NATIONAL TOXICOLOGY PROGRAM

EXECUTIVE SUMMARY OF SAFETY AND TOXICITY INFORMATION

TRIMETHYLOLPROPANE TRIACRYLATE

CAS Number 15625-89-5

October 4, 1991

Submitted to:

NATIONAL TOXICOLOGY PROGRAM

Submitted by:

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Board of Scientific Counselors Draft Report

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OVERVIEW[1]

Nomination History: Trimethylolpropane triacrylate was nominated by the NCI for multidose dermal carcinogenicity studies with a high priority based on its high and increasing production, widespread use, potential for exposure, lack of adequate chronic systemic toxicity, carcinogenicity and genotoxicity data on the acrylates chemical class, and interest in structure-activity relationships.

Chemical and Physical Properties: Trimethylolpropane triacrylate is a viscous, colorless liquid with an acrylic or pungent odor. Its boiling point has been reported to be > 200 ºC/1 mm Hg. The chemical is insoluble in water, is hygroscopic, light sensitive, and is incompatible with strong acids and bases. It may undergo spontaneous polymerization. However, it may be stabilized with the monomethyl ester of hydroquinone.

Production/Uses/Exposure: The production volume of trimethylolpropane triacrylate was reported in the public file of the EPA Toxic Substances Control Act (TSCA) Inventory in 1983 to be in the range of 120,000-1,200,000 pounds. Trimethylolpropane triacrylate has wide industrial application based on its use as a cross-linker in radiation curing. It is used to produce inks and coatings for wood, paper, glass, metal, textiles, vinyl and other plastics, and as an ingredient in coating formulations, print varnishes, inks, and other polymer systems. Trimethylolpropane triacrylate is used in colloidal dispersions for industrial baked coatings. Non-radiation curing uses of trimethylolpropane triacrylate include paper and wood impregnates, rubber crosslinking, wire and cable extrusion, and anaerobic adhesives. Trimethylolpropane triacrylate is also used as a chemical intermediate. Consumers are at potential risk of exposure from the many consumer products which contain trimethylolpropane triacrylate. Data from the National Occupational Exposure Survey (NOES) estimate that 4,179 employees, including 807 female employees, were exposed to trimethylolpropane triacrylate between 1981 and 1983. In addition, all workers involved in the manufacturing, processing, product handling, and application of trimethylolpropane triacrylate are at risk of exposure to this compound. The American Industrial Hygiene Association established a workplace environmental exposure level (WEEL) of 1 mg/m 3 (8 hour time weighted average) for trimethylolpropane triacrylate. No other exposure regulations/recommendations have been established for this compound.

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[1] The information contained in this Executive Summary of Safety and Toxicity Information (ESSTI) is based on data from current published literature. The summary represents information provided in selected sources and is not claimed to be exhaustive.

Toxicological Effects:

Human: Trimethylolpropane triacrylate has been shown to induce contact and allergic dermatitis in humans. Among workers involved in the manufacturing or handling of trimethylolpropane triacrylate-containing products (such as ink and paint), a number of cases of contact and allergic dermatitis have been reported. Three cases of irritant conjunctivitis have also been reported. Positive skin patch tests among these subjects have confirmed the sensitizing ability of

trimethylolpropane triacrylate. In the cases described, dermatitis began as irritation and itchiness of the hands, arms, neck, face, and ears. Gradual development of eczematous dermatitis occurred upon prolonged exposure to trimethylolpropane triacrylate. There were no data found on chemical disposition, or on the chronic, carcinogenic, reproductive, or teratogenic effects of trimethylolpropane triacrylate in humans.

Animal: Trimethylolpropane triacrylate was found to have low to moderate oral toxicity in rats. It is an acute skin and eye irritant upon direct application to rabbits. Trimethylolpropane triacrylate was corrosive to rabbit skin upon prolonged direct contact. Trimethylolpropane triacrylate has been found to be a skin sensitizer in numerous studies using guinea pigs. It has been demonstrated to have cross sensitivity with pentaerythritol triacrylate, methyl methacrylate, ethylene glycol dimethacrylate, triethylene glycol dimethacrylate and methyl vinyl ketone. Trimethylolpropane triacrylate did not induce skin lesions following prechronic exposure to mice. Trimethylolpropane triacrylate caused an increase in the number of large pyroninophilic cells in Iymph nodes in guinea pigs. No skin tumors or lesions were observed in mice following chronic dermal application of trimethylolpropane triacrylate to the shaved backs of mice. There were no data found on chemical disposition or on the reproductive or teratogenic effects of trimethylolpropane triacrylate in animals.

Genetic Toxicology: Trimethylolpropane triacrylate was non-mutagenic to Saccharomyces cerevisiae D4 and Salmonella tvphimurium with and without metabolic activation. Trimethylolpropane triacrylate was mutagenic to L5178 mouse Iymphoma cells and K1BH4 Chinese hamster ovary cells.

Structure Activity Considerations: Other multifunctional acrylates have been tested in chronic dermal toxicity studies using 50 male mice. Pentaerythritol triacrylate induced Iymphomas in 6 mice; triethyleneglycol diacrylate induced skin tumors in 6 mice and Iymphomas in 4 mice, and tetraethyleneglycol diacrylate caused an increased incidence of skin tumors in 6 mice.

I. NOMINATION HISTORY AND REVIEW

A. Nomination History

1. Source: National Cancer Institute [NCI, 1987a,b]

2. Date: July 1987

3. Recommendations: Multidose carcinogenicity studies

4. Priority: High

5. Rationale/Remarks:

·High and increasing production and use

·Potential for extensive human exposure

·Lack of adequate chronic toxicity and carcinogenicity data available

·Nominated as a representative multifunctional acrylate (MFA); need to evaluate structure-related differential carcinogenicity of mono- and multifunctional acrylates

· Existing mutagenicity tests for MFAs are inconsistent and inadequate and are of limited usefulness

·Known skin and eye irritant and dermal sensitizer

·Need for multidose response study using the skin as a target site and portal of systemic exposure

·Potential direct alkylating agent through double bond conjugate addition (i.e., Michael reaction)

B. Chemical Evaluation Committee Review

1. Date of Review: March 13, 1991

2. Recommendations:

·Chemical disposition

·Reproductive and developmental effects

·Carcinogenicity

3. Priority: Moderate to high

4. NTP Chemical Selection Principles: 3,8

5. Rationale/Remarks:

·Increasing use

·Potential for human exposure

·Lack of adequate data on carcinogenicity, reproductive and developmental effects

·Representative multifunctional acrylate

·Suspicion of carcinogenicity as a member of the multifunctional acrylate chemical class; some members of this class were shown to be carcinogenic or have potential for carcinogenic activity in dermal studies in mice.

C. Board of Scientific Counselors Review

1. Date of Review:

2. Recommendations:

3. Priority:

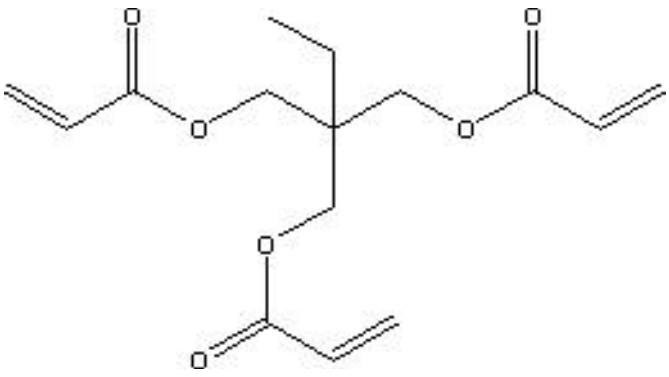
4. Rationale/Remarks:

D. Executive Committee Review

1. Date of Review:

II. CHEMICAL AND PHYSICAL DATA

A. Chemical Identifiers



TRIMETHYLOLPROPANE TRIACRYLATE

Molecular formula: $\mathbf{C_{15}H_{20}O_6}$ Molecular weight: **296.3**

CAS No. 15625-89-5

RTECS No. AT4810000

B. Synonyms and Trade Names

Synonyms: 2-propenoic acid, 2-ethyl-2-(((1-oxo-2-propenyl)oxy)methyl)-1,3-propanediol ester (9CI); acrylic acid, triester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol (8CI); A-TMPT; TMPTA; 1,1,1-trimethylolpropane triacrylate

Trade Names: Aronix M 3090®, Monosizer TD 1500A®, NK Ester A-TMPT®, SARTOMER SR 351®, Setalux UV 2241®, SR 351®, Viscoat®

C. Chemical and Physical Properties

Description: A viscous, colorless, liquid [Lenga, 1988] with an acrylic or pungent odor [NCI, 1987b]. The presence of impurities may produce a tan or amber color [AIHA, 1981].

Melting Point: < 0 ºC (<32 ºF) [AIHA, 1981; Celanese Chemical Company, Inc., date unspecified]

Boiling Point: >200 ºC (392 ºF)/1mm Hg [Alfa, 1990]

Specific Gravity: 1.1084 @ 25 ºC [ARCO, 1989]

1.1 @ 25 ºC [AIHA, 1981; Lenga, 1988]

1.5 [NFPA, 1986]

Density: 9.17 @ 77 ºF (lbs/gal)

1.18 @ 25 ºC (g/cc) [Celanese Chemical Company, Inc., date unspecified]

Vapor Density: 1.0 [Lenga, 1988]

Vapor Pressure: < 0.10 @ 100 ºC

<0.001 @ 25 ºC [Celanese Chemical Company, Inc., date unspecified]

<0.01 mm Hg (20 ºC) [Lenga, 1988]

< 1.0 mm Hg (25 ºC) [AIHA, 1981]

Refractive Index: 1.4736 @ 20 ºC [Lenga, 1988]

Solubility in Water: Insoluble [AIHA, 1981]

Solubility in other Solvents: No data were found

Log Octanol/Water Partition Coefficient: No data were found

Reactive Chemical Hazards: Incompatible with strong oxidizing agents, strong acids and bases; hygroscopic [Lenga, 1988; AIHA, 1981]. If exposed to extreme heat, possible rupture of container may occur [Lenga, 1988]. May undergo polymerization on exposure to direct sunlight and heat [Lenga, 1988; NFPA, 1986]. Decomposition products include carbon monoxide and carbon dioxide [Lenga, 1988]. May be inhibited with 100 ppm of the monomethyl ester of hydroquinone [Lenga, 1988; AIHA, 1981].

Flammability Hazards: · Combustible

· Flashpoint: > 110 º C (>230 ºF) CC [Lenga, 1988]

149 ° C (300 °F) OC [NFPA, 1986]

> 200 °C (> 392 °F) CC [Celanese Chemical Company, Inc., date unspecified]

< 93.3 °C (200 °F) [AIHA, 1981]

III. PRODUCTION/USE

A. Production

1. Manufacturing Process

No information on the specific manufacturing process of trimethylolpropane triacrylate was found. However, it is reported that polyfunctional acrylate monomers can be produced by direct or trans esterification methods, and that trimethylolpropane triacrylate is manufactured from trimethylolpropane [Kirk-Othmer, 1978].

2. Producers and Importers	
U.S. Producers:	**Reference**
-	-
Alcolac, Incorporated	USITC, 1989
Baltimore, Maryland	
-	-
Aldrich Chemical Company, Incorporated	Chemical Week Buyers'
Milwaukee, Wisconsin	Guide, 1989
-	-
Celanese Chemnical Company, Incorporated	USEPA, 1990
Pampa, Texas	
-	-
CL Industries, Incorporated	SRI, 1990
Georgetown, Illinois	
-	-

CPS Chemical Company, Incorporated	SRI, 1990
West Memphis, Arkansas	
-	-
Haven Chemical	USEPA, 1990
Philadelphia, Pennsylvania	
-	-
Hi-Tek Polymer	USITC, 1989
Louisville, Kentucky	
-	-
Monomer-Polymer and	Fitzgerald, 1989
Dajac Laboratories, Incorporated	
Trevose, Pennsylvania	
-	-
Neochem, Incorporated	Chemical Week Buyers'
Akron, Ohio	Guide, 1989
-	-
Radcure Specialties, Incorporated	SRI, 1990
Pampa, Texas	
-	-
Sartomer Company, Incorporated	SRI, 1990
West Chester, Pennsylvania	
-	-
Seegott, Incorporated	Fitzgerald, 1989
Solon, Ohio	

-	-
Thiokol Chemical Division	USEPA, 1990
Calvert City, Kentucky	
-	-
European Producers:	**Reference**
-	-
BASF Aktiengesellschaft	SRI, 1989
Ludwigshafen (Rheinland-Pfalz), Germany	
-	-
Degussa AG	SRI, 1989
Hanua 1 (Hessen), Germany	
-	-
Röhm GmbH Chemische Fabrik	SRI, 1989
Darmstadt, (Hessen), Germany	

No information on the importers of trimethylolpropane triacrylate is provided in the public file of the EPA Toxic Substances Control Act (TSCA) inventory [USEPA, 1990].

3. Volume

The production volume of trimethylolpropane triacrylate is reported in the public file of the EPA Toxic Substances Control Act (TSCA) Inventory. In 1983, 3 manufacturers listed as producers of trimethylolpropane triacrylate reported a total production volume ranging from 120,000-1,200,000 pounds. One additional producer did not report a total production volume [USEPA, 1990].

Celanese Chemical Company is expected to expand production of its seven multifunctional monomers (MFM) (including trimethylolpropane triacrylate) in the Pampa, Texas plant by fifty percent [American Chemical Society, 1990].

Trimethylolpropane triacrylate is listed in the United States International Trade Commission's publication Synthetic Organic Chemicals for the years 1979-1988; however, production data for this compound were not reported [2][USITC, 1980-1989]. In 1977 and 1978, trimethylolpropane triacrylate total production volume was reported to be 1,067,000 and 1,641,000 pounds, respectively [USITC 1978, 1979].

4. Technical Product Composition

Trimethylolpropane triacrylate is a di- and tri-acrylate ester of trimethyl propane with some dimers and trimers [AIHA, 1981]. Trimethylolpropane triacrylate is available in technical grade with 0.1% by weight maximum residual solvent content and 0.1% by weight maximum residual acrylic acid present as an impurity. The minimum ester rank for this compound is 2.70 [Celanese, 1982].

B. Use

·Widely used multifunctional monomer [Björkner, 1984]

·Cross-linking agent and reactive diluent [Björkner, 1984]

·Formulation in ultraviolet curable inks or electron beam irradiation curable coatings [Björkner, 1984; Celanese Chemical Company, Inc., date unspecified; Radak, 1990]

·Component of photopolymer and flexographic printing plates and photoresists [Radak, 1990]

·Ingredient in acrylic glues, adhesives, and anaerobic sealants [Björkner, 1984]

·Production of polymers and resins for specialty plastics, surface coatings, emulsion polymers, and latex coatings [Dearfield *et al.*, 1989]

·Colloidal dispersions for industrial baked coatings, waterborne alkyds, solvent-based alkyds, vinyl/acrylic nonwoven biners, and pressure sensitive adhesives [Celanese, 1982]

·Nonradiation curing uses include paper and wood impregnates, wire and cable extrusion, polymer impregnated concrete, polymer concrete structural composites, and uses as a chemical intermediate [Celanese, 1982]

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[2]Production statistics for an individual chemical are given only when there are three or more producers, no one or two of which may be predominant. Moreover, even when there are three or more producers, statistics are not given if there is any possibility that the publication would violate the statutory provisions relating to unlawful disclosure of information accepted in confidence by the Commission. Data are reported by producers for only those items where the volume of production or sales or value of sales exceeds certain minimums. Those minimums for all sections are 5,000 pounds of production or sales or $5,000 of value in sales with the following exeptions: plastics and resin materials-50,000 pounds or $50,000; pigments, medicinal chemicals, flavor and perfume materials, and rubber processing chemicals-1,000 pounds or $1,000.

IV. EXPOSURE/REGULATORY STATUS

A. Consumer Exposure

Although no quantitative data were reported, the widespread use of trimethylolpropane triacrylate in products such as latex paints and floor polishes increases the potential for consumer exposure to this compound [Dearfield *et al.*, 1989].

B. Occupational Exposure

Data from the National Occupational Exposure Survey (NOES) which was conducted by the National Institute for Occupational Safety and Health (NIOSH) estimated that 4,179 employees, including 807 female employees, were potentially exposed to trimethylolpropane triacrylate. The NOES database does not contain information on the frequency, level, or duration of exposure to workers of any chemicals listed therein [NIOSH, 1990].

Workers involved in the manufacturing, processing, product handling, and application of trimethylolpropane triacrylate are at risk of exposure to this compound [AIHA, 1981].

C. Environmental Occurrence

No environmental data were found on trimethylolpropane triacrylate.

D. Regulatory Status

OSHA has not established a permissible exposure limit (PEL) for trimethylolpropane triacrylate.

E. Exposure Recommendations

·ACGIH has not recommended an exposure limit for trimethylolpropane triacrylate.

·NIOSH has not recommended an exposure limit (REL) for trimethylolpropane triacrylate.

·The American Industrial Hygiene Association (AIHA) has set a workplace environmental exposure level (WEEL) of 1 mg/m^3 (8-hour time weighted average for a 40 hour work week) for trimethylolpropane triacrylate [AIHA, 1981].

V. TOXICOLOGICAL EFFECTS

A. Chemical Disposition

1. Human Data

No data were found on the chemical disposition of trimethylolpropane triacrylate in humans.

2. Animal Data

No data were found on the chemical disposition of trimethylolpropane triacrylate in animals.

B. Acute

1. Human Data

No data were found on the acute toxicity of trimethylolpropane triacrylate in humans.

2. Animal Data

Acute animal toxicity data for trimethylolpropane triacrylate are presented in Table 1.

Table 1. Trimethylolpropane Triacrylate Acute Animal Toxicity Data					
Route of Exposure	**Species (Sex) / Strain**	**Number of Animals**	**Acute Toxic Endpoint**	**Acute Toxic Value**	**Reference**
Oral	Rat (male) / Carworth Wistar	5	LD_{50}	5.19 (3.84-7.01 ml/kg)	Carpenter et al., 1974
Oral	Rat (NR)/NR	NR	LD_{50}	5 g/kg	Andrews and Clary, 1986
Oral	Rat (NR)/NR	NR	LD_{50}	500-5000 mg/kg	Celanese Chemical Company, Inc., date unspecified
-	-	-	-	-	-
Inhalation	Rat (NR)/NR	NR	LC_{50}	Unreported saturated vapor concentrations. No deaths with single dose.	Celanese Chemical Company, Inc., date unspecified
-	-	-	-	-	-
Skin	Rabbit (NR)/NR	NR	LD_{50}	200-2000 mg/kg	Andrews and Clary, 1986
Skin	Rabbit (male) / New Zealand	4	LD_{50}	6.35 (3.89-10.04) ml/kg	Carpenter et al., 1974
Skin	Rabbit (NR)/NR	NR	LD_{50}	5170 mg/kg for 24 hours	AIHA, 1981
Skin	Rabbit (NR)/NR	NR	LD_{50}	2000-20000 mg/kg	Celanese Chemical Company, Inc., date unspecified

-	-	-	-	-	-
Skin	Rabbit (male) / New Zealand	5	Irritant Scale (1-10)	3	Carpenter et al., 1974
Skin	Rabbit (NR)/NR	NR	--	Mild	Celanese Chemical Company, Inc., date unspecified
-	-	-	-	-	-
Eye	Rabbit (male) / New Zealand	4	Irritant Scale (1-10)	9	Carpenter et al., 1974
Eye	Rabbit (NR)/NR	NR	--	Moderate	Celanese Chemical Company, Inc., date unspecified

NR = Not Reported

inhalation, rat · Death occurred within 8 hours in rats exposed to concentrated trimethylolpropane triacrylate vapor. No other data were provided [Carpenter, *et al.*, 1983].

inhalation, species not specified · No deaths occurred in lab animals exposed to air saturated by sparging through trimethylolpropane triacrylate (composition not reported) for 6 hours at 60°C (140°F). No other data were provided [AIHA, 1981].

dermal, mice · Three pre-trial skin bioassays were conducted on C^3H/HeJ male mice to determine the appropriate dosing for a chronic skin bioassay (see section V.D). Fifty milligrams of undiluted trimethylolpropane triacrylate was applied to the interscapular region of 5 mice. Shortly after application, mice appeared lethargic, inactive, and salivating. All five mice died one day after treatment. In a second pre-trial study, 3 mice were treated with 50 milligrams of a 10% trimethylolpropane triacrylate solution in acetone 2 times per week for 2 weeks. Application produced epilated, crusty, and severely burned skin. In the third pre-trial, mice were treated with 50 milligrams of a 5% solution of trimethylolpropane triacrylate in mineral oil 2 times per week for 5 weeks. Only very slight crusting on the skin was observed. From these pre-trials, the authors recommended that 50 milligrams of a 5% solution of trimethylolpropane triacrylate be used for the chronic skin bioassay [Celanese Corporation, Inc, 1985].

dermal, rabbit · In the first part of the experiment, a single dose of trimethylolpropane triacrylate (unspecified concentration) applied to rabbit skin (unspecified strain and number) caused moderate irritation at 24 and 72 hours. Repeated application of trimethylolpropane triacrylate 5 days per week for 2 weeks caused corrosion, but not systemic effects. No other data were provided [Andrews and Clary, 1986].

eye, rabbit · Trimethylolpropane triacrylate caused corneal opacity in rabbit eyes which was reversible within 7 days. No other data were provided [Andrews and Clary, 1986].

C. Prechronic

1. Epidemiological Evidence/Case Reports

The case reports concern the skin irritation and skin sensitization properties of trimethylolpropane triacrylate.

Trimethylolpropane triacrylate-induced dermatitis is characterized by initial itching of the exposed skin, progressing to erythema and scaling upon prolonged exposure. The majority of the reported cases in which trimethylolpropane triacrylate has been identified as the acnegen entail exposure to ultraviolet inks. However, it is difficult to establish the potency of trimethylolpropane triacrylate because most cases describe individuals exposed to an industrial mixture of acrylates who have displayed positive reactions to two or more acrylates [Food and Chemical Toxicology, 1985]. Table 2 summarizes case reports found in the literature concerning trimethylolpropane triacrylate-induced dermatitis from occupational exposure. These case reports are described in greater detail below.

Table 2. Case Reports of Dermal Irritation in Workers Prechronically Exposed to Acrylates and Skin Patch Test Results with Trimethylolpropane Triacrylate

-	Number of Workers	Concentration (%)	-	-
Number	with Irritation/	Trimethylolpropane	Number Patch	-
of	Sensitization	Triacrylate in Skin	Test	-
Workers	Reactions	Patch Test (Time)	Positive	Reference
19	15	0.1 (48 hours)	2	Nethercott, 1978
26	5	0.2 (48 hours)	4	Emmett, 1977
-	-	Ink varnish containing	-	-
-	-	0.2% trimethylol	-	-
-	-	propane triacrylate	-	-

-	-	-	-	-
Unspecified	1	0.01 (2 and 4 days)	1	Maurice and Rycroft, 1986
-	-	0.1 (2 and 4 days)	-	-
-	-	-	-	-
Unspecified	4	0.0001	1	Dahlquist et al., 1983
-	-	0.03	3	-
-	-	0.1	4	-
-	-	-	-	-
Unspecified	6	0.1	3[a]	Bjorkner et al., 1980
-	-	0.5	4[b]	-
-	-	-	-	-
7	7	0.1	1	Nethercott et al., 1983
-	-	-	-	-
Unspecified	1	<0.5	neg	Cofield et al., 1985
-	-	0.5 (48 hours and 1 week)	1	-
-	-	-	-	-
47	47	0.2	2	NIOSH, 1983

[a]Only three workers were tested.

[b]Only four workers were tested.

dermal, human · Eight of nineteen workers who cured multifunctional acrylic monomers in ultraviolet curing inks (duration of exposure not reported) were diagnosed with irritant contact dermatitis. In addition, three were diagnosed with irritant contact conjunctivitis, and seven with allergic contact dermatitis. Three of these cases did not have direct contact with MFAs, therefore, it is suspected that contact was the result of airborne exposure. Dermatitis was characterized by itchy erythema, with scaly patches on the neck, arms, wrists, and face. Patients were tested for sensitivity to MFAs by a skin patch test. A concentration of 0.1%

trimethylolpropane triacrylate was applied to the subjects' upper back for 48 hours. Control subjects received hexane dioldeacrylate, a nonirritant. Two of the patients with allergic contact dermatitis had a positive(vesicular) skin reaction to trimethylolpropane triacrylate [Nethercott, 1978].

dermal, human · Following the introduction of 2 MFAs, trimethylolpropane triacrylate and pentaerythritol triacrylate, as components of radiation drying ink in an ink formulating facility, 5 of 26 employees who were potentially exposed to the radiation drying inks, developed eczematous dermatitis. The five case reports are as follows:

A 51 year-old male lye tank operator who cleaned the containers for ink ingredients developed vesicular dermatitis on his trunk, back, hands, and forearms. A 45 year-old male maintenance operator developed eczematous eruptions on his eyelids, wrists, hands, and fingers. A 53 year-old male, who weighed radiation-dried ink ingredients, developed dermatitis on his ears, arms, and fingers. A 63 year-old male mill-hand developed dermatitis on his forearms, hands, fingers, and groin area. A 37 year-old production manager developed erythema and papules on his left wrist. This dermatitis appeared related to his habit of holding his watch over an ink mill to observe the condensation of vapors on the metal watch case.

Patch tests using a varnish formulation containing 0.2% trimethylol-propane triacrylate and 0.2% trimethylolpropane triacrylate solution in petrolatum, demonstrated positive reactions in 4 of the 5 subjects described above. Although the 37 year-old production manager did not have a significant patch test reaction, he developed an irritant dermatitis to undiluted polyfunctional acrylates [Emmett, 1977].

dermal, human · The introduction of a water-based ink (containing a polyfunctional aziridine hardening agent, which contains trimethylolpropane triacrylate at unspecified concentrations) at a wallpaper printing company was correlated with an outbreak of contact dermatitis in 13 of the 51 workers (25%). Within 3-6 months, the following incidences of dermatitis occurred among workers: 6/8 (75%) ink mixers; 7/22 (32%) printers; and 0/21 workers not exposed to ink. The ink mixers reportedly handled undiluted aziridine hardener and the printers handled ink containing 2-4% aziridine [Garabrant, 1985].

dermal, human · A 37 year-old man involved in the manufacturing of optical fibers coated with ultraviolet-curing acrylate resins for 2 years (containing trimethylolpropane triacrylate and urethane acrylate) developed dermatitis on his hands, face, and eyelids. The dermatitis cleared within 1 week after removal from exposure. This subject had positive reactions to skin patch tests with 0.01% and 0.1% trimethylolpropane triacrylate in petrolatum at 2 and 4 days (0.1% only) [Maurice and Rycroft, 1986].

dermal, human · Four workers in a plastic floor manufacturing facility, handling a new varnish which contained an aziridine-based hardener (containing 3-5% trimethylolpropane triacrylate by weight), developed hand and face dermatitis after using the varnish for one year. The number of workers handling the varnish varied between ten and thirty. All four reacted positively to a skin patch test using 0.1% trimethylolpropane triacrylate in acetone. Three workers reacted positively to 0.03% trimethylolpropane triacrylate, and one worker reacted positively to 0.0001% trimethylolpropane triacrylate. The latter subject demonstrated the most severe skin reaction [Dahlquist *et al.*, 1983].

dermal, human · Six workers from different printing plants developed allergic dermatitis within 3-32 weeks of working with ultraviolet curing inks which contained trimethylolpropane triacrylate. The symptoms started with itchy forearms and irritation of the eyes and face. One or two weeks later, they developed into erythema and scaling. Upon continued exposure for several weeks, a severe contact eczematous reaction developed. All subjects tested were positive to skin patch tests with 0.5% and 0.1% trimethylolpropane triacrylate in acetone. Two of the subjects reacted very strongly to trimethylolpropane triacrylate. None of the 30 controls reacted to patch tests with the ink. However, the controls had weak irritation reactions to trimethylolpropane triacrylate [Björkner *et al.*, 1980].

dermal, human · Seven out of 10 workers exposed for unspecified periods to ultraviolet printing inks at a plastic food container manufacturing plant developed contact dermatitis. Dermatitis varied from severe eczematous dermatitis of the dorsal hands, forearms, arms, neck, and eyelids to erythematous scaling in distinct evanescent patches on the dorsal hands. One worker (a machine operator) tested positive for sensitization to 0.1% trimethylolpropane triacrylate in petrolatum [Nethercott *et al.*, 1983].

dermal, human · A 61 year-old painter, who had been employed for more than 25 years by a wood products company, developed eczematous dermatitis on his hands, arms, legs and trunk within several weeks of switching from an oil-based paint to an acrylic paint system that contained 1-3% of a polyfunctional aziridine cross-linking hardener. The cross-linking agent was made from aziridine and trimethylolpropane triacrylate, and contained 3-5% of residual trimethylolpropane triacrylate. The concentration of trimethylolpropane triacrylate in the acrylic paint system ranged from 0.03% to 0.15%. The dermatitis persisted even after the worker was no longer exposed in the workplace. The authors reported that the chronicity of his dermatitis may be explained by the fact that he continued to live in the same house, and may have had enough exposure to the allergen contamination in his home environment to keep his dermatitis "smoldering." The patient had demonstrated a positive skin reaction to full-strength primer containing cross-linker (1-3%) which persisted for weeks. The patient was tested with 0.1%, 0.5%, and 1.0% cross-linker in petrolatum and ethyl alcohol. Positive reactions were observed at all concentrations in both solvents. Normal volunteers (n=7) serving as controls had no reaction to the above test doses of cross-linker. In addition, 50 patients tested with 0.1% cross-linker in petrolatum had no reaction to a patch test. Skin patch tests with 0.5% trimethylolpropane triacrylate were positive at 48 hours and 1 week. However, lower concentrations (0.001%, 0.01%, 0.19%) of trimethylolpropane triacrylate were negative. The positive test site observed was pruritic, and the irritation persisted and worsened after one week. Of the 44 control patients tested with 0.5% trimethylolpropane triacrylate in petrolatum, 5 (11.4%) demonstrated irritant reactions which diminished after one week. Because the test subject reacted to lower concentrations of cross-linker than the trimethylolpropane triacrylate, the authors concluded that the subject was primarily allergic to the polyfunctional aziridine cross-linker [Cofield *et al.*, 1985].

dermal, human · In September 1983, NIOSH was requested to investigate complaints of dermatitis and possible respiratory problems associated with the use of UV-cured printing inks in a citrus juice bottling plant. In February 1984, a NIOSH medical officer interviewed and examined all 71 first and second shift workers assigned to the glass filling department (Vac-Pac). Another 43 workers from the carton filling department, where no UV-cured ink was used, were

interviewed and examined. On December 14-21, 1984, 47 Vac-Pac workers from the first and second shifts, 5 carton filling workers, and 2 workers from other departments were interviewed and examined. All of these employees were patch tested to the components of the UV-cured inks and solvents to detect skin sensitization.

Skin sensitivity and photo patch testing was done with 0.2% trimethylolpropane triacrylate in petrolatum. Two (4%) of the 47 subjects had strong positive allergic contact reactions to trimethylolpropane triacrylate. One of the subjects tested positive in an ordinary skin patch test. The other subjects tested positive to both a photo patch test and an ordinary patch test at 48 and 96 hours. Three persons (6%) reacted mildly to trimethylolpropane triacrylate in the standard skin patch test at 48 and 96 hours. Since few employees tested showed sensitization to trimethylolpropane triacrylate, the NIOSH investigators concluded that past skin reactions reported among the Vac-Pac workers were irritant, not allergic, reactions to the inks and their components [NIOSH, 1987].

2. Animal Data

dermal, guinea pig · Immunized, outbred Hartley guinea pigs (n=11) of either sex developed skin sensitization upon application of a 0.2 ml solution of 0.1%, 0.25%, and 0.5% trimethylolpropane triacrylate in acetone:olive oil (4:1) for 7 days. The number of test animals in each group was not reported. Average intensities (0=no reaction, 3=severe reaction) of 0.7, 1.4, and 1.9 were obtained following application of 0.1%, 0.25%, and 0.5% trimethylolpropane triacrylate, respectively [Parker and Turk, 1983].

dermal, guinea pig · Fifteen female albino Dunkin Hartley guinea pigs were used in a maximization test to determine skin sensitivity to, and cross sensitivity patterns of, multifunctional acrylates. Guinea pigs were topically induced with the commercial forms of both PETA-3 and PETA-4 (pentaerythritol tri- and tetra-acrylate) at a concentration of 25% in petrolatum. Animals sensitized with PETA-3 and PETA-4 were challenged not only with the commercial products, but also with the main fraction or "purified" compounds.

Guinea pigs were challenged twice, one week apart, on 6 test sites on the flank with 0.015 grams of PETA-3, PETA-4, or trimethylolpropane triacrylate in petrolatum. Forty-eight hours after the first challenge, guinea pigs received a booster of the sensitizing chemical (PETA-3, PETA-4) intradermally on the neck. Fifteen control animals were sensitized using the same test procedure but omitting the test substance. The control group also received olive oil as a booster. Ten (67%) of the fifteen guinea pigs became sensitized to commercial PETA-3. Six of these animals also reacted to purified PETA-3, 7 reacted to commercial PETA-4, 3 to purified PETA-4, and 7 to trimethylolpropane triacrylate. Only 1 animal of the 15 induced with commercial PETA-4 reacted to this compound in challenge tests. The same animal reacted to purified PETA-4, purified PETA-3, and trimethylolpropane triacrylate. No reaction was seen in control animals.

According to the manufacturer, the PETA-3 used in this investigation consisted mostly of pentaerythritol triacrylate. HPLC-analysis indicated that the compound contained a high degree of impurities, including PETA-4. Complete purification of this product was impossible and the "purified" form used in testing contained 1% PETA-4. Commercial PETA-4 had a higher degree of purity than PETA-3. Analysis of the "purified" PETA-4 showed two small peaks, the smaller of which was identified as PETA-3 (15% of main peak). From this study, the authors concluded

that PETA-3 is a stronger sensitizer than PETA-4, and guinea pigs sensitized to PETA-3 have the potential to cross-react with trimethylolpropane triacrylate [Björkner, 1984].

dermal, guinea pig · A maximization test for cross sensitivity reaction patterns of acrylates and methacrylate esters was carried out on outbred SSc:AL-female guinea pigs. Guinea pigs were induced on day 0 by 3 intradermal injections in the hairless shoulder with 2 x 50 µl of a suspension of Freund's Complete Adjuvant (FCA) in sterile water; a 2 x 50 µl solution of methyl methacrylate (MMA), ethyleneglycoldimethacrylate (EDMA), triethyleneglycoldimethacrylate (TEDMA), or trimethylolpropane trimethylacrylate (TMPTMA) in soy bean oil; and a 2 x 50 µl solution of the above test substances in emulsified FCA and water. Controls received the same dosing without the test substance. On day 7, approximately 250 milligrams of 10% SDS in petrolatum was applied to the same test area of the neck and left uncovered for 24 hours. On day 8, 400 µl of liquid test solutions (same substances as described above) or petrolatum were applied to the filter paper patch. The patch was left in place for 48 hours. On day 21, the guinea pigs were challenged with up to 6 patches containing 25 µl of MMA, EDMA, TEDMA, TMPTMA, 2-hydroxy-methacrylate, 1,6-hexane diolodiacrylate, pentaerythritol triacrylate or trimethylolpropane triacrylate. Sensitization determinations were made at 48 and 72 hours. The treatment was repeated on the virgin skin of the opposite flank of each guinea pig 35 days later. In guinea pigs induced with TMPTMA and challenged with 2% trimethylolpropane triacrylate, 14/19 had a positive skin sensitization reaction. Induction with MMA, EDMA, and TEDMA followed by a challenge with trimethylolpropane triacrylate, did not produce a cross sensitization reaction [Clemmensen, 1984].

dermal, guinea pig · Outbred Hartley guinea pigs (male or female, number not specified) were immunized by injection subcutaneously into the foot pad with 0.1 ml of an emulsion containing trimethylolpropane triacrylate in ethanol:saline (1:4) in FCA. In addition, 0.1 ml of the same emulsion was injected into the nape of the neck. Animals received a total of 11.5 micromoles of trimethylolpropane triacrylate. Skin tests were then performed with 0.02 ml of 0.25% and 0.5% trimethylolpropane triacrylate in acetone:olive oil (4:1) applied to the shaved flank of the guinea pig. Skin reactions were recorded at 24, 48, 72 and 96 hours after the skin tests. Skin sensitivity was graded on a scale of 0-3 (0=no reaction, 3=severe skin reaction). Skin reactions from trimethylolpropane triacrylate exposure, recorded 24 and 48 hours after testing are summarized in Table 3 [Parker *et al.*, 1985].

Table 3: Mean Skin Test Reactivity in Guinea Pigs Immunized with Trimethylolpropane Triacrylate in FCA

	7 days				**14 days**			
	24 hours		**48 hours**		**24 hours**		**48 hours**	
	0.25%	**0.5%**	**0.25%**	**0.5%**	**0.25%**	**0.5%**	**0.25%**	**0.5%**
TMPTA	0.7	0.9	1.5	1.6	1.3	1.9	1.4	1.9

dermal, guinea pig · Cross sensitivity tests with trimethylolpropane triacrylate were conducted

on outbred Hartley guinea pigs (n=5) immunized with methyl acrylate, methyl vinyl ketone, 4-vinyl pyridine, pentaerythritol (PETA) and trimethylolpropane triacrylate in FCA. Cross sensitivity was seen in mice immunized with methyl acrylate, methyl vinyl ketone, and PETA. Guinea pigs immunized with trimethylolpropane triacrylate demonstrated a cross sensitivity to methyl acrylate (20-60% of immunizer response), methyl vinyl ketone (60-80% of immunizer response) and PETA (> 80% of immunizer response) [Parker *et al.*, 1985].

dermal, guinea pig · Albino Hartley/Dalkin female guinea pigs (n=10) were induced, and subsequently challenged with, trimethylolpropane triacrylate. Each guinea pig received three pairs of intradermal injections in the shoulder region. The compositions of the injected materials were: (1) 0.1 ml of a 0.5% or 10% solution of trimethylolpropane triacrylate in propylene glycol; (2) 0.05 ml FCA and 0.05 ml trimethylolpropane triacrylate in propylene glycol as described in (1); (3) 0.1 ml FCA. One week after injection, 0.5% or 10% trimethylolpropane triacrylate in petrolatum was applied to the shaved shoulder of each guinea pig and then wrapped for 48 hours. Guinea pigs were then challenged 2 weeks after topical exposure with skin patches of non-irritant concentrations of trimethylolpropane triacrylate for 24 hours. Probit calculations were used to determine the percentage of animals sensitized and the intradermal concentration required to sensitize half of the animals. Of the 10 guinea pigs receiving 0.5% trimethylolpropane triacrylate, 4 (20%) became sensitized and 10 of the 20 (58.3%) guinea pigs receiving 10% trimethylolpropane triacrylate became sensitized. The intradermal sensitivity concentration for 50% of the animals ($IDSC_{50}$) was determined to be 5.4% [Nethercott *et al.*, 1983].

D. Chronic/Carcinogenicity

1. Human Data

No data were found on the chronic/carcinogenic effects of trimethylolpropane triacrylate in humans.

2. Animal Data

dermal, mice · As recommended by the pilot study (see section V.B), 5% trimethylolpropane triacrylate in mineral oil was tested at a dose of 50 milligrams twice weekly in 50 mice. In addition, a negative control group receiving mineral oil only, an untreated group, and a positive control group receiving 0.5% benzo(a)pyrene in mineral oil were tested (n=50). Materials were applied to the interscapular region of the shaven back for 80 weeks, or until a horny lesion grew to 1 mm^3. When a lesion appeared malignant, the mouse was sacrificed and the lesion was biopsied. After 80 weeks, all mice were sacrificed and 10% of the mice were histologically examined. In all control mice, "nothing remarkable" was noted. Slight epilated skin was observed in the test group. In addition, acanthosis of the epidermis and fibrosis of the dermis was observed in 46 and 38 trimethylolpropane triacrylate treated mice, respectively. No skin tumors or lesions were observed in the trimethylolpropane triacrylate treated group [Celanese Corporation, 1985].

E. Reproductive Effects and Teratogenicity

1. Human Data

No data were found on the reproductive or teratogenic effects of trimethylolpropane triacrylate in humans.

2. Animal Data

No data were found on the reproductive or teratogenic effects of trimethylolpropane triacrylate in animals.

F. Genetic Toxicology

1. Human Data

No data were found on the genetic toxicology of trimethylolpropane triacrylate in humans.

2. Prokaryotic Data

Salmonella typhimurium · Mutagenicity tests were conducted on *Salmonella typhimurium*, TA-1535, TA1537, TA1538, TA98, and TA100 with and without metabolic activation. Tests were conducted at dose levels of 0.1, 1.0, 5.0, and 10.0 µl/plate trimethylolpropane triacrylate. Positive (using various mutagens) and negative control tests were conducted. Trimethylolpropane triacrylate was non-mutagenic with and without metabolic activation in all *Salmonella* strains tested [Celanese Corporation, 1976].

3. Eukaryotic Data

mouse lymphoma cells · Trimethylolpropane triacrylate was analyzed for genotoxicity in the TK+/-heterozygote of the L5178Y mouse lymphoma cell line without exogenous activation at concentrations of 0.0, 0.6, 0.65, and 0.70 µg/ml. Trimethylolpropane triacrylate caused an increase in aberrations, micronuclei and mutant frequency. Trimethylolpropane triacrylate induced a clear dose response to a 494 x 10^{-6} frequency at a concentration of 0.65 µg/ml. The authors concluded that this chemical is mutagenic to mouse lymphoma cells [Dearfield *et al.*, 1989].

mouse lymphoma cells · Trimethylolpropane triacrylate was evaluated for mutagenicity in the absence of exogenous activation in the TK+/- heterozygote of L5178Y mouse lymphoma cells. In addition to the specific locus (*tk*) mutagenesis analysis, mouse lymphoma cells were evaluated for the frequency of gross chromosome aberrations. Trimethylolpropane triacrylate was tested at doses of 0.6, 0.65, and 0.70 µg/ml. The compound induced almost exclusively small colony TK mutants. The TK mutant frequency (small/large) for 0.0, 0.6, 0.65, and 0.70 µg/ml trimethylolpropane triacrylate was 37/29, 119/24, 151/38, and 232/51, respectively. In addition, trimethylolpropane triacrylate, at each concentration, induced chromosomal aberrations in mouse lymphoma cells. At a trimethylolpropane triacrylate concentration of 0.70 µg/ml, a total of 21 chromosomal aberrations were seen in 100 cells. The results from this study indicate that trimethylolpropane triacrylate is mutagenic in this assay [Moore *et al.*, 1989].

mouse lymphoma cells · Trimethylolpropane triacrylate induced an increase in mutations at the TK locus in L5178Y mouse lymphoma cells in the dose range of 1.0 to 2.5 nl/ml without activation and at 20.0 nl/ml with microsomal activation. The doses were moderately to highly toxic to the mouse lymphoma cells. These results indicate that trimethylolpropane triacrylate is mutagenic in the mouse lymphoma assay [Celanese Corporation, 1979].

Mouse lymphoma cells · It was reported in a paper submitted for publication that trimethylolpropane triacrylate was found to be mutagenic in a typical mouse lymphoma assay. L5178Y TK +/- 3.7.C mouse lymphoma cells were used to test the mutagenicity of trimethylolpropane triacrylate without exogenous metabolic activity and with liver S9 prepared from male Sprague-Dawley rats. Trimethylolpropane triacrylate was used at doses ranging from 3×10^{-7} to 3.3×10^{-6} M without S9, and from 3.34×10^{-5} to 1.11×10^{-4} M with S9. Of all chemicals tested in this study, trimethylolpropane triacrylate was the most toxic and induced a significant mutagenic response in the absence of metabolic activation (300 mutants per 10^6 survivors for 3.3×10^{-6} M trimethylolpropane triacrylate). The addition of S9 decreased both the toxicity and mutagenic response. The increase in the number of mutants was dose-dependent, but the required doubling in mutant frequency did not occur in cultures showing at least 10% relative total growth [Cameron, *et al*., 1990].

Chinese hamster ovary cells · Trimethylolpropane triacrylate was evaluated for mutagenicity in the absence of exogenous activation in a suspension adapted Chinese hamster ovary (CHO) assay using the K1BH4 cell line. In addition to the specific locus (HGPRT) mutagenesis analysis, CHO cells were evaluated for the frequency of gross chromosomal aberrations. Trimethylolpropane triacrylate was tested at doses of 0.2, 0.6, and 0.7 µg/ml . Results show that trimethylolpropane triacrylate did not show any consistent increase in the CHO/HGPRT mutant frequency (total mutant frequencies of 3, 9, 8, and 1 were observed at doses of 0.0, 0.2, 0.6, and 0.7 µg/ml respectively). However, trimethylolpropane triacrylate did induce chromosomal aberrations in CHO cells. The total number of aberrations in 100 cells was 1, 13, 34, and 37 for doses of 0.0, 0.2, 0.6, and 0.7 µg/ml respectively. The authors noted that the absence of genotoxicity at the HGPRT locus by a compound that is clastogenic to CHO cells indicates that the HGPRT locus may be inadequate for evaluating the clastogenic ability of a genotoxic compound [Moore, *et al*., 1989].

Saccharomyces cerevisiae · Mutagenicity tests were conducted on *Saccharomyces cerevisiae*, D4 with and without metabolic activation at dose levels of 0.1, 1.0, 5.0, and 10.0 µl/plate trimethylolpropane triacrylate. Positive (using various mutagens) and negative control tests were used. Trimethylolpropane triacrylate was non-mutagenic with and without metabolic activation in *Saccharomyces cerevisae* [Celanese Corporation, 1976].

G. Other Toxicological Effects

1. Immunotoxicity

dermal, guinea pig · A radioimmunoassay on trimethylolpropane triacrylate-immunized outbred Hartley female guinea pig serum did not detect anti-trimethylolpropane triacrylate antibodies. However, guinea pigs immunized with bovine gamma globulin (BGG) had high anti-trimethylolpropane triacrylate levels in sera.

An inhibition radioimmunoassay was conducted after incubating immunized serum dilutions (1/5000) for 2 hours with trimethylolpropane triacrylate/XOA (egg albumin), MeAc (methyl acrylate)/XOA, or 4VP (4-vinyl pyridine)/XOA in the range of 0.5 µg/ml to 5 mg/ml. A dose-dependent decrease in the amount of bound radiolabel was seen, indicating that the anti-trimethylolpropane triacrylate/BGG antibodies specifically reacted with trimethylolpropane triacrylate and cross-reacted with MeAc [Bull *et al.*, 1987].

dermal, guinea pig · Lymph nodes were extracted from trimethylolpropane triacrylate immunized guinea pigs 4-6 days after ear application of this compound and examined for T-lymphocyte proliferation (determined by the number of large pyroninophilic cells (LPC)).

A significant ($p<0.001$) increase in the number of LPC in lymph nodes was observed 4 days after epicutaneous application of 50 µmol of trimethylolpropane triacrylate, which was sustained for 6 days. The authors determined that there was a positive correlation between skin

contact reactions, and increases in lymph node weight and T-lymphocyte proliferation [Bull *et al.*, 1985]

2. Neurotoxicity

No data were found on the neurotoxic effects of trimethylolpropane triacrylate in humans or animals.

3. Biochemical Toxicology

No data were found on the biochemical toxicology of trimethylolpropane triacrylate in humans or animals.

VI. STRUCTURE ACTIVITY CONSIDERATIONS

Chronic dermal toxicity studies of eight MFAs have been conducted. For these studies, test groups of 50 male C^3H/HeJ mice were treated twice weekly for 80 weeks or until tumors were diagnosed or the animals became moribund or died. Of the MFAs tested, the following five compounds showed no increased incidence of skin or visceral tumors: trimethylolpropane triacrylate (TMPTA) {see section V.D for a description of the study}, trimethylolpropane trimethacrylate (TMPTMA), 1,6-hexanediol diacrylate (HDODA), tripropyleneglycol diacrylate (TRPGDA), and triethyleneglycol dimethacrylate (TTEGDMA). The remaining MFAs tested-pentaerythritol triacrylate (PETA), triethyleneglycol diacrylate (TREGDA), and tetraethyleneglycol diacrylate (TTEGDA) showed some potential for carcinogenicity/tumorigenicity. PETA (100 mg/kg) induced lymphomas with spleen or lymph node involvement in 6 of 50 mice. TREGDA (100 mg/kg) induced skin tumors in 6 mice and lymphomas in 4 mice. TTEGDA (100 mg/kg) caused an increased incidence of skin tumors in 6 mice. Forty-two (42) of 50 mice that received benzo[a]pyrene (positive control) developed squamous cell carcinomas of the skin and 1 animal in both the non-treatment and mineral oil negative control groups developed a skin papilloma.

In another study, neopentylglycol diacrylate (NPGDA) and PETA were tested for chronic dermal toxicity in 40 C^3H/HeJ male mice at 5 mg {approximately 200 mg/kg} and 3 mg {approximately

120 mg/kg} doses for NPGDA and PETA, respectively, for the lifetime of the animals. Eight NPGDA-treated animals developed skin tumors (5 papillomas and 3 carcinomas) compared to no tumor-bearing animals in the acetone control group. PETA did not show any evidence of carcinogenicity in this study, however, it was reported that no histological evaluation of internal organs was performed.

The authors report that the above findings suggest that MFAs are not strong skin carcinogens and that the increased incidence of lymphomas induced by PETA and TREGDA have "raised concerns" that MFAs can be absorbed and cause tumors of viscera [Andrews and Clary, 1986].

Figure 1. Structures of Multifunctional Acrylates

1,6-Hexanediol diacrylate (HDODA)	Tripropyleneglycol diacrylate (TRPGDA)

Neopentylglycol diacrylate (NPDGA) *

R = H	*n* = 3	Triethyleneglycol diacrylate (TREGDA)*
R = H	*n* = 4	Tetraethylenegycol diacrylate (TTEGDA)*
R = CH_3	*n* = 4	Tetraethyleneglycol dimethacrylate (TTEGDMA)

R = H	$R_1 = C_2H_5$	Trimethylolpropane triacrylate (TMPTA)
R = CH_3	$R_1 = C_2H_5$	Trimethylolpropane trimethylacrylate (TMPTMA)
R = H	$R_1 = CH_2OH$	Pentaerythritol triacrylate (PETA)*

* indicates chemicals which have the potential for carcinogenicity

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APPENDIX I. ON-LINE DATABASES SEARCHED		
-	**DATE OF SEARCH**	**TIME PERIOD**
BRS:	-	-
HZDB	November, 1989	-
-	-	-
DIALOG:	-	-
Agricola	November, 1989	1970-1990

Agris International	November, 1989	1974-1990
Aquatic Sciences Abstracts	November, 1989	1974-1990
Biosis Previews	November, 1989	1969-1990
CAB Abstracts	November, 1989	1972-1990
Cancerlit	November, 1989	1963-1990
Chem Bus Newsbase	November, 1989	1984-1990
Chemical Exposure	November, 1989	1974-1987
Compendex Plus	November, 1989	1970-1990
CRIS USDA	November, 1989	-
Embase	November, 1989	1974-1990
Environline	November, 1989	1970-1990
Environmental Bibliography	November, 1989	1974-1990
Federal Register	November, 1989	1977-1990
Foods Adlibra	November, 1989	1974-1990
FSTA	November, 1989	1969-1990
Life Sciences Collection	November, 1989	1978-1990
Medline	June, 1990	1966-1990
NTIS	November, 1989	1964-1990
Occupational Safety and Health	November, 1989	1973-1990
PTS Newsletter	November, 1989	1987-1990
PTS Prompt	November, 1989	1972-1990
Pollution Abstracts	November, 1989	1970-1990
Trade and Industry ASAP	November, 1989	1983-1990
-	-	-

MEAD:	-	-
Nexis/Lexis-BNA ENV	June, 1990	-
-	-	-
NLM:	-	-
Chemline	November, 1989	-
CCRIS	June, 1990	-
ETIC	June, 1990	-
HSDB	November, 1989	-
RTECS	November, 1989	-
Toxline 65	November, 1989	1965-1980
Toxline	June, 1990	1981-1990
Toxlit	June, 1990	1981-1990
Toxlit 65	June, 1990	1965-1980
-	-	-
STN:	-	-
CA	June, 1990	1967-1990
Chemlist	June, 1990	-

APPENDIX II. SAFETY INFORMATION

·HANDLING AND STORAGE

Trimethylolpropane triacrylate rapidly polymerizes at temperatures above 32ºC (89.6ºF) . Exposure to free radical initiators and oxidizing agents may initiate polymerization. Trimethylolpropane triacrylate is light-sensitive and may undergo polymerization on exposure to direct sunlight. This compound may be reactive after 12 months of storage. Trimethylolpropane triacrylate can be stabilized with free radical polymerization inhibitor (monomethyl ester of hydroquinone at 100 ppm ± 25) [AIHA, 1981]. Upon exposure to extreme heat, container rupture may occur [Lenga, 1988].

·EMERGENCY FIRST AID PROCEDURES

Eye: First check the victim for contact lenses and remove if present. Flush victim's eyes with

water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center. Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician. IMMEDIATELY transport the victim to a hospital even if no symptoms (such as redness or irritation) develop.

Skin: IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently was affected skin areas thoroughly with soap and water. If symptoms such as inflammation or irritation develop, IMMEDIATELY call a physician or go to a hospital for treatment.

Inhalation: IMMEDIATELY leave the contaminated area and take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.

Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used.

Ingestion: If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician.

If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. Immediately transport the victim to a hospital.

·PROTECTIVE EQUIPMENT

Eye: Safety goggles

Gloves: Two pairs of dissimilar protective gloves shall be worn when handling the neat chemical, otherwise one pair. When contact with this chemical has been known to occur, change gloves immediately.

Clothing: Minimally, a disposable laboratory suit (e.g. Tyvek ®) shall be worn, as specified in the most current NTP Statement of Work or the NTP Health and Safety Minimun Requirements.

Respiratory A NIOSH-approved chemical cartridge respirator with an

Protection: organic vapor cartridge.

·EXTINGUISHANT

Dry chemical, carbon dioxide or halon extinguisher

·MONITORING PROCEDURES

There is no NIOSH analytical method reported in the NIOSH Manual of Analytical Methods for trimethylolpropane triacrylate.

· SPILLS AND LEAKAGE

Persons not wearing the appropriate protective equipment and clothing shall be restricted from areas of spills until cleanup has been completed. When exposure to unknown concentrations may occur, air-purifying respirators may not be used. Chemical cartridge respirators with organic vapor cartridges may not be used when airborne concentrations exceed 1000 ppm.

If trimethylolpropane triacrylate is spilled the following steps shall be taken:

1. If a liquid solution is spilled, use vermiculite, sodium bicarbonate, sand, or paper towels to contain and absorb the spill.

2. Clean the spill area with dilute alcohol (approximately 60-70%) followed by a strong soap and warm water washing.

3. Dispose of all absorbed material as hazardous waste.

· DECONTAMINATION OF LABORATORY EQUIPMENT

TDMS Terminal: Whenever feasible, a protective covering (e.g., plastic wrap) shall be placed over the keyboard when in use.

General Equipment: Before removing general laboratory equipment (i.e., lab carts, portable hoods and balances) from animal dosing rooms and/or chemical preparation areas, a decontamination process shall be conducted in addition to routine housekeeping procedures.

· WASTE MANAGEMENT AND DISPOSAL PROCEDURES

Waste Management: If an inhalation study is to be conducted, all exhaust air from the inhalation chamber must be cleaned with appropriate air cleaning devices unless the laboratory has informed local and state air pollution regulatory agencies of both the laboratory's operating practices and the potential hazards of the chemicals in use. Compliance with all federal, state and local air pollution laws and regulations is required. A specific air cleaning system design must consider the specific conditions of the laboratory (eg., air flow rates and volumes, mixing of exhaust streams, size of inhalation chamber, etc.) and the dosing regimen selected. Air cleaning systems designs must be described by the laboratory and approved by the NTP Office of Laboratory Health and Safety.

Waste Disposal: Securely package and label, in double bags, all waste material. All potentially contaminated material (e.g., carcasses, bedding, disposable cages, labware) shall be disposed of by incineration in a manner consistent with federal (EPA), state, and local regulations or disposed of in a licensed hazardous waste landfill.