Safety and Health. May be fatal if swallowed. Wash thoroughly with soap and water after handling and before eating or smoking. Use with adequate ventilation."

(2) The "If on Skin" must be revised to read "If on skin, wash with plenty of soap and water and get medical attention."

(3) The word "WARNING" must be deleted from under the "Physical and Chemical Hazards."

Review: Series 7680

(1) Acute Oral Toxicity Study: Bio/dynamics, Inc.; Project #6041-79; February 15, 1980; (Series 7680).

Procedure: Five groups consisting of 5M and 5F rats each received one of the following doses: 2.5, 3.5, 5.0, 7.1, and 10 g/kg. Observations made daily for 14 days. Necropsy performed on all animals.

Results: At 5 g/kg, 3M and 3F died; at 7.1 g/kg, 4M and 4F died; at 10 g/kg, 5M and 5F died. Clinical signs observed included clear ocular discharge, piloerection, motor activity decrease, rales, gray oral discharge, respiratory rate decrease, red oral discharge, soft stool, clear oral discharge, urinary staining, fecal staining, ataxia, prostration, fine tremors, general poor conditions, unthrify, labored breathing, alopecia in anogenital region, respiratory rate increase, irregular breathing, gray oral discharge, wet rales, loss of hair-middle of back, hypothermia, red nasal discharge, abdominal gripping.

Necropsy revealed lungs: dark red foci throughout; adrenals: pale red; red nasal discharge; urinary staining; lungs: mottled, bright red; stomach: pronounced vascularization, contains viscous tan fluid; intestines: distended with gas; fecal staining of the abdomen; brain:

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blood vessels [illegible]ed, meninges red in color; liver: clear edges; stomach: fundus-distended three times normal, highly vascularized, inside walls had a red discharge, pyloric region-empty, constricted at cardiac-pylcric junction, contains thick green substance; duodenum: empty; spleen: diminished, pale, roughened; kidney: mottled pale; adrenals: bright red; testis: undescended, vascularized; urinary bladder: empty; stomach: strong odor, yellow urinary staining; lungs: bright red, black patches; stomach extended with gas and white fluid; cecum: vascularized, contains dark yellow fluid. LD50 was 6 g/kg with 95% confidence levels between 4.6 and 7.4 g/kg.

Study Classification: Core Guideline Data.

Toxicity Category: IV - CAUTION.

(2) Acute Dermal Toxicity Study: Bio/dynamics, Inc; Project #6042-79; December 26, 1979; (Series 7680).

Procedure: 5M and 5F rabbits with abraded skin were administered 2 g/kg of the test material, under occlusive wrap for 24-hour exposure.

Results: No mortalities. Well defined erythema (score of 2) and slight to severe edema (scores 1, 2, 3, 4). Other symptoms included activity decrease, fecal staining, soft stool, nasal discharge, urinary staining, ocular discharge, piloerection, food consumption decrease, exfoliation of treated areas, haunches raised.

Necropsy revealed lungs: mottled dark red; liver: mottled pale, roughened; kidneys: pale; lungs: mottled brow, bright red, pale; liver: irregular edges, pitted, mottled pale and tan; spleen: irregular pitted vascularized, pale: kidneys: vascularized, dark patch; intestines: pronounced vascularization.

LD50 was greater than 2 g/kg.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.

(3) Acute Inhalation Toxicity Study: 5M and 5F Sprague-Dawley rats were exposed for 4 hours to a concentration of 0.3 mg/l of the test material in a 100 liter plexiglass chamber under adequate chamber conditions. Nominal concentration was 15 mg/l; temperature was 72°F; relative humidity was 70%; average partical size was 3.89 micrometers. Observations made for 28 days. Necropsy performed on all animals.

Results: No mortalities at a concentration of 0.3 mg/l for four hours. Symptoms observed included increased incidence of scabbing; blistering; loss of hair; scaly skin; salivation; labored breathing; reduced activity; wet fur; lacrimation; mucoid nasal discharge; dried material around the facial area; irregular breathing and yellow anogenital fur, gasping and dry rales.

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Necropsy revealed lungs: discoloration, foci; kidney: moderately pale, green-brown.

LC_{50} was determined to be greater than 0.3 mg/l.

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING.

(4) Eye Irritation Study: Bio/dynamics, Inc.; Project #6043-79; December 26, 1979; (Series 7680).

Procedure: Nine New Zealand rabbits received 0.1 ml of the test material in one eye each. The eyes of 3 of the rabbits were washed for one minute 20-30 seconds posttreatment. Observations made at 24, 48, and 72 hours; 4 and 7 days after treatment. If signs of irritation are present on day 7, observations are made on days 9, 11, and 14 or until no signs of irritation are present.

Results: At 24 hours in the unwashed group 6/6 had corneal opacity (1/6=10, 3/6=20, 2/6=40); 2/6 iris irritation (2/6=5); 6/6 conjunctive redness (1/6=2, 5/6=3); chemosis (1/6=1, 2/6=2, 3/6=3); discharge (3/6=2, 3/6=3). At day 4, 5/6 corneal opacity (3/6=20, 2/6=40); 6/6 redness (3/6=1, 3/6=2); 5/6 chemosis (3/6=1, 2/6=2); 4/6 discharge (3/6=1, 1/6=2). At day 7, 4/6 corneal opacity (3/6=20, 1/6=40); 3/6 redness (2/6=1, 1/6=2); 4/6 chemosis (3/6=1, 1/6=2); 1/6 discharge (1/6=1). At day 15, 4/6 corneal opacity (4/6=20). Alopecia around eyes, stippling and ulcerations observed.

At 24 hours in the washed group, 3/3 had corneal opacity (1/3=10, 1/3=20, 1/3=30); redness (1/3=2, 2/3=3); chemosis (1/3=2, 2/3=3); discharge (1/3=2, 2/3=2). At day 4, 3/3 corneal opacity (3/3=20); 2/3 redness (2/3=1); 3/3 chemosis (3/3=1). At day 7, 1/3 corneal opacity (1/3=20); 1/3 redness (1/3=1); chemosis (1/3=1). At day 15, no corneal opacity or conjunctive irritation present. Alopecia around eyes and stippling was observed.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.

(5) Primary Dermal Irritation Study: Bio/dynamics, Inc.; Project #6044-79; December 26, 1979; (Series 7680).

Procedure: Six New Zealand rabbits at 2 abraded and 2 intact sites per animal received 0.5 ml of the test material under occlusive wrap for 24-hour exposure. Observations made at 24.5 hours and 72 hours after treatment, then daily for remainder of 14-day observation period.

Results: At 24 hours, slight to well defined erythema (scores 1 and 2) and slight to moderate edema (scores 1, 2, & 3). Peeling also observed.

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At 72 hours, 5/6 had severe erythema (score of 4) and 1/6 slight erythema (score of 1) and slight to moderate edema (score 1, 2 & 3). Eochen present and peeling. Severe irritation through day 14.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.

(6) Dermal Sensitization Study: Bio/dynamics, Inc.; Project #6688-81; September 3, 1981; (Series 7680).

Procedure: Ten guinea pigs were used for test and control mixtures which were administered in a volume of 0.2 ml under occlusive wrap for six hours and removed. This was repeated three times a week for three weeks for a total of nine insults. Fourteen days after the last sensitization exposure, the challenge treatment was administered. Eight days after initial challenge, a second challenge was performed.

Results: Under conditions of this study, Hempel's 7680 Antifouling Marine Paint showed little or no potential to produce sensitization in the guinea pig.

Study Classification: Core Guideline Data

Toxicity Category: Non-sensitizing.

Review: Series 7687

(1) Acute Oral Toxicity Study: Bio/dynamics, Inc.; Project #6826-81; November 23, 1981; (Series 7687).

Procedure: Five groups consisting of 5M and 5F Sprague-Dawley rats received one of the following doses: 1.4, 1.8, 2.3, 2.9 and 3.7 g/kg. Observations made twice daily for 14 days. Necropsy performed on all animals.

Results: At 1.4 g/kg, 1/5M and 1/5F died; at 1.8 g/kg, 3/5F died; at 2.3 g/kg, 1/5M and 3/5F died; at 2.9 g/kg, 2/5M and 5/5F died; at 3.7 g/kg, 3/5M and 5/5F died.

Clinical signs observed included wet rales, oral, ocular discharge, soft stool, fecal staining, ataxia, hypopnea, hypoactivity, food consumptions decreased, emaciation, alopeua, unthrifty coat and variety of other signs.

Necropsy revealed discoloration of gastrointestinal contents and walls; thickening of the stomach wall. Other observations were generally considered to represent post mortem changes.

LD50 for males was 3.2 g/kg with 95% confidence limits between 2.4 and 4.0 g/kg. LD50 for females was 1.85 g/kg with 95% confidence limits between 1.45 and 2.25 g/kg. Combined LD50 for males and females was 2.4 g/kg with 95% confidence limits between 2.0 and 2.8 g/kg.

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Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.

(2) Acute Dermal Toxicity Study: Bio/dynamics, Inc.; Project #6827-81; November 23, 1981; (Series 7687).

Procedure: 5M and 5F rabbits received 2 g/kg of the test material at abraded skin sites under occlusive wrap for 24-hour exposure. Observations made daily for 14 days. Necropsy performed on all animals.

Results: No mortalities. Severe erythema and edema at 24 hours. Necrosis, eschar, fissuring, exfoliation present also. Other symptoms observed included nasal discharge, oral discharge, fecal staining, food consumption decrease. Necrosis at dosing site, eschar at dosing site. Necropsy revealed lungs: mottled, bright red, dark red patch, pale red, light brown; stomach: brown patch; spleen: roughened, wrinkled, irregular, small; ovaries: clear spots. LD50 greater than 2 g/kg.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.

(3) Eye Irritation Study: Bio/dynamics, Inc.; Project #6828-81; November 17, 1981; (Series 7687).

Procedure: Nine New Zealand rabbits received 0.1 ml of the test material in one eye each. The eyes of three of the rabbits were washed for one minute 20 seconds posttreatment. Observations made twice daily for 14 days.

Results: At 24 hours in unwashed group 5/6 had corneal opacity (1/6=10, 4/6=20); 6/6 iris irritation (6/6=3). At day 4, 6/6 no corneal opacity; 1/6 iris irritation (1/6=5); redness (2/6=1, 4/6=2); chemosis (6/6=3); 4/6 discharge (2/6=1, 2/6=2). At day 7, redness (2/6=1, 4/6=2); chemosis (1/6=2, 5/6=3); 1/6 discharge (1/6=1). Irritation clear by day 14 except for slight chemosis in 1/6 animals (1/6=1). Exfoliation, necrosis, alopecia, desquamation on outer lids, necrotic upper and lower lids and ulceration of lower lid observed.

At 24 hours in washed group, 3/3 corneal opacity (3/3=20); iris irritation (3/3=5); redness (3/3=3); chemosis (1/3=3, 2/3=4); discharge (3/3=3). At day 4, redness (3/3=2), chemosis (2/3=2, 1/3=3); 2/3 discharge (2/3=1). At day 7, redness (3/3=2); chemosis (2/3=2, 1/3=3); discharge (2/3=1). At day 14, all irritations clear except slight redness (1/3=1) and chemosis (1/3=1) in one animal.

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING.

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(4) Primary Dermal Irritation Study: Bio/dynamics, Inc.; Project #6829-81; November 16, 1981; (Series 7687).

Procedure: Six New Zealand rabbits received 0.5 ml of the test material at two abraded and two intact skin sites under occlusive wrap for 24-hour exposure. Observations were made at 24 and 72 hours, then daily through 14 days.

Results: At 24 and 72 hours, severe erythema and edema with majority of animals having a score of 4. Necrosis, eschar, desquamation and exfoliation present. Severe irritation persisted through day 14.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.

Review: Series 7690

(1) Acute Oral Toxicity Study: Bio/dynamics, Inc.; Project #6830-81; November 23, 1981; (Series 7690).

Procedure: Five groups, each consisting of 5M and 5F Sprague-Dawley rats received one of the following doses: 1.4, 1.8, 2.3, and 3.7 g/kg. Observations made daily for 14 days. Necropsy performed on all animals.

Results: At 1.4 g/kg, 1/5 F died; at 1.8 g/kg, 1/5 M and 5/5 F died; at 2.3 g/kg, 1/5 M and 4/5 F; at 2.9 g/kg, 4/5 M and 5/5 F died; at 3.7 g/kg, 4/5 M and 5/5 F died.

Toxicologic signs observed included nasal, oral and ocular discharge, soft stool, urinary and fecal staining, wet rales, dyspnea, ataxia, hypoprea, hypoactivity, food consumption decrease, emaciation, unthrifty coat, hypothermia, hair under cage, compulsive tail biting, end of tail missing on one female.

Necropsy revealed discoloration of gastrointestinal contents and walls; thinning, thickening and roughening of stomach walls; adhesion of liver or spleen to the stomach; other observations were generally considered to represent postmortem changes.

LD50 for males was 2.5 g/kg with 95% confidence limits between 2.0 and 3.2 g/kg. LD50 for females was 1.8 g/kg with 95% confidence limits between 1.4 and 2.2 g/kg. Combined LD50 for males and females was 2.3 g/kg with 95% confidence limits between 2.1 and 2.5 g/kg.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.

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(2) Acute Dermal Toxicity Study: Bio/dynamics, Inc.; Project #6831-81; November 18, 1981; (Series 7690).

Procedure: 5M and 5F New Zealand rabbits received 2 g/kg of the test material at abraded skin sites under occlusive wrap for 24-hour exposure. Observations made daily for 14 days. Necropsy performed on all animals.

Results: No mortalities. Severe corrosive dermal effects. Necrosis, eschar formation, exfoliation, desquamation, reddened of the nictitating membrane in one animal, fissuring, soft stool, fecal staining, nasal and ocular discharge, alopacia were observed. Necropsy revealed red subcapsular fluid in kidney. LD50 greater than 2 g/kg.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.

(3) Eye Irritation Study: Bio/dynamics, Inc.; Project #6832-81; November 16, 1981; (Series 7690).

Procedure: Nine New Zealand rabbits received a 0.1 ml of the test material in one eye each. The eye of three of the rabbits were washed for one minute 20 seconds posttreatment. Observations were made at days 7, 11, and 14 or until no signs of irritation were present.

Results: At 24 hours in the unwashed group, 4/6 corneal opacity (1/6=10, 2/6=20, 1/6=30); 1/6 iris irritation (1/6=5); 6/6 conjunctive redness (6/6=3); chemosis (1/6=3, 5/6=4); discharge (2/6=2, 4/6=3). At day 4, 6/6 redness (6/6=2); chemosis (1/6=3, 5/6=4); discharge (2/6=1, 4/6=2). At day 7, 6/6 redness (6/6=1); chemosis (4/6=2, 2/6=3); 3/6 discharge (3/6=1). At day 14, 3/6 redness (3/6=1); chemosis (3/6=1).

At 24 hours in the wash group, 2/3 corneal opacity (2/3=20); 3/3 conjunctive redness (3/3=3); chemosis (2/3=3, 1/3=4); discharge (2/3=2, 1/3=3). At day 4, 3/3 redness (3/3=2); chemosis (3/3=4); discharge (2/3=1, 1/3=2). At day 7, 3/3 redness (1/3=1, 2/3=2); chemosis (2/3=2, 1/3=2). At day 14, 1/3 redness (1/3=1).

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING.

(4) Primary Dermal Irritation Study: Bio/dynamics, Inc.; Project #6833-81; November 16, 1981; (Series 7690).

Procedure: Six New Zealand rabbits received 0.5 ml of the test material at two abraded and two intact skin sites per animal under occlusive wrap for 24-hour exposure. Observations were made at 24 and 72 hours after treatment, then daily for 14 days.

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Results: At 24 and 72 hours severe erythema (score 4) and moderate to severe edema (scores 3 and 4). Eschar formation, necrosis, desquamation, exfoliation, atonia and fissuring present.

Study Classification: Core Guidline Data.

Toxicity Category: I - DANGER.

Review: Series 7697

(1) Acute Oral Toxicity Study: Bio/dynamics, Inc.; Project #6834-81; November 23, 1981; (Series 7697).

Procedure: Five groups consisting of 5M and 5F Sprague-Dawlay rats each received one of the following doses: 1.4, 1.8, 2.3, 2.9, and 3.7 g/kg. Observations were made daily for 14 days. Necropsy performed on all animals.

Results: At 1.4 g/kg, 1/5 F died; at 1.8 g/kg, 3/5 F died; at 2.3 g/kg, 1/5 M and 3/5 F died; at 2.9 g/kg, 4/5 M and 2/5 F died; at 3.7 g/kg, 3/5 M and 5/5 F died.

Toxicologic signs observed included nasal, oral, and ocular discharge, wet rales, soft stool, urinary and fecal staining, ataxia, hypopnea, hypoactivity, food consumption decrease, emaciation, unthrifty coat, hair under cage, hypothermia, compulsive tail biting in one female.

Necropsy revealed discoloration of gastrointestinal contents and walls; thinning, thickening, and roughening of stomach wall. Other observations were generally considered to represent postmortem changes.

LD50 for males was 2.7 g/kg with 95% confidence limits between 2.1 and 3.3 g/kg. LD50 for females was 2.4 g/kg with 95% confidence limits between 1.8 and 3.0 g/kg. Combined LD50 for males and females was 2.45 g/kg with 95% confidence limits between 2.05 and 2.85 g/kg.

Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.

(2) Acute Dermal Toxicity Study: Bio/dynamics, Inc.; Project #6835-81; November 23, 1981; (Series 7697).

Procedure: 5M and 5F New Zealand rabbits received 2 g/kg of the test material at abraded skin sites under occlusive wrap for 24-hour exposure. Observations made daily for 14 days. Necropsy performed on all animals.

Results: No mortalities. Severe corrosive dermal effects. Necrosis, eschar, exfoliation, fissuring, decreased food consumption, and nasal discharge. Necropsy revealed discoloration of liver and pitting. LD50 greater than 2 g/kg.

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Study Classification: Core Guideline Data.

Toxicity Category: III - CAUTION.

(3) Eye Irritation Study: Bio/dynamics, Inc.; Project #6836-81; November 17, 1981; (Series 7697).

Procedure: Nine New Zealand rabbits received a 0.1 ml of the test material in one eye each. The eyes of three of the rabbits were washed for one minute 20 seconds posttreatment. Observations made 24, 48, and 72 hours and 4 and 7 days. If irritation was present at 7 days, observations were made at 9, 11, 14 days or until no signs of irritation were present.

Results: At 24 hours in unwashed group, 5/6 had corneal opacity (5/6=20); 3/6 iris irritation (3/6=5); 6/6 conjunctive redness (6/6=3); chemosis (1/6=3, 5/6=4); discharge (2/6=2, 4/6=3). At day 4, 2/6 iris irritation (2/6=5); 6/6 conjunctive redness (2/6=1, 4/6=2); chemosis (3/6=3, 3/6=4); discharge (2/6=1, 3/6=2, 1/6=3). At day 7, 2/6 iris irritation (2/6=5); 6/6 conjunctive redness (6/6=1); chemosis (4/6=2, 2/6=3); 2/6 discharge (2/6=1). At day 14, 2/6 conjunctive redness (2/6=1), 6/6 chemosis (6/6=1); 1/6 discharge (1/6=1).

At 24 hours in washed group, 3/3 corneal opacity (3/3=20); conjunctive redness (3/3=3); chemosis (2/3=2, 1/3=30); discharge (2/3=1, 1/3=2). At day 4, 3/3 conjunctive redness (1/3=1, 2/3=2); chemosis (1/3=2, 1/3=3, 1/3=4); discharge (2/3=1, 1/3=2). At day 7, 3/3 redness (3/3=1); chemosis (2/3=2, 1/3=3); 2/3 discharge (2/3=1). At day 14, all irritation clear. Necrosis, exfoliation, ulceration, red patch on nictitating membrane, disquamation, and alopecia present.

Study Classification: Core Guideline Data.

Toxicity Category: II - WARNING.

(4) Primary Dermal Irritation Study: Bio/dynamics, Inc.; Project #6837-81; November 16, 1981; (Series 7697).

Procedure: Six New Zealand white rabbits received 0.5 ml of the test material at two abraded and two intact skin sites per animal under occlusive wrap for 24-hour exposure. Observations were made at 24 and 72 hours and daily for remainder of 14 days.

Results: At 24 and 72 hours severe erythema (score 4) and slight to severe edema (1, 2, 3, and 4) and persisted through day 14. Necrosis, eschar, exfoliation, desquamation, fissuring, white and red discharge present.

Study Classification: Core Guideline Data.

Toxicity Category: I - DANGER.

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TBTO Scientific Reviews

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