UN..ED STATES ENVIRONMENTAL PRO..CTION AGENCY

Rec'd 10/16/79.

DATE: September 18, 1979

SUBJECT: Lonza Formulation 68-16, EPA Registration No. 6836-37
Caswell Nos. 613A, 331A, 392A, 438, 507

FROM: Carlos A. Rodriquez Carlos A. Rodriquez 10-12-79
Toxicology Branch/HED (TS-769)

TO: John H. Lee, P.M. 31
RD (TS-767)

Registrant: Lonza Inc.
22-10 Route 208
Fair Lawn, New Jersey 07410

Action Requested: Resubmission with toxicology data.

Recommendations:

1. A teratogenic evaluation of your formulation is required. Ethylenediamine tetraacetate (EDTA), as the diethanolamine salt, has been accepted as an RPAR candidate on the basis of teratogenicity (and further testing is needed).

2. This product causes irreversible eye damage in the rabbit eye at 7 and 14 days observation period. ~~Please, submit a rabbit washed irritation eye test to determine if after washing the eye, the damage will subside. The washing procedure is defined as flushing the treated eye for one minute with lukewarm water starting no sooner than 20-30 seconds after~~ omit cc instillation.

3. Revise the statement under "Danger" "Harmful or fatal if swallowed" to read "Harmful or fatal if swallowed or absorbed through the skin."

4. [redacted]

INERT INGREDIENT INFORMATION IS NOT INCLUDED

EPA FORM 1320-6 (REV. 3-76)

5. [redacted]

Formulation of Lonza 68-16

Active Ingredients:

Octyl decyl dimethyl ammonium chloride	4.5%
Dioctyl dimethyl ammonium chloride	2.25%
Didecyl dimethyl ammonium chloride	2.25%
Tetrasodium ethylenediamine tetraacetate	2.28%
Isopropyl alcohol	3.60%
Inert Ingredients	85.12%
	100.00%

Uses: Cleaner, Disinfectant, Deodorizer, Virucide for hospital and institutional use.

Use dilution: For organic soil in hospitals, nursing homes, schools, institutional and industrial uses, add 2 ounces per gallon of water.

For routine disinfecting add one ounce per gallon of water.

Method of Application: With a cloth or mop.

Review of Toxicology Data submitted:

Acute Rat Oral LD_{50} with Lonza Formulation 68-16, Report No. E-1711, (Wells Laboratories, Inc., April 14, 1972)

5 male and 5 female rats weighing between 100-150 grams were used per dose level of 3, 4, 5, 6 and 7 ml/kg of the test material by oral administration. The animals were observed following dosing and over a subsequent fourteen day observation period. At the conclusion the survivors were sacrificed and subjected to necropsy.

Results: LD_{50}= 4.2 (3.55-4.96)ml/kg

Slope and 19/20 confidential limits= 1.31 (1.13-1.50)

Toxic signs: 2 deaths at 3 ml/kg
4 deaths at 4 ml/kg
7 deaths at 5 ml/kg
9 deaths at 6 ml/kg
10 deaths at 7 ml/kg

No other toxic signs reported.

Autopsy findings: cloudy liver and kidneys, Petechiae throughout the alimentary tract.

TOX. Category: III

Classification: Core-Minimum Study.

Primary Eye Irritation in Rabbits, Lonza Formulation 68-16, (Wells Laboratories, Inc., March 29, 1972).

0.1 ml of the test sample was instilled into the right eye of 6 rabbits, the left eye remaining untreated to serve as control. Observations of ocular lesions were made on the rabbits eyes after 24,48,72 hours and at 4,5,6,7,8,9,10,11,12,13 and 14 days after instillation. At these intervals the extent and degree of irritation were scored.

Results:

Draize score at 24 hours = 43/110
Draize score at 4 days = 75/110
Draize score at 7 and 14 days = 110/110

Corneal opacity, iritic reaction and conjunctival irritation generally increased to maximum scores during the first 7 days after application. No reductions were noted during the 14 day observation period.

TOX. Category: I

Classification: Core-Minimum Data.

Acute Primary Skin Irritation Study (Rabbits) with Lonza Formulation 68-16 (Wells Laboratories, Inc., Lab Report No. E-1712, March 24, 1972).

0.5 ml of the test material was applied to the intact and abraded skin of each of 6 albino rabbits clipped free of hair. The

material was introduced under a square patch of surgical gauze (1 inch x 1 inch). The animals were immobilized with the patches secured in place with adhesive tape. The entire trunk was wrapped with an impervious material to maintain the test patches in position and retard evaporation. After 24 hours of exposure, the patches were removed. Readings were made at 24 and 72 hours. Draize scoring system was used.

Results:

Primary skin irritation index = 3.0

Erythema and eschar formation - Intact (24 hours) 1/8
Abraded (24 hours) 2/8

Edema Formation - Intact (24 hours) 1/8
Abraded (24 hours) 2/8

Classification: Core-Minimum Study.

TOX. Category: III

Acute Dermal LD_{50} in rabbits with Disinfectant Cleaner 68-16
(Leberco Laboratories, Assay No. 73137, February 7, 1977).

32 rabbits (16 male and 16 females) weighing betweeen 2.2 and 3.6 kilo, had 10% of their body hair clipped from their backs. One half the animals in each sex had their skin abraded on one side. The animals were divided into 4 groups. Each group contained 4 female and 4 male rabbits. Group #1 received a dose of 3 ml/kg, group #2 received 2 ml/kg, group #3 received 1 ml/kg and group #4 received 0.5 ml/kg. The application site of each animal was covered with gauze and the entire animal was wrapped in a sleeve. The material remained in contact with the skin for 24 hours. After 24 hours the gauze and sleeve were removed and the animals washed with warm water and towel dried. They were observed for 14 days for toxic effects.

Results: LD_{50} = 0.97 (0.65-1.46) ml/kg.

Slope Value = 1.80

All animals showed severe erythema and edema when the covering was removed.

At 3 ml/kg - 7/8 died.
At 2 ml/kg - 6/8 died.
At 1 ml/kg - 6/8 died.
At 0.5 ml/kg - 1/8 died.

TOX. Category: II

Classification: Core-Minimum Study.

Subacute Dermal Toxicity Texting on Rabbits using Lonza Formulation 68-16, (Wells Laboratories, Laboratory No. E-1714, May 25, 1972, submitted by Lonza, Inc.).

Six adult rabbits, two rabbits per dose were utilized at each of three dose levels. The hair was clipped from their backs and flanks. One half of each test area was abraded as required, while the remainder was left intact. The test material was diluted 1:64 in water prior to use in test. The material was applied daily to 10% of the total body surface. Doses applied were 1.0 ml/kg, 2.0 ml/kg and 4.0 ml/kg. These were repeated for 20 consecutive days after each application of the test material, the torsos were wrapped with a rubberized fabric to prevent grooming by the rabbit with possible inhalation or ingestion of test material. The animals were observed for 2 weeks after the last application when all animals were autopsied. Blood and urine studies were performed. Food intake excretion and behavior were observed daily.

Results:

Hematology and Urine - findings were within normal parameters. Toxic signs - at 4.0 ml/kg moderate erythema and edema and persisted through day 21. At 2.0 ml/kg minimal erythema and minimal edema Hyperemia and edema became more pronounced on day 19 of the study. These findings persisted through day 21. Skin irritation was alleviated within 5 days of cessation of treatment. Histological findings were similar to those found in control rabbits. Gross findings in the test animals were not significant.

NEL = 2.0 ml/kg of 1:64 dilution.

Classification: Core-Minimum Data.