CASE FILE

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

AUG 5 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: TRIADINE 3; hexahydro-1,3,5,tris (2 hydroxyethyl)-s-triazine. EPA ID# 1258-01071; Subm # S383667

To: John Lee/Martha Delaney, P.M. 31
Disinfectants Branch
Registration Division (H7507C)

Tox Chem No 481C
Proj. No. 0-2008

From: Joycelyn E. Stewart, Ph.D. 7/25/91
Section II, Toxicology Branch I
Health Effects Division (H7509C)

Thru: Marion Copley, D.V.M., Head Marion Copley 7/25/91
Section IV, Toxicology Branch I
Health Effects Division (H7509C) 7/26/91

Registrant: Olin Chemicals
Stamford, Connecticut 06904

Action Requested: Review submission to determine whether available data are adequate to support the proposed new use. The proposed use is the preservation of aqueous analytical and diagnostic reagents used in chemical and clinical analyses.

Background: Triadine 3 is hexahydro 1,3,5 tris(2 hydroxyethyl)-s-triazine, 78.5% a.i. The inert ingredients are not listed on the label. The end use product is to be regulated by the Food and Drug Administration. Triadine 3 has been previously registered for use as an industrial antimicrobial agent to inhibit the growth of bacteria in aqueous based metal working fluids. The chemical is subject to the Antimicrobial Data Call-In Notice.

Conclusion: The data in Toxicology Branch's files indicate that there are data gaps for acute oral toxicity (81-1), acute inhalation toxicity (81-3) and mutagenicity data (84-4). These data gaps should be satisfied prior to registration of the chemical.

Data Requirements (Antimicrobial Data Call-In Notice)

Technical		Required	Satisfied
81-1	Acute Oral Toxicity	Y	N
81-2	Acute Dermal Toxicity	Y	Y
81-3	Acute Inhalation Toxicity	Y	N
81-4	Primary Eye Irritation	Y	Y
81-5	Primary Dermal Irritation	Y	Y
81-6	Dermal Sensitization	Y	Y
81-7	Acute Delayed Neurotoxicity	N	-
Tier I Studies 1/			
82-1	90 day feeding	Y	Y
82-3	90 day dermal	Y	Y
83-3	Teratogenicity (1 species)	Y	Y
84-2	Mutagenicity-gene mutation	Y	Y
84-2	Mutagenicity-chromosomal aberration	Y	Y
84-4	Mutagenicity-other genotoxic effects	Y	N

1/ This chemical is subject to tier testing. Additional teratology, Tier 2, and Tier 3 studies may be required based on the results of the Tier 1 studies and/or exposure data.

TOXICOLOGY PROFILE

GUIDE#	CITATIONS	RESULTS
81-1	Acute oral LD50 Species: mice Consultox Lab Ltd. ACC#1: 260195 Date: 3/73 CORE - SUPPLEMENTARY DOC#s: 005165	LD50 = 1.30 (1.14-1.48) ml/kg.
81-2	Acute Dermal LD50 Species: rabbit Hill Top Res. Inc. Study#: 85-0866-21 ACC#1: 260195 Date: 8/30/85 CORE - MINIMUM DOC#s: 005165	LD50 > 2 g/kg.
81-4	Primary eye irritation Species: rabbit Safepharm Lab limited Study#: 371/8408 ACC#1: 260195 Date: 9/3/1984 CORE - MINIMUM DOC#s: 005165	Primary eye irritant. Draize score = 239; cornal opacity, iritis, discharge, chemosis, conjunctival necrosis.
81-5	Primary dermal irritation Species: rabbit Safepharm Lab limited Study#: 317/8505 ACC#1: 260195 DOC#s: 005165	Not a primary skin irritant.
81-6	Dermal sensitization Species: rabbit Consultox Lab Ltd. ACC#1: 260195 Date: 7/74 CORE - MINIMUM DOC#s: 005165	Not a dermal sensitizer.

GUIDE#	CITATIONS	RESULTS
81-6	Dermal sensitization Species: guinea pig Consultox Lab Ltd. ACC#1: 260195 Date: 1978 CORE - SUPPLEMENTARY DOC#s: 005165	
81-6	Dermal sensitization Species: guinea pig Consultox Lab Ltd. ACC#1: 260195 Date: 1984 CORE - SUPPLEMENTARY DOC#s: 005165	Grotan BK caused derrmal sensitization in 20-74% of guinea pigs tested.
82-1(a)	Feeding-13 week Species: rat MRID#: 414830-01 Date: 4/25/90 CORE - MINIMUM DOC#s: 008099	NOEL (M&F) = 50 mg/kg/day. LEL = 100 mg/kg/day (based on lymphocytic infiltration - females; erosion of gastric mucosa and prominence of limiting ridge of the stomach - males).
82-1(a)	Feeding-13 week Species: rat MRID#: 414830-01 Date: 1/25/90 CORE - MINIMUM DOC#s: 008099	Males & Females: NOEL = 50 mg/kg/day. LEL = 100 mg/kg/day (based on lymphocyte infiltration - females; erosion of gastric mucosa and prominence of limiting ridge of the stomach - males).
82-2	Dermal-3 week . Species: rat Study#: 508/8411 ACC#1: 260195 Date: 7/19/85 CORE - MINIMUM DOC#s: 005165	Systemic NOEL = 1000 mg/kg (HDT). Local NOEL < 100 mg/kg. levels tested in Sprague-Dawley str: 0, 100, 500 and 1000 mg/kg

GUIDE#	CITATIONS	RESULTS
82-3	Dermal-13 week Species: rat MRID#: 414830-02 Date: 4/26/90 CORE - MINIMUM DOC#s: 008099	Dermal NOEL (M&F) = 5 mg/kg/day. Dermal LEL = 50 mg/kg/day (based on erythema and edema).
83-3(a)	Developmental Toxicity Study Species: rat MRID#: 411618-01 Date: 7/8/89 CORE - MINIMUM DOC#s: 007684	Maternal NOEL = 500 mg/kg/day. Maternal LEL = 750 mg/kg/day (HDT). Toxicity = decreased body wt. gain; ulcerations and/or scarring of the stomach mucosa. Developmental Toxicity > 750 mg/kg/day. Doses tested by gavage in Sprague-Dawley rats: 0, 250, 500, 750 mg/kg/day
84-2(a)	Mutagenic-Ames Species: Safepharm Lab limited ACC#1: 260195 Date: 9/11/84 CORE - UNACCEPTABLE DOC#s: 005165	Positive in salmonella typhimurium TA96 with metabolic activation; positive in TA1538 with and without m. a.
84-2(a)	Mutagenic-Ames Species: salmonella Safepharm Lab limited MRID#: 412317-02 Date: 2/8/89 CORE - ACCEPTABLE DOC#s: 007685	Negative for reverse gene mutation in Salmonella strains exposed to toxic levels (200 ug/plate), with/without activation.
84-2(b)	Mut- Chrom aberr. in vivo Species: mice Safepharm Lab limited MRID#: 412317-01 Date: 2/3/89 CORE - ACCEPTABLE DOC#s: 007685	Negative for inducing micronuclei in bone marrow cells of CD-1 mice treated orally up to 80% of the LD50 (855 mg/kg).

GUIDE#	CITATIONS	RESULTS
84-4	Mutagenic-micronucleus assay Species: rat Safepharm Lab limited ACC#1: 260195 Date: 1976 CORE - UNACCEPTABLE DOC#s: 005165	Negative
84-4	Mutagenic-unscheduled DNA synt Species: rat hepatocytes Microbiological Associates Study#: T8102.380 MRID: 412623-01 Date: 7/20/88 CORE - UNACCEPTABLE DOC#s: 008045	Positive response (increased net nuclear grain count; increased percent of cells with > 5 nng > at 0.10 ug/ml. Results should be confirmed by duplicate assay. Doses tested: 0, 0.001, 0.03, 0.01, 0.03 & 0.1 ug/ml.

Data Gaps

Based on the data available, the following data gaps are identified:

Technical

81-1 Acute Oral Toxicity
81-3 Acute Inhalation
84-4 Mutagenicity-other mechanisms

Action Being Taken To Obtain the Missing Information

Registration Division is to inform the registrant that these data gaps exist.

Pending Regulatory Actions Against this chemical

Toxicology Branch is not aware of of any pending regulatory actions against this chemical.

Toxicological Issues

There are no immediate toxicological issues of concern.