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DATE: 6/26/78

SUBJECT: EPA Reg. No. 1839-50 Onyl CD1.6 Cleaner, Disinfectant
Caswell #16 C and 19

FROM: William Dykstra, Ph.D
Toxicology Branch

TO: James Banks PM 33

Registrant: Onyx Chemical Co.
190 Warren Street
Jersey City, New Jersey 0732

Action Type: Review teratology data and state what other toxicology data are needed to complete the new requirements for the Onyx CD1.6 formulation.

Recommendations:

1. In order to evaluate the human hazards based on the proposed use patterns as a disinfectant, etc. for food and non-food contact items, the registrant must reference or submit the following toxicology studies on the formulated product:

   a. Skin sensitization study which evaluates formulated product and the use dilution concentrations of the formulated product.

   b. 21-day-Subacute dermal toxicity study in rabbits, with a NOEL which evaluates the formulated product and the use dilution concentrations of the formulated product.

2. In order to evaluate the human hazards based on the proposed use patterns for food equipment or other food contact items only the registrant must reference or submit the following toxicology studies on each active ingredient in the formulation:

   a. Mutagenicity testing - Multi-test evidence.

   b. Reproduction study -1 species.

   c. Teratology study - 2 species.

   d. Chronic/oncogenic study - 1 species.

   e. Chronic/oncogenic study with dietary nitrite (when evaluating quaternary amines) - 1 species.

3. The teratology study is acceptable as core-minimum data. The results show a dose-related occurrence in rudimentary ribs. This skeletal variation indicates that the embryotoxic range of dosage is being approached by treatment with BTC-C-2125M. Therefore, although no teratogenic effects were observed, an embryotoxic effect was observed at the lowest treatment level (5 mg/kg) during Days 6 to 15 of gestation. This embryotoxic effect is considered sufficient for Toxicology Branch to recommend against the proposed use pattern for food equipment or other food contact items at a level of 200 ppm of quaternaries as stated on the label. The reason for this decision is that at an exposure level of 200 ppm of quaternaries, the oral consumption of only 10 ml of treated water would result in consumption of 2 mg of quaternaries. For a 60 kg woman, this results in an acute exposure of .03 mg/kg. Since the 5mg/kg (lowest treatment) level in the teratology study revealed embryotoxic effects, the imposition of a theoretical 100-fold safety factor (based on possible inter- and intraspecies differences) at this level suggests that exposure at a margin of safety level of 0.05 mg/kg could result in human embryotoxic effects. Toxicology Branch therefore concludes that the potential risks of human embryotoxic effects at exposure levels of 200 ppm of quaternaries are not toxicologically supported.

Product Name: Onyx CD1.6 Cleaner. Disinfectant. Deodorizer. Fungicide

Ingredient	Percent Weight
Alkyl (60% C_{14}, 30% C_{16}, 5% C_{12}, 5%C_{18}) dimethyl benzyl ammonium chloride	0.8
Alkyl (68% C_{12}, 32% C_{14}) dimethyl ethylbenzyl ammonium chloride	0.8
[redacted]	
	100.0

Use Directions

For light duty cleaning, sanitizing and deodorizing, use two ounces per gallon.

For heavy duty cleaning and disinfecting and fungicidal activity against pathogenic funga use 4.5 ounces per gallon.

For best results, use (0.16 with a cloth or mop and apply to walls, floors and other hard surfaces. If used on food equipment or other food contact items, limit level to 200 ppm of quaternaries.

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For extra heavy industrial cleaning and sanitizing, use a second application. Do not mix with soap or anionic solutions. (0.16 is non-corrosive in use dilutions or inanimate surfaces.

Rinse empty container thoroughly with water and discard it.

NOTE: BTC C-E is part of active ingredients.

Review

1. Teratologic evaluation of BTC-E-2125M in Rats (Food and Drug Research Laboratories, Inc. Report No. 5433a, Sept. 30, 1977).

   Test material: BTC-E-2125

   Notebook #1607-3695; Activity 80% pp 909; clear yellow viscous liquid.

   Sexually mature BLU:(SD) BR female albino rats, 200-25gm BW were mated 1:1 with sexually mature BLU:(SD) male albino rats, 300 gm BW, in sufficient numbers to produce 120 pregnant females. BTC-E-2125M was administered orally to three groups of 20 pregnant females at doses of 5, 15 and 50 mg/kg BW from Days 6 to 15 of gestation. In addition, a positive control group (aspirin 250 mg/kg) and a negative control group each consisting of 30 pregnant females were established. Test materials were prepared fresh weekly and administered as a aqueous solutions on 10 ml/kg basis. Parameters on dams observed were general appearance and behavior, body weight and food consumption. On day 20 of gestation, all dams were sacrificed with an overdose of chloroform and subjected to caesarean section. The following observations were recorded for each female. number of implantation sites, resorption sites live fetus and body weight of live fetuses. All fetuses were examined grossly for presence of external congenital abnormalities. One third of the fetuses from each litter were examined by Wilson technique for visceral abnormalities. The remaining two-thirds of fetuses from each litter were eviscerated fixed in 70% isopropyl alcohol, macerated in 12% KOH solution, stained with Alizaun - Red 5 dye, cleared in glycerine and examined under low power magnification for skeletal abnormalities. All animals were evaluated according to normally accepted degrees of development for a 20 day old fetus.

Results

There were no differences between negative control and treatment groups for pre-implantation loss, implant sites, resorptions, dead fetuses or live fetuses (Ave/dam; M/F; Ave. wt). The percent of dams and fetuses which were affected is shown below:

Dose	Fetuses affected	Dams affected
mg/kg	%	%
0	2.2(1.0-5.5)	12.5(2.0-34)
5	5.2(2.0-11.5)	34.8(13-64)
15	8.1*(3.5-16.5)	35(12-66)
50	13.6*(7.5-22)	59.1*(30-83.5)

*Significantly different from control P1..01 Values in ( ) indicate range for 99% confidence interval, according to report.

A summary of the skeletal findings revealed the following results:

Group	13th Rudimentary Ribs (Fetuses/ Number of litters affected)
0	6/4
250 mg/kg Aspirin	54/21
5 mg/kg test material	10/8
15 mg/kg " "	13/7
50 mg/kg " "	26/13

There appears to be a dose-related effect in the occurrence of rudimentary ribs, which indicates that the embryotoxic range of dosage is being approached (Environment and Birth Defects. J. Wilson, p. 188 Academic Press (1973). This embryotoxic effect is considered to be due to delayed ossification. No abnormal incidence of soft tissue anomalies was observed in any test group when compared with the controls. The body weight of dams was similar for all groups throughout gestation.

Conclusion:

The test material did not produce any terata when administered during days 6 to 15 of gestation at dosages of 5, 15 and 50 mg/kg. However an embryotoxic dose-related effect was seen as increased 13th rudimentary ribs. Therefore, the embryotoxic "no observable effect level" has not been demonstrated for this study.

Classification: Core Minimum Data.

R/D Tox/init: G.E. Whitmore 6/20/78
gjl
E for GEW 6/28/78