NATIONAL TOXICOLOGY PROGRAM

EXECUTIVE SUMMARY OF SAFETY AND TOXICITY INFORMATION

PENTAERYTHRITOL TRIACRYLATE

CAS No. 3524-68-3

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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: *Pentaerythritol triacrylate (PETA) was nominated by NCI in 1987 for multidose dermal carcinogenicity studies with a high priority. The request was based on its high and increasing production, widespread use, potential for exposure, lack of adequate chronic and carcinogenicity data, as well as the lack of adequate genotoxicity data on the acrylates class, and structure-activity relationships.*

Chemical and Physical Properties: *PETA is a colorless or light amber non-volatile liquid or white crystalline solid (up to 40 °C) with a melting range of 25-40 °C (77-104 °F) and a boiling point of >315 °C (>599 °F) @ 760 mm Hg. This chemical is practically insoluble in water, hygroscopic, and incompatible with strong oxidizing agents, strong acids, and strong bases. PETA may polymerize in the presence of localized heat and ultraviolet light. It is stabilized with the monomethyl ether of hydroquinone.*

Production/Uses/Exposure: *The total production volume of PETA was reported in the public file of the EPA Toxic Substances Control Act (TSCA) Inventory in 1983 by three manufacturers, to range from 100,000-1,002,000 pounds. No production data were available from the United States International Trade Commission's Publication Sythetic Organic Chemicals or from SRI's Chemical Economics Handbook. This compound has a wide industrial application as a polymer cross-linker in radiation curing. PETA is also used as an ingredient in printing inks, coatings, print varnishes, and other polymer systems. Non-radiation curing uses of PETA include paper and wood impregnates, wire and cable extrusion, and polymer impregnated concrete. Workers involved in the manufacturing, processing, product handling, and application of PETA are at risk of exposure to this compound. Data from the National Occupational Exposure Survey (NOES) conducted during 1981-1983 estimate that 62 employees, including 41 females, were potentially exposed to PETA. The American Industrial Hygiene Association established a workplace environmental exposure level (WEEL) of 1 mg/m ^{3} (8-hour time-weighted average) for this compound. No other exposure regulations/recommendations have been established. Although no quantitative data were reported, the potential for consumer exposure to this chemical, from its use in such products as paints and floor polishes, exists.*

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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: *PETA has been shown to induce contact and allergic dermatitis in workers handling printing inks, paints, coatings, and aziridine hardeners containing the compound. In addition, a number of cases of irritant skin reactions and irritant conjunctivitis have been reported upon exposure to these formulations containing PETA. Positive skin patch tests among these subjects have confirmed the sensitizing ability of this compound. In most cases, the dermatitis began as irritation and itchiness of the hands, arms, neck, face, and ears. Gradual development of eczematous dermatitis occurred upon prolonged exposure. There were no data found on the chemical disposition, or on the chronic, carcinogenic, teratogenic, or reproductive effects of PETA in humans.*

Animal: *PETA was found to have a slight to moderate oral toxicity in rats (LD_{50}>500-5000 mg/kg) and a moderate dermal toxicity in rabbits (LD_{50} >200-2000 mg/kg). Applications of this chemical to the rabbit eye caused severe and corrosive irritation as well as corneal opacity. Prechronic studies show that PETA acts as a skin sensitizer and allergen in guinea pigs. Studies investigating the cross-reactivity patterns of PETA in guinea pigs indicate the compound has cross-sensitivity with trimethylolpropane triacrylate, triethyleneglycol dimethacrylate, methylmethacrylate, and other compounds of similar structure. In a subchronic dermal toxicity study in rabbits, PETA induced dermal effects including severe necrosis of the epithelium. However, no evidence of systemic toxicity resulting from this compound was observed. In another prechronic dermal toxicity study, in addition to dermal effects, PETA treated animals exhibited symptoms including weight loss, hypoactivity, hypopnea, and nasal discharge. At necropsy, numerous black foci were observed on the stomach of 2/6 animals. The authors concluded that this study failed to demonstrate the presence or absence of test compound-induced systemic toxicity. Repeated dermal exposure to PETA did not induce a significant number of skin tumors in male mice, but it did increase the incidence of lymphomas. However, the conclusions presented in this study have been disputed. In a chronic dermal study, PETA treated mice had an increase in hepatic tumors when compared to*

the acetone control group. This increased incidence, however, was not statistically significant when compared to historic controls. In addition, dermal treatment with PETA caused an increase in the number of large pyroninophilic cells in lymph nodes in the guinea pig, indicating T-lymphocyte proliferation. In an intraperitoneal LD_{50} study, PETA, at 30 and 300 mg/kg, caused neurological abnormalities in male and female rats. These abnormalities included ataxia, body and limb tone flaccidity, and abnormal visual-placing and righting reflex. At 10 mg/kg, this compound caused neurological abnormalities in 50% of the test animals. PETA was not found to be teratogenic to rats and no data on the compound's reproductive effects were found. No data were found on the chemical disposition of this compound.

Genetic Toxicology: *This chemical was non-mutagenic to Salmonella strains TA98, TA100, TA1535, TA1537 and TA1538 with and without metabolic activation. This compound was also non-mutagenic to Saccharomyces cerevisiae strain D4. PETA was found to cause an increase in mutant frequency in L51784 mouse lymphoma cells and to induce an increase in the number of aberrations and micronuclei.*

Structure Activity Relationships: *PETA is structurally similar to other multifunctional acrylates, including triethyleneglycol diacrylate (TREGDA) and tetraethyleneglycol diacrylate (TTEGDA), which were shown to have the potential for carcinogenicity in a chronic dermal study in C3H/HeJ mice. The multifunctional acrylate neopentylglycol diacrylate (NPGDA) was found to be carcinogenic to C3H/HeJ male mice in another dermal toxicity study.*

I. NOMINATION HISTORY AND REVIEW

A. Nomination History

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

2. Date: July 1987

3. Recommendations: Multidose dermal 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
   - Existing but inadequate evidence of potential carcinogenicity: caused spleen lymphoma induction in male mice in a limited (one species, one dose, one sex) skin painting study
   - Nominated as a representative multifunctional acrylate (MFA): need to evaluate structure-related differential carcinogenicity of mono- and multi-functional acrylates
   - Existing mutagenicity tests for MFAs are inconsistent, inadequate, and of limited usefulness
   - 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 (Michael reaction)

B. Chemical Evaluation Committee Review

1. Date of Review: August 8, 1991

2. Recommendation:
   - Chemical disposition and metabolism
   - Carcinogenicity

3. Priority:
   - High for chemical disposition and metabolism
   - Moderate for carcinogenicity

4. NTP Chemical Selection Principle(s): 2, 3, 8

5. Rationale/Remarks:

   - High and increasing production and use
   - Potential for occupational exposure
   - 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**

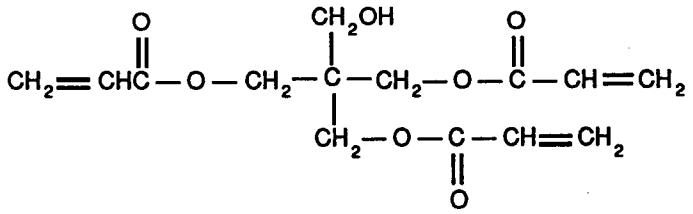
1. Date of Review:
2. Recommendations:
3. Priority:
4. Rationale/Remarks:

D. **Executive Committee Review**

1. Date of Review:
2. Decision:

II. CHEMICAL AND PHYSICAL DATA

A. Chemical Identifiers



PENTAERYTHRITOL TRIACRYLATE

CAS No. 3524-68-3
RTECS No. UD3370000

Molecular formula: $C_{14}H_{18}O_7$ Molecular weight: **298.3**

B. Synonyms and Trade Names

Synonyms: acrylic acid, triester with pentaerythritol (8CI); 2-propenoic acid, 2-(hydroxymethyl)-2-(((1-oxo-2-propenyl)oxy)methyl)-1,3-propanediyl ester (9CI); pentaerythrityl triacrylate; PETA, PETIA; tetramethylolmethane triacrylate

Trade Names: Aronix M 305®, NK Ester A-TMM3®, Setalux UV 2242®, SR 444®, Viscoat 300®

C. Chemical and Physical Properties

Description: A colorless or light amber, non-volatile liquid [AIHA, 1981], or white semi-solid [Lenga, 1988] to crystalline solid [Celanese, 1979] up to 40°C (104°F) [AIHA, 1981] with a characteristic acrylate odor [Radcure, 1990b].

Melting Point: 25-40°C (77-104°F) [Radcure, 1990a; AIHA, 1981; Celanese, date unspecified].

Boiling Point: >315°C (>599°F) @760 mm Hg (estimated) [AIHA, 1981]

Density: 9.84 @ 25°C (lbs/gal) [Radcure, 1990a, Celanese, date unspecified]
1.18 @25°C (g/cc) [Aldrich, 1990; Radcure, 1990a; Celanese, date unspecified].

Vapor Pressure:	<0.001 mm Hg (25°C) <0.01 mm Hg (100°C) [Radcure, 1990a; Celanese, date unspecified] <1.0 mm Hg @ 150°C [AIHA, 1981].
Refractive Index:	1.4840 @ 20°C [Aldrich, 1990] 1.4864 @ 20°C [Lenga, 1988].
Solubility in Water:	practically insoluble [Radcure, 1990b] insoluble [AIHA, 1981].
Solubility in other Solvents:	This compound has been tested in acetone, DMSO, mineral oil, methyl ethyl ketone and alcohol for toxicological evaluation (see section V).
Log Octanol/Water Partition Coefficient:	No data were found.
Reactive Chemical Hazards:	Hygroscopic; incompatible with polymerization initiators including peroxides, strong oxidizing agents, copper, copper alloys, carbon steel, iron, rust, strong bases [Radcure, 1990b] and strong acids [Lenga, 1988]. May polymerize on exposure to sources of free radicals [Radcure, 1990a], direct light, and localized heat. Decomposition products include toxic fumes of carbon monoxide and carbon dioxide [Radcure, 1990b; Lenga, 1988]. Uncontrolled polymerization may occur at high temperatures resulting in explosions and ruptures of storage containers [Radcure, 1990b]. Inhibited with 100 ppm hydroquinone monomethyl ether [Lenga, 1988; Aldrich, 1990].
Flammability Hazards	• Flashpoint: by Pensky-Martens Closed Cup Method: > 110°C (230°F) [Lenga, 1988]. > 93.3°C (200°F) [Radcure, 1990b; Celanese, 1982a].

III. PRODUCTION/USE

A. Production

1. Manufacturing Process

No information on the specific manufacturing process of pentaerythritol triacrylate was found. However, polyfunctional acrylate monomers can be produced by direct or trans esterification methods [Kirk-Othmer, 1978].

Pentaerythritol is manufactured by the reaction of acetaldehyde with formaldehyde in alkaline medium such as sodium or calcium hydroxide. First, the alpha-hydrogen atoms of the acetaldehyde condense with the formaldehyde in three sequential aldol reactions to form pentaerythrose. The pentaerythrose is reduced to pentaerythritol in a crossed Cannizzaro reaction with formaldehyde. Pentaerythritol esters have been synthesized by the usual methods of esterification using organic acids, acid anhydrides, or acid chlorides [Kirk-Othmer, 1978]. Mono acrylates can be prepared by dehydration of the corresponding hydroxyalkanoic acid, saponification of the alkene nitrile, catalytic hydration of acetylene and carbon monoxide, or the reaction of acetone with hydrocyanic acid [Clayton and Clayton, 1981].

2. Producers and Importers

U.S. Producers	Reference
Alcolac Incorporated Baltimore, Maryland	USEPA, 1991
Aldrich Chemical Company, Incorporated Milwaukee, Wisconsin	Chemical Week Buyers' Guide, 1990
Celanese Chemical Company, Incorporated Pampa, Texas	USEPA, 1991
CL Industries, Incorporated Georgetown, Illinois	SRI, 1990
Haven Chemical Philadelphia, Pennsylvania	USEPA, 1991
Monomer-Polymer and Dajak Laboratories, Incorporated Trevose, Pennsylvania	Chemical Week Buyers' Guide, 1990
Polysciences, Incorporated Warrington, Pennsylvania	Chemical Week Buyers' Guide, 1990

Radcure Specialties, Incorporated Pampa, Texas	SRI, 1990
Sartomer Company, Incorporated Westchester, Pennsylvania	SRI, 1990; USEPA, 1991; Chemical Week Buyers' Guide, 1990
Thiokol Chemical Division Calvert City, Kentucky	USEPA, 1991

European Producers :

- No data were available on European producers

Importers:

- No information on the importers of pentaerythritol triacrylate is provided in the public file of the EPA Toxic Substances Control Act (TSCA) inventory [USEPA, 1991].

3. Volume

The production volume of pentaerythritol triacrylate is reported in the public file of the EPA Toxic Substances Control Act (TSCA) Inventory. In 1983, 5 manufacturers were listed as producers of pentaerythritol triacrylate. Three manufacturers reported a total production volume ranging from 100,000 pounds to 1,002,000 pounds. Two manufacturers did not report a production volume. Of the latter two, one plant was classified as a small manufacturer, i.e., less than 100,000 pounds of pentaerythritol triacrylate were produced at this plant [USEPA,1991].

Pentaerythritol triacrylate is not listed in the United States International Trade Commission's publication Synthetic Organic Chemicals for the years 1986-1989. However, the United States International Trade Commission has reported a total production volume of 159,618,000-252,285,000 pounds for polyhydric alcohol esters, a class with includes pentaerythritol triacrylate, for the years 1979-1988 [USITC, 1980-1989].

Pentaerythritol triacrylate was listed in SRI's Chemical Economics Handbook; however, no production data were provided [SRI, 1991].

In 1984, Celanese Chemical Company, Incorporated reported that it was expanding its production of multifunctional monomers, including pentaerythritol triacrylate, by 50% at its Pampa, Texas plant [Chemical Engineering, 1984]. The American Industrial Hygiene Association predicts the production of multifunctional acrylates (including pentaerythritol triacrylate) may be several million pounds per year, depending on demand [AIHA, 1981].

4. Technical Product Composition

Commercial grade pentaerythritol triacrylate is mainly a mixture of tri- and tetra-acrylate esters of pentaerythritol with some dimers and trimers containing 3.3 acrylate groups per molecule [AIHA, 1981]. Technical grade pentaerythritol triacrylate supplied by Aldrich is a mixture of di-, tri- and tetra-acrylates and other esters [Aldrich, 1990]. Technical grade pentaerythritol triacrylate is available with 0.10% by weight maximum water content and 0.10 % by weight maximum residual acrylic acid as impurity, and 900 ppm maximum residual solvent. The minimum ester rank for pentaerythritol triacrylate is 3.2 [Radcure, 1990a], and the maximum is 3.45 [Celanese, 1982a]. It was also reported that commercial pentaerythritol triacrylate can be a mixture of the diacryalate, triacrylate, and tetraacrylate forms in various ratios. Other impurities known to occur in pentaerythritol triacrylate include cyclic dimers with a 1,3-dioxane structure and acrylates of dipentaerythritol [Newmark and Palazzotto, 1990].

Celanese Chemical Company, Incorporated reported the composition of its crystalline pentaerythritol triacrylate mixture based on liquid chromatographic analysis. Although the concentrations were found to vary with process variables, the typical composition was 1.4 % by weight pentaerythritol diacrylate (PEDA), 42.6 % by weight pentaerythritol triacrylate (PETA), and 56.0 % by weight pentaerythritol tetraacrylate (PETA-4). Celanese Chemical Company also reported that the liquid form of pentaerythritol triacrylate is composed principally of PEDA, PETA and PETA-4, and their dimers in relative amounts that differ from the crystalline product [Celanese, 1982b].

B. Use

- Component of a formulation for electron beam irradiation curable coatings [Björkner, 1984].
- Cross-linking agent and reactive diluent utilized in ultraviolet curing processes for printing inks and coatings [Nethercott, 1978; Björkner 1984].
- Component of ultraviolet curable decorative coatings and fast-drying ink systems for lithographic and web offset printing inks [Celanese, 1982a].
- Reactive monomer in radiation-cured and photocurable coatings of urethanes and epoxy resins [Newmark and Palazzatto, 1990].
- Ingredient in acrylic glues, adhesives, and anaerobic sealants [Björkner, 1984].
- Acrylic component of photopolymer and flexographic printing plates, flexographic inks, photoresists (an etch resist for printed circuit boards), and ultraviolet cured letterpress [Bjorkner, 1984].

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

- Component of polyfunctional aziridine hardeners used to cross-link water-borne acrylic emulsions, solvent-born acrylic lacquers, and water-born urethanes found in paints, paint primers, lacquers, topcoats and other protective coatings [Cofield *et al.*, 1985].

- Modifier for polyesters and fiberglass [ACS, 1990].

- Inorganic filled, molded, extruded polymer by ultraviolet, beta, and gamma radiation [ACS, 1990].

- Non-radiation end use: colloidal dispersion for industrial baked coatings, waterborne alkyds, solvent-based alkyds, vinyl/acrylic emulsions non-woven binders, pressure sensitive adhesives, paper and wood impregnates, wire and cable extrusion, polymer impregnated concrete, polymer concrete structural composites, and chemical intermediate [Celanese, 1982a].

IV. EXPOSURE/REGULATORY STATUS

A. Consumer Exposure

No quantitative data were found on consumer exposure to pentaerythritol triacrylate. However, because of the widespread and increasing use of this compound and related compounds in products such as latex paint, and floor polishes, the potential for consumer exposure exists [Dearfield *et al.* , 1989]. Some consumer products that are made from high-impact acrylic molding powders containing pentaerythritol triacrylate include outboard motor shrouds, housings and containers, nameplates, toys, business machine components, and blow-molded bottles [NCI, 1987b].

B. Occupational Exposure

Data from the National Occupational Employee Survey (NOES), which was conducted by the National Institute for Occupational Safety and Health (NIOSH) during the years 1981 to 1983, estimated that 62 employees, including 41 female employees, were potentially exposed to pentaerythritol triacrylate. The NOES database does not contain information on the frequency, level, or duration of exposure to workers of any chemicals listed therein [NIOSH, 1991].

As an ingredient of ultraviolet curing inks, pentaerythritol triacrylate is widely encountered in both the printing and photographic industries. The potential for occupational exposure exists for workers handling products containing this compound (printing inks, paints, coatings) [Parker and Turk, 1983]. In addition, the possibility exists for exposure to pentaerythritol triacrylate through air contamination in facilities using high speed printing presses [Björkner *et al.*, 1980].

C. Environmental Occurrence

No data were found on the occurrence of pentaerythritol triacrylate in the environment.

D. Regulatory Status

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

E. Exposure Recommendations

- ACGIH has not recommended an exposure limit for pentaerythritol triacrylate.
- NIOSH has not recommended an exposure limit (REL) for pentaerythritol triacrylate.
- The American Industrial Hygiene Association (AIHA) has set a work place environmental exposure level (WEEL) of 1 mg/m^3 (8-hour time-weighted average for a 40-hour week) [AIHA, 1981].

V. TOXICOLOGICAL EFFECTS

A. Chemical Disposition

1. Human Data

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

2. Animal Data

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

B. Acute

1. Human Data

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

2. Animal Data

Data on the acute toxicity of pentaerythritol triacrylate in animals are presented in Table 1. Additional data are described below.

Table 1. Acute Toxicity of Pentaerythritol Triacrylate in Animals

Route	Species (sex/strain)	Number of Animals	Dose (Confidence Limits)*	Reference
Oral	Rat (NR/NR)	NR	LD_{50} = 1350 mg/kg	AIHA, 1981
Oral	Rat (m or f/ Carworth-Wistar)	NR	LD_{50} = 2.46 ml/kg (1.79-3.39)	Carpenter *et al.*, 1974
Oral	Rat (NR/NR)	NR	LD_{50} > 500-5000 mg/kg	Andrews and Clary, 1986; Celanese, date unspecified
Inhalation	Rat (NR/NR)	NR	No deaths	Celanese, date unspecified
Intraperitoneal	Rat (m and f/ Sprague-Dawley)	5m/5f	LD_{50} = 25 mg/kg (12.5-37.5)	Celanese, 1982c
Intraperitoneal	Rat (m/Sprague-Dawley)	5	LD_{50} = 18.5 mg/kg (not calculated)	Celanese 1982c
Intraperitoneal	Rat (f/Sprague-Dawley)	5	LD_{50} = 27 mg/kg (2-53 mg/kg)	Celanese, 1982c
Dermal	Rabbit (NR/NR)	NR	LD_{50} >2000 mg/kg	AIHA, 1981
Dermal	Rabbit (m/New Zealand)	NR	LD_{50} = 4.00 ml/kg (1.50-10.6)	Carpenter *et al.*, 1974
Dermal	Rabbit (NR/NR)	NR	LD_{50} >200-2000 mg/kg	Andrews and Clary, 1986; Celanese, date unspecified

NR=not reported
m=male
f=female
*=if not listed in the table, the limits were not provided in the study

inhalation, rats

- Carpenter *et al.* reported that in a concentrated vapor inhalation study the maximum time for no deaths was 8 hours for rats exposed to concentrated vapors of pentaerythritol triacrylate. No other data were provided [Carpenter *et al.*, 1974].

intraperitoneal,rats

- Sprague-Dawley albino rats (either sex) were used to determine the intraperitoneal LD_{50} of pentaerythritol triacrylate and the acute toxicity of the chemical when administered by intraperitoneal injection. Any neurological effects produced by this type of acute administration were also noted. Prior to the determination of the LD_{50} value, a range-finding screen was conducted using 20 rats treated with pentaerythritol triacrylate at doses ranging from 3 mg/kg to 300 mg/kg (1 rat/sex/dose level). Based on the mortality observed within 14 days, the doses used for the LD_{50} determination were 3, 10, 30, and 100 mg/kg of pentaerythritol administered by intraperitoneal injection as a 10% solution in dimethyl sulfoxide (DMSO). Control animals received intraperitoneal injections of DMSO.

  For each concentration and control, ten rats (5 males and 5 females) were injected with the chemical and then observed for viability twice daily for two weeks. Each animal was weighed prior to dosing, on the day of dosing, and days 7 and 14 following dosing. In addition, the animals were observed for pharmacologic and toxicologic signs 1, 2, and 4 hours after dosing and daily thereafter for fourteen days. Neurological examinations were conducted 1, 2, 4, and 24 hours after dosing in all animals and then daily through day 14 for animals in the 30 mg/kg dose group. Animals in the 10 mg/kg group that exhibited neurological abnormalities at 24 hours were observed daily thereafter through day 7, and animals that continued to exhibit abnormalities at day 7 were observed through day 14. Animals that succumbed were weighed and necropsied at the time of death, and survivors were weighed, sacrificed, and necropsied at the end of the 14 day observation period.

  From the mortality data of all test animals, the intraperitoneal LD_{50} value for pentaerythritol triacrylate was determined to be 25 mg/kg with confidence limits of 12.5 -37.5 mg/kg. For male rats, the value was found to be 18.5 mg/kg (confidence limits not calculated) and for female rats the LD_{50} value was 27 mg/kg (confidence limits of 2-53 mg/kg). Six of the eight animals that died after receiving 30 mg/kg showed substantial (P value not reported) weight loss at the time of death. Also, weight gains in survivors (2/10) at the 30 mg/kg dose level and in males survivors (5/5) at the 10 mg/kg dose level were lower than those in control animals (P value not reported). Two of the 5 females in the 10 mg/kg group exhibited weight loss at 7 or 14 days. Weight gain in the remaining three animals of this group were comparable to controls.

Signs of neurological toxicity, including ataxia, flaccid limb and body tone, and abnormal righting and visual placing reflexes, were seen in all or most animals at the 30 and 100 mg/kg dose levels, and in 5/10 animals at the 10 mg/kg dose level. No abnormalities were observed in animals that received 3 mg/kg of pentaerythritol triacrylate. More specific data on neurotoxicity are presented in section G.2. Signs of acute toxicity (decreased activity, decreased respiration rates, and abdominal writhing) were seen in the animals at the 10, 30, and 100 mg/kg dose levels on the day of treatment and throughout the post-dose period. The two female survivors in the 30 mg/kg dose group, and 2/5 survivors in the 10 mg/kg group, exhibited decreased activity and respiration rates and decreased food consumption. These animals also exhibited urinary and fecal staining and unthrifty coat. Animals treated with 3 mg/kg of pentaerythritol triacrylate were free of abnormalities except for the presence of swollen eyelids and/or ocular discharge in two animals between days 8 and 14. The authors, however, concluded for unstated reasons, that these symptoms did not represent effects of the test material.

Necropsy observations of all animals that were killed after 14 days revealed abnormalities exclusive to test groups as well as abnormalities that were seen in both test and control groups. Survivors from the control group and groups treated with pentaerythritol triacrylate (3, 10 and 30 mg/kg) showed dark red foci (all test and control animals) and mottled dark red areas on the lungs (5/10 controls, 5/10 in the 3 mg/kg group, 1/10 in the 10 mg/kg group, 1/2 in the 30 mg/kg group). The survivors in the 3 mg/kg dose group did not have any abnormalities that were considered by the authors to represent an effect of pentaerythritol triacrylate. Survivors in the 10 mg/kg group exhibited rounded edges of the liver (3/5 males, 1/5 females), swollen eyes (2/5 males), and pale red adrenals (2/5 females). These symptoms were not seen in control animals, except for one female control that had rounded edges of the liver. In the 30 mg/kg dose group, the two female survivors exhibited swollen eyes, urinary staining alopecia, distended abdomen, rounded edges of the liver, adherence of the liver to the diaphragm, a distended large intestine containing green fluid, and pale red adrenals. Again, these abnormalities were not seen in control groups. No P values were reported for these results.

Necropsy performed on animals that died during the study also showed several abnormalities that were not present in control animals, most of which appeared in the abdominal viscera. For conciseness, Table 2 summarizes the abnormalities found in male and female rats that were treated with 30 or 100 mg/kg pentaerythritol triacrylate and that had expired during the study. Since no P values were provided, only those observations that were seen in three or more animals at either dose have been reported [Celanese, 1982c].

Table 2: Necropsy Findings in Rats Found Dead (Treated with 30 or 100 mg/kg Pentaerythritol Triacrylate)

Necropsy Observation	30 mg/kg*		100 mg/kg**	
	males	females	males	females
Lungs				
pale red	2/5	1/3	4/5	3/5
bright red	3/5	2/3	1/5	4/5
Stomach				
red walls	---	---	5/5	4/5
brown/yellow/green fluid or substance	4/5	2/3	---	---
Small Intestine				
red walls	2/5	1/3	0/5	4/5
distended	1/5	2/3	---	---
mottled red	1/5	2/3	---	---
orange/yellow/green fluid	2/5	2/3	0/5	4/5
brown fluid	2/5	1/3	---	---
Large Intestine				
mottled red	1/5	2/3	---	---
brown fluid	4/5	1/3	---	---
Adrenals				
dark red/red	4/5	3/3	5/5	2/5
Body Cavity				
yellow fluid	---	---	5/5	3/5
red fluid	1/5	2/3	---	---
Miscellaneous				
ocular discharge	4/5	0/3	---	---
urinary staining	1/5	2/3	---	---

--- = did not occur in three or more animals
* = five males and three females examined
** = five males and five females examined

dermal, mice

- In a pilot study conducted prior to a long-term bioassay, C3H/HeJ male mice were used to examine the toxicity and potential for cutaneous irritancy of pentaerythritol triacrylate. The investigation consisted of a single dose dermal experiment and a repeated application test to determine a suitable solvent and test concentration for long-term skin painting. First, five mice were treated with 50 mg of neat pentaerythritol triacrylate to the interscapular area of the shaved backs. The behavior of the mice was observed and the number of deaths were recorded. The next segment of the study involved the application of 50 mg of a 10% solution of pentaerythritol triacrylate in acetone (5 mg/mouse of the test chemical)[2] to the backs of three mice. The mice were treated twice a week for two weeks. The final step involved similar applications using further dilutions of pentaerythritol triacrylate in white mineral oil. No information was given on control animals.

  After receiving the undiluted dose of the chemical, all mice appeared lethargic and inactive. Some (unspecified number) were salivating. After the first day of treatment, 3 of the 5 mice had died and 4 had died after the second day. When the mice were treated with 50 mg of the 10% solution of pentaerythritol triacrylate in acetone (5 mg/mouse), the skin became epilated, crusted and severely burned. Finally, the investigators observed that 50 mg of a 5% solution of pentaerythritol triacrylate in mineral oil (2.5 mg/mouse of the test chemical) did not result in any toxic effects. No signs of toxicity were seen after five weeks. From this data, it was recommended that future long-term skin paint studies (see section V.D.) use pentaerythritol triacrylate as a 5% solution in mineral oil, at doses of 50 mg twice per week, for a final concentration of 2.5 mg/mouse pentaerythritol triacrylate [Celanese, 1982d].

dermal, rabbit

- Studies on the acute effects of dermal application of pentaerythritol triacrylate have shown that the compound has low to moderate dermal toxicity in rabbits. For example, on an irritation scale from 1-10 (10=severe), pentaerythritol triacrylate scored a 2 when tested on male New Zealand albino rabbits at an unspecified dose [Carpenter *et al.*, 1974; DePass, 1982]. In another study, a single dose of an unreported concentration of pentaerythritol triacrylate caused moderate irritation at 24 and 72 hours in the rabbit (unspecified sex and strain). Repeated exposure caused corrosive effects, but no systemic effects were noted [Andrews and Clary, 1986; Celanese, date unspecified]. Finally, a 500 mg unoccluded dose of the compound was reported to result in mild skin irritation [Lenga, 1988; Sax and Lewis, 1989].

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[2]The amount of pentaerythritol triacrylate received by the test animals was interpreted as 50 mg of a 10% solution in acetone (as opposed to as a 10% solution), which would result in a final dosage of 5.0 mg/mouse of pentaerythritol triacrylate. Although unreported by the authors, the calculated values for the final concentrations of pentaerythritol triacrylate (expressed as mg/mouse) for both the acetone and mineral oil solutions, have been reported in this summary.

ocular, rabbits

- Studies on the acute toxicity of pentaerythritol triacrylate to the eye of rabbits indicate that this compound has severe to corrosive effects. In one report, an unspecified dose to the eyes of New Zealand albino rabbits scored a 10 on an irritancy scale of 1-10 (10 indicates severe irritation) [Carpenter *et al.*, 1974]. Another study reported that a single exposure of an unreported dose of pentaerythritol triacrylate was corrosive to the rabbit eye (unspecified sex and strain), with corneal opacity not reversible within seven days [Andrews and Clary, 1986; Celanese, date unspecified]. In addition, 1 mg of pentaerythritol triacrylate applied to the rabbit's eye resulted in severe irritation [Lenga, 1988; Sax and Lewis, 1989].

C. Prechronic

1. Human Data/Case Reports

dermal, human

- Pentaerythritol triacrylate was experimentally tested for sensitization potential in eleven human volunteers ages 18-25. For each subject, a 10% solution of pentaerythritol triacrylate was applied to the extensor surface of the arm on "A1-Test-Strips" covered with Dermicel tape. The patch was removed daily and reapplied if there was no evidence of inflammation. The duration of the induction period was unreported. Eight of the eleven subjects participated in the challenge tests four weeks after the initial patches were applied. Patches containing 0.1% pentaerythritol triacrylate in petrolatum were applied to subjects' upper backs in a similar fashion to the induction tests. The patches were removed after 48 hours and the pressure effects of the strips were allowed to fade. The sites were then examined and scored on a scale from 0 to 3+, with a 0 score indicating a negative reaction. Positive reactions were observed in 6 subjects. One subject had only macular erythema (1+), four exhibited a oedematous or vesicular reaction (2+), and one subject had a severe spreading, ulcerative reaction (3+). In this experiment, pentaerythritol triacrylate was shown to be a cutaneous sensitizer in humans [Nethercott, 1978].

A summary of the following case reports concerning potential exposure to acrylates and the subsequent patch tests conducted with pentaerythritol triacrylate is presented in Table 3.

dermal, human

- Six workers at four different printing plants where a new printing method had recently been introduced developed symptoms of dermatitis after exposure to ultraviolet curing inks. The symptoms started in three patients 3-4 weeks after exposure, in 2 patients 6 months after exposure, and in one patient 8 months after exposure. The sixth patient was reported to have had atopic dermatitis as a child. In each patient the symptoms began as itching on the forearms, face, and eyes with some skin irritation, and developed into dermatitis with erythema and scaling. Upon continued exposure, a severe contact eczematous reaction developed.

All subjects were patch tested with each component of the printing ink, as well as the ink itself. They were also patch tested with pentaerythritol triacrylate, a multifunctional acrylate, also reported to be used in this type of ink. The duration of the tests was not reported. Although six patients tested positive to patch tests with 0.5% and 0.1% trimethylolpropane triacrylate (TMPTA) in acetone, the multifunctional acrylate present in this ink formulation, only 4 out of 6 subjects tested positive to 0.1% pentaerythritol triacrylate in acetone. The four workers positive to pentaerythritol triacrylate reported previous exposure to similar ultraviolet printing inks. However, since no information was available on the composition of these inks, it was impossible to determine whether a cross-reaction between pentaerythritol and trimethylolpropane triacrylate occurred. None of the 30 control subjects reacted to the ink. Four additional control workers, however, showed slight brown-red outlined erythema without infiltration with pentaerythritol triacrylate and TMPTA. These were considered to be weak irritant reactions. [Bjorkner *et al.*, 1980].

<u>*dermal, human*</u>

- A 61-year-old male painter, who had been employed for more than 25 years by a wood products company, developed eczematous dermatitis of the hands, arms, trunk, and legs within weeks after his company switched from oil-based paint to an acrylic paint system. The new system employed by the company contained 1-3% of a polyfunctional aziridine cross-linking hardener, which was composed of a multifunctional acrylic monomer, such as pentaerythritol triacrylate, at residual concentrations ranging from 3-5%. The concentrations of the multifunctional acrylic monomer (in this case trimethylolpropane triacrylate) in the paint system ranged from 0.03-0.15%. The patient was exposed to the acrylic paint system while mixing the paint, loading the paint sprayer, and standing in the mist created by this rapidly moving, high-pressure sprayer. He did not wear protective clothing and did not work in a well-ventilated area. The patients dermatitis persisted long after he left his job due to potential contamination in his home environment.

  Patch tests on the patient were done with 0.2% pentaerythritol triacrylate, full strength primer (without cross-linker), and the full strength cross-linker, all in petrolatum. The pentaerythritol triacrylate was applied to the upper portion of the back and kept in place for 48 hours. The primer and the cross-linker were applied as open patch tests to the anterior upper portion of the patient's arm and kept in place for 48 hours. The results were read 15 minutes after the patches were removed, and at one week. Positive reactions were seen to both the pentaerythritol triacrylate and the full strength cross-linker at 48 hours and one week. The reaction to the cross-linker persisted for weeks. To rule out an irritant reaction, the patient was tested with the cross-linker at concentrations of 1.0%, 0.5%, and 0.1% in petrolatum and ethyl alcohol. Positive reactions were seen to all concentrations in both solvents; the reactions to the petrolatum mixtures were more severe. Normal volunteers (n=7) serving as controls had no reaction to the above test doses of the cross-linker in petrolatum. Also, 50 additional subjects showed no reactions to 0.1% cross-linker in

petrolatum. The study also noted that since the patient had been exposed only to a cross-linker composed of trimethylolpropane triacrylate, his reaction to pentaerythritol triacrylate could be attributed to cross-sensitization [Cofield *et al.*, 1985].

dermal, human

- Four workers in an industry producing plastic flooring material developed contact dermatitis on the hands and face after a one-year exposure to a new varnish top coat. The number of workers handling the varnish varied between 10 and 30. The varnish consisted of a polyurethane dispersion and a polyfunctional aziridine hardener (about 3% by weight), and additives. The hardener was made by reacting propyleneimine (maximum of 0.1%) with a polyfunctional acrylate (3-5% by weight). Although the hardener in this case was composed of trimethylolpropane triacrylate (TMPTA), pentaerythritol triacrylate can also be substituted as the hardener in the varnish.

  All four patients tested positive to patch tests (duration unspecified) with 0.1% (v/v) hardener in acetone, and to a 0.1% (v/v) solution in acetone of the polyfunctional acrylate found in the hardener (trimethylolpropane triacrylate). Two patients also reacted to 0.1% pentaerythritol triacrylate in acetone. Patch tests done with the polyurethane dispersion and the other components of the top coat were negative. Patch tests with the hardener at 1% in acetone were given to 12 control subjects, while tests with the hardener at 0.1% in acetone were given to 33 subjects. All control tests were negative. In addition, the batch formulation (specifications not reported) that had produced the original positive allergic reactions in the four patients did not result in any reactions in 10 controls. The authors concluded that the hardener (TMPTA), and not the other products used in the flooring material, caused the dermatitis. The reactions to pentaerythritol triacrylate may be attributed to cross-sensitization [Dahlquist, *et al.*, 1983].

dermal, human

- The addition of 2 new multifunctional acrylates, trimethylolpropane triacrylate and pentaerythritol triacrylate, as components of a radiation drying ink in an ink formulation facility, was associated with eczematous dermatitis in 5 of 26 employees (duration of exposure not reported). 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, who also cleaned containers, developed eczematous eruptions on his eyelids, wrists, hands, and fingers. This subject reportedly rubbed his eyes when his hands were contaminated with ink ingredients. A 53-year-old male, who weighed radiation-dried ink ingredients, developed eczematous dermatitis on his ears, forearms, and fingers. A 63-year-old male mill hand developed eczematous dermatitis on his forearms, hands, fingers, and loin area. Finally, a 37-year-old male production manager developed erythema and isolated papules on his left wrist, which 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 testing was done individually with each component of the ultraviolet inks used in the plant, including a 0.2% solution of pentaerythritol triacrylate in petrolatum. All dilutions were previously determined to be non-irritating. Tests were also performed with three ink varnish formulations containing 0.2% of the pentaerythritol triacrylate in petrolatum. Results were recorded after 48 hours. Four of the five patients reacted positively to pentaerythritol triacrylate and the three varnish formulations containing pentaerythritol triacrylate. Although the fifth patient did not have significant reactions at 48 or 72 hours, he did exhibit an irritant dermatitis following patch testing with pentaerythritol triacrylate. No reactions were seen to the other components of these varnish formulations. All subjects sensitized to pentaerythritol triacrylate also reacted to trimethylolpropane triacrylate, a similar polyfunctional acrylate monomer. However, since all subjects had potential exposure to both compounds, it could not be determined whether the multiple reactivity was a result of cross-sensitization or concomitant sensitization. No data were provided on control group testing [Emmett, 1977].

dermal, human

- Approximately 58 employees in one plant were potentially exposed to an ultraviolet cured ink manufacturing process between February and June of 1975. Between March and June, eight men, ages 24-62, developed symptoms consistent with allergic contact dermatitis. Of the affected workers, four worked as weighers or foremen in the mixing room, three as weighers or millhands in the milling operations, and one as a stockman. None of the patients had a past history of skin disease or atopy. Symptoms included recurrent, pruritic and erythematous eruptions, often accompanied by papules, vesicules and scaling. These eruptions occurred on areas of the body consistently exposed and unprotected (face, forearms, neck, ears, and hands). In 6 of the 8 cases, the symptoms were observed 1-2 days after working with the ultraviolet inks. In one case (stockman), no correlation was seen between the exacerbation of his dermatitis and handling of a particular chemical.

  For all patch tests, the test materials were applied to the upper back on 3.8 square centimeter patch test plasters and occluded with surgical tape. Patches were removed after 48 hours and the sites were examined one hour later. In cases of mild or questionable readings, additional data were recorded 72 hours after application. All compounds were tested at concentrations found to be non-irritating in patch tests on normal, unaffected volunteers. For pentaerythritol triacrylate, all patients were tested with a 0.2% solution in petrolatum. Other acrylates tested included trimethylolpropane triacrylate and 1,6-hexanediol diacrylate. The results of the patch test show 4 of the tested subjects had positive reactions to pentaerythritol triacrylate, and in three cases, the results were categorized as strong edematous or vesicular reactions. The fourth case showed a weak (nonvesicular) reaction and the fifth patient had a doubtful reaction. From this data, the authors concluded that the multifunctional acrylic monomer, pentaerythritol triacrylate, is a strong allergen capable of sensitizing a significant percentage of the work force exposed to the compound. The authors noted that some of the observed reactions represent cross-reactions, but since the employees were potentially

exposed to each of the materials, cross-sensitization could not be evaluated [Emmett and Kominsky, 1975; Emmett and Kominsky, 1977].

dermal, human

- In an ink manufacturing plant, 19 workers exposed to ultraviolet inks for an unspecified time developed skin and conjunctival reactions. Twelve employees developed itchy rashes on various skin sites including the arms, hands, wrists, face, neck and thighs. Seven workers exhibited irritation of the eyes and eyelids, and one mixer developed swelling of the face, lips, and hands (case 18). Two cases with dermatitis and one with conjunctivitis displayed symptoms without having direct contact with the ink when working near mills grinding ultraviolet ink. This observation suggests an airborne method of exposure.

  The patients were patch tested with several acrylate compounds, including a 0.1% solution of pentaerythritol triacrylate in petrolatum. This concentration was shown to be non-irritating to 15 control subjects. Patches were applied to the upper back on "A1-Test-Strips" and the sites were examined after 48 hours once the pressure effect of the strips had resolved. Case 18 was not tested, since his symptoms (swelling of face and lips) were determined not to be occupationally related. Seven of the patients tested reacted positively to pentaerythritol triacrylate. Four exhibited a severe spreading, bullous or ulcerative reaction (3+ score); two showed a oedematous or vesicular reaction (2+ score); and one had a less acute macular erythema (1+ score). The authors concluded that these seven cases were sensitized to pentaerythritol triacrylate, which was handled by each worker as a raw material. The remaining cases were classified as either irritant contact dermatitis or irritant contact conjunctivitis [Nethercott, 1978].

dermal, human

- Seven out of ten workers (2 males, 5 females) who worked in a plant that manufactured plastic food containers developed various cutaneous conditions. The symptoms ranged from severe eczematous dermatitis of the dorsal hands, forearms, arms, neck, and eyelids to erythematous scaling in distinct patches on the dorsal hands. The affected employees were involved in an offset printing process that applied print to the exterior of plastic containers and then dried the ink with intense ultraviolet lamps. Exposure to the inks (duration unreported) occurred when the workers filled reservoirs, mixed the ink formulations, and cleaned the presses. Due to poor safety practices (gloves were seldom worn), the workers were at risk to skin contamination with any of the components of this ultraviolet curing system.

  All seven patients were patch tested with several potential allergens, including pentaerythritol triacrylate, urethane acrylate, and several epoxy acrylate resins. Each substance was tested at a concentration of 0.1% in petrolatum. This dose had been shown to be non-irritating in 20 healthy volunteers. Patches were applied to the upper back of each subject on "A1-Test-Strips" secured with Dermicel tape and then removed after 48 hours. Once the pressure effect of the patches had resolved (30 minutes), the sites were examined and scored. Reexamination was done at 72 and

96 hours. The scoring system used was recommended by the International Contact Dermatitis Group.

Although 5 out of 7 workers tested positive to urethane acrylate, only one patient also showed a positive reaction to pentaerythritol triacrylate. This machine operator exhibited a spreading, ulcerative reaction (3+ score) at both 48 and 96 hours. Since the chemical structures of these two compounds differ, and no contamination of urethane acrylate with pentaerythritol triacrylate was shown by chemical analysis and the individual had been exposed to both substances, the investigators concluded that these reactions did not represent cross-sensitization, but rather concurrent sensitization [Nethercott, *et al.*, 1983].

dermal, human

- In 1976, a factory installed three flatbed letterpresses to economize its commercial printing process. To ensure rapid drying of the ink and avoid smudging of the print during its passage through the system, ultraviolet inks containing acrylate polyesters were used. In January of 1977, months after the new presses had been installed, a press minder had developed an erythematous pruritic rash on his hands and face. The rash would disappear when he was not exposed to the ultraviolet inks. Also, since the press minder was exposed to direct and reflected ultraviolet light during a process to confirm register or print definition, the possibility of photosensitivity existed. Days later, a second press minder reported similar skin eruptions. Neither worker had any history of atopy or skin disease.

  Each man was patch tested with the three colored inks (red, black, and gold) diluted to 10% in methyl ethyl ketone and with the reducer (pentaerythritol triacrylate). Positive reactions were seen with pentaerythritol triacrylate and the black and gold inks that contained pentaerythritol triacrylate. No reaction was seen with red ink, which did not contain pentaerythritol triacrylate. To clarify the results, a second series of patch tests were run. This time the men were patch tested with pentaerythritol triacrylate at 1.0% and 0.1% in methyl ethyl ketone, the other components of the inks, and two alternative acrylates, trimethylolpropane triacrylate and tripropylene glycol triacrylate. The length of the patch tests was not reported. Both patients had positive patch tests with pentaerythritol triacrylate and the two alternative acrylates, but not with any other component of the inks. No data were provided on control subjects. The investigators concluded that pentaerythritol triacrylate is a strong allergen capable of producing sensitization in a significant percentage of the work force. Positive reactions observed with the two alternative acrylates were believed to be due to cross-sensitization [Smith, 1977].

dermal, human

- The abstract of a Czechoslovakian study reported that, during the course of 5 months, 59 cases of skin disorders of the hands were observed after use of protective gloves made from modified polyvinyl chloride (PVC). The condition reportedly developed after the manufacturers modified the formulation for the gloves by the addition of pentaerythritol triacrylate at 2.2% to improve the mechanical and chemical resistance of the product. Symptoms consisted of a sparse papulovesicular rash on reddened skin of the dorsum of the hand and of the wrist. Patch tests with 0.2% pentaerythritol triacrylate in alcohol produced intense allergic reactions and the concentration of the compound was reduced to 0.1% in vaseline®. In five of the subjects examined following patch testing with 0.1% pentaerythritol triacrylate in vaseline, an annular reaction was observed. The author concluded that the use of pentaerythritol triacrylate, a strong sensitizing agent, for protective gloves was unsuitable [Kalensky, 1987].

Table 3. Case Reports of Workers Prechronically Exposed to Acrylates and the Results of Skin Patch Tests with Pentaerythritol Triacrylate

Number of Workers Potentially Exposed	Number of Workers with Irritation/ Sensitization Reactions	Concentration (%) in Skin Patch Tests (Time)	Number Positive in Patch Test	Reference
unspecified	6	0.1 in ace (NR)	4	Björkner *et al.*, 1980
unspecified	1	0.2 in pet (48 hrs)	1	Cofield *et al.*, 1985
10–30	4	0.1 in ace (NR) 0.01 in ace (NR)	1 1	Dahlquist *et al.*, 1983
26	5	0.2 in pet(48 hrs.)	4	Emmett, 1977
58	8	0.2 in pet (48 hrs.)	4	Emmett and Kominsky, 1975
unspecified	19*	0.1 in pet (48 hrs.)	7/18	Nethercott, 1978
10	7	0.1 in pet (48 hrs.)	1	Nethercott *et al.*, 1983
unspecified	2	1.0 in mek (NR) 0.1 in mek (NR)	2 2	Smith, 1977
unspecified	59	0.2 in alcohol 0.1 in vaseline®	NR** 5	Kalensky, 1987

pet=petrolatum
ace=acetone
mek=methyl ethyl ketone
NR=not reported
NR**=not reported in abstract
* = only 18 workers were patch tested

3. Animal Data

dermal, guinea pigs

- The sensitization potential of pentaerythritol triacrylate was tested using 15 albino Hartley/Dalkin guinea pigs (unspecified sex) in a typical guinea pig maximization test. The animals were exposed to pentaerythritol in stages. Prior to the first stage, topical and intradermal irritancy tests were performed on 20 control animals. For the first stage, the animals received a row of three intradermal injections into each shoulder for a total of 6 injections. The injections were composed of (1) 0.1 ml Freund's complete adjuvant (FCA), (2) 0.1 ml of 0.05% pentaerythritol triacrylate in propylene glycol, and (3) 0.05 ml of 0.1% pentaerythritol triacrylate in propylene glycol with 0.05 ml of FCA. After one week, the shoulder was clipped and shaved. A 25% solution of pentaerythritol triacrylate in petrolatum was applied to the injection sites and the patches were held in place by elastic adhesive bandages for 48 hours. After a two-week non-treatment period, the animals were challenged with patches containing 10% pentaerythritol triacrylate in petrolatum applied to a shaved area of the flank. The patches were kept in place for 24 hours. Twenty-four hours after removal of the bandages, the sites were examined and scored on a scale from 0 to 3+, with 0 indicating no reaction and 3+ indicating intense redness and swelling. Thirteen of the fifteen test animals reacted positively to pentaerythritol triacrylate and three of these reactions scored greater than 1. The specific scores for each animal were not reported. At concentrations greater than 10%, pentaerythritol triacrylate caused inflammation in control animals [Nethercott, 1978].

dermal, guinea pigs

- Albino Hartley/Dalkin female guinea pigs were used in a guinea pig maximization test to examine the sensitization potential of pentaerythritol triacrylate. In a preliminary study, 10 control guinea pigs were used in irritancy tests to determine the concentrations of pentaerythritol triacrylate to be used in the induction and challenge tests.

  Induction was performed in two stages. First, each animal was injected intradermally on either side of the shoulder region with the following formulations (3 pairs of injections per animal): (1) 0.1 ml of 0.001% pentaerythritol triacrylate (5 animals), 0.01% pentaerythritol triacrylate (15 animals), 0.05% pentaerythritol triacrylate (5 animals) or 0.5% pentaerythritol triacrylate (10 animals) in propylene glycol; (2) 0.05 ml of FCA mixed with 0.05 ml of the appropriate concentration (0.001, 0.01, 0.05 or 0.5%) of pentaerythritol triacrylate in propylene glycol; (3) 0.1 ml of Freund's complete adjuvant (FCA). After one week, the shoulder region was clipped and pentaerythritol triacrylate in petrolatum at the appropriate concentration (0.001, 0.01, 0.05, or 0.5%) was applied to the injection site on Whatman filter paper. The patch was kept in place for 48 hours. Two weeks after this topical exposure, the animals were subjected to challenge patch tests. Pentaerythritol triacrylate was applied at a non-irritating concentration (unreported) to a shaved area of the flank as described in the induction procedure. After 24 hours, the patch was removed. At 48 hours, the sites were examined for evidence of a reaction.

Using probit analysis, the percentage of animals sensitized at each concentration was calculated. At 0.001%, only 15.4% (2/5) of the animals were sensitized to pentaerythritol triacrylate. This percentage increased to 55.6% (8/15) for animals induced with 0.01% pentaerythritol triacrylate, 93.3% (4/5) for animals induced with 0.05% pentaerythritol triacrylate, and 100% (10/10) for the 0.5% pentaerythritol triacrylate induced group. The intradermal concentration required to sensitize half the guinea pigs ($IDSC_{50}$) was calculated to be 0.005%. This value indicates that pentaerythritol triacrylate possesses a high potential to induce cutaneous allergy in guinea pigs [Nethercott *et al.*, 1983].

dermal, guinea pigs

- Outbred Hartley guinea-pigs of both sexes were used to examine the contact sensitization potential of pentaerythritol triacrylate using five different immunization protocols: the Polak method, the split adjuvant method, the maximization method, and two epicutaneous methods. Unless stated, the number of guinea pigs used for each procedure was unreported.

  Polak method: On the first day of this procedure, the test animals received 4 footpad injections of a 0.1 ml emulsion containing 2 mg/ml pentaerythritol triacrylate in ethanol:saline (1:4), in Freund's complete adjuvant (FCA). Another injection of 0.1 ml of the emulsion was given into the nape of the neck, resulting in a total dose of 1 mg pentaerythritol triacrylate per animal. On day 7, open skin testing was done by dropping 0.02 ml of a solution of pentaerythritol triacrylate in acetone:olive oil (4:1) onto a shaved flank of the animal. Pentaerythritol triacrylate was used at concentrations of 0.1 and 0.25%, which were described as the maximum concentrations that did not result in non-specific irritation. The skin tests were repeated weekly at different sites on the flank for up to 12 weeks.

  Split adjuvant method: On day zero, 0.05 ml of FCA was injected into 5 sites on the dorsal shaved flank of the guinea pig. One day later, 0.1 ml (100 µg) of pentaerythritol triacrylate in ethanol:saline (1:100) was injected intradermally into the same five sites. Finally, on day 14, skin tests were begun, as described in the Polak method, and continued for 12 weeks.

  Maximization method: On day zero, guinea pigs received intradermal injections onto shaved sites on the back of the neck. Each animal received two injections of 0.1 ml FCA, 0.1 ml of 1% pentaerythritol triacrylate in saline, and 0.1 ml of 1% pentaerythritol triacrylate in FCA. At day 14, skin tests (as described above) were done for up to 12 weeks.

  Epicutaneous method (A): On day zero, 0.1 ml of a 0.3 M solution of pentaerythritol triacrylate in 95% ethanol:2-methoxyethanol:Tween 80 (9:9:2) was dropped onto a marked area of the animal's shaved flank. This procedure was repeated on days 2, 4, 7, 9, and 11. On day 28, the weekly skin testing was begun (as described above) and continued for up to 12 weeks.

Epicutaneous method (B): On day zero, 0.1 ml of 0.25% pentaerythritol triacrylate in acetone:olive oil (1:1) was applied to a marked and shaved area of the back of the neck on six test animals. This was repeated on days 1, 2, 3, 4, 7, 8, 9, 10, and 11. On day 21, the skin test procedures began (as described above) and continued for up to 12 weeks.

All skin test sites were observed at 24, 48, and 72 hours. The data reported show that both the Polak method and the epicutaneous (B) method were able to induce contact sensitivity to pentaerythritol triacrylate. With the Polak method, six guinea pigs exhibited positive skin reactions on the 14th day of the skin test studies. The reactions were scored using a 0-3 scale (0= no reaction, 3 = a red and elevated reaction). Scores of 1.1 using 0.1% pentaerythritol triacrylate and 1.4 using 0.25% pentaerythritol triacrylate were determined. When immunized using the epicutaneous method (B), 5 out of 6 animals were sensitized to the compound. The severity of the reactions was not specified. Results concerning the other methods of induction were not reported. However, it can be assumed that pentaerythritol triacrylate did not induce sensitization reactions using these protocols. Information concerning control groups was not reported [Parker and Turk, 1983].

dermal, guinea pigs

- Albino female guinea pigs of the Dunkin-Hartley strain were used in a guinea pig maximization test to determine whether animals sensitized with trimethylolpropane triacrylate would exhibit cross-sensitivity when challenged with other multifunctional acrylates including pentaerythritol triacrylate. Prior to induction studies, control guinea pigs were used to determine the optimal sensitization concentration that would not result in systemic toxicity and challenge patch test concentrations that would not give irritant reactions.

  For induction, an unreported number of test animals were given three intradermal injections into each side of the shoulder region. The formulations were: (1) 0.1 ml of Freund's complete adjuvant (FCA) mixed with an equal amount of water; (2) 0.1 ml of 1.0% trimethylolpropane triacrylate in olive oil and; (3) 0.1 ml of 1.0% trimethylolpropane triacrylate in olive oil with an equal amount of FCA. One week after the injections, a topical patch consisting of 25% trimethylolpropane triacrylate in petrolatum was applied to the reshaved injection sites on Whatman paper. The patch was held in place for 48 hours. Two weeks after this induction procedure, 24 animals were challenged with patch tests of 0.5 and 0.1% pentaerythritol triacrylate in petrolatum. For these tests, an occluded patch was applied to a clipped and shaved area of the flank for 24 hours and then removed. Each site was examined for evidence of a positive reaction. During induction, control groups (unspecified number of animals) were intradermally injected with FCA and olive oil, and treated topically with only olive oil. In challenge tests, 24 control animals were also patch tested with pentaerythritol triacrylate at the same concentrations.

The results of the challenge tests show that 18/24 guinea pigs (75%) sensitized to trimethylolpropane triacrylate gave positive reactions when challenged with 0.5% pentaerythritol triacrylate. Twelve of 24 animals (50%) reacted to pentaerythritol triacrylate in a 0.1% test concentration. Control animals, tested simultaneously, did not react to challenge with pentaerythritol triacrylate. In this study, trimethylolpropane triacrylate sensitized 67% of the guinea pigs and is consequently considered a strong allergen. Since 75% of the trimethylolpropane triacrylate-sensitized animals also reacted to pentaerythritol triacrylate, cross-sensitivity between the two compounds is suggested [Björkner, 1980].

dermal, guinea pigs

- Guinea pig maximization studies were conducted to determine the sensitizing capacity of multifunctional acrylates including pentaerythritol triacrylate and the simultaneous reaction pattern of pentaerythritol triacrylate with other structurally-related acrylic compounds. Thirty female albino guinea pigs of the Dunkin/Hartley strain were used for each acrylate tested: 15 as test animals and 15 as control animals. In the first stage of induction, guinea pigs were intradermally injected with the commercial form of pentaerythritol triacrylate (PETA-3) or pentaerythritol tetraacrylate (PETA-4) in olive oil:acetone (9:1). The final intradermal concentration for PETA-3 and PETA-4 was 1% (w/w). For the subsequent topical induction, patches containing 25% PETA-3 or PETA-4 in petrolatum were applied to the animals under the same conditions as the study described above [Björkner, 1980]. Control animals were sensitized using the same procedure.

  Guinea pigs were given challenge patch tests with the commercial forms of PETA-3 and PETA-4, the "purified" forms of PETA-3 and PETA-4, pentaerythritol, and two structurally similar acrylates, all in petrolatum. In two separate tests, one week apart, approximately 0.015 g of each chemical was applied to test sites on a shaved area of the animal's flank. The duration of exposure was not reported in this study. The control animals were challenged with the same chemicals at the same doses. Forty-eight hours after the first challenge, test animals received a booster dose consisting of a 1% solution of the sensitizing chemical (PETA-3 or PETA-4) in olive oil:acetone (9:1) injected intradermally into the neck. For control animals, the booster injections consisted of only olive oil.

  Of the animals sensitized to commercial PETA-3, 10/15 (67%) reacted to commercial pentaerythritol triacrylate in challenge tests. Six of these animals also reacted to purified PETA-3, seven to commercial PETA-4, 3 to purified PETA-4, 3 to pentaerythritol, and 7 to trimethylolpropane triacrylate (TMPTA). Only one animal of the 15 sensitized to commercial PETA-4 reacted to this compound in challenge tests. The same animal reacted to purified PETA-4, purified PETA-3, and TMPTA. Two other animals that did not react to PETA-4 reacted to PETA-3 (commercial form only). None of the control animals reacted positively to any of the compounds tested.

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 shows 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. In addition, the possibility of cross-reactivity between pentaerythritol triacrylate and TMPTA was supported by the results of this study [Björkner, 1984].

dermal, guinea pigs

- In a study to determine whether lymph node cell proliferation correlates with the induction of a positive immunologic response in guinea pigs (see section V.G), outbred Hartley guinea pigs of either sex were used to assess the contact sensitization potential of pentaerythritol triacrylate using the Polak method of immunization. Five guinea pigs were injected subcutaneously into the 4 footpads with a 0.1 ml emulsion containing pentaerythritol triacrylate in ethanol:saline (4:1), in Freund's complete adjuvant. Another 0.1 ml injection of the same composition was given into the nape of the neck. Although the specific concentration of pentaerythritol triacrylate was not reported in this study, the final dose received by the test animals was approximately 11.5 µmol of pentaerythritol triacrylate. In addition to this immunization procedure, five guinea pigs were sensitized epicutaneously by applying 50 µl of a 1M solution of pentaerythritol triacrylate in acetone:olive oil (4:1) to the dorsum of the animal's right ear. One and two weeks after induction, open skin tests were conducted by dropping 0.02 ml of a solution of pentaerythritol triacrylate in acetone:olive oil (4:1) onto a shaved area of the flank. Pentaerythritol triacrylate was used at concentrations of 0.1 and 0.25%, which had been shown not to produce any nonspecific irritation. The reactions were then read at 24, 48, 72 and 96 hours after skin testing, assessed according to degree of severity, and rated on a scale from 0-3 (0=no change, 3=red and elevated). The scores from five animals were averaged for each skin test concentration.

  Immunization with pentaerythritol triacrylate by the Polak method resulted in positive skin reactions in the guinea pigs, whereas sensitization was not induced by epicutaneous application. The reported skin test scores, recorded one and two days after skin test patches were removed, are presented below in Table 4 [Bull *et al.*, 1985].

Table 4. Mean Skin Test Reactivity in Guinea Pigs From Patch Tests One and Two Weeks After Sensitization to Pentaerythritol Triacrylate

Induction Method	7 Days				14 days			
	24 hours		48 hours		24 hours		48 hours	
	0.1%	0.25%	0.1%	0.25%	0.1%	0.25%	0.1%	0.25%
Polak	0.2	0.5	0.8	1.5	0.8	1.3	1.2	2.1
Epicutaneous	0.1	0.1	0.1	0.2	0.1	0.2	0.2	0.2

dermal, guinea pigs

- In a paper by Parker *et al.*, the study described above [Bull *et al.*, 1985] was extended to examine the ability of pentaerythritol triacrylate to induce a tolerance to the contact reactions seen in guinea pigs. The cross-reactivity patterns of pentaerythritol triacrylate were also examined. In this investigation, the Polak method of induction, the skin test protocol, and the scores of these tests (Table 4) described above were re-reported for completeness. The details will not be re-described here.

  For tolerance and cross-reactivity tests, outbred Hartley guinea pigs of either sex were used. To assess cross-reactivity, groups of five test animals were immunized with pentaerythritol triacrylate and skin tested with pentaerythritol triacrylate, as well as additional acrylates of similar structure (concentrations unspecified). The procedure for all patch tests is described in detail in the study above. In an attempt to induce tolerance epicutaneously, 0.1 ml of a solution of 10% pentaerythritol triacrylate in acetone was applied to the dorsum of the animals ear 14 and 7 days before immunization with methyl acrylate or trimethylol propane triacrylate (concentrations unspecified). The control group was not pretreated with pentaerythritol triacrylate. Skin tests on the test animals and the control animals were conducted with the immunizing compound on day 7 after induction. Methyl acrylate was skin tested at 1% and 5%, while trimethylol propane triacrylate was tested at 0.25% and 0.5%. Again, for skin tests at each concentration, the mean reactivity score of 5 animals was reported 24 and 48 hours after the patches were removed.

  Animals sensitized to pentaerythritol triacrylate also reacted to trimethylolpropane triacrylate (TMPTA), 4-vinyl pyridine (4VP), methyl acrylate (MeA), and methyl vinyl ketone (MVK). The relative degree of cross-reactivity was assessed as a percentage of the contact reaction induced by the immunizing chemical. In the case of TMPTA, greater than 80% of the reaction was induced by pentaerythritol triacrylate, while 60-80% of the reaction to 4VP was induced by this compound. For MeA and MVK, only 20-60% of the contact reactions seen were induced by pentaerythritol triacrylate. These numbers indicate that pentaerythritol triacrylate does have the potential to cross-react with several other chemicals.

The results of the tolerance study show that treatment with pentaerythritol triacrylate prior to immunization does not suppress the contact reactions to methyl acrylate or trimethylolpropane triacrylate. For example, without pretreatment, immunization with 5% MeA produced a skin test reaction of 0.9±0.6 and 1.7±0.4 at 24 and 48 hours, respectively. With a pretreatment application of pentaerythritol triacrylate, skin test scores were 1.3±0.6 and 1.4±0.9 at 24 and 48 hours, respectively. Immunization with 0.5% TMPTA without epicutaneous application of pentaerythritol triacrylate resulted in skin test scores of 0.4±0.4 and 1.5±0.9 for the two time points. With application of pentaerythritol triacrylate, the scores were 0.2±0.2 and 1.2±1.0 for 24 and 48 hours, respectively. According to these results, pentaerythritol triacrylate was determined not to induce epicutaneous tolerance to these compounds. The authors also concluded that strong cross-reactivity between compounds is not alone sufficient to produce epicutaneous tolerance [Parker *et al.*, 1985].

dermal, guinea pigs

- The cross-reaction patterns of pentaerythritol triacrylate and other selected acrylates were investigated using the guinea pig maximization test on female outbred SSc:AL guinea pigs. Prior to induction, naive guinea pigs were used to determine the minimally irritating and maximally non-irritating concentrations (irritation threshold) for intradermal and topical doses. Induction was carried out with the following di- and tri- methacrylates: triethyleneglycol dimethacrylate (TEDMA), methylmethacrylate (MMA), trimethylolpropane trimethacrylate (TMPTMA), and ethyleneglycol dimethacrylate (EDMA). The challenge tests of relevance were done using pentaerythritol triacrylate.

  For the first stage of induction (day 0), three pairs of intradermal injections were given to the animal in a shaved area of the shoulder. The injections were as follows: (1) 2 x 50 µl of Freund's complete adjuvant (FCA) in sterile water (1:1); (2) 2 x 50 µl of a 5% solution of the test chemical in soy bean oil; and (3) 2 x 50 µl of a 5% solution of the test chemical in FCA and water (1:1). The control animals received the same treatment without the test substance. On day 7, the same area of the neck was clipped and 250 mg of 10% sodium dodecyl sulfate in petrolatum was applied to the site and left uncovered for 24 hours. On day 8, 400 µl of the test compound (100%) were applied to the test area on a piece of Whatman filter paper which was left in place for 48 hours. The control group received the same treatment, substituting the test substance with petrolatum. Challenge patch tests were conducted on day 21 on a shaved area of the animal's flank. Up to six patches, containing 25 µl of 2% pentaerythritol triacrylate, were applied and secured for 24 hours. Readings were made 48 and 72 hours after the application of the patches and the sites were scored on a scale of 0-3 (0=no reaction, 3=intense erythema and marked edema). Controls received identical treatment.

Seven out of twenty animals induced with TEDMA and 9/19 animals induced with TMPTMA also reacted to pentaerythritol triacrylate in challenge patch tests. No cross-reaction with pentaerythritol triacrylate was seen in animals induced with either MMA or EDMA. No reactions were seen in the control animals. The author concluded that pentaerythritol triacrylate is a potent sensitizer that can cross-react [Clemmensen, 1985].

dermal, rabbits

- Twenty New Zealand White rabbits (5 males and 5 females for both test and control groups) were used to assess the dermal irritation caused by pentaerythritol triacrylate. Prior to treatment, hair was clipped from the exposure site on the back of each animal. For five animals (3M and 2F or 2M and 3F), these exposure sites were further treated by abrading the area with an inverted clipper prior to treatment and twice weekly thereafter. A solution of pentaerythritol triacrylate (vehicle unreported) was applied to the test sites at a dose level of 200 mg/kg daily, 5 days a week for two weeks unoccluded. Animals were observed daily for evidence of dermal or toxic effects. After the last day of treatment, six animals per group (3 abraded, 3 nonabraded of either sex) were sacrificed and the remaining animals (4/group) were sacrificed after day 30. Animals were observed daily for dermal or systemic effects, and the weights of each animal were taken prior to treatment, weekly during treatment, and after death. All animals survived the treatment period, and complete necropsies were performed on all animals after sacrifice.

  From the results, it was found that the weight gain in test animals was comparable to the weight gain in the control group, with the exception of one male and one female that exhibited slight weight losses (-0.2 kg). Motor activity decrease and nasal discharge also occurred in several animals, primarily during the treatment period. Gross dermal observations revealed that all test animals treated with pentaerythritol triacrylate exhibited severe erythema with necrosis and eschar formation, fissuring, desquamation, and slight to moderate edema and atonia. While edema, atonia and fissuring subsided during the post-treatment period, the other signs persisted through termination of the study. Exfoliation of eschar tissue occurred during the last week of the post-treatment period. Other than a few rabbits with slight erythema and desquamation, control animals were free of abnormalities. Gross post-mortem observations of selected tissues revealed discolorations of the lungs and kidneys in animals after two weeks of treatment with pentaerythritol triacrylate. In rabbits held for 2 weeks post-treatment, mottled, dark red foci were observed on the surface of the lungs. However, since similar abnormalities were seen in organs of control animals, the authors concluded that they were probably due to infectious etiology and were not treatment related.

Microscopic examinations of treated or exposed skin from rabbits sacrificed following two weeks of treatment (2 males/4 females) revealed severe necrosis of the epithelium and subepithelium (2 males/3 females and 2 males/1 female, respectively) and congestion of the dermis (2 males/3 females). These effects were not observed in control animals. In addition, inflammatory cell infiltrates were seen in the subepithelial connective tissue of all animals treated with pentaerythritol triacrylate. Such infiltrates were only seen in one control animal (female). Other abnormalities seen in treated skin, but not in controls, include subcutaneous edema (1 male/3 females), epithelial hyperplasia (2 females), and hyperkeratosis (2 females). Pathological examination of animals sacrificed at four weeks revealed that the epithelium was intact, but evidence of prior moderate to severe irritation was present. For example, healing of the skin with re-epithelization (hyperplasia), was observed in 2/2 males treated with pentaerythritol triacrylate. These animals also had regions of dense subepithelial fibrosis and regions where normal follicular structures had been destroyed. Control animals examined at four weeks did not show any abnormalities related to treatment with pentaerythritol triacrylate

Microscopic examination of other selected tissues from animals sacrificed after two and four weeks revealed various inflammatory changes in the liver, kidneys, brain, and lungs. However, these lesions were also seen in control rabbits and were not considered by the pathologist to be treatment related. No evidence of systemic toxicity resulting from administration of pentaerythritol triacrylate was observed [Celanese, 1979].

dermal, rabbits

- A 2 week exposure/2 week recovery dermal toxicity study of pentaerythritol triacrylate was done for Celanese Chemical Company in 1981. Again, 20 New Zealand White rabbits were used (5 males and 5 females for test and control groups) and pretreatment of the skin was similar to the procedure described above [Celanese, 1979]. In this study, pentaerythritol triacrylate was applied to the skin of the rabbits at a dose level of 500 mg/kg/day and as a 25 % (w/w) solution in mineral oil. Applications were made daily, five consecutive days a week, for two weeks. The animals were checked twice daily for viability and daily for signs of toxicity and dermal irritation. Weights were recorded prior to treatment and weekly during treatment. A control group consisting of an equal number of rabbits received the same treatment using only mineral oil applications at a concentration of 2.0 g/kg/day. For the test group, necropsies were performed on 6 animals (4 males, 2 females) that died during days 7-15 of treatment. The four survivors were sacrificed, weighed, and necropsied after two weeks. They were not held for the additional two- week recovery period. Six animals from the control group (3 intact, 3 abraded of either sex) were sacrificed after two weeks, and 4 were sacrificed after four weeks. Selected tissues were evaluated for histopathology.

All animals treated with pentaerythritol triacrylate exhibited weight loss (0.1 to 0.7 kg) during the first week of study. Rabbits that survived beyond day 7 continued to lose weight until death or sacrifice. Overall, weight loss ranged from 0.3 to 1.0 kg. All control animals exhibited normal weight gain or no change (one female) during the first two weeks and continued to gain weight during the two-week recovery period. Dermal observations revealed that at day 7, all animals in the test group exhibited moderate to severe erythema and edema, which persisted until death or sacrifice (day 15). At the time of death (spontaneous or sacrifice) most animals also exhibited necrosis and eschar formation (9/10 and 8/10, respectively) and atonia (8/10). A few also showed slight desquamation (4/10) and/or fissuring (2/10). Most animals exhibited hypoactivity, hypopnea, nasal discharge, and food consumption decrease. Some also exhibited soft stool, fecal staining, emaciation, piloerection, hypothermia, and respiratory arrhythmia. Individual animals exhibited ataxia, dry rales, and prostration. Other signs which, according to the authors, probably represent irritation from the test material include hair loss and irritation of the eyes and scrotum. Toxicological signs were generally similar in animals that died spontaneously and those that survived through day 15. Control animals treated with mineral oil showed little or no evidence of dermal irritation or toxicity throughout the study, with the exception of ocular irritation and decreased food consumption in a few animals.

Gross observations from the post-mortem examination of the four test animals sacrificed after two weeks (1 male/3 females) revealed morphological abnormalities of the skin, which were recorded as a slight dark red coloring with red areas accompanied by thickened, hairless scabs. Similar abnormalities were seen on the skin of the six animals (4 males/2 females) that died during the study. Numerous black foci were observed on the stomach of 2 of the 6 animals that died during the study. These foci were not seen in any control animals. Other gross abnormalities seen in animals that were sacrificed, animals that spontaneously expired, and control animals were sporadic and inconsistent. The pathologist concluded that they did not appear related to administration of the test compound.

Histological examination of rabbits treated with pentaerythritol triacrylate and sacrificed at two weeks revealed extensive degeneration of the subcutis and severe epidermal necrosis and ulceration in all 4 animals. Other abnormalities seen in these animals included dermal and subcutis edema (1 male/1 female), dermal hemorrhage and inflammation (2 females), and subcutis inflammation (3 females). The authors report that the absence of epidermal hyperplasia, epidermal hyperkeratosis, and dermal fibrosis or granular tissue reactions suggests marked toxicity and a suppression of tissue repair attempts. All animals that died during the study exhibited degeneration and edema of the dermis and degeneration and inflammation of the subcutis. Microscopic evaluation of these animals also revealed epidermal necrosis (3 males/2 females), epidermal atrophy (2 males), and dermal hemorrhage (2 males, 1 female). A variety of inflammatory changes were also observed in the kidneys, lungs, brain,

and other organs of treated and control animals. These changes were random and without predilection to treatment groups and were interpreted by the pathologist as spontaneous. Other changes were too few or mild to demonstrate definite systemic effect. The pathology report concluded that the evaluation of the animals failed to conclusively demonstrate the presence or absence of systemic toxicity with pentaerythritol triacrylate [Celanese, 1981].

D. Chronic/Carcinogenicity

1. Human Data

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

2. Animal Data

dermal, mice

- A group of forty male C3H/HeJ mice were used to assess the dermal oncogenic potential of a mixture consisting of approximately 25% pentaerythritol triacrylate, 65% of the tetraacrylate, and 10% of the diacrylate. An approximate dose of 3 mg of the test material was applied as a 15% solution in acetone three times per week to a clipped area of the back of each mouse. In preliminary studies, this concentration did not cause gross irritation or weight gain. Two negative control groups were administered acetone, and a positive control group was given 0.03 mg of 0.2% methylcholanthrene. Each control group contained 40 animals. The mice were treated for their complete lifespan, and necropsies were performed at death.

  Mice treated with the test mixture of pentaerythritol triacrylate showed no incidence of skin tumors, in contrast to the positive control group in which 36/40 mice treated with methylcholanthrene developed skin tumors. No clinical or histological signs of chronic toxicity were observed in the animals treated with the test material. The survival rate of test material-treated mice (25 after one year, 16 after 1.5 years, and 5 after 2 years) was not unusual when compared to the acetone controls (P values not reported). According to the results of this study, the authors concluded that the test material is not oncogenic [DePass, 1982; DePass *et al.*, 1985].

dermal, mice

- Forty C3H/HeJ male mice were used to assess the dermal carcinogenic potential of a pentaerythritol acrylate-HF[3], composed principally of pentaerythritol triacrylate. The test substance was applied to the clipped backs of each mouse three times per week by skin painting for the lifespan of the animal. Pentaerythritol triacrylate was used as a 15% solution in acetone at an average dose of 0.0026 grams/mouse/application. A negative control group of 40 mice received similar skin paintings of acetone at an average dose of 0.012 grams/mouse/application. All mice were examined monthly for neoplasms, and necropsies were performed on all animals at the time of death.

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[3]The term "HF" is a Union Carbide Corporation (UCC) definition for "high functionality." Although the test compound contained some pentaerythritol tetracrylate, UCC believes that it is essentially the same material tested by Celanese Chemical company (Celanese, 1981) [Union Carbide, 1988].

No skin tumors were found in mice treated with pentaerythritol acrylate-HF. Only one mouse in the negative control group developed a squamous cell carcinoma of the skin, which may or may not have been related to acetone treatment. Mice in the test group, however, did exhibit an increase in gross hepatic tumors when compared to the acetone-treated group (13/39 v. 4/34, respectively). In those mice examined histologically, the incidences of hepatic tumors in test and control groups were 13/14 and 4/5, respectively. The authors reported that in this study, histological examination was only carried out to confirm gross findings or if unusual lesions were discovered during gross observation. Consequently, there are histology data only for selected tissues of several mice.

Historic control data for the same test species indicate that the incidence of gross hepatic tumors in other negative control groups was not numerically or statistically different (P value not reported) than the incidence seen in the animals of this study treated with pentaerythritol acrylate-HF. The number of hepatic tumors observed in previous studies was higher (13/36) than those observed in the concurrent negative control group of this experiment (4/34). The gross observations of mouse liver tumors, while statistically significant (P value not reported) in this study, would be equivocal when compared to historic controls. Based on this data, Union Carbide Corporation believes that the results of this study do not contain substantial risk information under TSCA Section 8(e) [Union Carbide, 1979; Union Carbide, 1988].

dermal, mice

- C3H/HeJ male mice were used to assess the carcinogenic potential and the chronic dermal toxicity of pentaerythritol triacrylate. Twice a week, 50 mice were given a dose of 50 mg of 5% pentaerythritol triacrylate in white mineral oil (2.5 mg/mouse-see footnote #2). This concentration and solvent were determined in a pilot study to be non-irritating. Three control groups of 50 mice each were also tested. One group received only mineral oil (vehicle control), one group went untreated (negative control), and a third group received 0.5% benzo(a)pyrene in mineral oil (positive control). All substances were applied to the interscapular region of the shaven backs for 80 weeks or until a 1 mm^3 horny lesion appeared on the surface of the skin. When such neoplasms exhibited characteristics of malignancy, the animal was sacrificed and autopsied. In the rare event of tumor regression, treatment was resumed for the duration of the experiment or until the appearance of another tumor. Mice that did not develop neoplasms were sacrificed and autopsied at the end of the treatment period. All surviving mice were observed daily for tumors and signs of toxicity. In addition to gross and histological observations, complete microscopic examinations were done on all mice.

Gross observations of the skin sites indicate that pentaerythritol triacrylate applied repeatedly in non-irritating doses to the same area results in slightly epilated and crusted skin. Similar irritant reactions were not seen in mice treated with mineral oil. Pathological results show that of the 43 test compound-treated mice examined, all developed acanthosis of the epidermis and 39/43 had fibrosis of the dermis. These responses were also found in the negative control and vehicle control groups, and are most likely due to the repeated shavings. Hyperkeratosis was noted in 11 of the test animals and in none of the vehicle or negative control animals.

Only one mouse treated with pentaerythritol triacrylate developed a neoplasm during the skin painting study. By histological examination, this tumor was determined to be a squamous cell carcinoma. The incidence of tumors in mice treated with pentaerythritol triacrylate was much lower that the incidence seen in the positive control group (44/48) (P values not reported). One mouse in the negative control group developed a squamous cell carcinoma, while none of the mice in the vehicle control group developed any type of neoplasm. Mice treated with pentaerythritol triacrylate also exhibited atropy of the gonads, prostatitis, prostatic hyperplasia, and mononuclear infiltrates in the adrenals. In addition, there was an increased incidence of lymphomas in animals treated with pentaerythritol triacrylate (P value not reported). Six mice treated with pentaerythritol triacrylate had lymphomas with spleen or lymph node involvement, while the incidence of lymphomas was 1/49 and 0/48 in the vehicle and negative control groups, respectively. From these data, the investigators concluded that although pentaerythritol triacrylate does not seem to be tumorigenic to mouse skin, it may be absorbed and act as an internal carcinogen to the lymphoid systems [Celanese, 1982d].

dermal, mice

- A peer review of the microscopic evaluation of the Celanese study described above [Celanese, 1982d] was conducted by three pathologists from E. I. DuPont de Nemours. These pathologists analyzed the histology slides from the skin painting study and compared them with the diagnoses and conclusions presented in the original pathology report. The three DuPont pathologists were in substantial disagreement with several of the study's diagnoses. In particular, they believed that lymphoid, granulocytic, and erythrocytic hyperplasia were mistakenly diagnosed as lymphoma in six of the pentaerythritol triacrylate treated mice. As a result, the original study's conclusion of a compound-related increase in malignant lymphoma was found to be invalid. The review pathologists found no evidence of any compound-related increase in neoplasia. In addition, the reviewers believed that liver and kidney sections were inconsistently available and all other tissues were only sporadically present with many histology slides missing from the review material. The tissue recovery rate, therefore, was inadequate to support any conclusions with regard to systemic toxicity or carcinogenicity [E.I. DuPont, 1988].

This review was submitted to the United States Environmental Protection Agency (EPA)[4] and evaluated by a Senior Science Advisor for the Health and Environmental Review Division. After scrutinizing the DuPont report, the advisor concluded that the EPA should not overturn the "limited positive evidence of carcinogenicity" of pentaerythritol triacrylate supported by the study conducted by Celanese Chemical Company for several reasons. First, due to missing material (histology slides), there is no way to determine if the sections available to the DuPont review pathologists were the same sections on which the original conclusion was made. Second, the EPA cannot choose to believe the conclusions of one laboratory over the conclusions of another. A third review would be equally uninformative due to the missing slides. Finally, a pilot experiment for the Celanese study found the acrylates, including pentaerythritol triacrylate, to be systemically toxic, which prompted the complete histological examination. The EPA has recommended that the current categorization of pentaerythritol triacrylate be maintained until a similar long-term dermal exposure study can be completed [USEPA, 1988].

[4]Pentaerythritol triacrylate is listed in the EPA's Toxic Substances Control Act (TSCA) Inventory for 1990. Section 8(a) of TSCA requires chemical manufacturers and processors to report production and exposure-related data on any chemical listed in section 712.18(a). Although the EPA may regulate the chemical in accordance with this information, a listing in TSCA does not confirm the existence of regulation.

E. Reproductive Effects and Teratogenicity

1. Case Reports

No data were found on the reproductive effects or teratogenicity of pentaerythritol triacrylate in humans.

2. Animal Data

unspecified, rats

- In study to examine the teratogenic potential of multifunctional acrylates, 20 pregnant rats (unspecified strain) were given a single dose of pentaerythritol triacrylate during days 6-15 of gestation. The concentration of the chemical, 100 mg/kg, was determined in a preliminary study to be the maximum dose at which slight maternal toxicity was observed (*i.e.* weight gain). Observations during the treatment period included number of implantations, number of live and dead fetuses, number of early and late resorptions, and number of corpora lutea. Any fetal malformations were also noted.

  The results from exposure to pentaerythritol triacrylate present equivocal findings at a clearly maternally toxic (unspecified) dose level. At 100 mg/kg, the test chemical caused uncommon malformations in a small number of fetuses/litter. However, in a second study in which pentaerythritol triacrylate was given at a level (dose not reported) that caused minimal maternal toxicity, teratogenic effects were not noted. From these results, the authors concluded that pentaerythritol triacrylate was not a teratogen [Andrews and Clary, 1986].

F. Genetic Toxicology

1. Human Data

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

2. Prokaryotic Data

Salmonella typhimurium

- Pentaerythritol triacrylate has been tested in a preincubation modification of the *Salmonella* / microsome test in the absence of metabolic activation and in the presence of liver S-9 from Arochlor-induced male Sprague-Dawley rats and Syrian hamsters. The assay was conducted in *Salmonella* strains TA98, TA100, TA1535, and TA1537 at doses of pentaerythritol triacrylate in dimethyl sulfoxide ranging from 0.0 (solvent control)-10,000.0 µg/plate. Pentaerythritol triacrylate was found to be non-mutagenic in all strains of *Salmonella* tested [Zeiger, *et al.*, 1987].

Salmonella, typhimurium

- Pentaerythritol triacrylate was examined for mutagenic activity in a series of *in vitro* microbial assays employing *Salmonella* (strains TA98, TA100, TA1535, TA1537, and TA1538). The compound was tested directly and in the presence of liver microsomal enzyme preparations from Aroclor-induced Sprague-Dawley male rats at the following concentrations: 0.1 µl, 1.0 µl, 5.0 µl, and 10.0 µl pentaerythritol triacrylate, in an unspecified solvent, per plate. The low dose in all cases was below a concentration that demonstrated any toxic effect, and the high dose level was found to induce some physiological changes (results unreported). Pentaerythritol triacrylate was found to be non-mutagenic under all test conditions in all strains [Celanese, 1976].

3. Eukaryotic Data

Saccharomyces, cerevisiae

- Pentaerythritol triacrylate was examined for mutagenic activity in a series of *in vitro* microbial assays employing *Saccharomyces cerevisiae* (strain D4). The compound was tested directly and in the presence of liver microsomal enzyme preparations from Aroclor-induced Sprague-Dawley male rats at the following concentrations: 0.1 µl, 1.0 µl, 5.0 µl, and 10.0 µl pentaerythritol triacrylate, in an unspecified solvent, per plate. The low dose in all cases was below a concentration that demonstrated any toxic effect and the high dose level was found to induce some physiological changes (results unreported). Pentaerythritol triacrylate was found to be non-mutagenic under all test conditions in this strain of *Saccharomyces cerevisiae* [Celanese, 1976].

in vitro, mouse lymphoma cells

- Pentaerythritol triacrylate was tested for the induction of mutations, aberrations and micronuclei using the TK+/- heterozygote of L51784 mouse lymphoma cells in the absence of exogenous activation. Triplicate cultures were treated (2 for mutation analysis, and 1 for cytogenetics) with pentaerythritol triacrylate in dimethyl sulfoxide at concentrations ranging from 0.01 - 0.05 µg/ml. Cells were cloned in the presence and absence of triflourothymidine (TFT) selection. Bromodeoxyuridine was added to cultures to be used for cytogenetic analysis. For aberration analysis, cells were incubated with colcemid for the last 2 hours, and for the micronucleus analysis, cultures were harvested 12 or 13 hours after the addition of cytocholasin B.

  In the three experiments, pentaerythritol triacrylate induced a dose-responsive increase in mutant frequency. The highest increase in mutant frequency observed was 416 x 10^{-6} at a pentaerythritol triacrylate concentration of 0.37 µg/ml (15% survival). Increases in mutant frequency were primarily due to the induction of small-colony TFT-resistant mutants. Pentaerythritol triacrylate also induced a dose-responsive increase in the number of aberrations and micronuclei observed. The highest frequency observed was 50 aberrations per 100 cells scored and 38 micronuclei per 1000 cells scored at a concentration of 0.350 µg/ml pentaerythritol triacrylate (15% survival).

The authors concluded that the genotoxicity of pentaerythritol triacrylate is elicited via a direct-acting clastogenic mechanism because no metabolic activation is required. The induced level of micronuclei paralleled the increased aberration frequency and small-colony formation, adding further support that small-colony formation may correlate with clastogenic activity and that pentaerythritol triacrylate is indeed clastogenic [Dearfield, *et al.* 1989].

G. Other Toxicological Effects

1. Immunotoxicity

epicutaneous, guinea pigs

- An assessment of T-lymphocyte proliferation and lymph node weight was carried out to determine their predictive value for identifying contact sensitizers. Lymph nodes were extracted from outbred Hartley guinea pigs (either sex) 4-6 days after epicutaneous immunization with 50 µmol of pentaerythritol triacrylate (see section V.C). The lymph nodes from five animals were weighed, fixed, and processed for histological examination. The sections were evaluated for T-lymphocyte proliferation by counting the number of large pyroninophilic cells (LPC) in the area of maximal proliferation in the paracortex. Control animals were tested in an identical procedure, without the test chemical.

  Four days after the epicutaneous application, a significant increase in weight in the homolateral auricular, homolateral cervical, and contralateral cervical lymph nodes was observed in animals treated with pentaerythritol triacrylate (numbers not reported). There was also evidence of increased T-lymphocyte proliferation, as measured by an increase in LPC, in the paracortical areas of these lymph nodes when compared to the control values ($P<0.001$). For example, in the homolateral auricular lymph nodes, 39 cells (per microscopic field of 270 µm diameter) were found in test animals as compared to 15 LPC in the control animals. These results were consistent after 6 days for the homolateral auricular nodes. From this study, the authors concluded that a positive correlation exists between skin sensitization reactions, increases in lymph node weight, and T-lymphocyte proliferation [Bull, *et al.*, 1985]

2. Neurotoxicity

intraperitoneal, rats

- In an intraperitoneal LD_{50} study previously described (see section V.B), ten Sprague-Dawley albino rats (5 males, 5 females) were used to determine the neurological effects produced by a single intraperitoneal injection of pentaerythritol triacrylate. This chemical was administered at dose levels of 3, 10, 30, and 100 mg/kg of pentaerythritol triacrylate as a 10% solution in dimethyl sulfoxide. Neurological examinations were conducted 1, 2, 4, and 24 hours after dosing for all animals, and then daily through day 14 for animals in the 30 mg/kg dose group. Animals at the 10 mg/kg dose level that exhibited neurologic abnormalities at 24 hours were observed daily thereafter through day 7. Animals that continued to exhibit abnormalities at day 7 were observed daily through day 14. Other details of the procedure can be found in section V.B.

  Table 5 summarizes the principal signs of neurological toxicity seen in animals who were found dead after treatment with 30 or 100 mg/kg of pentaerythritol triacrylate (5 males/3 females and 5 males/5 females, respectively) at some point prior to death. The two survivors (females) in the 30 mg/kg group continued to exhibit ataxia, body and limb flaccidity, and/or abnormal righting and visual placing reflexes throughout most or all of the 14-day post-dose observation period. One female also exhibited compulsive biting between days 7 and 14. In both dose groups (30 and 100 mg/kg), a few animals that died also exhibited convulsions, toe pinch, abnormal startle reflexes, abnormal pupil or corneal reflexes, and uncoordinated eye movements prior to death.

  Neurological abnormalities were noted in 5 of the 10 animals in the 10 mg/kg group (3 males, 2 females) and consisted of ataxia (1 male, 2 females), flaccid limb and body tone (2 males, 2 females), and abnormal righting and visual placing reflexes (2 females). The males were free of neurological abnormalities by day 5. One of the females was free of abnormalities by day 10, but the second continued to exhibit an abnormal righting reflex through the termination of the study (day 14). No neurological abnormalities were observed in animals that received 3 mg/kg of pentaerythritol triacrylate or in control animals receiving only mineral oil [Celanese, 1982b].

Table 5: Neurological Abnormalities in Rats Treated with 30 and 100 mg/kg Pentaerythritol Triacrylate

Sign	Dose 30 mg/kg male/female	Dose 100 mg/kg male/female
Ataxia	5/3	5/5
Body tone flaccidity	4/2	4/4
Limb tone flaccidity	4/1	3/3
Abnormal righting reflex	5/3	5/5
Abnormal visual-placing reflex	4/1	4/3

3. Biochemical Toxicology

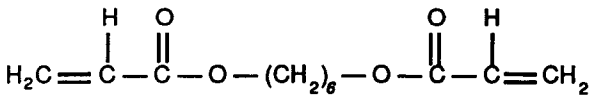
No data were found on the biochemical toxicology of pentaerythritol triacrylate in humans or animals.

VI. STRUCTURE ACTIVITY RELATIONSHIPS

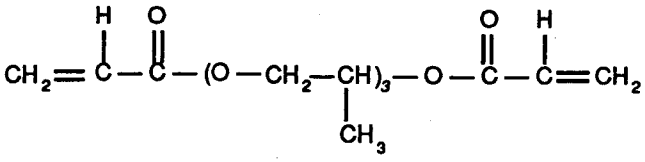
Pentaerythritol triacrylate is a member of the multifunctional alkyl acrylates (MFAs) chemical class. Some members have been found to have potential for carcinogenicity in mice in a dermal toxicity study {see Figure 1, Structures of Multifunctional Acrylates (next page)}. Eight MFAs were tested on 50 male C3H/HeJ mice twice weekly for 80 weeks, or until tumors were diagnosed, or 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), trimethylolpropane trimethacrylate (TMPTMA), 1,6-hexanediol diacrylate (HDODA), tripropyleneglycol diacrylate (TRPGDA), and triethyleneglycol dimethacrylate (TTEGDMA). The remaining MFAs tested, pentaerythritol triacrylate (see section V. D for a description of the study), triethyleneglycol diacrylate (TREGDA), and tetraethyleneglycol diacrylate (TTEGDA), showed some potential for carcinogenicity/tumorigenicity. TREGDA (100 mg/kg) induced skin tumors in 6/50 mice and lymphomas in 4/50 mice. TTEGDA (100 mg/kg) caused an increased incidence of skin tumors in 6 mice. Forty-two of 50 mice that received benzo[a]pyrene (positive control) developed squamous cell carcinomas of the skin and 1 animal in both the negative and vehicle control groups developed a skin papilloma [Andrews and Clary, 1986].

In another study, two multi-functional acrylates, neopentylglycol diacrylate (NPGDA) and pentaerythritol triacrylate (PETA), were tested for chronic dermal toxicity in 40 C3H/HeJ male mice at varying doses three times weekly for the lifetime of the animals. The results for pentaerythritol triacrylate are discussed in section V.D. Eight of the 40 mice treated with 5 mg doses of NPGDA developed skin tumors (5 papillomas and 3 carcinomas). In the positive control group, 35 of the 40 mice treated with 0.03 mg doses of methylcholanthrene developed skin tumors. None of the mice in the vehicle (acetone) control groups developed tumors. The authors concluded that NPGDA was oncogenic to mice under the conditions of this study [Depass, *et al.*, 1985].

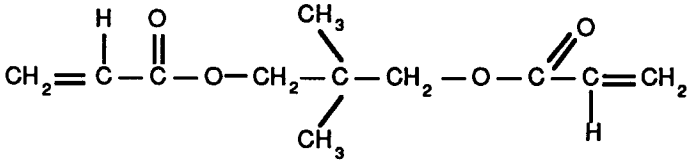
Figure 1. Structures of Multifunctional Acrylates



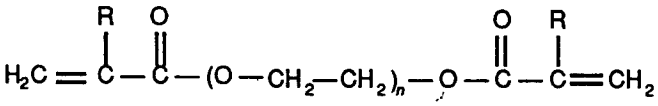
1,6-Hexanediol diacrylate (HDODA)



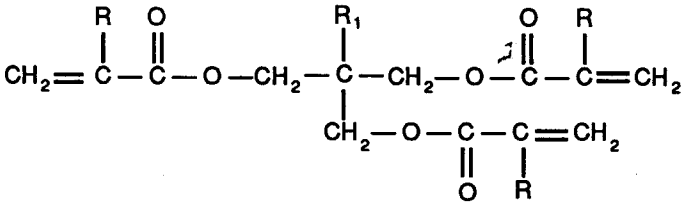
Tripropyleneglycol diacrylate (TRPGDA)



Neopentylglycol diacrylate (NPGDA)*



R = H	$n = 3$	Triethyleneglycol diacrylate (TREGDA)*
R = H	$n = 4$	Tetraethyleneglycol 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	January, 1991	
CIS		
TSCAPP	January, 1991	
DIALOG:		
Analytical Abstracts	January, 1991	1980-1990
Biosis Previews	January, 1991	1969-1991
Cancerlit	January, 1991	1963-1990
Chem Bus Newsbase	January, 1991	1984-1991
Chem Safety Newsbase	January, 1991	1984-1991
CIN	January, 1991	
Commerce Bus Daily	January, 1991	1982-1990
Compendex Plus	January, 1991	1970-1990
Current Contents	January, 1991	Current
Embase	January, 1991	1974-1991
Energy Sci Technol	January, 1991	1983-1990
Informat Int'l Bus	January, 1991	1984-1991
Life Sciences Collection	January, 1991	1978-1990
Medline	January, 1991	1966-1991
Occ Safety & Health	January, 1991	1973-1990
NTIS	January, 1991	1964-1990
Paperchem	January, 1991	1967-1990
Pascal	January, 1991	1983-1990
PTS Newsletter	January, 1991	1987-1991
PTS Prompt	January, 1991	1972-1991
Scisearch	January, 1991	Current
SPIN	January, 1991	1975-1990
Thomas Register Online	January, 1991	
Trade and Industry ASAP	January, 1991	1983-1991
MEAD:		
Nexis/Lexis-BNA ENV	January, 1991	
NLM:		
Chemid	January, 1991	
Chemline	January, 1991	
HSDB	January, 1991	
RTECS	January, 1991	
IRIS	January, 1991	
Toxline 65	January, 1991	1965-1980
Toxline	January, 1991	1981-1991
Toxlit	January, 1991	1981-1991
Toxlit 65	January, 1991	1965-1980
Dart	January, 1991	1989-1991
Eticback	January, 1991	1950-1989

Emicback	January, 1991	
CCRIS	January, 1991	
STN:		
CA	January, 1991	1967-1991
CAold	January, 1991	pre 1965
CApreviews	January, 1991	Updated Weekly
Chemlist	January, 1991	1979-1991
Registry	January, 1991	
Beilstein	January, 1991	1830-1979

APPENDIX II. SAFETY INFORMATION

- **HANDLING AND STORAGE**

Pentaerythritol triacrylate is hygroscopic and may undergo rapid and violent polymerization at high temperatures [Radcure 1990b]. Exposure to free radical initiators [Radcure,1990a], light, peroxides, oxidizing agents, copper, copper alloys, carbon steel, iron, rust, strong bases [Radcure, 1990b], and strong acids [Lenga, 1988] may initiate polymerization [Radcure, 1990b, Lenga 1988]. Uncontrolled polymerization occurring at high temperatures may result in explosions and ruptures of the storage container [Radcure, 1990b]. Pentaerythritol triacrylate is inhibited with 100 ppm hydroquinone monomethyl ether [Lenga, 1988; Aldrich, 1990].

- **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:	Splash-proof 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 Minimum Requirements.
Respiratory Protection:	A NIOSH-approved chemical cartridge respirator with an organic vapor and high-efficiency particulate filter 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 pentaerthritol 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 pentaerythritol triacrylate is spilled the following steps shall be taken:

1. Remove all source of ignition.
2. Ventilate the area of the spill.
3. If a liquid solution is spilled, use vermiculite, sodium bicarbonate, sand, or paper towels to contain and absorb the spill.
4. Place the absorbed material under a fume hood and allow sufficient time for the liquid to evaporate.
5. Clean the spill area with dilute alcohol (approximately 60-70%) followed by a strong soap and warm water washing.
6. 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 chemical's 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 (i.e., 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.