FOREWORD INTRODUCTION

HYDROXYPROPYL ACRYLATE

CAS N°: 25584-83-2

SIDS Initial Assessment Report

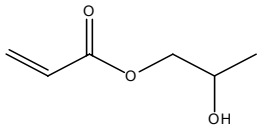
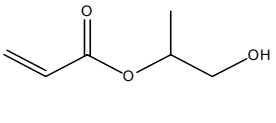
For

SIAM 20

Paris, France, 19-22 April 2005

1. Chemical Name:	Hydroxypropyl acrylate
2. CAS Number:	25584-83-2
3. Sponsor Country:	United States Oscar Hernandez Director, Risk Assessment Division (7403M) U.S. Environmental Protection Agency 1200 Pennsylvania Ave, N.W. Washington, DC 20460 Phone: 202-564-7641
4. Shared Partnership with:	HEA/HPA Consortium
5. Roles/Responsibilities of the Partners:	The HEA/HPA Consortium prepared the initial documents, which were then reviewed by U.S. EPA.
• Name of industry sponsor /consortium	Elizabeth Hunt, HEA/HPA Consortium 941 Rhonda Place SE Leesburg, VA 20175 703-669-5688
• Process used	Data searches included published scientific literature, databases and handbooks as well as the internal files of the member companies of the consortium.
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme?	The IUCLID Data Set has been revised and the SIAR prepared by a consortium of chemical industry producers in 2004. Data searches included published scientific literature, databases and handbooks as well as the internal files of the member companies of the consortium.
7. Review Process Prior to the SIAM:	See 5 above
8. Quality check process:	U.S. EPA reviewed the information in the industry sponsor's submission.
9. Date of Submission:	
10. Date of last Update:	December 2005
11. Comments:	

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	25584-83-2
Chemical Name	Hydroxypropyl Acrylate (Acrylic Acid, Monoester with Propane-1,2,-Diol)
Structural Formula	 2-Hydroxypropyl acrylate  1-Methyl-2-hydroxyethyl acrylate A typical commercial sample of hydroxypropyl acrylate contains approximately 75-80% 2-hydroxypropyl acrylate and 20-25% 1-methyl-2-hydroxyethyl acrylate. The purity of the salable product is at least 97% combined isomers

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The kinetics of hydroxypropyl acrylate have not been studied. However, results from oral, inhalation, and dermal single dose studies with the closely related, hydroxyethyl acrylate (CAS No. 818-61-1), indicated rapid metabolism via hydrolysis of the ester functionality, similar to many other acrylic acid esters. For hydroxyethyl acrylate, rapid metabolism to CO_2 and urinary metabolites was not route-dependent. The half-lives of elimination of radioactivity were approximately 14 hours for urine and 17 hours for CO_2. The half-life of elimination of radioactivity from plasma was approximately 26 hours. Based on the similarity of the results for hydroxyethyl acrylate with other acrylic acid esters, similar kinetics of hydroxypropyl acrylate is anticipated.

Acute toxicity studies with experimental animals indicate oral and dermal LD_{50} values of 820 mg/kg bw (rat) and 306 mg/kg bw (rabbit), respectively. In an acute inhalation study, exposure to a saturated vapor for eight hours did not result in deaths. In standard primary irritation studies, hydroxypropyl acrylate is a severe skin irritant. Upon eye contact, hydroxypropyl acrylate may cause severe irritation with corneal injury which may result in permanent impairment of vision or blindness. Skin sensitization studies in animals and humans indicate that hydroxypropyl acrylate is likely to be a sensitizer and will cross-react with other acrylates in some exposed individuals.

Repeated exposure to vapors of hydroxypropyl acrylate (6 hr/day, 5 days/week for 21 or 20 exposures to rats and mice and rabbits and dogs, respectively) results in severe irritation of the upper respiratory tract, resulting in death due to respiratory failure at higher concentrations and concentration-related local irritation at sublethal exposures. The LOAEC for subchronic exposure, based on irritation, was 5 ppm (27 mg/m^3) for hydroxypropyl acrylate. Except for irritant effects, no systemic toxicity was observed.

Hydroxypropyl acrylate was not mutagenic to *Salmonella typhimurium* (bacterial reverse mutation assay) *in vitro* with or without metabolic activation but was positive with metabolic activation when tested with two *E. coli* strains. In mammalian cells *in vitro*, hydroxypropyl acrylate was negative in a gene mutation assay but had clastogenic activity in cytogenetic and chromosomal aberration assays. In these mammalian cell assays, positive results occurred only at concentrations that resulted in significant cell death. Thus, the positive results are considered equivocal. Hydroxypropyl acrylate was not mutagenic in an *in vivo* mouse micronucleus study. Overall, hydroxypropyl acrylate is considered not to have mutagenic potential *in vivo* based on available data.

Hydroxypropyl acrylate had no effect on male reproductive organs in four species following repeated exposures via inhalation for 30 or 31 days (20 or 21 exposures). The principal treatment-related effects observed following 18 months exposure of laboratory rats to 5 ppm of the closely related, hydroxyethyl acrylate, were related to irritation of the respiratory tract, without significant evidence of systemic toxicity. Histopathological examination of the reproductive organs revealed effects in the arteries of the testes (fibrinoid degeneration in the

vascular channels — an age-related lesion) and uterus (inflammation) which were interpreted as neither treatment-related nor adverse to reproduction.

In a well-conducted inhalation study exposing pregnant rats to hydroxypropyl acrylate from gestation day 6 to 20, maternal body weights were reduced at the two highest exposure concentrations (5 and 10 ppm; 27 and 53 mg/m^3), but no embryo-fetal or developmental toxicity was observed. Overall, based on the available studies, hydroxypropyl acrylate does not show evidence for developmental toxicity.

Environment

The melting point is – 23.4°C and the boiling point is 205.7°C. The vapor pressure is 0.038 hPa at 25°C. The measured log Kow is 0.35. The water solubility of hydroxypropyl acrylate is estimated to be 307 g/L (25°C) and specific gravity is 1.049 g/cm^3 at 25°C.

Hydroxypropyl acrylate is photodegraded by reaction with hydroxyl radicals in the atmosphere with a half-life of 7.4 hours (calculated). The hydrolysis rate of hydroxypropyl acrylate is pH dependent with hydrolysis half-lives of > 490 days and >230 days at pH 3 and pH 7, respectively. The hydrolysis half-life at pH 11 is 0.056 days.

Distribution modeling using Mackay Level I indicates hydroxypropyl acrylate released into the environment partitions almost completely (99.8%) to the water phase. Fugacity model Level III with 100% of the hydroxypropyl acrylate release to air distribution is: <1% (air), 27% (water), 73% (soil) and <0.1% (sediment). Fugacity model Level III distribution with 100% of the hydroxypropyl acrylate release to water is: <0.1% (air), 100% (water), <0.1% (soil) and <1% (sediment). Fugacity model Level III distribution with 100% of the hydroxypropyl acrylate release to soil is: <0.1% (air), 21% (water), 79% (soil) and <0.1% (sediment). Fugacity model Level III distribution with equal distribution of hydroxypropyl acrylate release to air, water and soil is: <0.1% (air), 45% (water), 55% (soil) and <0.1% (sediment)

A low bioaccumulation potential is expected based on the partition coefficient of Log Kow of 0.35. Based on an OECD Guideline 301C study, hydroxypropyl acrylate is readily biodegradable (83% degraded over 28 days).

The 96-hour LC_{50} for fathead minnow was 3.1 mg/L (measured), the 48-hour EC_{50} for *Daphnia magna* was 24 mg/L (nominal) and the 96-hour EC_{50} values for biomass and growth rate of algae (*Selenastrum capricornutum*) were 3.53 and 6.67 mg/L (nominal), respectively.

Exposure

The worldwide production volume of hydroxypropyl acrylate is estimated to be 6000 to 7000 tonnes per year. The US production is estimated to be 5000 tonnes per year. Hydroxypropyl acrylate is produced and primarily used in closed systems. Its principle use is either as a co-monomer in the manufacture of polymers or as a chemical reactant in the manufacture of chemical intermediates. The polymers and chemical intermediates made with hydroxypropyl acrylate find applications in automotive top coatings, architectural coatings, photocure resins, and adhesives.

Based on the use pattern of the substance, significant environmental releases are unlikely. Impact on the environment is expected to be low due to photolysis, biodegradation and lack of bioaccumulation. Results from workplace measurements at a US production site indicated that hydroxypropyl acrylate did not exceed the TLV of 0.5 ppm in 87 samples collected over 20 years. Worker exposure is limited by the use of enclosed processing systems, industrial hygiene controls and personal protective measures. Hydroxypropyl acrylate has a characteristic acrylic odor, which can provide a measure of warning of the presence of vapors. End-use consumer products contain only trace levels of acrylic acid and esters (as a result of polymerization). Therefore, consumer exposure to acrylate monomers is not anticipated.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is currently of low priority for further work. The chemical has properties indicating a hazard for human health (severe eye irritation with corneal injury, which may result in permanent impairment of vision, even blindness, skin and upper respiratory tract irritation, potential skin sensitization, and acute toxicity from inhalation exposure). Based on exposure data presented by the Sponsor Country (relating to

production in one country which accounts for approximately 80% of global production and relating to the use pattern in several countries), this chemical is currently of low priority for further work. Countries may wish to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment: This chemical has properties indicating a hazard for the environment (fish, invertebrate, algae). However, the chemical is of low priority for further work for the environment because of its ready biodegradability and the limited potential for bioaccumulation.

SIDS Initial Assessment Report

1 IDENTITY

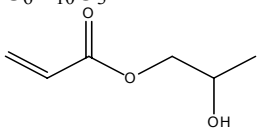
1.1 Identification of the Substance

CAS Number: 25584-83-2 - this CAS RN represents the commercial product as routinely produced that contains approximately 75-80% 2-hydroxypropyl acrylate (CAS No 999-61-1) and 20-25% 1-methyl-2-hydroxyethyl acrylate CAS No 2918-23-2)

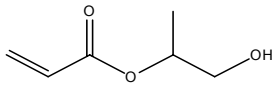
IUPAC Name: Acrylic acid, monoester with 1,2-propanediol

Molecular Formula: $C_6H_{10}O_3$

Structural Formula:



2-Hydroxypropyl acrylate



1-Methyl-2-hydroxyethyl acrylate

Molecular Weight: 130.14

Synonyms: Hydroxypropyl acrylate
Acrylic acid, 2-hydroxypropyl ester
Acrylic acid, monoester with propylene glycol
β-Hydroxypropyl acrylate
1,2-Propanediol-1-acrylate
1,2-Propanediol, monoacrylate
2-Propenoic acid,2-hydroxypropyl ester
Propylene glycol acrylate
Propylene glycol monoacrylate

1.2 Purity/Impurities/Additives

A typical commercial sample of hydroxypropyl acrylate contains approximately 75-80% 2-hydroxypropyl acrylate and 20-25% 1-methyl-2-hydroxyethyl acrylate. The purity of the salable product is at least 97% combined isomers. A typical commercial sample of hydroxypropyl acrylate may contain acrylic acid (≤ 0.98% w/w), other esters (≤ 1.8% w/w), propylene glycol diacrylate (≤0.2% w/w) and propylene oxide (ca. 0.001% w/w). Methyl ethyl hydroquinone may be added at 250 to 650 ppm as an inhibitor of spontaneous polymerization.

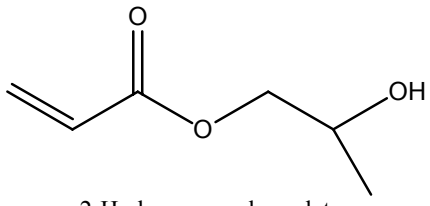
1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

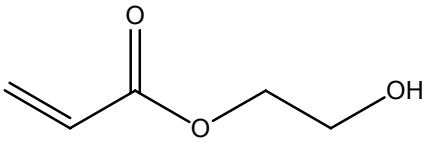
Property	Value	Reference
Physical state	Liquid	
Melting point	-23.4 °C	Rowley et al. in DIPPR, 2004
Boiling point	205.7 °C at 1013 hPa	Rowley et al. in DIPPR, 2004
Density	1.049 g/cm^3 at 25°C	DOW, 2002
Vapour pressure	0.038 hPa at 25°C	Rowley et al. in DIPPR, 2004
Water solubility	307 g/L @ 25°C (Considered miscible)	U.S. EPA, 2000a
Partition coefficient n-octanol/water (log value)	0.35 @ ca. 25°C	Tanii and Hashimoto, 1982
Henry's law constant	0.00161 Pa x m^3 / mol	HENRYWIN v 3.10

1.4 Analogue Justification

Justification for Use of Limited Hydroxyethyl Acrylate Data to Support Hydroxypropyl Acrylate for Mammalian Toxicity: Hydroxyethyl acrylate (CAS RN 818-61-1) is a member of the acrylate ester family with similar structure, physical/chemical properties and fate and effects profile as hydroxypropyl acrylate. The molecules are very similar structurally with the addition of a single carbon on the ester chain of hydroxyethyl acrylate. The structures are shown below:



2-Hydroxypropyl acrylate



2-Hydroxyethyl acrylate

As noted in the mammalian toxicity study reviews below, the LOAEC values from inhalation studies for the two chemicals are similar (5 ppm for hydroxypropyl acrylate and hydroxyethyl acrylate) and are based on local irritation. As with other acrylates, at sublethal levels, the major effects of both chemicals are related to irritation at the site of contact (stomach from gavage dosing, nasal and respiratory irritation from inhalation exposure, skin irritation from cutaneous exposure). Therefore, where appropriate for mammalian toxicity endpoints, hydroxyethyl acrylate data are included herein to support the toxicological profile of hydroxypropyl acrylate.

2 GENERAL INFORMATION ON EXPOSURE

The worldwide production volume of hydroxypropyl acrylate is estimated to be 6000 to 7000 tonnes per year. The US production is estimated to be 5000 tonnes per year.

Release of hydroxypropyl acrylate into the environment is unlikely based on the use pattern (closed system) and virtually complete polymerization in the final products. Small accidental releases are considered to be the only potential source of hydroxypropyl acrylate environmental contamination.

Hydroxypropyl acrylate is a chemical monomer, manufactured and processed within closed systems. The primary routes of potential exposure to hydroxypropyl acrylate are skin contact and vapor inhalation. The lower vapor pressure (0.038 hPa at 25ºC) helps reduce potential vapor inhalation exposure. In an industrial setting, ingestion is not an anticipated route of exposure. The primary use of hydroxypropyl acrylate in the production of polymeric coatings (used predominantly in the automotive industry) results in virtually no unreacted monomer in the finished coatings. The potential exposure to aerosols of hydroxypropyl acrylate is, therefore, highly unlikely.

Consumer exposure to hydroxypropyl acrylate is expected to be negligible because hydroxypropyl acrylate is used as a co-monomer in polymers (virtually complete polymerization occurs in the final products) or a reactant to make chemical intermediates and consumer products do not contain unreacted hydroxypropyl acrylate.

2.1 Production Volumes and Use Pattern

The worldwide annual production volume of hydroxypropyl acrylate for the SIDS-sponsoring companies (Cognis Performance Chemicals UK Limited, Degussa/Röhm GMBH & Co. KG, The Dow Chemical Company, Nippon Shokubai Co., Ltd., and Rohm and Haas Company) is in the range between 6000 and 7000 tonnes (2001 data).

Hydroxypropyl acrylate is mainly used either as a co-monomer in the manufacture of polymers or as a chemical reactant in the manufacture of chemical intermediates. In the manufacture of polymers, hydroxypropyl acrylate can be co-polymerized with acrylic acid, acrylates, methacrylates, vinyl acetate, vinyl chloride, vinylidene chloride, styrene, butadiene, and the like. Co-reactants with hydroxypropyl acrylate include aromatic and aliphatic isocyanates, anhydrides, and epoxides. The polymers and chemical intermediates made with hydroxypropyl acrylate find applications in automotive top coatings, architectural coatings, photocure resins, and adhesives. Examination of the Substances in Preparations in Nordic Countries database indicated no additional uses.

The Western Europe consumption of commodity acrylate esters by end use in 1984 was as follows (ECETOC, 1994).

Table 2 Western Europe consumption of commodity acrylate esters

End Use	Percent
Surface Coatings	35-40%
Adhesives / Sealants	15%
Textiles	10-15%
Paper Coating	15-20%
Fibers and Plastics Comonomers	10%
Others	10%

In 2000, the U.S. consumption of commodity acrylate esters was (SRI, 2001):

Table 3 United States consumption of commodity acrylate esters

End Use	Percent
Surface Coatings	44%
Adhesives / Sealants	18%
Textiles	15%
Plastics Additives	9%
Paper	5%
Others	9%

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

Releases of hydroxypropyl acrylate into the environment: Release of hydroxypropyl acrylate into the environment is unlikely based on the use pattern (closed system) and virtually complete polymerization in the final products. Small accidental releases are considered to be the only potential source of hydroxypropyl acrylate environmental contamination. For example,. no releases existed to require a Toxics Release Inventory (TRI) submission in the United States in the past decade.. The TRI is a publicly available EPA database that contains information on toxic chemical releases and other waste management activities reported annually. This inventory was established under the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) and expanded by the Pollution Prevention Act of 1990.

2.2.2 Photodegradation

The indirect photodegradation of hydroxypropyl acrylate by reaction with hydroxyl radicals in the atmosphere is estimated to occur with a half-life of approximately 7.4 hours (U.S. EPA, 2000b).

2.2.3 Stability in Water

The hydrolysis rate of hydroxypropyl acrylate, as with other acrylates, is pH dependent with little hydrolysis at acid and neutral pH and rapid hydrolysis in alkaline conditions. The hydrolysis half-lives determined at pH 3, 7, and 11 were > 490 days, >230 days, and 0.056 days, respectively (Gonsior *et al.*, 1997).

2.2.4 Transport between Environmental Compartments

The theoretical distribution of hydroxypropyl acrylate has been estimated using the fugacity model of Mackay, Level I (Canadian Environmental Modeling Centre, 1999). According to this model, hydroxypropyl acrylate, when released into the environment, partitions almost completely (99.8%) to the water phase.

Table 4 Estimated Distribution Between Environmental Compartments (Level I)

Compartment	%
Air	0.03
Water	99.8
Soil	0.2
Sediment	0.004

The environmental distribution of hydroxypropyl acrylate has also been examined using the Level III fugacity model (U.S. EPA, 2000c). Results are shown in the table below.

Table 5 Estimated Distribution Among Air, Water, Soil, and Sediments Under Various Emission Scenarios (Level III)

Emission Scenario	Percentage distributed to			
	Air	Water	Soil	Sediment
1,000 kg/hr to Air	1.38 %	26.6 %	71.9 %	4.5×10^{-2} %
1,000 kg/hr to Water	7.4×10^{-5} %	99.8 %	3.9×10^{-3} %	0.17 %
1,000 kg/hr to Soil	0.013 %	21.0 %	78.9 %	3.6×10^{-2} %
1,000 kg/hr simultaneously to Air, Water, and Soil	0.4 %	46.3 %	53.2 %	7.6×10^{-2} %

Conclusion

Hydroxypropyl acrylate has very high water solubility, very low vapor pressure, and very low log K_{ow}. These properties dictate that the material has low potential to volatilize from water to air or adsorb to soil and sediments. When released to water (the most likely emission scenario), the material will remain dissolved in water and will be removed through biodegradation and hydrolysis. Since hydroxypropyl acrylate is susceptible to destructive reactions such as indirect photolysis and biodegradation.

2.2.5 Biodegradation

In a biodegradation assay according to OECD Guideline 301 C, hydroxypropyl acrylate was 83% biodegraded after 28 days (MITI, 2001). In a biodegradation assay according to OECD Guideline 301 D, hydroxypropyl acrylate showed 34.9% biodegradation after 28 days expressed as ThOD (Wu, 1996). A third study reported no degradation after 5 days but toxicity of hydroxypropyl acrylate to the organisms, Polyseed, could not be ruled out (Schaefer, 1995). A fourth study, employing methods similar to current OECD Guideline 302 testing, that used industrial effluent (i.e. acclimated sludge) showed HPA was approximately 73% biodegraded after 20 days (Dow Chemical Company, 1975). Based on the OECD Guideline 301C study, hydroxypropyl acrylate is readily biodegradable.

The difference in results for the OECD 301C and 301D studies is considered to be affected by two factors: First, the inoculum concentration used in the 301D study is lower than for the 301C study. A number of studies have investigated the effect of inoculum concentration on results of the ready biodegradation tests. Three basic observations have been made: first, precision among repeated tests or different labs is improved with increasing inoculum concentration; second, the lag phase, or

time for onset of biodegradation, is typically shortened with increased inoculum concentration (one study suggests that one order of magnitude difference in competent cell concentration can result in about one week difference in the lag phase); and third, the composition/diversity of wastewater microbial populations will differ with time and location, and is mostly determined by organic composition of the wastewater. These observations are linked to the number of "competent" organisms (i.e. capable of degrading the substance) initially present in the test mixtures, and whether these competent organisms will survive and grow under the conditions of the test. A higher total inoculum concentration is expected to result in higher number of competent organisms initially present, and thus, a shortened lag phase during the test. In the case of 301C vs. 301D for HPA, a longer lag phase is expected in the 301D test. However, degradation equal to that in the 301C test would eventually be attained with extended incubation of the 301D test beyond the standard 28 days.

In addition to the above, there is inherent variability in biodegradation assays performed with these types of chemicals dependant on laboratory variability, solubility of the test substance and a variety of other variables. Overall, the high degradation in the 301C study clearly indicates that HPA is readily biodegradable under the conditions of the assay which is consistent with its classification in Japan and elsewhere.

2.2.6 Bioaccumulation

No experimental data on bioaccumulation is available. With a measured log K_{ow} of 0.35, a low bioaccumulation potential is expected.

2.3 Human Exposure

2.3.1 Occupational Exposure

Hydroxypropyl acrylate is a chemical monomer, manufactured and processed within closed systems. The primary routes of exposure to hydroxypropyl acrylate are skin contact and inhalation. The lower vapor pressure (0.038 hPa at 25ºC) helps reduce potential inhalation exposure. In an industrial setting, ingestion is not an anticipated route of exposure.

Exposure may occur during manufacture, transportation and industrial use. Results from workplace measurements at a US production site indicated that hydroxypropyl acrylate did not exceed the ACGIH TLV of 0.5 ppm in 87 samples collected over 20 years. Worker exposure is limited by the use of enclosed processing systems, industrial hygiene controls and personal protective measures. Hydroxypropyl acrylate has a characteristic acrylic odor, which can provide a measure of warning of the presence of hydroxypropyl acrylate vapors.

Loading, unloading, and transportation of tank trucks, railroad tankers, and drums are potential activities that could lead to dermal and inhalation exposure. However, dedicated systems designed to handle hydroxypropyl acrylate are typically used for loading and unloading purposes and procedures are typically in place to prevent spills or leaks during transportation. In addition, the use of personal protective equipment during the loading and unloading operation along with good personal hygiene practices reduces the risk of a potential exposure.

Current occupational exposure limit values for hydroxypropyl acrylate:

Table 6 International Occupational Exposure Limits

ACGIH TLV	0.5 ppm TWA, Skin
German MAK	0.5 ppm TWA, Skin
Belgium	0.5 ppm
Italy	0.5 ppm, Skin
Norway	0.5 ppm, Skin
UK	0.5 ppm, Skin
Sweden	1.0 ppm, Skin

2.3.2 Consumer Exposure

It is highly unlikely that any consumer product contains unreacted hydroxypropyl acrylate because hydroxypropyl acrylate is used by chemical manufacturers as a co-monomer in polymers (virtually complete polymerization occurs in the final products) or a reactant to make chemical intermediates. Consumer exposure to hydroxypropyl acrylate is expected to be negligible.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Studies in Animals

In vivo Studies

No reliable studies were identified for hydroxypropyl acrylate. However, 2-hydroxyethyl acrylate (HEA) has been evaluated in a study that examined metabolism and excretion in male Fischer 344 rat using oral, intraperitoneal, dermal and inhalation routes of exposure (Dow Chemical Company, 1992a). For the oral and intraperitoneal routes of exposure the rats (four animals/dose level/route of exposure) received a single dose of ^{14}C-HEA at 2.5 or 50 mg/kg body weight. For the inhalation exposure, six rats were exposed to a target concentration of 8 ppm ^{14}C-HEA for six hours in a head only inhalation chamber. For the dermal exposure, four rats were treated with ^{14}C-HEA at a dose of 50 mg/kg. No qualitative differences in urinary metabolites between routes were observed, indicating no marked route-dependent differences in the metabolic fate of HEA. The results of the study indicate that once the chemical becomes systemically available it is rapidly metabolized and eliminated from the body as either CO_2 in the expired air or urinary metabolites with approximately equal percentage of administered/exposed dose eliminated by each route. The half-lives of elimination of radioactivity were approximately 14 hours for urine and 17 hours for CO_2. The half-life of elimination of radioactivity from plasma was approximately 26 hours although the label was not associated with parent HEA. The available metabolic data on HEA is consistent with information on studies with other acrylates where hydrolysis of the ester functionality is the primary metabolic pathway. By analogy with ethyl acrylate and acrylic acid, it is expected that a minor metabolic pathway for HEA will be via conjugation with glutathione with the resulting mercapturic acid derivatives being excreted in the urine. Based on the similarity of the results for HEA with other acrylic acid esters, similar kinetics of hydroxypropyl acrylate is anticipated.

Conclusion

Animal studies with hydroxyethyl acrylate indicated rapid metabolism *via* hydrolysis of the ester functionality with the subsequent rapid metabolism of the hydrolysis products to produce exhaled CO_2 or urinary metabolites (mercapturic acid derivatives). There were no marked route-dependent differences in the metabolic fate of hydroxyethyl acrylate when administered by the oral, intraperitoneal, dermal or inhalation routes of exposure.

3.1.2 Acute Toxicity

Studies in Animals

Inhalation

No reliable studies determining the LC_{50} for hydroxypropyl acrylate were identified. When six rats were exposed to a substantially saturated vapor of hydroxypropyl acrylate for eight hours, no deaths occurred (Union Carbide, 1971). When four rats were exposed to saturated vapor of hydroxypropyl acrylate at room temperature for seven hours or for one hour when the test substance was placed in a water bath at 100ºC, no deaths occurred. However, after 4.25 hours of exposure to the material warmed to 100ºC, all five exposed animals died (Dow Chemical Company, 1964).

Dermal

The acute dermal LD_{50} in rabbits was 306 mg/kg body weight (Rohm and Haas, 1983). In this study, groups of six male rabbits received a single occluded application of undiluted hydroxypropyl acrylate for 24 hours at doses of 0, 115, 132, 152, 174, 180, 192, 206, 220, 250, 304, 370, and 450 mg/kg. The skin of half the rabbits in each group was abraded. Mortality was 0/6, 0/6, 0/6, 0/6, 0/6, 1/6, 1/6, 0/6, 0/6, 1/6, 3/6, 4/6 and 6/6, respectively. The signs of toxicity included passiveness, hypothermia, ataxia, iritis, skin irritation (erythema and edema) and eschar. At necropsy, black foci on stomach mucosa; pitted, mottled kidneys; and tan and congested liver were noted.

Other acute LD_{50} values ranging from approximately 117 to 214 mg/kg were reported as shown in the following table:

Species	Result	Reference
Rabbit LD_{50}	214 mg/kg	Carreon *et al.*, 1981
Rabbit LD_{50}	168 mg/kg (0.16 ml/kg)	Union Carbide, 1967
Rabbit LD_{50}	117 mg/kg (0.112 ml/kg)	Union Carbide, 1971

Oral

For the key study evaluating the acute oral toxicity of hydroxypropyl acrylate in rats, the LD_{50} was 820 mg/kg body weight (Rohm and Haas, 1983). In this study, groups of 10 male rats were administered hydroxypropyl acrylate at 0 (distilled water, control), 840, 1000, 1410, and 2000 mg/kg and a group of 20 male rats were dosed at 710 mg/kg and the animals were observed for 14 days. The mortality was 0/10, 4/20, 5/10, 9/10, 10/10 and 10/10 for the 0, 710, 840, 1000, 1410 and 2000 mg/kg groups, respectively. The clinical signs included ataxia, salivation, and passiveness. Animals that died during the study showed stained muzzle; lungs, stomach and intestines red and fluid filled; and enlarged stomach.

Other acute LD_{50} values ranging from approximately 252 and 1300 mg/kg were reported in various sources as shown in the following table:

Species	Result	Reference
Rat LD_{50}	1290 mg/kg (1.23 ml/kg)	Union Carbide, 1967
Rat LD_{50}	1180 mg/kg (1.13 ml/kg)	Union Carbide, 1971
Rat LD_{50}	> 252 and < 500 mg/kg	Dow Chemical Company, 1964

Conclusion

Hydroxypropyl acrylate has a moderate acute toxicity by oral and dermal routes of exposure. It does not pose an acute vapor inhalation hazard at ambient temperatures due to its low vapor pressure.

3.1.3 Irritation

Skin Irritation

Studies in Animals

Hydroxypropyl acrylate is highly irritating to skin but is not a corrosive. The available studies are summarized in the following table:

Species	Exposure Conditions	Result	Reference
Rabbit	0.5 ml; 24 hr; semi-occluded	Highly irritating	Ciba-Geigy, 1976a,b
Rabbit	0.5 ml; 4 hr; occluded	Highly irritating	Rohm and Haas, 1983
Rabbit	0.25 ml; 24 hr; occluded	Highly irritating	BP Chemicals Inc., 1981
Rabbit	4 hr DOT test	Not corrosive	Dow Chemical Company, 1973
Rabbit	4 hr DOT test	Not corrosive	Dow Chemical Company, 1981
Rabbit	10% solution; 9 applications to the ear (intact) and 1 application to the abdomen (intact and abraded) Undiluted solution: one application as above	No irritation – ear; Moderate burn and severe edema – abdomen (severe scar remained after 21 days); The single rabbit treated with undiluted test substance died	Dow Chemical Company, 1964
Rabbit	12.6% solution (252 mg/kg) 24 hr 50% solution (252 mg/kg) 24 hr 50% solution (500 mg/kg) 24 hr	0/2 dead; severe hyperemia and swelling; 1/2 dead; moderate hyperemia and edema; 2/2 dead	Dow Chemical Company, 1964

DOT = Department of Transportation

Conclusion

Hydroxypropyl acrylate is severely irritating to the skin.

Eye Irritation

Studies in Animals

Hydroxypropyl acrylate applied in the eyes of rabbits was moderately to severely irritating. The available studies are summarized in the following table:

Species	Exposure Conditions	Result	Reference
Rabbit	0.1 ml; 3 of 6 eyes washed after 30 seconds	Moderately irritating	Ciba-Geigy, 1976c
Rabbit	0.1 ml; (undiluted material instilled onto the corneal surface of the eye) 3 of 9 eyes washed after 30 seconds	Severely irritating	Rohm and Haas, 1983
Rabbit	0.1 ml; 3 of 6 eyes washed after 30 seconds	Moderately irritating	Ciba-Geigy, 1976d
Rabbit	Instilled undiluted; (washed and unwashed eyes)	Unwashed eye: severe and extensive conjunctival and corneal injury including swelling of the eyeball resulting in total loss of vision; Washed eye: Moderate to severe conjunctival irritation and corneal injury resulting in some permanent impairment of vision	Dow Chemical Company, 1964

Conclusion

Upon eye contact, hydroxypropyl acrylate may cause severe irritation with corneal injury which may result in permanent impairment of vision, even blindness.

3.1.4 Sensitisation

Studies in Animals

Skin

Hydroxypropyl acrylate has been tested in a number of studies using experimental animals. These studies are summarized in the following table:

Species	Exposure Conditions	Result	Reference
Guinea pig	Induction with HPA or HEA Induction with HEMA	Positive (12/12) with HPA challenge Positive (2/15) with HPA challenge	Clemmensen, 1984
Guinea pig	Induction with HPMA	Negative to HPA challenge	Bjoerkner, 1984
Guinea pig	Topical induction	Negative	Rao *et al.*, 1981
Guinea pig	Topical induction	Positive (4/10)	Dow Chemical Company, 1970

HPA = Hydroxypropyl acrylate; HEA = Hydroxyethyl acrylate;
HEMA = Hydroxyethyl methacrylate; HPMA = Hydroxypropyl methacrylate

Conclusion

Hydroxypropyl acrylate may cause skin sensitization in experimental animals.

Studies in Humans

Skin

In human patch tests, three out of 24 patients showing irritation to initial exposure to acrylates including hydroxypropyl acrylate, showed sensitization reactions to hydroxypropyl acrylate exposure (Kanerva *et al.*, 1988).

A number of case reports (see IUCLID Dossier) are presented for exposure to hydroxypropyl acrylate. These reports suggest that hydroxypropyl acrylate is likely to cause sensitization and cross-react with other acrylates in some exposed individuals. The human exposure to hydroxypropyl acrylate, however, is extremely limited since the only potential for repeated exposure is in workplace environments that have stringent protective procedures to avoid contact with the highly irritating chemical.

Conclusion

Hydroxypropyl acrylate may cause skin sensitization in humans. Cross-reactivity with and to other acrylate exposure is possible.

3.1.5 Repeated Dose Toxicity

Studies in Animals

Several studies, summarized below, were conducted with male animals of several species via inhalation exposure. In addition, a 28-day repeated-dose toxicity study and a 18-month chronic toxicity study on the closely related, hydroxyethyl acrylate (CAS RN 818-61-1) are used to address this endpoint.

Inhalation

Studies with Hydroxypropyl Acrylate

An inhalation study with rats, mice, rabbits and dogs was conducted with hydroxypropyl acrylate (Quast and Rampy 1983). Three groups of animals per species, consisting of 10 male Sprague-Dawley rats, 20 male Swiss-Webster mice, 4 male New Zealand white rabbits, or 2 male beagle dogs, were used in the study. The animals were exposed (whole body) to hydroxypropyl acrylate vapors at 0 (unexposed control), 5 ppm (27 mg/m^3) or 10 ppm (53 mg/m^3). Exposures were 6 hours/day, 5 days/week for a total of 21 exposures for the rats and mice and 20 exposures for rabbits and dogs. Food and water were available at all times except during exposure. Food and water were removed from the control animals for 6 hours on the first day of exposure only. The tissues examined for each species included adrenal glands, parathyroid glands, thyroid glands, aorta, sternum, bone marrow, kidneys, urinary bladder, prostate, accessory sex glands, epididymides, testes, urethra, brain, pituitary gland, spinal cord, peripheral nerve, large intestine, small intestine, esophagus, salivary gland, stomach, pancreas, liver, lung, skin, larynx, trachea, nasal turbinates, heart, lymph nodes, spleen, thymus, skeletal muscle, mammary tissue, gall bladder (except rats) and eyes.

In the rat study, no mortality was observed. Five of 10 rats exposed to 10 ppm developed slight cloudiness of the cornea. No treatment-related decreases in mean body weights were found, and the absolute and relative organ weights were not affected. No treatment-related effects on the hematological measurements, red cell counts, white cell counts, differential white cell counts,

hemoglobin concentration, and packed cell volume, the clinical chemistry measurements, BUN, glucose, SGPT, and alkaline phosphatase or the urinalysis parameters, specific gravity, pH, glucose, protein, and the presence or absence of ketones, bilirubin and blood were identified. At necropsy, focal corneal cloudiness was noted in 8 of 10 rats from the high exposure group suggesting an irritant effect. Histologically, a small increase in the number of animals with changes in the lungs at 10 ppm (subacute pneumonitis) and the nasal mucosa (both concentrations) was observed. No other treatment-related effects in the examined tissues were observed and no systemic toxicity was identified. The LOAEC was 5 ppm (27 mg/m^3) based on the effects in the nasal mucosa.

In the mouse study, no mortality was observed. Three of 20 mice exposed to 10 ppm, but none exposed to 5 ppm showed signs of eye irritation. No compound-related, statistically significant effects on mean body weights were found. However, the high dose mice showed a slightly lower body weights during weeks 1, 3 and 4 of exposure (up to 4.5% lower in week 1) which recovered during the weekend without treatment. No gross or histopathological changes related to exposure were observed. The NOAEC was 5 ppm (27 mg/m^3).

In the rabbit study, no mortality was observed. All rabbits exposed to 10 ppm and 2 of 4 animals exposed to 5 ppm developed slight rhinitis and eye irritation (moderate conjunctivitis). No treatment-related effects on mean body weight were observed and all groups gained a similar amount of weight during the study. The absolute and relative organ weights were not affected. No treatment-related effects on the hematological measurements, red cell counts, white cell counts, differential white cell counts, hemoglobin concentration, and packed cell volume or the clinical chemistry measurements, BUN, glucose, SGPT, SGOT and alkaline phosphatase were identified. Gross and histopathological changes related to exposure were found in the upper respiratory system (rhinitis, squamous metaplasia, and ulcerations), trachea and lungs (bronchitis, focal pneumonitis) of both hydroxypropyl acrylate exposure groups. The tracheal changes varied from no effect in some low dose animals to focal ulceration, squamous metaplasia and tracheitis in the high dose group. The most marked effects were seen in the upper respiratory system of all rabbits, especially those in the 10 ppm group that were characterized by mucopurulent rhinitis with squamous metaplasia and ulceration of the nasal turbinate mucosa. The LOAEC was 5 ppm (27 mg/m^3) based on effects on the upper respiratory system.

In the dog study, no mortality was observed. During the exposures, both dogs exposed to 10 ppm lost body weight (from 2 to 10%) and exhibited nasal irritation (exudative rhinitis) and eye irritation (bilateral corneal cloudiness, slight corneal edema, and bilateral suppurative conjunctivitis). The body weights showed some recovery during the weekends when no exposures occurred. One dog exposed to 5 ppm exhibited exudative rhinitis approximately half way through the study. At necropsy, exudative rhinitis, tracheitis, and suppurative bronchopneumonia were observed in all hydroxypropyl acrylate-exposed dogs. Microscopic lesions included suppurative rhinitis, squamous metaplasia and hyperplasia of the lining epithelium and focal area of ulceration in the mucosa of the nasal turbinates. These lesions extended to the trachea and lungs of the high exposure group resulting in bronchopneumonia. The LOAEC was 5 ppm (27 mg/m^3) based on effects on the upper respiratory system.

Studies with Hydroxyethyl Acrylate

A 28-day inhalation study with hydroxyethyl acrylate in male rats at concentrations of 0, 5, 10 and 25 ppm (0, 24, 48 and 120 mg/m^3) was reported (Leong and Trice, 1970). Groups of 15-20 animals (5 –10 animals sacrificed at 10 days) were exposed 7 hours/day for five days/week. The 25 ppm group was exposed for only 10 days due to excessive toxicity. Eight animals in the 25 ppm group died in the first 10 days and 9 additional died after cessation of dosing. One animal in the 10 ppm group died. At 5 ppm, only irritation of the cornea was observed. Ulcerative corneal changes, nasal irritation and decreased body weight were found in the 10 ppm survivors. However, the animals

were able to recover weight during the weekend when no exposures occurred. In the high exposure group, nasal irritation and sever respiratory distress occurred within two days. Thereafter, the animals lost weight and died of respiratory failure. It was concluded that the respiratory system and the eyes are the only affected systems following vapor exposure. The LOAEC based on minimal irritation was 5 ppm (24 mg/m^3). This value compares well with the minimal irritation observed at 10 ppm (54 mg/m^3) in rats exposed to hydroxypropyl acrylate under a similar regimen.

In a chronic inhalation study, male and female Sprague-Dawley rats (99 or 100 animals per dose group) were exposed to hydroxyethyl acrylate 6 hours per day, 5 days/week for 18 months at doses of 0.5 ppm (2.4 mg/m^3) or 5 ppm (24 mg/m^3) (Kociba *et al.*, 1979). The control group, consisting of 100 animals of both sexes, was exposed to air. After termination of treatment, the male and female animals were left for a recovery period of 5 and 6 months respectively before being killed for examination *post mortem*. The study included a 12-month interim kill for clinical and histopathological evaluation. Body weights, terminal organ weights and cumulative mortality, urinalysis, clinical chemistries and hematology did not appear to be altered by chronic hydroxyethyl acrylate exposure. Treatment was not associated with adverse effects except that the rats in the 5 ppm treatment group developed yellow staining of the fur and a marginal increase in *Mycoplasma*-induced pneumonia which was interpreted as being treatment related. No treatment-related effects were seen in the 0.5 ppm group. Overall, chronic inhalation exposure to hydroxyethyl acrylate at a dose of 5 ppm caused only a minimal toxicological effect while no toxicity was seen at 0.5 ppm. Gross and histopathological examination of tissues showed no indication of chronic toxicity or a carcinogenic effect in either the 5 or 0.5 ppm treatment groups, however nasal tissues were not examined. In addition, animals were treated for 18 months and, although maintained untreated for a further 6 months (approximately), the study does not meet current guideline requirements of a 24 month exposure period. Despite these and other limitations (e.g. bacterial infection), the data provide some evidence that hydroxyethyl acrylate was not carcinogenic *via* inhalation, which is potentially a significant route of occupational exposure.

Conclusion

Hydroxypropyl acrylate and the closely related, hydroxyethyl acrylate, are highly irritant at vapor concentrations greater than approximately 10 ppm (approximately 50 mg/m^3) resulting in severe localized effects and, in some cases, death due to respiratory distress. Exposure below lethal concentrations results in concentration-related irritant effects of the nasal passages and respiratory system. The systemic toxicity for either chemical was minimal with all of the effects observed in various studies related to the irritant properties.

3.1.6 Mutagenicity

Studies in Animals

In vitro Studies

Hydroxypropyl acrylate was tested in the bacterial reverse mutation assay test (OECD Guideline 471) with *Salmonella typhimurium* TA98, TA100, TA1535, and TA1537 at concentrations up to 5000 µg/plate with and without metabolic activation. Hydroxypropyl acrylate was considered not mutagenic under the conditions of the assay (Roehm, 1995a). Hydroxypropyl acrylate was positive in two *E. coli* strains (WP2UVrA/PKM101 and WP2/PKM101) and negative in two *Salmonella typhimurium* strains (TA 102 and TA 2638) when tested only with metabolic activation (Watanabe *et al.*, 1996).

A mammalian cell (CHO V79) mutation assay (OECD Guideline 476) was negative with and without metabolic activation at concentrations up to 150 µg/ml. Cytotoxicity was observed in this assay, however, at concentrations as low as 30 µg/ml (Roehm, 1995c).

Hydroxypropyl acrylate was tested in a cytogenetic assay (CHO V79 cells) according to OECD Guideline 473 at concentrations up to 100 µg/ml and was positive with and without metabolic activation in this assay (Roehm, 1995b).

In a chromosomal aberration assay (CHO cells), hydroxypropyl acrylate up to 5000 µg/ml was positive for chromosomal damage. Cytotoxicity was observed at all concentrations in the assay with viable cells ranging from 3 to 75% of control in a concentration-related manner (Roehm, 2000).

Other (meth)acrylates, including acrylic acid, methyl (meth)acrylate, ethyl (meth)acrylate, 2-ethylhexyl acrylate, 2-hydroxyethyl acrylate, and several multifunctional (meth)acrylates (Moore and Doerr, 1990), have been evaluated in *in vitro* mutagenicity assays with mammalian cells. In these studies, positive results were reported at concentrations that led to a clearly reduced cell survival rate. Studies have indicated that there is an association between chromosomal aberrations and cytotoxicity at exposure concentrations which reduce cell growth to less than 50% of the control value (Galloway, 2000 and references cited therein). These data suggest that the increase in mutagenicity reported in some of the chromosomal aberration assays with hydroxypropyl acrylate may be an artifact of the experimental method.

In vivo Studies

A mouse micronucleus study with hydroxypropyl acrylate conducted in compliance with OECD Guideline 474 (Hamann, 2000) indicated that, as with other acrylates (e.g. methyl acrylate and ethyl acrylate; see respective SIAR documents) , hydroxypropyl acrylate is not mutagenic in this assay and further support the conclusion above that the positive *in vitro* findings noted above in in vitro studies are possibly an artifact of the assay design and cytotoxicity of the test chemical.

Conclusion

Based on the results of the reliable studies, hydroxypropyl acrylate shows no potential to induce gene mutations, at least in mammalian cells, and no potential to induce chromosomal aberrations *in vivo*.

3.1.7 Carcinogenicity

In vivo Studies in Animals

No carcinogenicity studies were identified for hydroxypropyl acrylate. As reviewed for Repeated Dose toxicity, no evidence of carcinogenicity was observed for the closely related, hydroxyethyl acrylate, following 18 months of inhalation exposure (Kociba *et al.*, 1979; Rampy *et al.*, 1978).

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility

No reproductive toxicity studies are available. In the inhalation studies described under Repeated Dose Toxicity (Quast and Rampy, 1983), the prostate, accessory sex glands, epididymides, and testes, were examined for males of four species (rats, mice, rabbits, and dogs) exposed to hydroxypropyl acrylate vapor at 5 or 10 ppm (27 or 53 mg/m^3). No effects on any reproductive

organs were identified following 20 or 21 exposures to concentrations that resulted in significant irritation of the nasal passages and respiratory system. Similarly no effects on reproductive organs were seen with the closely related hydroxyethyl acrylate following a 28-day exposure study in males at 5, 10, or 25 ppm (24, 48, or 120 mg/m^3, respectively) (Leong and Trice, 1970).

As part of the chronic inhalation study described above (Kociba *et al*., 1979) a detailed pathological examination of the male and female reproductive organs from the animals on study was conducted. The analysis indicated that the female rats in the 5 ppm group showed an increased incidence of uterine inflammation as compared to the negative control animals. The incidence of uterine inflammation was 2/21, 1/3 and 11/27 for controls, 0.5 and 5 ppm groups, respectively. No other statistically significant differences for histopathologic observations of the female reproductive organs were found, including the ovaries.

An evaluation of the histopathological data from the male animals exposed to 5 ppm indicated a statistically significant increase from the controls in the incidence of fibrinoid degeneration in the vascular channels of the testes which was a local vascular manifestation of mesenteric periarteritis syndrome observed as age-related lesion in this rat strain (8/14 in controls *vs.* 17/19 for the 5 ppm group). The authors of the study indicate that the fibrinoid degeneration in the testes was not a substance-specific toxic effect as the laboratory conducting this study commonly observed this lesion in aging rats of this strain at similar incidence as was observed in this study (the historical control incidence of this lesion from seven chronic toxicity/oncogenicity studies ranged from 37 to 85%). Polyarteritis (polyarteritis or periarteritis nodosa) is the most conspicuous inflammatory lesion of the blood vessels of rats. The etiology is unknown and the incidence varies among strains and colonies (Mitsumori, K. (1990) Chapter 29 in Pathology of the Fischer Rat. Eds: Boorman et al., Academic Press, Inc. p 477). Common sites in male rats are the arteries of the testicle and to a lesser extent the arteries of the spermatic cord (Burek, J.D. (1978) Pathology of the Aging Rat, CRC Press p. 87). Carlton and Engelhardt (Polyarteritis, In: Cardiovascular and Musculoskeletal Systems Eds: Jones, T.C., Mohr, U. and Hunt, R.D., Springer-Verlag, 1991, p 71) also indicate that this lesion can be present in spermatic arteries.

Developmental Toxicity

The developmental toxicity of hydroxypropyl acrylate was evaluated in Sprague-Dawley rats after inhalation exposure for 6 hours/day, on gestation days 6 to 20 (Saillenfait *et al.*, 1999). The exposure concentrations were 0, 1, 5, or 10 ppm (0, 5.3, 27, or 53 mg/m^3). Dose groups consisted of 20 to 22 pregnant rats. Maternal body weights were lower than control for the 10 ppm group and weight gain was reduced for the 5 and 10 ppm groups. There was no significant difference in the numbers of implantation sites and live fetuses, in the incidence of non-live implants and resorptions, or in the fetal sex ratio, or fetal body weight between control and treated animals. No treatment-related increase in embryo/fetal lethality or fetal malformations was observed at any dose level. The incidence of external, visceral, and skeletal variations was similar to controls. The NOAECs were 1 ppm (5.3 mg/m^3) for maternal toxicity and >10 ppm (53 mg/m^3) for embryo-fetal toxicity and teratogenicity.

The closely related hydroxyethyl acrylate was similarly tested in the study design and at the exposure concentrations described above for hydroxypropyl acrylate (Saillenfait *et al.*, 1999). Exposure to 10 ppm hydroxyethyl acrylate caused maternal toxicity evidenced by a transient decrease in body weight change, a decrease in absolute weight gain and a continuous reduction of food consumption during exposure. There were no effects in dams exposed to 5 ppm hydroxyethyl acrylate. The NOAECs were 5 ppm (24 mg/m^3) for maternal toxicity and > 10 ppm (48 mg/m^3) for embryo-fetal toxicity and teratogenicity.

Conclusion

Based on results of animal studies evaluating exposure to hydroxypropyl acrylate and hydroxyethyl acrylate vapors, no reproductive toxicity is anticipated for hydroxypropyl acrylate. Hydroxypropyl acrylate is not selectively toxic to the embryo or fetus and is not teratogenic via inhalation exposure. This conclusion is supported by a similar study with the analog chemical, hydroxyethyl acrylate.

3.2 Initial Assessment for Human Health

Studies with experimental animals indicate that the acute oral and dermal toxicity of hydroxypropyl acrylate is moderate. The acute oral and dermal LD_{50} values for hydroxypropyl acrylate are 820 mg/kg (male rats) and 306 mg/kg (rabbits), respectively. In an acute inhalation study, exposure to a saturated vapor for eight hours did not result in deaths. In standard primary irritation studies, hydroxypropyl acrylate is a severe skin and eye irritant. It may cause corneal injury which may result in permanent vision impairment or blindness. Skin sensitization studies in animals and humans indicate that hydroxypropyl acrylate is likely to be a sensitizer and will cross-react with other acrylates in some exposed individuals. Repeated dose studies in rats via inhalation with hydroxypropyl acrylate and the closely related, hydroxyethyl acrylate, indicate that systemic toxicity is minimal. Exposure to vapors of these two monomers results in severe irritation of the upper respiratory tract, resulting in death due to respiratory failure at higher concentrations and concentration-related local irritation at sublethal exposures. The LOAEC for subchronic exposure, based on irritation, was 10 ppm (53 mg/m^3) for hydroxypropyl acrylate and 5 ppm (24 mg/m^3) for hydroxyethyl acrylate. Only minor irritant effects, no systemic toxicity, including effects on reproductive organs, and no carcinogenicity was observed following 18 months exposure to 5 ppm of hydroxyethyl acrylate.

Hydroxypropyl acrylate was not mutagenic to *Salmonella typhimurium* (Salmonella reverse mutation assay) *in vitro* with or without metabolic activation but was found to be positive with metabolic activation when tested with two *E. coli* strains. In mammalian cells *in vitro*, hydroxypropyl acrylate was found to be negative in a gene mutation assay but had clastogenic activity in cytogenetic and chromosomal aberration assays. In these mammalian cell assays, positive results occurred only at concentrations that resulted in significant cell death. Thus, the positive results are considered equivocal. Hydroxypropyl acrylate was not mutagenic in an *in vivo* mouse micronucleus study. Overall, hydroxypropyl acrylate is considered not to have mutagenic potential *in vivo* based on available data.

Hydroxypropyl acrylate had no effect on male reproductive organs in four species following repeated exposures via inhalation for 30 or 31 days (20 or 21 exposures). The principal treatment-related effects observed following 18 months exposure of laboratory rats to 5 ppm of the closely related, hydroxyethyl acrylate, were related to irritation of the respiratory tract, without significant evidence of systemic toxicity. Histopathological examination of the reproductive organs revealed effects in the arteries of the testes (fibrinoid degeneration in the vascular channels – an age-related lesion) and uterus (inflammation) which were interpreted as not treatment-related nor adverse to reproduction. No evidence of a carcinogenic effect was observed. In a well-conducted inhalation study exposing pregnant rats to hydroxypropyl acrylate from gestation day 6 to 20, maternal body weights were reduced at the two highest exposure concentrations (5 and 10 ppm; 27 and 53 mg/m^3), but no embryo-fetal or developmental toxicity or teratogenicity was observed. Overall, based on the available animal studies, hydroxypropyl acrylate is not toxic to reproduction or development and is not teratogenic.

Knowledge of the effects of hydroxypropyl acrylate exposure in humans is minimal and based primarily on isolated incidence reports. These reports along with animal data indicate the primary hazard from exposure to hydroxypropyl acrylate in humans is irritation. It is anticipated that there

is potential for sensitization from hydroxypropyl acrylate exposure and cross reactivity with other acrylates in some exposed individuals. However, use of personal protective equipment during production prevents exposure and there is virtually no exposure to residual hydroxypropyl acrylate following polymerization.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute Toxicity Test Results

Acute toxicity to fish (Geiger *et al.*, 1986; Russom *et al.*, 1988) yielded a 96-hour LC_{50} for fathead minnows of 3.1 mg/L (NOEC = 1.8 mg/L). This study followed ASTM (1980) guidelines using a flow-through design. Nominal exposure concentrations ranged from 1.8 to 9.8 mg/L and analyses at 96 hours ranged from 1.2 to 10.6 mg/L. Mortality occurred in the three highest concentrations (3.99, 6.54 and 10.6 mg/L, measured). The LC_{50} was determined based on analytical values.

An acute toxicity study with *Daphnia magna* (Dow Chemical Company, 1992b) indicated the 48-hour EC_{50} was 24 mg/L (NOEC = 10 mg/L). This study followed OECD Guideline 202 and Directive 84/449/EEC, C.2 using a static design. Nominal exposure concentrations ranged from 1.0 to 100 mg/L; no analytical confirmation was performed. Immobilization occurred in the four highest concentrations (18, 32, 56 and 100 mg/L, nominal).

A toxicity study with *Pseudokirchneriella subcapitata* (formerly known as *Selenastrum capricornutum)* (Scheerbaum, 2004) indicated the 96-hour EC_{50} values for biomass and growth rate were 3.53 mg/L and 6.67 mg/L, respectively and the 96-hour NOECs were 0.625 mg/L and 5 mg/L, respectively. This study followed OECD Guideline 201 using a static design. Nominal exposure concentrations ranged from 0.625 to 10 mg/L. Growth inhibition of algae was observed at concentrations of 2.5 mg/L and greater. The EC_{50} values were determined based on nominal values.

Toxicity to Microorganisms

Toxicity to Microorganisms: Seven studies (see Robust Summaries) examining the bacterial inhibition of hydroxypropyl acrylate are reported in different species. The MIC values range from 20 to 10,000 mg/L. Based on the broad range of results, no conclusion as to the potential toxicity of hydroxypropyl acrylate to specific microorganisms can be made.

4.2 Terrestrial Effects

No data available

4.3 Other Environmental Effects

No data available

4.4 Initial Assessment for the Environment

Although hydroxypropyl acrylate is produced in high volumes, releases to the environment are small. Hydroxypropyl acrylate has a low vapor pressure and would not be expected to extensively volatilize in the environment. Based on the Level III fugacity modeling, the majority of the releases are expected in water and soil with little in the air or sediment compartments. Modeling data indicate that hydroxypropyl acrylate is degraded rapidly in air with a half-life of 7.4 hours. Based

on the OECD Guideline 301C study, hydroxypropyl acrylate is readily biodegradable (83% degraded over 28 days).

Hydroxypropyl acrylate is toxic to aquatic organisms. The LC_{50} value for fish in standard laboratory tests is approximately 3.1 mg/L and the EC_{50} value for daphnia is 24 mg/L and for biomass and growth rate of algae are 3.53 and 6.67 mg/L, respectively. Due to the low log K_{ow} of 0.35, the bioaccumulation potential is very limited.

5 RECOMMENDATIONS

Human Health

The chemical is currently of low priority for further work. The chemical has properties indicating a hazard for human health (severe eye irritation with corneal injury, which may result in permanent impairment of vision, even blindness, skin and upper respiratory tract irritation, potential skin sensitization, and acute toxicity from inhalation exposure). Based on exposure data presented by the Sponsor Country (relating to production in one country which accounts for approximately 80% of global production and relating to the use pattern in several countries), this chemical is currently of a low priority for further work. Countries may wish to investigate any exposure scenarios that were not presented by the Sponsor country.

Environment

This chemical has properties, indicating a hazard for the environment (fish, invertebrate, algae). However, the chemical is of low priority for further work for the environment because of its ready biodegradability and the limited potential for bioaccumulation.

6 REFERENCES

Bjoerkner, B. 1984. Contact allergy to 2-Hydroxypropyl-Methacrylate (2-HPMA) in an ultraviolet curable ink, Acta Derm.-Venerol. 64 (3):264-267.

BP Chemicals Inc. 1981. Initial Submission: Irritation and Mutagenicity tests of Hydroxyethyl methacrylate and related studies with cover letter dated 082892; Microfiche No.: OTS0556083; Carpanini Dr. F.M.B., date produced: 03/10/81.

Burek, J.D. (1978) Pathology of the Aging Rat, CRC Press p. 87).

Canadian Environmental Modelling Centre. 1999. Level I Model, Version 2.11; Computer software available from www.trentu.ca

Carlton, W.W. and Engelhardt, J.A. Polyarteritis, Rat, In: Cardiovascular and Musculoskeletal Systems. Eds: Jones, T.C., Mohr, U. and Hunt, R.D., Springer-Verlag, 1991, p 71).

Carreon, R.E., Young, J.T. and Wall, J.M. 1981. Hydroxypropyl acrylate: Acute percutaneous absorption potential. Unpublished report. Toxicology Research Laboratory, Dow Chemical Company, Midland, MI, USA.

Ciba-Geigy. 1976a. Skin irritation in the rabbit after single application of TK 12116, Ciba-Geigy Limited, Basle, Switzerland, 4p.

Ciba-Geigy. 1976b. Skin irritation in the rabbit after single application of TK 12117, Ciba-Geigy Limited, Basle, Switzerland, 4p.

Ciba-Geigy. 1976c. Eye Irritation in the rabbit of TK 12116, Ciba-Geigy Limited, Basle, Switzerland, 4p.

Ciba-Geigy. 1976d. Eye Irritation in the rabbit of TK 12117,Ciba-Geigy Limited, Basle, Switzerland, 4p.

Clemmensen, S. 1984. Cross-reaction patterns in guinea pigs sensitized to acrylic monomers. Drug and Chemical Toxicology 7(6):527-540.

Dow Chemical Company. 1964. Results of Range-Finding Toxicological Test on 2-Hydroxypropyl Acrylate. Unpublished report, February 19, 1964. The Dow Chemical Company, 5p.

Dow Chemical Company. 1970. Guinea pig skin sensitization study on 2-hydroxypropyl acrylate. Unpublished report, June 30, 1970. The Dow Chemical Company Biochemical Research Laboratory, 1p.

Dow Chemical Company. 1973. DOT Test for Corrosiveness Conducted on: Hydroxypropyl Acrylate. Unpublished report, March 14, 1973. Dow Chemical Company, USA, 1p.

Dow Chemical Company. 1975. The pollutional evaluation of compounds. Unpublished report, February 26, 1975. Dow Chemical Company, USA, 5 p.

Dow Chemical Company. 1981. DOT (Department of Transportation) Test for Corrosiveness to the Skin of 2-Hydroxypropyl Acrylate. Unpublished report, Lab No. 485, September 1, 1981. Dow Chemical Company, USA, 1p.

Dow Chemical Company. 1992a. Unpublished Report: Domoradzki, J.Y., Freshour, N.L., Dryzga, M.D., Hiser, M.F., Smith, F.A., and Waechter, Jr., J.M., 2-Hydroxyethyl Acrylate:

Pharmacokinetics in Male Fischer 344 Rats Following Administration by Four Routes. See also Domoradzki *et al.* (1992). The Toxicologist, Abstracts of the 31st Annual Meeting, 12(1):570.

Dow Chemical Company. 1992b. 2-Hydroxypropylacrylate, Acute toxicity to Daphnia magna, Unpublished report, Project No. 44/991, Safepharm Laboratories Limited, U.K., Sponsor: Dow Europe S.A., 22p.

Dow Chemical Company. 2002. Product Stewardship Manual (October 2002).

ECETOC. 1994. ECETOC JACC Report No. 28. Joint Assessment of Commodity Chemicals No. 28 (Ethyl Acrylate). ECETOC - European Centre for Ecotoxicology and Toxicology of Chemicals. ISSN-0773-6339-28.

Galloway, S. 2000. Cytotoxicity and Chromosomal Aberrations in vitro: Experience in Industry and the Case for an Upper Limit on Toxicity in the Aberration Assay. Environmental and Molecular Mutagenesis 35:191-201.

Geiger, D.L., Poirier, S.H., Brooke, L.T. and Call, D.J. (eds.). 1986. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas), Volume III. Center for Lake Superior Environmental Studies, University of Wisconsin-Superior, ISBN 0-9614968-2-7.

Gonsior, S.J., Goodwin, P.A. and Tryska, T.J. 1997. Hydrolysis of Hydroxyethyl Acrylate (HEA) and Hydroxypropyl Acrylate (HPA) in Buffered Solutions. R & D report of The Dow Chemical Company.

Hamann, U. 2000. Mammalian Micronucleus Test of Murine Bone Marrow Cells with 2-Hydroxypropylacrylate. BSL Bioservice Project No.: 001524 A. BSL Bioservice Scientific Laboratories GmbH, Planegg/München, Germany.

Kanerva, L., Estlander, T. and Jolanki, R. 1988. Sensitization to patch test acrylates. Contact Dermatitis 18:10-15.

Kociba, R.J., Keyes, D.G., Schuetz, D.J., Yakel, H.O., Balmer, M.F. and Rampy, L.W. 1979. Results of a Two-Year Inhalation Toxicity Study of 2-Hydroxyethyl Acrylate (HEA) in Rats. Unpublished Report of The Dow Chemical Company.

Leong, B.K.J. and Trice, V.R. 1970. Effects of Repeated Inhalation Exposures of Rats and Single Exposure of Humans to Vapours of Hydroxy Ethyl Acrylate. R & D report of The Dow Chemical Company.

Mitsumori, K. (1990) Chapter 29 In: Pathology of the Fischer Rat. Eds: Boorman et al., Academic Press, Inc. p 477).

METI (2001). Ready Biodegradability: modified METI method. METI official gazzette

Moore, M.M. and Doerr, C.L. 1990. Comparison of chromosome aberration frequency and small-colony TK-deficient mutant frequency in L5178Y/TK+/- 3.7.2C mouse lymphoma cells. Mutagen. 5:609-614.

Quast, J.F. and Rampy, L.W. 1983. Repeated Inhalation Toxicity of Hydroxypropyl Acrylate. Dow Chemical, USA; Final Report, July 7, 1983; 35p.

Rampy, L.W. *et al.* 1978. Toxicol. Appl. Pharmacol. 45:310.

Rao, K.S., Betso, J.E. and Olson, K.J. 1981. A collection of guinea pig sensitization test results - grouped by chemical class. Drug and Chemical Toxicology 4(4):331-351.

Roehm. 1995a. Salmonella typhimurium reverse mutation assay with Hydroxypropylacrylat, CCR Robdorf, Unpublished report, Project no. 517701, Roehm GmbH, Chemische Fabrik, Darmstadt, 30p.

Roehm. 1995b. In vitro chromosome aberration assay in Chinese hamster V79 cells with Hydroxypropyl acrylate, Roehm GmbH, Chemische Fabrik, Darmstadt, 29p.

Roehm. 1995c. Gene Mutation Assay in Chinese Hamster V79 Cells in Vitro (V79/HPRT) with Hydroxypropyl acrylate, CCR Robdorf, Unpublished report, Project no. 517703, Roehm GmbH, Chemische Fabrik, Darmstadt, 29p.

Roehm. 2000. 2-Hydroxypropyl Acrylate chromosome Aberrations in Chinese Hamster Ovary Cells in Vitro. Unpublished report. RTC Report no. 7384-M-04899 Roehm GmbH, Chemische Fabrik, Darmstadt, 26p.

Rohm and Haas. 1982. Results, Microbial Mutagen Assay (Ames): Rocryl 430 (HPA). Rohm and Haas, Spring House, 3p.

Rohm and Haas. 1983. Toxicity report. Unpublished report no. 82R 0224. Rohm and Haas, toxicology department, Spring House, PA, 16p.

Rowley, R.L., Wilding, W.V., Oscarson, J.L., Yang, Y., Zundel, N.A., Daubert, T.E., Danner, R.P. (2004) DIPPR® Data Compilation of Pure Chemicals Properties, Design Institute for Physical Properties, AIChE, New York, NY.

Russom, C.L., Drummond, R.A. and Hoffman, A.D. 1988. Acute toxicity and behavioural effects of acrylates and methacrylates to juvenile fathead minnows. Bull. Environ. Contam. Toxicol. 41:589-596.

Saillenfait, A. *et al.* 1999. Relative Developmental Toxicities of Acrylates in Rats Following Inhalation Exposure. Toxicological Sciences 48:240-245.

Schaefer, E. 1995. Chemical Oxygen Demand and Biochemical Oxygen Demand Test Results. Wildlife International LTD. Project Number: 408E-101.

Scheerbaum, D. 2004. Hydroxypropyl Acrylate (HPA): Alga, Growth Inhibition Test with Pseudokirchneriella subcapitata, 96 H (formerly Selenastrum capricornutum). Project-No. 031022HH from Dr. U. Noack-Laboratorien, Sarstedt, Germany for HEA/HPA Consortium, 941 Rhonda Place SE, Leesburg, VA 20175, USA.

SRI. 2001. CEH Marketing Research Report, Acrylic Acid and Esters, 606.4000A, Chemical Economics Handbook –SRI International.

Tanii H. and Hashimoto, K. 1982. Structure-toxicity relationship of acrylates and methacrylates. Toxicol. Lett. 11:125-129.

Union Carbide Corporation. 1967. 2-Hydroxypropyl Acrylate Range Finding Toxicity Studies. Unpublished report. Chemical Hygiene Fellowship, Mellon Institute, Industrial Fellowship 274-30.

Union Carbide Corporation. 1971. Hydroxypropyl Acrylate Range Finding Toxicity Studies. Unpublished report no. 34-3. Chemical Hygiene Fellowship, Mellon Institute, Carnegie-Mellon University, PA. Submission with cover letter dated July 29, 1992, US EPA Doc. # 88-920004579.

U.S. EPA (U.S. Environmental Protection Agency). 2000a. EPI Suite™, Version 3.11; WSKOWWIN Program, Version 1.41; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

U.S. EPA (U.S. Environmental Protection Agency). 2000b. EPI Suite™, Version 3.11; AOPWIN Program, Version 1.91; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

U.S. EPA (U.S. Environmental Protection Agency). 2000c. EPI Suite™, Version 3.11; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Watanabe, K., Sakamoto, K. and Sasaki, T. 1996. Comparisons on chemically-induced mutagenicity among four bacterial strains, Salmonella typhimurium TA102 and TA2638, and Escherichia coli WP2/pKM101 and WP2 uvrA/pKM101: Collaborative study I. Mutation Research 361:143-155.

Wu, H. 1996. Determination of ready biodegradability: Closed bottle test, Ethyl Acrylate (EA), Methyl Acrylate (MA), Hydroxyethyl Acrylate (HEA), Hydroxypropyl Acrylate (HPA), Butyl Acrylate (BA). Unpublished report Weston Study No. 96-016. Roy F. Weston, Inc., Lionville, PA, USA

S I D S

Dossier

Existing Chemical	:	ID: 25584-83-2
CAS No.	:	25584-83-2
EINECS Name	:	acrylic acid, monoester with propane-1,2-diol
EC No.	:	247-118-0
Molecular Formula	:	C6H10O3

Producer related part

Company	:	Hydroxyethyl Acrylate/Hydroxypropyl Acrylate Consortium
Creation date	:	15.01.2003

Substance related part

Company	:	Hydroxyethyl Acrylate/Hydroxypropyl Acrylate Consortium
Creation date	:	15.01.2003
Status	:	
Memo	:	
Printing date	:	23.08.2005
Revision date	:	
Date of last update	:	23.08.2005
Number of pages	:	112
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type :
Name : Cognis Performance Chemicals UK
Contact person :
Date :
Street :
Town : S045 3ZG Hardley, Hythe, Southampton
Country : United Kingdom
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

03.01.2005

Type :
Name : Degussa/Rohm GMBH & Co. KG
Contact person :
Date :
Street :
Town : D-64275 Darmstadt
Country : Germany
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

03.01.2005

Type :
Name : Nippon Shokubai Co., Ltd.
Contact person :
Date :
Street :
Town : 541-0043 Osaka
Country : Japan
Phone :
Telefax :
Telex :
Cedex :
Email :
Homepage :

27.12.2004

Type :
Name : Rohm and Haas Company
Contact person :
Date :
Street :
Town : 19477 Spring House, Pennsylvania
Country : United States
Phone :
Telefax :

Telex	:	
Cedex	:	
Email	:	
Homepage	:	

27.12.2004

Type	:	
Name	:	The Dow Chemical Company
Contact person	:	
Date	:	
Street	:	
Town	:	48674 Midland, Michigan
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

27.12.2004

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	Acrylic acid, monoester with 1,2-propanediol
Smiles Code	:	
Molecular formula	:	C6 H10 O3
Molecular weight	:	130.14
Petrol class	:	
Remark	:	CAS RN 25584-83-2: A typical commercial sample of hydroxypropyl acrylate contains approximately 75-80% 2-hydroxypropyl acrylate and 20-25% 1-methyl-2-hydroxyethyl acrylate. The purity of the salable product is at least 97% combined isomers.

07.01.2004

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	organic
Physical status	:	liquid
Purity	:	> 97 % w/w
Colour	:	colorless
Odour	:	characteristic acylic odor

02.01.2004

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1,2-Propanediol, monoacrylate

02.01.2004

1,2-Propanediol-1-acrylate

02.01.2004

2-Propenoic acid,2-hydroxypropyl ester

02.01.2004

Acrylic acid, 2-hydroxypropyl ester

02.01.2004

Acrylic acid, monoester with propylene glycol

02.01.2004

beta-Hydroxypropyl acrylate

02.01.2004

Hydroxypropyl acrylate

02.01.2004

Propylene glycol acrylate

02.01.2004

Propylene glycol monoacrylate

02.01.2004

1.3 IMPURITIES

Purity :
CAS-No :
EC-No :
EINECS-Name : Other esters
Molecular formula :
Value : <= 1.8 % w/w

02.01.2004

Purity :
CAS-No : 79-10-7
EC-No : 201-177-9
EINECS-Name : acrylic acid
Molecular formula :

Value : <= .98 % w/w

02.01.2004

Purity :
CAS-No :
EC-No :
EINECS-Name : Propylene glycol diacrylate
Molecular formula :
Value : <= .2 % w/w

02.01.2004

Purity :
CAS-No :
EC-No :
EINECS-Name : Propylene oxide
Molecular formula :
Value : ca. .001 % w/w

02.01.2004

1.4 ADDITIVES

Purity type :
CAS-No :
EC-No :
EINECS-Name : Methyl Ethyl Hydroquinone
Molecular formula :
Value : ca. .02 - .065 % w/w
Function of additive : other: Stabilizer - to prevent polymerization

27.12.2004

1.5 TOTAL QUANTITY

Quantity : ca. 6000 - 7000 tonnes produced in 2001

Remark : (estimated world-wide production)
08.08.2005

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Remark : Hydroxypropyl acrylate is mainly used either as a co-monomer in the manufacture of polymers or as a chemical reactant in the manufacture of chemical intermediates. In the manufacture of polymers, hydroxypropyl acrylate can be co-polymerized with acrylic acid, acrylates, methacrylates,

vinyl acetate, vinyl chloride, vinylidene chloride, styrene, butadiene, and the like. Co-reactants with hydroxypropyl acrylate include aromatic and aliphatic isocyanates, anhydrides, and epoxides. The polymers and chemical intermediates made with hydroxypropyl acrylate find applications in automotive top coatings, architectural coatings, photocure resins, and adhesives. Examination of the Substances in Preparations in Nordic Countries database indicated no additional uses.

10.08.2005

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value : = -23.4 °C
Sublimation :
Method : other: (estimated) Constantinou method
Year :
GLP :
Test substance :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
03.01.2005 (14)

2.2 BOILING POINT

Value : = 205.7 °C at
Decomposition :
Method : other: (estimated) Constantinou method
Year :
GLP :
Test substance :

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
27.12.2004 (14)

Value : = 191 °C at
Decomposition :
Method :
Year :
GLP :
Test substance : other TS

Test substance : hydroxypropyl acrylate
Reliability : (2) valid with restrictions
18.03.2003 (35)

2.3 DENSITY

Type :
Value : = 1.049 g/cm³ at 25 °C

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.02.2003 (22)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .038 hPa at 25 °C
Decomposition :
Method : other (calculated): Riedel's method

Year	:	
GLP	:	
Test substance	:	
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

27.12.2004 (14)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	
Log pow	:	= .35 at 25 °C
pH value	:	
Method	:	other (measured): Shake flask method
Year	:	1982
GLP	:	no
Test substance	:	other TS: 2-Hydroxypropyl acrylate, Tokyo Kasei Co. Japan
Test condition	:	Both phases were saturated with the other solvent prior to the experimental determination. The TS was dissolved in dist. water at a concentration <1.0 mM. The ratio water/n-octanol was 6:4. Subsequent shaking was continued for 1h, followed by centrifugation at 2500 rpm for 30 min, and GC/FID analysis.
Reliability	:	(2) valid with restrictions Basic data given (comparable to guidelines/standards)
Flag	:	Critical study for SIDS endpoint

03.01.2005 (50)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 307 g/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: EPIWIN (v 3.11) WSKOWWIN Submodel (v 1.41)
Year	:	2003
GLP	:	
Test substance	:	
Remark	:	The EPIWIN model was run using the following physical chemical properties: Vapor Pressure (mm Hg) : 0.028 Log Kow (octanol-water): 0.35 Boiling Point (deg C) : 205.70 Melting Point (deg C) : -23.35
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

30.12.2003 (51)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

DIRECT PHOTOLYSIS

Halflife t1/2	:	= 7.4 hour(s)
Degradation	:	% after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated): EPIWIN (v3.11) AOPWIN (v 1.91)
Year	:	2003
GLP	:	
Test substance	:	
Remark	:	The EPIWIN model estimated the rate constant and atmospheric half-life using the 1-methyl-2-hydroxyethyl acrylate isomer, using the global average for hydroxyl radical concentrations (1.5E6 OH/cm3) and 12hr per day as the duration of the reaction. Other physical chemical properties for HEA are as follows: Vapor Pressure (mm Hg): 0.028 (0.038 hPa) Log Kow (octanol-water): 0.35 Boiling Point (deg C): 205.70 Melting Point (deg C): -23.35
Result	:	Overall OH rate constant = 17.4 E-12 cm3/molecule-sec t1/2 = 7.4 hours (12-hr day; 1.5E6 OH/cm3 The model output shows the 1-methyl-2-hydroxyethyl acrylate isomer.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

23.08.2005 (52)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Deg. product	:	
Method	:	other: TSCA section 796.3500 Hydrolysis as a Function of pH at 25C
Year	:	1997
GLP	:	yes
Test substance	:	other TS
Method	:	Hydrolysis study at pH 3, 7 and 11 was conducted following the TSCA guidelines, section 796.3500 Hydrolysis as a Function of pH at 25C. Test material was added to the buffered solutions at a concentration of less than 1 mM (15 ul test material/150mL solution). Approximate nominal concentration for HPA was 105 mg/L. The concentration of HPA was at least several orders of magnitude below the water solubility (307 g/L). Portions (10mL) of the test solutions were transferred to uniquely labeled 10-mL serum bottles and sealed with Teflon-coated rubber septa and aluminum crimp seals. The test solutions were incubated in the dark for 28 days at 25+/-1C. Periodically, test solutions were removed for measurement of pH and the analysis of test material remaining in the solution. Single test samples were removed at each time point and analyzed in triplicate by reverse phase HPLC using UV detection. For test samples at pH 11, 20-ul portions of

formic acid were added prior to analysis to adjust the dample to the pH range of 5 to 6 to minimize further hydrolysis. The following sampling schedule is described in the TSCA guidelines:

Procedure 1- If 60-70% conversion occurs within 28 days, then a minimum of six measurements will be made at regular intervals between 20 and 70% hydrolysis.

Procedure 2- If the reaction is too slow to conveniently follow the hydrolysis to a high conversion in 28 days, but is still rapid enough to attain at least 20% conversion, then the test solution should be analyzed at 15- 20 time points at regular intervals after 10% conversion is attained.

Procedure 3- If less than 20% conversion occurs after 28 days, then the concentration of test chemical after 28 days will be determined, and a half-life of >x days reported.

For each hydrolysis experiment, the natural logarithm of the test substance concentration was plotted as a function of time. At a constant pH, a straight line was obtained, indicating pseudo-first order kinetics. The slope of the linear regression line was equal to -Kh, where Kh was the pseudo-first order rate constant. Using the relationship T1/2=ln 2/Kh, the half-life of the hydrolysis reaction was determined. The following relationship holds for hydrolysis reactions in buffered systems:

Kh=Ka[H+]+Kb[OH-]+Kn where Ka, Kb, and Kn are the second-order rate constants for acid and base catalyzed, and neutral water hydrolysis reactions, respectively, and Kh is the measured pseudo-first order rate constant. At a given pH, the equation contains three unknowns, Ka, Kb, and Kn; therefore, three equations are required to determine the three unknown values. This was accomplished by measuring the hydrolysis rates at pH 3, 7 and 11.

Result : Hydrolysis of HPA in Buffered Solutions at 25C

Time	pH 3		pH 7	
(days)	Ave mg/L	Std dev	Ave mg/L	Std dev
0	111.3	0.4	110.3	0.1
5	112.1	0.2	111.0	0.9
7	112.0	0.3	109.8	0.9
15	112.3	0.1	109.5	1.4
21	109.3	0.7	105.0	1.6
28	107.1	0.3	101.6	0.7

Time	pH 11	
(hours)	Ave mg/L	Std dev
0	103.8	0.7
0.5	81.2	0.1
1	61.7	0.2
2	37.5	0.1
3	20.3	0.0
4	11.9	0.0
5	8.1	0.2
6	4.8	0.0
7	3.0	0.1

Results for Hydrolysis Studies for HPA

pH	K(a) (days-1)	half-life (days)	correlation coefficient (r2)
2.85	0.0014	>490	-
7.03	0.003	>230	-
10.90	12.27	0.056	0.9983

(a) pseudo-first-order rate constant determined at indicated pH

Calculated kA, kB and kN second order rate constants:

Ka (M-1day-1)=4.26 x 10-2, Kb (M-1day-1)=15,500 and
Kn (day-1)=1.34X10-3

HPA hydrolyzed rapidly at pH 11, with a half-life of 0.056 days. In contrast, slow hydrolysis was observed at pH 3 and pH 7, with half-lives greater than 230 days. These results were explained by the presence of ester functional groups in HPA which are more susceptible to hydrolysis at high pH. Based on the hydrolysis rate constant determined for HPA, half-lives of 35 to 40 days would be expected at pH 8.

Test substance : Test material was received from The Dow Chemical Company with a reported purity of 98.21%.

Reliability : (2) valid with restrictions
2b- Test material was not characterized in accordance with GLPs.

23.08.2005 (24)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level I
Year : 2004

Remark : Input Parameters for Level I Model:

Chemical Type = 1, Indicates chemical can partition into all environmental compartments

Molecular Mass (g/mol) 130.14
Data Temperature (deg C) 25
Log Kow 0.35
Est. Water Solubility (g/m3) 3.07E+05 (from EPIWIN Calc)
Est. Henry's Law Constant 1.61E-03 (from Level I Calc)
Vapor Pressure (Pa) 3.8 (0.038 hPa)
Melting Point (deg C) -23.35
Simulated Emission (kg) 100000 (Level I Default)

Predicted equilibrium distribution:

Air: 3.0E-02% (32 kg)
Water: 99.8% (99800 kg)
Soil: 2.0E-01% (198 kg)
Sediment: 4.0E-03% (4 kg)

Result : Air (Level I) = 0.03%
Water (Level I) = 99.8%

Soil (Level I) = 0.2%

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
23.08.2005 (6)

Media : other: air (emission rate to air of 1000 kg/hr)
Method : Calculation according Mackay, Level III
Year : 2003

Remark : The EPIWIN model (v3.11) was run using the following physical chemical properties:
Vapor Pressure (mm Hg) : 0.028
Log Kow (octanol-water): 0.35
Boiling Point (deg C) : 205.70
Melting Point (deg C) : -23.35

Result : Concentration (%):
Air - 1.4
Water - 27
Soil - 72
Sediment - < 0.1

Level III Fugacity Model (Full-Output):
==========
Chem Name : 2-Propenoic acid, monoester with 1,2-propanediol
Molecular Wt: 130.14
Henry's LC : 1.58e-008 atm-m3/mole (Henrywin program)
Vapor Press : 0.028 mm Hg (user-entered)
Log Kow : 0.35 (user-entered)
Soil Koc : 0.918 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	1.38	13.5	1000
Water	26.6	360	0
Soil	71.9	360	0
Sediment	0.0452	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	8.62e-012	235	45.9	23.5	4.59
Water	5.37e-014	170	88.4	17	8.84
Soil	5e-012	460	0	46	0
Sediment	4.46e-014	0.0723	0.003	0.00723	0.0003

Persistence Time: 332 hr
Reaction Time: 384 hr
Advection Time: 2.47e+003 hr
Percent Reacted: 86.6
Percent Advected: 13.4

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 13.52
Water: 360
Soil: 360
Sediment: 1440
Biowin estimate: 3.212 (weeks)

Advection Times (hr):
Air: 100
Water: 1000

Sediment: 5e+004

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
23.08.2005 (53)

Media : other: water (emission rate to water of 1000 kg/hr)
Method : Calculation according Mackay, Level III
Year : 2003

Remark : The EPIWIN model (v3.11) was run using the following physical chemical properties:
Vapor Pressure (mm Hg): 0.028 (0.038 hPa)
Log Kow (octanol-water): 0.35
Boiling Point (deg C): 205.70
Melting Point (deg C): -23.35

Result : Concentration (%):
Air - < 0.1
Water - 99.8
Soil - < 0.1
Sediment - 0.2

Level III Fugacity Model (Full-Output):
==========

Chem Name : 2-Propenoic acid, monoester with 1,2-propanediol
Molecular Wt: 130.14
Henry's LC : 1.6958e-009008 atm-m3/mole (Henrywin program)
Vapor Press : 0.028 mm Hg (user-entered)
Log Kow : 0.35 (user-entered)
Soil Koc : 0.918 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	7.41e-005	13.5	0
Water	99.8	360	1000
Soil	0.00386	360	0
Sediment	0.17	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	4.76e-018	0.013	0.00254	0.13	0.000254
Water	2.07e-013	658	342	65.8	34.2
Soil	2.77e-016	0.0254	0	0.00254	0
Sediment	1.72e-013	0.279	0.0116	0.0279	0.00116

Persistence Time: 342 hr
Reaction Time: 520 hr
Advection Time: 1e+003 hr
Percent Reacted: 65.8
Percent Advected: 34.2

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 13.52
Water: 360
Soil: 360
Sediment: 1440
Biowin estimate: 3.212 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
23.08.2005 (53)

Media : other: soil (emission rate to soil of 1000 kg/hr)
Method : Calculation according Mackay, Level III
Year : 2003

Remark : The EPIWIN model (v3.11) was run using the following physical chemical properties:
Vapor Pressure (mm Hg) : 0.028
Log Kow (octanol-water): 0.35
Boiling Point (deg C) : 205.70
Melting Point (deg C) : -23.35

Result : Concentration (%):
Air - < 0.1
Water - 21
Soil - 79
Sediment - < 0.1

Level III Fugacity Model (Full-Output):
==========
Chem Name : 2-Propenoic acid, monoester with 1,2-propanediol
Molecular Wt: 130.1
Henry's LC : 1.58e-008 atm-m3/mole (user-entered
Vapor Press : 0.028 mm Hg (user-entered
Log Kow : 0.35 (user-entered
Soil Koc : 0.918 (calc by model

	Mass Amount (percent)	Half-Life (hr)	Emission (kg/hr)
Air	0.0136	13.5	0
Water	21	360	0
Soil	78.9	360	1000
Sediment	0.0357	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	1.2e-013	3.26	0.637	0.326	0.0637
Water	5.95e-014	189	98.1	18.9	9.81
Soil	7.72e-012	709	0	70.9	0
Sediment	4.95e-014	0.0802	0.00333	0.00802	0.000333

Persistence Time: 467 h
Reaction Time: 518 h
Advection Time: 4.73e+003 h
Percent Reacted: 90.
Percent Advected: 9.8

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin)
Air: 13.5
Water: 36
Soil: 36
Sediment: 144
Biowin estimate: 3.212 (weeks

Advection Times (hr)
Air: 10
Water: 100
Sediment: 5e+00

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
23.08.2005 (53)

Media : other: air, water, soil (emissions to each compartment = 1000 kg/hr)
Method : Calculation according Mackay, Level III
Year : 2003

Remark : The EPIWIN model (v3.11) was run using the following physical chemical properties:
Vapor Pressure (mm Hg) : 0.028
Log Kow (octanol-water): 0.35
Boiling Point (deg C) : 205.70
Melting Point (deg C) : -23.35

Result : Concentration (%):
Air - 0.4
Water - 46
Soil - 53
Sediment - < 0.1

Level III Fugacity Model (Full-Output):
==========

Chem Name : 2-Propenoic acid, monoester with 1,2-propanediol
Molecular Wt: 130.14
Henry's LC : 1.58e-008 atm-m3/mole (user-entered)
Vapor Press : 0.028 mm Hg (user-entered)
Log Kow : 0.35 (user-entered)
Soil Koc : 0.918 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.408	13.5	1000
Water	46.3	360	1000
Soil	53.2	360	1000
Sediment	0.0786	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	8.74e-012	239	46.6	7.95	1.55
Water	3.21e-013	1.02e+003	528	33.9	17.6
Soil	1.27e-011	1.17e+003	0	39	0
Sediment	2.66e-013	0.432	0.0179	0.0144	0.000598

Persistence Time: 380 hr
Reaction Time: 471 hr
Advection Time: 1.99e+003 hr
Percent Reacted: 80.8
Percent Advected: 19.2

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 13.52
Water: 360
Soil: 360
Sediment: 1440
Biowin estimate: 3.212 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
23.08.2005 (53)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 100 mg/l related to Test substance
related to
Contact time : 28 day(s)
Degradation : 83 (±) % after 28 day(s)
Result : readily biodegradable
Deg. product : no
Method : OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year : 2000
GLP : yes
Test substance : other TS

Remark : Conditions of cultivation
Concentration of test substance = 100 mg/L
Concentration of activated sludge = 30 mg/L (conc. of suspended solid)
Volume of test solution = 300 ml
Cultivation temperature 25 ºC
Cultivation duration = 28 days

		BOD			
Vessel	Description	Day 7	Day 14	Day 21	Day 28
1	Sludge + Test Substance	13.8	38.2	42.8	47.0
2	Sludge + Test Substance	26.1	40.1	44.7	48.4
3	Sludge + Test Substance	23.4	38.7	42.5	46.0
4	Sludge + Aniline	51.1	64.4	67.9	68.3
5	Contol Blank	2.1	2.4	3.4	4.3
6	Water + Test Substance	0.3	0.3	0.3	0.3

TOC = 93%
Test substance : 2-hydroxypropyl acrylate 68%, 1-methyl-2-hydroxyethyl acrylate 28%
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
08.08.2005 (38)

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 3 mg/l related to Test substance
related to
Contact time : 28 day(s)
Degradation : = 34.9 (±) % after 28 day(s)
Result : other: not readily biodegradable
Kinetic of testsubst. : 0 day(s) = 0 %
7 day(s) = 0 %
14 day(s) = 5.8 %
21 day(s) = 11.6 %
28 day(s) = 34.9 %
Control substance : Benzoic acid, sodium salt
Kinetic : 7 day(s) = 71.9 %
28 day(s) = 95.8 %
Deg. product : not measured
Method : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year : 1996
GLP : yes
Test substance : other TS

Method : A closed bottle test was conducted on hydroxypropyl acrylate (HPA). The test measured the dissolved oxygen (DO) uptake by the microbial population during biodegradation of the test substance correct for uptake by the blank inoculum run in parallel. Percentage of biodegradation was obtained by comparing the BOD result with ThOD. TOC analysis of HPA indicated the following: Theoretical TOC (mg C/mg active) = 0.55; Measured TOC = 0.58. The reference substance used in the study was sodium benzoate. The theoretical and measured TOC for the reference substance was 0.583 and 0.593, respectively. The dilution water (test medium) was deionized water containing MgSO4, CaCl, phosphate buffer, and FeCl. The water was aerated to bring the DO to ~ 9.0 mg/L.

At test initiation, 150 ml of dilution water was added to 9 BOD bottles. HPA was added in stock solution to provide 3 mg active/L and the bottles filled with test medium. The initial DO concentration was determined in one replicate and the bottle discarded. The remaining bottles were capped and placed in an incubator in the dark at 20 +- 0.2 °C. At 7, 14, 21, and 28 days, two bottles were analyzed for DO. Inoculum blanks and reference controls were run simultaneously.

Remark : The difference in results for this study compared to the OECD 301 C is considered to be affected by two factors: 1) The inoculum concentration used in the 301D study is lower than for the 301C study. A number of studies have investigated the effect of inoculum concentration on results of the ready biodegradation tests. Three basic observations have been made: first, precision among repeated tests or different labs is improved with increasing inoculum concentration; second, the lag phase, or time for onset of biodegradation, is typically shortened with increased inoculum concentration. One study suggests that one order of magnitude difference in competent cell concentration can result in about 1 week difference in the lag phase; and third, the composition/diversity of wastewater microbial populations will differ with time and location, and is mostly determined by organic composition of the wastewater. These observations are linked to the number of "competent" organisms (i.e. capable of degrading the substance) initially present in the test mixtures, and whether these competent organisms will survive and grow under the conditions of the test. A higher total inoculum concentration is expected to result in higher number of competent organisms initially present, and thus, a shortened lag phase during the test. In the case of 301C vs. 301D for HPA, a longer lag phase is expected in the 301D test. However, degradation equal to that in the 301C test would eventually be attained with extended incubation of the 301D test beyond the standard 28 days.

In addition to the above, there is inherent variability in biodegradation assays performed with these types of chemicals dependant on laboratory variability, solubility of the test substance and a variety of other variables. Overall, the high degradation in the 301C study clearly indicates that HPA is readily biodegradable under the conditions of the assay which is consistent with its classification in Japan and elsewhere.

Result : HPA showed 34.9% ThOD by Day 28. The test substance was not considered readily biodegradable but can be considered inherently biodegradable.

Test substance : Hydroxypropyl acrylate (> 97% pure)

Reliability : (1) valid without restriction

08.08.2005 (57)

Type : aerobic
Inoculum : other: Polyseed
Contact time : 5 day(s)
Degradation : = 0 (±) % after 5 day(s)
Result : under test conditions no biodegradation observed
Control substance : other: glucose-glutamic acid

Kinetic : %
%
Deg. product : not measured
Method : other: COD/BOD APHA 17th Addition, 1987
Year : 1995
GLP : no
Test substance : other TS

Method : The COD was determined by a procedure based on Hach Method Number 8000. Stock solution of HPA was prepared at a nominal concentration of 1 mg/mL in distilled water. Triplicate COD determination were performed. The reference standard was potassium hydrogen phthalate.

The BOD determination was based on the methods described in "Standard Methods for the Examination of Water and Wastewater", APHA 17th Edition, 1987. HPA was administered to the test chambers by direct addition. The reference standard was dextrose and glutamic acid. The biological seed used was Polyseed (Polybac, Bethlehem, PA).

Result : The COD measurement for HPA was 1.7 +- 0.1 g O2/g test substance and the ThOD was 1.72 g/g.

At concentrations from 2 to 66 mg/L, the oxygen depletion over 5 days was less than 1 mg/L. Oxygen depletion was required to be >= 2 g/L to perform a valid BOD calculation. Therefore, no degradation was evident. The authors noted that HPA may have inhibited the microbial inoculum.

The dilution water and glucose-glutamate control results were within the acceptable range established for the test. The average observed DO depletion for the dilution water was 0.15 mg O2/L and the average BOD(5) result for the glucose-glutamic acid control was 180 mg/L.

Test substance : Hydroxypropyl acrylate (purity not stated)
Reliability : (2) valid with restrictions
The test substance may have been toxic to the Polyseed organisms

07.01.2005 (47)

Type : aerobic
Inoculum : activated sludge, industrial, adapted
Contact time : 20 day(s)
Degradation : 73 (±) % after 20 day(s)
Result :
Kinetic of testsubst. : 5 day(s) 37 %
10 day(s) 59 %
20 day(s) 73 %
%
%
Deg. product : not measured
Method : other: Standard Methods for Examination of Water and Wastewater (1971). 13th Edition.
Year : 1975
GLP : no
Test substance : other TS

Method : Comparable to OECD Guideline 302.
Remark : The seed material used in this study was filtered 437 Secondary Effluent (effluent from the Midland plant of the Michigan Division general wastewater treatment system).
Result : The test substance was not considered readily biodegradable but can be considered ultimately biodegradable, as it degradaded 73%, relative to theoretical BOD, over 20 days.
Test substance : Hydroxypropyl acrylate; purity not provided.
Reliability : (2) valid with restrictions
03.01.2005 (21)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : flow through
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = 3.1
EC50 : = 1.9
Method : other
Year : 1986
GLP : no data
Test substance : other TS

Method : According to ASTM (1980), Standard practice for conducting acute toxicity tests with fishes, macroinvertebrates and amphibians. American Society for Testing and Methods Comittee E-35.

Flow-through exposures were made with a continuous flow modified mini-diluter. One chemical stock solution was prepared and used for the entire test.

Gas-liquid chromatography (flame-ionisation detector) was used to analyze test substance concentrations in water samples from the exposure chambers. All test exposure chambers were sampled at approximately mid-depth at 0, 24, 48, 72 and 96 hours. All samples were analyzed immediately or adequately preserved for later analysis.

The fish were not fed 24 hours before or during the test. The tests were initiated by adding 20 fish per treatment and control groups. The number of dead fish was noted every 24 hours after the beginning of the test at which time they were also removed from the chambers. Observations of fish behavior and toxic signs were made at 2-8, 24, 48, 72 and 96 hours. Upon test termination, individual control fish were weighed (wet weight) and measured (standard length). Four surviving fish each from the control, the lowest concentration and the concentration nearest the LC50 were preserved for possible future histopathologic evaluation.

Result : The LC50 and EC50 values were calculated using the corrected averages of the analyzed tank concentrations and the Trimmed Spearman-Karber Method. EC50's were based upon loss of equilibrium.

Analytical Results (in mg/l):

Nominal Conc. (mg/l)	Hours 0	24	48	72	96	Corrected Averages*
Control	<0.5	<0.5				<0.5
1.8	1.2	1.5	1.4	1.4	1.2	1.51
2.7	1.9	2.3	2.0	2.2	2.2	2.39
4.2	3.4	3.5	3.5	3.6	3.7	3.99
6.4	5.5	5.6	5.6	6.1	6.2	6.54
9.8	8.6	8.4	9.6	9.8	10.6	10.6

*Corrected for analytical recoveries of spiked water samples.

Fish exposed to HPA showed behavioral and morphological signs indicative of neurotoxicants. They lost schooling behavior and swam near the tank surface in a corkscrew/spiral pattern. They were hyperactive and overreactive to external stimuli, had increased respiration, rigid musculature, and showed signs of edema, were deformed, and lost equilibrium prior to death.

Cumulative Mortality (total number of animals in each group = 20):

Concentration (mg/l)	Number of deaths Time (hours) 24	48	72	96
0	0	0	0	0
1.8	0	0	0	0
2.7	0	0	0	0
4.2	0	0	0	20
6.4	0	0	15	20
9.8	3	5	20	20

Number of animals with effects (total number of animals in each group = 20):

Concentration (mg/l)	Time (hours) 24	48	72	96
0	0	0	0	0
1.8	0	0	0	0
2.7	0	0	0	20
4.2	0	0	0	20
6.4	0	0	20	20
9.8	9	12	20	20

These results are from a second test, the first test resulted in an LC50 value of 3.61 mg/L.

Test condition : Species: P. promelas,
Age: 28-34 days,
Weight: 0.092 +/- 0.030 g,
Length: 19.4 +/- 2.41 mm,
Loading: 0.92 g/l
Test medium: filtered Lake Superior water,
Water quality parameters as measured during the test:
Temperature = 24.7 degrees C;
Dissolved oxygen = 6.7 mg/l;
pH = 7.87;
Total hardness = 45.9 mg/l CaCO3; and
Total alkalinity = 45.0 mg/L CaCO3.

Test substance : 2-hydroxypropyl acrylate, Scient. Polymer Prod., purity >97%

Reliability : (1) valid without restriction
Equivalent to guideline

Flag : Critical study for SIDS endpoint

04.04.2003 (23) (45)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : = 10
EC0 : = 10
EC50 : = 24
EC100 : = 56
Analytical monitoring : no
Method : other: OECD 202 and Directive 84/449/EEC, C.2

Year : 1992
GLP : yes
Test substance : other TS

Method : The test material was administered to the test vessels as an aqueous solution to obtain a concentration of 0 (control), 1.0, 1.8, 3.2, 5.6, 10, 18, 32, 56 and 100 mg/L . The concentration and stability of the test material in the test solutions were not determined. The water temperature was recorded daily, pH and oxygen concentration were recorded a 0 and 48 hours.

Young daphnids were selected at random and maintained in groups of ten in glass jars containing 200 ml of test media under static test conditions. Each exposure concentration was run in duplicate (20 daphnids/concentration) with a loading factor of 20 ml test solution per daphnid.

The criterion of effect used was that daphnids were considered to be immobilized if they were unable to swim for approximately 15 seconds after general agitation. The number of immobilized daphnids were recorded after 24 and 4 hours.

Remark : 95% confidence limits: 20-29 mg/l

Result : Exposure to the test material resulted in immobilisation of daphnia at nominal concentrations of 18, 32, 56, 100 mg/l, whereas no immobilisation occurred at concentrations of 1.0, 1.8, 3.2 and 5.6 and 10 mg/l (nominal).

Cumulative immobilisation

Conc. (mg/L)	24 hours	48 hours	Total no. immobilised
0	0	0	0/20
1.0	0	0	0/20
1.8	0	0	0/20
3.2	0	0	0/20
5.6	0	0	0/20
10	0	0	0/20
18	5	6	6/20
32	11	13	13/20
56	13	20	20/20
100	20	20	20/20

Test condition : Animals: 20 (2 groups of 10) daphnia per concentration,
Age: 24 hours,
Medium: dechlorinated and aged tap water,
Water quality: total hardness= 50mg/L as CaCO3,
pH = 7.6 - 7.7,
Oxygen Conc. = 7.9 - 8.6 mg/O2/L,
Temperature: 22 degrees C,
Lighting: 16 hours light and 8 hours dark,
Nominal conc.: 0 (control), 1.0, 1.8, 3.2, 5.6, 10, 18, 32, 56 and 100 mg/L.

Test substance : 2-Hydroxypropyl acrylate (purity min 97%; 1% acrylic acid)

Reliability : (2) valid with restrictions
Analytical verification was not performed.

Flag : Critical study for SIDS endpoint

03.04.2003 (20)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : other: biomass and growth rate
Exposure period : 96 hour(s)
Unit : mg/l

Limit test	:	
Analytical monitoring	:	no
Method	:	EPA OPPTS 850.5400
Year	:	2003
GLP	:	yes
Test substance	:	other TS
Method	:	Also conducted according to OECD Test Guideline 201
Remark	:	A preliminary test at concentrations of HPA at 0, 1, 10, 100 and 1000 mg/L (2 replicates/concentration) was conducted in which biomass and growth rate were monitored at 0, 24, 48, 72 and 96 hours. Based on the results of the preliminary study, the definitive 96-hour static EC50 test was conducted with nominal concentrations of 0, 0.625, 1.25, 2.5, 5, and 10 mg/L. The test was carried out under static conditions. The test was initiated with exponentially growing cells (3 days old). The pH was measured at the beginning of the study on an extra replicate for each concentration. Water temperature was recorded hourly. Room temperature was monitored continuously. Light intensity was measured prior to the start of the study. After 96 hours of growth, the pH was measured in pooled samples from each concentration. Changes in cell development or appearance, such as cell clumping, cell morphology, cell color, cell shape, and cell size were reported. After 96 h, 5 mL of alga suspension from the 5 and 10 mg/L concentrations were transferred to fresh medium and allowed to grow for 3-4 days to determine reversibility of any test chemical effects. CRITERIA FOR A VALID STUDY: Exponential cell growth should be demonstrated in the control replicates. The temperature during the test must be in the range of 24 ± 2 ºC and the pH of the control replicates should not deviate more than 1.0 unit during the test. STATISTICS: The EbC50 and ErC50 values and confidence intervals were calculated by probit analysis. The NOEC and LOEC were determined by calculation of statistical significance of biomass and growth rates using One Way Analysis of Variance (ANOVA) and Dunnett's test or Bonferroni t-test. An Equal Variance Test was conducted prior to the ANOVA and a normality test and homogeneity test were conducted prior to the Bonferroni t-test determination. A significance level of 0.05 was used for all tests. The following is a summary of the test conditions: Test species: Pseudokirchneriella subcapitata; formerly known as Selenastrum capricornutum Duration of test: 96 hours Culture medium: Algal growth medium (according to OECD Guideline) Testing medium: Algal growth medium (according to OECD Guideline) Temperature: 24 ± 2°C Light quality: Fluorescent Light intensity: (66.5 ± 10% µE.mE-02.sE-01) Photoperiod: Continuous (24 hours) Test vessel size: Clear glass 250-mL Erlenmeyer flasks Nutrient/test solution volume: 100 mL pH of the nutrient solution: Recommended = 7.5 ± 0.2 Age of test plants: 3 days Number of cells per test vessel: 1 x 104 cells/mL Definitive test concentrations: 0, 0.625, 1.25, 2.5, 5, and 10 mg/L Number of replicate test vessels/concentration in definitive test: 3 replicates per test concentration; 6 replicates for control Measured endpoints: Cell density measured daily using a Chlorophyll-a-fluorescence excitation at 435 nm Calculated endpoints: Area under the growth curve (biomass), growth

rate
Statistical endpoints: 72- and 96-hour ECb50 (based on area under the growth curve), 72- and 96-hour ECr50 (based on growth rate).

Result : Based on nominal concentrations:
Growth:
ErC50 (72h) = 6.98 mg/L (95% CI = 5.82 - 8.38 mg/L)
ErC50 (96h) = 6.67 mg/L (95% CI = 5.63 - 7.90 mg/L)
NOEC (72h) = 2.5 mg/L
LOEC (72h) = 5 mg/L
NOEC (96h) = 2.5 mg/L
LOEC (96h) = 5 mg/L
Biomass (area under the curve):
EbC50 (72h) = 3.88 mg/L (95% CI = 3.55 - 4.24 mg/L)
EbC50 (96h) = 3.53 mg/L (95% CI = 3.25 - 3.82 mg/L)
NOEC (72h) = 0.625 mg/L
LOEC (72h) = 1.25 mg/L
NOEC (96h) = 0.625mg/L
LOEC (96h) = 1.25 mg/L

For the preliminary test, inhibition based on biomass was 98, 100 and 100% of control at 10, 100 and 1000 mg/L, respectively. Corresponding inhibition based on growth rate was 73, 100 and 100%.

Microscopic evaluation of the cells at the end of the incubation period revealed no morphological abnormalities. Environmental conditions (pH, water temperature) were within acceptable limits. The pH ranged from 7.49 to 7.64 at time 0 and 8.48 to 8.89 at 96 hours for the six concentrations. Based on an estimated half-life for hydrolysis of HPA at pH 8 of 35 to 40 days, the pH changes that occurred over the 96 hours in this study are unlikely to have resulted in significant decrease in HPA concentrations. The water temperature ranged from 23.8 to 24.3 deg C.

The following table provides a summary of cell density, area under growth curves and growth rate for the definitive test:

Nominal Conc. (mg/L)	Average Cell Counts (x 10,000) 24 h	48 h	72 h	96 h	Inhibition of Biomass (%)	Rate-Related Inhibition (%)
0	8.4	46	201	453		
0.625	7.8	51	203	447	-3.4	-1.2
1.25	7.9	46	177	352	7.7	-1.4
2.5	7.7	39	164	362	17	3.3
5	5.4	16	29	45	78	36
10	3.9	5.0	6.9	7.7	94	65

Test substance : 2-Hydroxypropyl acrylate (HPA; CAS RN 25584-83-2);
Purity: 98.81%

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
23.08.2005 (48)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : other: heterotrophic
Species : Candida albicans (Fungi)
Exposure period :
Unit : g/l
MIC : = 5
Analytical monitoring : no
Method : other: Determination of Minimal Inhibition Concentration (MIC)
Year :

GLP : no
Test substance :

Test condition : Strain: C. albicans, ATCC 10231,
Incubation: 12-15 hours at 28 degree C,
Evaluation: bacterial growth,
MIC: test concentration at which no increase of turbidity was observed due to bacterial growth.
Test substance : Hydroxypropyl acrylate, BMC Acryl-Chemie
Reliability : (2) valid with restrictions
Only basic data are given (summary of test results)

03.02.2003 (2)

Type : other: heterotrophic
Species : Escherichia coli (Bacteria)
Exposure period :
Unit : g/l
MIC : = 10
Analytical monitoring : no
Method : other: Determination of Minimal Inhibition Concentration (MIC)
Year :
GLP : no
Test substance :

Test condition : Strain: E. coli, ATCC 11229,
Incubation: 12-15 hours at 28 degree C,
Evaluation: bacterial growth,
MIC: test concentration at which no increase of turbidity was observed due to bacterial growth.
Test substance : Hydroxypropyl acrylate, BMC Acryl-Chemie
Reliability : (2) valid with restrictions
Only basic data are given (summary of test results)

03.02.2003 (2)

Type : other: heterotrophic
Species : Pseudomonas aeruginosa (Bacteria)
Exposure period :
Unit : g/l
MIC : = 10
Analytical monitoring : no
Method : other: Determination of Minimal Inhibition Concentration (MIC)
Year :
GLP : no
Test substance :

Test condition : Strain: P. aeroginosa, ATCC 15442,
Incubation: 12-15 hours at 28 degree C,
Evaluation: bacterial growth,
MIC: test concentration at which no increase of turbidity was observed due to bacterial growth.
Test substance : Hydroxypropyl acrylate, BMC Acryl-Chemie
Reliability : (2) valid with restrictions
Only basic data are given (summary of test results)

03.02.2003 (1)

Type : other: heterotrophic
Species : Staphylococcus aureus (Bacteria)
Exposure period :
Unit : g/l
MIC : = 10
Analytical monitoring : no
Method : other: Determination of Minimal Inhibition Concentration (MIC)

Year	:	
GLP	:	no
Test substance	:	
Test condition	:	Strain: S. aureus, ATCC 6538, Incubation: 12-15 hours at 28 degree C, Evaluation: bacterial growth, MIC: test concentration at which no increase of turbidity was observed due to bacterial growth.
Test substance	:	Hydroxypropyl acrylate, BMC Acryl-Chemie
Reliability	:	(2) valid with restrictions Only basic data are given (summary of test results)

03.02.2003 (1)

Type	:	other: lithotrophic
Species	:	Nitrobacter sp. (Bacteria)
Exposure period	:	
Unit	:	mg/l
MIC	:	= 20
Analytical monitoring	:	no
Method	:	other: Determination of Minimal Inhibition Concentration (MIC)
Year	:	
GLP	:	no
Test substance	:	
Test condition	:	Strain: Nitrobacter K62, Incubation: 12-15 hours at 28 degree C, Evaluation: nitrite consumption, MIC: test concentration at which an inhibition of more than 5% compared to control occurred.
Test substance	:	Hydroxypropyl acrylate, BMC Acryl-Chemie
Reliability	:	(2) valid with restrictions Only basic data are given (summary of test results)

03.02.2003 (1)

Type	:	other: lithotrophic
Species	:	Nitrobacter sp. (Bacteria)
Exposure period	:	
Unit	:	mg/l
MIC	:	= 200
Analytical monitoring	:	no
Method	:	other: Determination of Minimal Inhibition Concentration (MIC)
Year	:	
GLP	:	no
Test substance	:	
Test condition	:	Strain: Nitrobacter winogradskyi, Incubation: 12-15 hours at 28 degree C, Evaluation: nitrite consumption, MIC: test concentration at which an inhibition of more than 5% compared to control occurred.
Test substance	:	Hydroxypropyl acrylate, BMC Acryl-Chemie
Reliability	:	(2) valid with restrictions Only basic data are given (summary of test results)

03.02.2003 (1)

Type	:	other: lithotrophic
Species	:	Nitrosomonas sp. (Bacteria)
Exposure period	:	
Unit	:	mg/l
MIC	:	= 40
Analytical monitoring	:	no

Method	:	other: Determination of Minimal Inhibition Concentration (MIC)
Year	:	
GLP	:	no
Test substance	:	
Test condition	:	Strain: Nitrosomonas M22, Incubation: 12-15 hours at 28 degree C, Evaluation: formation of nitrite, MIC: test concentration at which an inhibition of more than 5% compared to control occurred.
Test substance	:	Hydroxypropyl acrylate, BMC Acryl-Chemie
Reliability	:	(2) valid with restrictions Only basic data are given (summary of test results)

03.02.2003 (1)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : = 820 mg/kg bw
Species : rat
Strain :
Sex : male
Number of animals : 70
Vehicle :
Doses : 0, 710, 840, 1000, 1410 and 2000 mg/kg
Method : other: Acute oral toxicity
Year : 1982
GLP : no data
Test substance : other TS

Method : Ten male rats (CRCD) per group (except for the 710 mg/kg group which had 20/group) were fasted overnight prior to oral administration of the test substance at doses of 0, 710, 840, 1000, 1410 or 2000 mg/kg at a constant dose volume of 5 ml/kg. The control group was dosed with distilled water at a dose volume of 5 ml/kg. Animals weighed between 220 and 235 g at the start of the study. Animals were observed for 14 days post dosing for mortality and clinical signs. A necropsy was performed on all animals at the time of death an on all survivors at the end of the observation period.
Remark : Confidence limits: 760 - 910 mg/kg
Result : Signs of toxicity, including passiveness, ataxia and salivation, were observed in several animals.

Mortality

Dose group (mg/kg)	No. Dead/ No. Dosed
0	0/10
710	4/20
840	5/10
1000	9/10
1410	10/10
2000	10/10

No gross lesions were observed in any animal that was sacrificed at the end of the 14-day observation period. The following observations were noted in animals that died during the study: stained muzzle; lungs, stomach and intestines red and fluid-filled; and enlarged stomach.
Test substance : Rocryl 430 (Hydroxypropyl acrylate, purity 97%)
Reliability : (2) valid with restrictions
Basic data given (comparable to guidelines/standards)
Data were audited by QAU but no reference to GLP standard.
Flag : Critical study for SIDS endpoint
14.03.2003 (44)

Type : LD50
Value : = 1290 mg/kg bw
Species : rat
Strain : Wistar
Sex : male
Number of animals : 15

Vehicle : other: none
Doses : 0.5, 1.0 and 2.0 ml/kg (525, 1050 and 2100 mg/kg bw)
Method : other: not specified
Year : 1967
GLP : no
Test substance :

Method : Five male Wistar rats (90-120 grams and 2 to 4 weeks old) per group were administered the test substance undiluted via stomach intubation. Animals were not fasted prior to dosing. Animals were observed for 14 days postdosing. The LD50 was calculated by the moving average method.
Remark : LD50 = 1.23 ml/kg (1290 mg/kg bw)
Confidence limits: 0.89 to 1.70 ml/kg (934 to 1780 mg/kg bw)
Result : Animals in the 2.0 ml/kg group were prostrate soon after dosing. Animals in the 0.5 ml/kg were sluggish.

Mortality

Dose group (ml/kg)	No. Dead/ No. Dosed
0.5	0/5
1.0	1/5
2.0	5/5

Gross lesions observed at the time of necropsy included: hemorrhage of the lungs and intestines; congested livers, stomachs, kidneys and adrenals.
Test substance : Purity not provided.
Reliability : (2) valid with restrictions
Basic data given (comparable to guidelines/standards)

27.12.2004 (54)

Type : LD50
Value : = 1180 mg/kg bw
Species : rat
Strain : Wistar
Sex : male
Number of animals : 10
Vehicle : other: none
Doses : 1.0 and 2.0 ml/kg (1050 and 2100 mg/kg bw)
Method : other: not specified
Year : 1971
GLP : no
Test substance : other TS

Method : Five male Wistar rats (90-120 grams and 2 to 4 weeks old) per group were administered the test substance undiluted via stomach intubation. Animals were not fasted prior to dosing. Animals were observed for 14 days postdosing. The LD50 was calculated by the moving average method.
Remark : LD50 = 1.13 ml/kg (1180 mg/kg bw)
Confidence limits: 0.583 to 2.16 ml/kg (612 to 2270 mg/kg bw)
Result : Animals in the 2.0 ml/kg group had wet fur 30 minutes after dosing. Animals in the 1.0 ml/kg group were sluggish five minutes after dosing. All deaths occurred one day following dosing.

Mortality

Dose group (ml/kg)	No. Dead/ No. Dosed
1.0	5/5
2.0	2/5

Gross lesions observed at the time of necropsy of animals that died included: congestion throughout the lungs, liver, kidneys and adrenals.

Test substance : hydroxypropyl acrylate (3 parts 2-hydroxy-1-propyl acrylate: 1 part 1-hydroxy-2-propyl acrylate);
Purity not provided.

Reliability : (2) valid with restrictions
Basic data given (comparable to guidelines/standards)

27.12.2004 (55)

Type : other: acute oral toxicity
Value :
Species : rat
Strain :
Sex : no data
Number of animals : 4
Vehicle : water
Doses : 0.252 and 0.50 g/kg
Method : other: not specified
Year : 1964
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : The test substance was dosed as a 10% solution in water at dose levels of 0.252 and 0.5 g/kg.

Result : Mortality: No deaths occurred the 0.252 g/kg dose group. All animals (2/2) in the 0.5 k/kg group died one day following dosing.
Gross necropsy of all animals on study revealed no apparent treatment-related lesions.

Test substance : 2-hydroxypropyl acrylate

Reliability : (2) valid with restrictions
minimal details provided

18.03.2003 (16)

5.1.2 ACUTE INHALATION TOXICITY

Type : other:
Value :
Species : rat
Strain : no data
Sex : no data
Number of animals : 6
Vehicle :
Doses : substantially saturated vapor - no analysis performed
Exposure time : 8 hour(s)
Method : other: substantially saturated vapor
Year : 1971
GLP : no data
Test substance : other TS

Method : Substantially saturated vapor is prepared by spreading 50 grams of chemical over 200 cm2 area on shallow tray placed near the top of a 120-liter glass chamber which is then sealed for at least 16 hours while an intermittently operated fan agitates the internal chamber atmosphere. Rats are then introduced in a gasketed drawer-type cage designed and operated to minimize vapor loss.

Result : No deaths occurred. Observations during exposure included: extremities irritated within 4 hours; slight loss of coordination at 6 hours but normal at 8 hours.

Test substance : hydroxypropyl acrylate (3 parts 2-hydroxy-1-propyl acrylate: 1 part 1-hydroxy-2-propyl acrylate);

Purity not provided.
Reliability : (2) valid with restrictions
Basic data given
27.12.2004 (55)

Type : other: saturated atmosphere
Value :
Species : rat
Strain :
Sex :
Number of animals : 13
Vehicle :
Doses :
Exposure time :
Method : other: Saturated atmosphere
Year : 1964
GLP : no
Test substance : other TS

Method : Rats were exposed to saturated atmospheres of the test substance according to the following study design:

Bath Temperature	Length of Exposure	No. Rats Exposed
100 C	1 hour	4
100 C	4.25 hours	5
Room	7 hours	4

Result : Mortality

Bath Temperature	Length of Exposure	No. Dead/ No. Exposed
100 C	1 hour	0/4
100 C	4.25 hours	5/5
Room	7 hours	0/4

Responses:
1-hour exposure with 100 degree C bath: Animals had wet noses and closed eyes when removed, but were conscious. They recovered normally.
4.25-hour exposure with 100 degree C bath: After thirty minutes in the chamber, rats were puffing, ataxic and held their eyes shut. At the end of the exposure, one rat was dead and the others were unconscious. All were dead an hour later.
7-hour exposure with room temperature bath: Animals normal during and after exposure.
Test substance : 2-hydroxypropyl acrylate
Reliability : (2) valid with restrictions
Minimal details provided.
18.03.2003 (16)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : = 306 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 72
Vehicle :
Doses : 0, 115, 132, 152, 174, 180, 192, 206, 220, 250, 304, 370 and 450 mg/kg

Method : other: Acute dermal toxicity
Year : 1982
GLP : no data
Test substance : other TS

Method : Six male New Zealand white rabbits per group, approximately 2 to 2.5 kg were exposed to the test substance via the dermal route at doses of 0, 115, 132, 152, 174, 180, 192, 206, 220, 250, 304, 370 and 450 mg/kg. The test substance was applied to the clipped skin and held under an impervious wrap for 24 hours. The skin of half of the animals was abraded. After the 24-hour exposure, the wrapping was removed and the application site was wiped gently to remove the test substance. The animals were observed for 14 days post-application. A necropsy was performed on all animals at the time of death and on all survivors at the end of the observation period.

Result : Signs of toxicity, including passiveness, hypothermia, ataxia and iritis, were observed. Skin irritation (erythema and oedema) was found on day 1 and desiccation on day 4. Skin irritation persisted through day 14 in all dose groups. Small areas of eschar were observed to be sloughing off on day 14 and new hair growth was observed beneath the eschar.

Mortality

Dose group (mg/kg)	No. Dead/ No. Dosed
115	0/6
132	0/6
152	0/6
174	0/6
180	1/6
192	1/6
206	0/6
220	0/6
250	1/6
304	3/6
370	4/6
450	6/6

Necropsy observations seen in the majority of the animals that died during the study included: erythema and edema at dosing site; and black foci on stomach mucosa. Other gross lesions observed in single incidences at the time of necropsy included: blanching and eschar at dosing site; kidneys pitted; clear fluid-filled stomach; and tan area on liver. The majority of the surviving animals had eschar and blanching of the dosing site at the time of necropsy. Other gross lesions observed in one to two surviving animals included: pale and/or mottle kidneys; red foci on kidneys; and tan foci on liver. Aside from the skin irritation at the dosing site, no gross lesions were observed in any animal in the 115 mg/kg that was sacrificed at the end of the 14-day observation period.

Test substance : Rocryl 430 (Hydroxypropyl acrylate, purity 97%)
Reliability : (2) valid with restrictions
Basic data given (comparable to guidelines/standards)
Data were audited by QAU but no reference to GLP standard.
Flag : Critical study for SIDS endpoint
27.12.2004 (44)

Type : LD50
Value : = 168 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 8
Vehicle : other: none

Doses : 0.1 and 0.2 ml/kg (105 and 210 mg/kg bw)
Method : other: not specified
Year : 1967
GLP : no
Test substance :

Method : The test substance was administered to the clipped, intact skin of four male New Zealand White rabbits (3 to 5 months of age) per group. The dose sites were wrapped with impervious sheeting for 24 hours. After the 24-hour exposure period, excess test substance was removed to prevent ingestion. Animals were observed for 14 days postdosing.
Remark : Confidence limits: 0.097 to 0.26 ml/kg
Result : Edema, necrosis and ecchymosis was observed at the test site of the animals.

Mortality

Dose group (mg/kg)	No. Dead/ No. Dosed
1.0	0/4
2.0	3/4

Gross lesions observed at the time of necropsy included: hemorrhage and congestion of the lungs; congested livers and mottle kidney surfaces.
Test substance : Purity not provided.
Reliability : (2) valid with restrictions
Basic data given (comparable to guidelines/standards)

03.01.2005 (54)

Type : LD50
Value : = 117 mg/kg bw
Species : rabbit
Strain : other: albino
Sex : male
Number of animals : 12
Vehicle : other: none
Doses : 0.05, 0.10 and 0.20 ml/kg (52.4, 105 and 210 mg/kg bw)
Method : other: not specified
Year : 1971
GLP : no
Test substance : other TS

Method : The test substance was administered to the clipped, intact skin on the trunk of four male albino rabbits (3 to 5 months of age) per group. The dose sites were wrapped with impervious sheeting for 24 hours. After the 24-hour exposure period, excess test substance was removed to prevent ingestion. Animals were observed for 14 days postdosing.
Remark : Confidence limits: 0.0528 to 0.239 ml/kg
Result : Ecchymosis and edema were noted on the test sites in all dose groups. In addition, necrosis was observed on the test sites of animasl in the 0.20 ml/kg dose group. All deaths occurred one or two days following dosing.

Mortality

Dose group (mg/kg)	No. Dead/ No. Dosed
0.05	0/4
0.10	2/4
0.20	3/4

Gross lesions observed at the time of necropsy included: congestion throughout the lungs, spleens and kidneys; livers mottled with prominent

acini; urinary bladder empty or with sediment or solid contents.

Test substance : Hydroxypropyl acrylate (3 parts 2-hydroxy-1-propyl acrylate: 1 part 1-hydroxy-2-propyl acrylate);
Purity not provided.

Reliability : (2) valid with restrictions
Basic data given (comparable to guidelines/standards)

29.12.2004 (55)

Type : LD50
Value : = 214 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 12
Vehicle : other: none
Doses : 130, 250 and 400 mg/kg bw
Method : other
Year : 1981
GLP : no data
Test substance :

Method : Twenty-four hours prior to application, the entire trunk of two male and two female New Zealand White rabbits per group was clipped free of hair. The undiluted test substance was applied to the intact skin at dose levels of 130, 250 or 400 mg/kg and covered with an occlusive plastic wrap for 24 hours. After the 24-hour exposure period, the wraps were removed and the skin was washed with a mild soap and water, rinsed thoroughly and dried with a soft disposable towel. The topical response at the test sites was evaluated after removal of the plastic wrap. The rabbits were then fitted with a plastic collar to prevent ingestion of any residual test material. The collars were removed at least 72 hours later. The animal were observed frequently during exposure and for two weeks following exposure for signs of toxicity. Body weights were recorded before and after the 24-hour exposure period and at and 2 weeks post-treatment. A gross necropsy was performed on all surviving rabbits following the 2-week post-treatment observation period. The acute percutaneous absorption LD50 was calculated by the moving average method of Thompson and Weil (Thompson, W.R. and C.S. Weil. Biometrics, (1952) 8:1:51-54. as implemented in a computer program (Stephan, C., 1978. personal communication).

Remark : Confidence limits: 140 - 293 mg/kg

Result : LD50 = 214 mg/kg

Mortality

Dose group (mg/kg)	No. Dead/ No. Dosed
130	0/4
250	3/4
400	4/4

Deaths occurred within two days of dosing.

Topical responses observed on the application sites of 6 test rabbits 24 hours post-treatment included: moderate to marked redness, moderate to marked swelling and slight necrosis. Animal observations during the two-week post-treatment observation period included: lethargy (all groups); loss of appetite and decreased activity at 130 mg/kg; and shallow breathing at 400 mg/kg. A gross necropsy was performed on four surviving animals in the 130 mg/kg dose group and one in the 250 mg/kg dose group. No treatment-related internal lesions were noted in these animals.

Test substance : Hydroxypropyl acrylate;

Purity not provided.
Reliability : (2) valid with restrictions
well documented report (comparable to guidelines/standards)
29.12.2004 (7)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	highly irritating
Classification	:	
Method	:	
Year	:	1959
GLP	:	no
Test substance	:	

Method : other: Patch test according to "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics" (US-AFDO).
Result : The primary skin irritation index which presents the mean value of the sum of all scores (abraded and non-abraded, 24 and 72 h) from 6 animals was established to be 7.9 (maximum possible score 8). On the basis of this value, the test compound was regarded as severely irritant.
Test condition : Animals: 3 male and 3 female rabbits (Himalayan),
Body weight: 1.5 - 2 kg,
Dose: 0.5 ml (gauze patch 2.5 x 2.5 cm),
Exposure: 24 hours (semi-occlusive), abraded and non-abraded skin (back and flank),
Observations:immediately and 48 h after patch removal (24 and 72 h after initiation).
Test substance : TK 12116 (2-Hydroxypropyl acrylate), Batch No. 7/76;
Purity not provided.
Reliability : (2) valid with restrictions
Only basic data given (summary of test results)
03.01.2005 (10)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	other: none
PDII	:	7
Result	:	highly irritating
Classification	:	irritating
Method	:	other: Acute skin irritation
Year	:	1982
GLP	:	no data
Test substance	:	other TS

Method : 0.5 ml of the test substance was applied to the clipped intact skin of six male New Zealand white rabbits and held under a patch covered with an

impervious cuff for 4 hours. After the 4-hours exposure period, the patches and cuffs were removed and the application sites wiped gently with a paper towel to remove any residual test substance. Test sites were scored at 0.5, 24 and 72 hours and 7 and 14 days following patch removal.

Result : The 72-h mean irritation score (sum of the mean erythema and oedema values after 72 h) was 7.0. On the basis of this value, the test compound was regarded as severely irritant. Severe erythema, eschar formation and dessication but only slight oedema remained after 7 days.
Test substance : Rocryl 430 (Hydroxypropyl acrylate, purity 97%)
Reliability : (2) valid with restrictions
Basic data given (comparable to guidelines/standards)
Data were audited by QAU but no reference to GLP standard.

14.03.2003 (44)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result : highly irritating
Classification :
Method :
Year : 1959
GLP : no
Test substance :

Method : other: Patch test according to "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics" (US-AFDO).
Result : The primary skin irritation index which presents the mean value of the sum of all scores (abraded and non-abraded, 24 an 72 h) from 6 animals was established to be 7.7 (maximum possible score 8). On the basis of this value, the test compound was regarded as severely irritant.
Test condition : Animals: 3 male and 3 female rabbits (Himalayan),
Body weight: 1.5 - 2 kg,
Dose: 0.5 ml (gauze patch 2.5 x 2.5 cm),
Exposure: 24 hours (semi-occlusive), abraded and non-abraded skin (back and flank),
Observations:immediately and 48 h after patch removal (24 and 72 h after initiation).
Test substance : TK 12117 (2-Hydroxypropyl acrylate), Batch No. 7/76;
Purity not provided.
Reliability : (2) valid with restrictions
Only basic data given (summary of test results)

03.01.2005 (11)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result : highly irritating
Classification :
Method : Draize Test
Year : 1980
GLP : no data
Test substance :

Remark	:	Application: 0.25 ml, occlusive, abraded and non abraded skin Number of animals: 6 Primary irritation score: 5.4 (24 hours) Draize score HPA was found to be a severe irritant producing necrosis, subcutaneous hemorrhage and pitting edema over a wide area of skin in rabbits.
Test substance	:	Source: British Petroleum Co. Ltd.; Purity not provided.
Reliability	:	(2) valid with restrictions Only summary of the toxicological study available. Without detail documentation but acceptable for assessment.

29.12.2004 (4)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	other: DOT test for corrosiveness
Year	:	1973
GLP	:	no data
Test substance	:	other TS
Method	:	A sample of hydroxypropyl acrylate as submitted for evaluation of corrosiveness to skin in accordance with the Department of Transportation Hazardous Materials Regulation of the Code of Federal Regulations, Title 49, Section 173.240. A corrosive material is one that causes irreversible change or destruction to the intact skin of an albino rabbit after an exposure period of 4 hours. The test procedure used is described in Paragraph 191.11 of 21 CFR Part 191 (revised as of January 1, 1970).
Result	:	Hydroxypropyl acrylate is non-corrosive.
Test substance	:	Hydroxypropyl acrylate; Purity not provided.
Reliability	:	(2) valid with restrictions Minimal details provided.

29.12.2004 (18)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	other: DOT test for corrosiveness
Year	:	1981
GLP	:	no data
Test substance	:	other TS
Method	:	A sample of 2-hydroxypropyl acrylate was submitted for evaluation of corrosiveness to skin by the DOT (Department of Transportation) Test. A corrosive material is one that causes irreversible change or destruction to the intact skin of an albino rabbit after an exposure period of 4 hours or less. The test procedure used is described in the Code of Federal

Regulations, Title 49, Section 173.240, Appendix A.

Result : A 4-hour exposure to the test material resulted in slight-moderate redness, severe swelling, and superficial necrosis (1/6) to the skin of 6 albino rabbits (New Zealand albino rabbits). The test material is considered not corrosive by this test.

Test substance : 2-hydroxypropyl acrylate;
Purity not provided.

Reliability : (2) valid with restrictions
Minimal details provided.

29.12.2004 (19)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
Vehicle :
PDII :
Result :
Classification :
Method : other: not specified
Year : 1964
GLP : no
Test substance : other TS

Method : The rabbit(s) had three test sites: the ear, abraded abdominal skin and intact abdominal skin. A 10% solution of the test substance in water was applied to the intact skin of the ear for 9 applications; and to the intact and abraded abdominal skin of the same rabbits for 1 application.

One rabbit had the undiluted test substance applied to each of the three test sites mentioned above for one application.

Result : The rabbit on the undiluted test material died overnight after one application to each of the three test sites.

Essentially no irritation was observed after 9 applications to the ear. Moderate burn accompanied by severe edema was observed on the intact and abraded skin of the abdomen after one application. Severe scar remained on these test sites after 21 days.

Test substance : 2-hydroxypropyl acrylate;
Purity not provided.

Reliability : (2) valid with restrictions
minimal details provided

29.12.2004 (16)

Species : rabbit
Concentration :
Exposure : no data
Exposure time : 24 hour(s)
Number of animals : 6
Vehicle : water
PDII :
Result :
Classification :
Method : other: Cuff Technique
Year : 1964
GLP : no
Test substance : other TS

Method : Rabbits were exposed to the test substance at the following concentrations (in water) and dose levels for 24 hours:
12.6% solution at 0.252 g/kg

50% solution at 0.252 g/kg
50% solution at 0.5 g kg

Result : Mortality

Concentration	Dose (g/kg)	No. Dead/ No. Exposed
12.6%	0.252	0/2
50%	0.252	1/2
50%	0.50	2/2

Responses:
12.6% solution at 0.252 g/kg: Severe hyperemia and swelling observed upon removal of the cuff. Animals recovered normally but had slight scabs in two weeks.
50% solution at 0.252 g/kg: One animal died overnight; the other had moderate hyperemia and edema upon removal of the cuff. This animal recovered normally, but had scabs in two weeks.
50% solution at 0.5 g/kg: One animal died overnight; the other was very sick and had severe hyperemia and moderate edema upon removal of the cuff. This animal died later on that day.

Test substance : 2-hydroxypropyl acrylate;
Purity not provided.

Reliability : (2) valid with restrictions
Minimal details provided.

29.12.2004 (16)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : moderately irritating
Classification :
Method :
Year : 1959
GLP : no
Test substance :

Method : other: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (US-AFDO).

Result : The mean irritation indices were 18.1 for the cornea (maximum score 80), 0.5 for the iris (maximum score 10) and 10.4 for the conjunctivae (maximum score 20). Therefore, the test article caused an overall eye irritation index of 29 (maximum score 110) in rabbits which was regarded as moderate (26 - 56).

Test condition : Animals: 3 male and 3 female rabbits (Himalayan),
Body weight: 1.5 - 2 kg,
Dose: 0.1 ml (conjunctival sac, left eye),
Exposure: in 3 of the 6 animals, eyes were flushed with lukewarm water after 30 seconds,
Observations:on day 1, 2, 3, 4 and 7.

Test substance : TK 12116 (2-Hydroxypropyl acrylate), Batch No. 7/76;
Purity not provided.

Reliability : (2) valid with restrictions
Only basic data are given (summary of test results)

03.01.2005 (8)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	other: not rinsed in 6 rabbits and rinsed after 20-30 seconds in 3 rabbits
Number of animals	:	9
Vehicle	:	none
Result	:	highly irritating
Classification	:	irritating
Method	:	other: Acute eye irritation
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Method	:	Nine New Zealand White rabbits (male/female) had 0.1 ml of the test substance instilled onto the corneal surface of the eye. The eyes were held open momentarily after dosing and then released. Twenty to 30 seconds after instillation, three of the nine animals had their eyes flushed with water for approximately 60 seconds. The eyes were scored 24, 48 and 72 hours and 7, 14 and 21 days after dosing.
Remark	:	Some deviations exist between the report summary (page 2) and the raw data (page 12 of 14) concerning the number and sex of animals used. The observation times in the raw data are illegible.
Result	:	Corneal, irital and conjunctival irritation with opacification, and blood vessel encroachment of the cornea, were observed throughout the 21-day observation period. The iris was unscorable due to the density of the opacity. The compound was regarded as severely irritating on the basis of the duration of the ocular effects.
Test substance	:	Rocryl 430 (Hydroxypropyl acrylate, purity 97%)
Reliability	:	(2) valid with restrictions Only basic data are given (summary of test results) Data were audited by QAU but no reference to GLP standard.

14.03.2003 (44)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure time	:	
Comment	:	
Number of animals	:	
Vehicle	:	
Result	:	moderately irritating
Classification	:	
Method	:	
Year	:	1959
GLP	:	no
Test substance	:	
Method	:	other: Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics (US-AFDO).
Result	:	The mean irritation indices were 16.4 for the cornea (maximum score 80), 0.0 for the iris (maximum score 10) and 10.8 for the conjunctivae (maximum score 20). Therefore, the test article caused an overall eye irritation index of 27.2 (maximum score 110) in rabbits which was regarded as moderate (26 - 56).
Test condition	:	Animals: 3 male and 3 female rabbits (Himalayan), Body weight: 1.5 - 2 kg, Dose: 0.1 ml (conjunctival sac, left eye),

Exposure: in 3 of the 6 animals, eyes were flushed with lukewarm water after 30 seconds,
Observations:on day 1, 2, 3, 4 and 7.

Test substance : TK 12117 (2-Hydroxypropyl acrylate), Batch No. 7/76; Purity not provided.

Reliability : (2) valid with restrictions
Only basic data are given (summary of test results)

03.01.2005 (9)

Species : rabbit
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle : none
Result :
Classification :
Method : other: not specified
Year : 1964
GLP : no
Test substance : other TS

Method : Material was instilled undiluted. Both washed (with water) and unwashed eyes were evaluated.

Result : Unwashed eye: Moderate pain upon direct contact followed by severe and extensive conjunctival and corneal injury including swelling of the eyeball essentially resulting in total loss of vision.
Washed eye: Moderate to severe conjunctival irritation and corneal injury resulting in some permanent impairment of vision.

Test substance : 2-hydroxypropyl acrylate; Purity not provided.

Reliability : (2) valid with restrictions
minimal details provided

29.12.2004 (16)

5.3 SENSITIZATION

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification :
Method : other: Magnusson, B. and Kligman, A.M. (1970)
Year :
GLP : no
Test substance :

Remark : The cross-reaction patterns of selected acrylate and methacrylate esters were investigated.

Result : Following the induction with Hydroxyethyl methacrylate (HEMA), 2 out of 15 animals showed positive reactions after a challenge application of 0.3% HPA, whereas after induction with either HEA or HPA, all guinea pigs (12/12) of both groups reacted positive to a challenge with HPA.

Test condition : Animals: 12-15 females (SSc:AL) for each groups,
Age: 1 month,
Body weight: 300-350 g,
Induction: HEMA (i.d. 25%, dermal 100%),
HEA (i.d. 10%, dermal 100%),

HPA (i.d. 0.5%, dermal 25%),
Challenge: HPA (dermal 0.3 %).

Test substance : 2-Hydroxypropyl acrylate, ICN-K&K, New York
Reliability : (2) valid with restrictions
Acceptable, well documented publication which meets basic scientific principles.

29.12.2004 (12)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : not sensitizing
Classification :
Method : other: Magnusson, B. and Kligman, A.M. (1970)
Year :
GLP :
Test substance :

Remark : The cross-reaction patterns of selected acrylate and methacrylate esters were investigated.
Result : None of the animals reacted to 2-HPA.
Test condition : Animals: 10 each for control and treatment groups,
Replicates: 2,
Induction: 2-Hydroxypropyl methacrylate (HPMA) (i.d. 5%, dermal 25%)
Challenge: 2-HPA (dermal 2%).
Test substance : 2-hydroxypropyl acrylate, Pfaltz & Bauer USA, purity 95%
Reliability : (2) valid with restrictions
Acceptable, well documented publication which meets basic scientific principles.

03.01.2005 (3)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : not sensitizing
Classification :
Method :
Year :
GLP : no
Test substance :

Method : other: according to Maguire, H.C., 1973 (modified)
Result : HPA caused no skin sensitisation in the tested animals (0/9).
Test condition : Animals: 9 male guinea pigs (Hartley),
Body weight: approx. 300 g,
Induction: topical applications of 0.1 ml of test compound four times in 10 days (clipped back); at the time of 3rd application, 0.2 ml Freund's adjuvant was injected i.d. adjacent to the insult site,
Challenge: after 2 weeks, topical to the clipped flank,
Observation: at 24 an 48 hours after challenge.
Test substance : Purity not provided.
Reliability : (2) valid with restrictions
Only basic data are given (summary of test results)

29.12.2004 (37)

Type : Patch-Test
Species : human
Number of animals :

Vehicle :
Result : sensitizing
Classification :
Method : other: Patch test
Year :
GLP : no
Test substance :

Result : Three of 24 patients were actively sensitised to HPA and other acrylates. Irritation was observed in the initial patch test with HPA. These test sites became positive after 18-19 days, indicating active sensitisation. Sensitisation to HPA was confirmed by re-testing in 2 patients.
Test condition : Volunteers: 3 patients, actively sensitised with, e.g. HPA,
Conc.: 0.5% (w/w) HPA in petrolatum,
Testing: initial patch test and re-testing (2 patients),
Exposure: 24 hours, skin of the back or thighs,
Observation: 24, 48 and 96-120 hours after patch removal.
Test substance : 2-hydroxypropyl acrylate (Chemotechnique, 2)
Reliability : (2) valid with restrictions
Acceptable, well documented publication which meets basic scientific principles.

03.01.2005 (30)

Type : other: skin sensitization
Species : guinea pig
Concentration : 1st: Induction
2nd:
3rd:
Number of animals : 30
Vehicle : other: 9:1 mixture of Dowanol DPM:Tween 80
Result : sensitizing
Classification : sensitizing
Method : other: not specified
Year : 1970
GLP : no data
Test substance : other TS

Method : A 0.5% (w/v) solution of 2-hydroxypropyl acrylate in a 9:1 mixture of Dowanol DPM:Tween 80 was used for the induction and challenge phases of the study. The solution was applied to a clipped and chemically depilated area on the shoulders of male and female guinea pigs twice a week for 3 weeks. After a two week rest period, the animals were challenged by exposing the clipped skin on the flanks with the test solution and, also the solvent surfactant system. The negative control animals received the Dowanol DPM:Tween 80 mixture twice a week for 3 weeks and were challenged after a 2 week rest period with the solvent surfactant mixture. Positive control animals received DER-331 in Dowanol DPM:Tween 80 and were likewise challenged after a two week rest period, with the DER-331 in the solvent surfactant system, as well as with the solvent surfactant system alone.
Result : Material # sensitized/# treated
2-hydroxypropyl acrylate 4/10
DER-331 10/10
Dowanol DPM:Tween 80 0/10
Test substance : 2-hydroxypropyl acrylate;
Purity not provided.
Reliability : (2) valid with restrictions
minimal details provided

29.12.2004 (17)

5.4 REPEATED DOSE TOXICITY

Type	:	
Species	:	rat
Sex	:	male
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	31 days
Frequency of treatm.	:	6 hours/day, 5 days/week, total of 21 exposures
Post exposure period	:	
Doses	:	5 and 10 ppm (27 and 53 mg/m3)
Control group	:	yes, concurrent no treatment
NOAEL	:	< 5 ppm
LOAEL	:	= 5 ppm
Method	:	other: no data available
Year	:	1983
GLP	:	no
Test substance	:	other TS

Method :

Three groups of animals, each consisting of 2 male beagle dogs, 4 male New Zealand white rabbits, 10 male Sprague-Dawley rats and 20 Swiss-Webster mice were used in the study. The animals were exposed (whole body) to hydroxypropyl acrylate (HPA) vapors at 0 (unexposed control), 5 ppm (27 mg/m3) or 10 ppm (53 mg/m3). Exposures were 6 hours/day, 5 days/week for a total of 21 exposures for the rats. Food and water were available at all times except during exposure. Food and water were removed from the control animals for 6 hours on the first day of exposure only.

HPA vapor was generated by injection into a countercurrent vaporization column heated to approximately 140°C for the 5 ppm chamber and 180°C for the 10 ppm chamber. Air flow was maintained at 1.0 liter/minute in the 3.7 cubic meter chambers. The concentration of the vapor was determined 3-6 times daily by gas chromatography. Both isomers eluted in a single peak that was used for quantitation.

Animals were observed for signs of toxicity and irritation throughout the study. Body weights were recorded 3-4 times weekly. Hematology determination, including red cell counts, white cell counts, differential white cell counts, hemoglobin concentration, and packed cell volume were conducted on 7 rats/group at termination. Urine was collected from the same 7 rats/group and specific gravity, pH, glucose, protein, and the presence or absence of ketones, bilirubin and blood were determined. Clinical chemistry determinations were also made for the 7 rats/group including BUN, glucose, SGPT, and alkaline phosphatase.

A necropsy was performed on all animals. The brain, heart, liver, kidneys and testes were weighed. The following organs were retained in fixative: adrenal glands, parathyroid glands, thyroid glands, aorta, sternum, bone marrow, kidneys, urinary bladder, prostate, accessory sex glands, epididymides, testes, urethra, brain, pituitary gland, spinal cord, peripheral nerve, large intestine, small intestine, esophagus, salivary gland, stomach, pancreas, liver, lung, skin, larynx, trachea, nasal turbinates, heart, lymph nodes, spleen, thymus, skeletal muscle, mammary tissue, eyes, gross lesions.

Histologic examination of the tissues listed above was conducted for five rats/group.

Statistical analyses of hematological, biochemical and body weight data were carried out using an analysis of variance and Dunnett's test ($p<0.05$).

Result : Average chamber concentrations were measured before the study to be approximately 77% f the nominal concentrations. Therefore, the amount of HPA was adjusted to provide 4.49 +- 1.17 and 9.87 +- 0.72 ppm measured concentrations for the low and high exposure groups respectively.

No mortality was observed during the study. Five of 10 rats exposed to 10 ppm developed slight cloudiness of the cornea. All rats (including control) showed swelling of the salivary glands (interpreted as sialodacryoadenitis). No treatment-related decreases in mean body weights were found, and the absolute and relative organ weights were not affected. Hematological investigations, clinical chemistry and urinalysis indicated no treatment-related effects.

At necropsy, focal corneal cloudiness was noted in 8 of 10 rats from the high exposure group suggesting an irritant effect. Histologically, a small increase in the number of animals with changes in the lungs at 10 ppm (subacute pneumonitis) and nasal mucosa (both concentrations) was observed. These were considered related to HPA exposure.

Pathologic Finding	0 ppm	5 ppm	10 ppm
Focal subacute pneumonities, minimal	1/5	1/5	2/5
, moderate	0/5	1/5	2/5
Subacute inflammatory infiltrate, nasal mucosa	0/5	3/5	1/5

No systemic toxicity was identified from the gross and microscopic pathological examinations. The LOAEC was 5 ppm (27 mg/m3) based on the effects in the nasal mucosa.

Test substance : Hydroxypropyl acrylate (purity 97.09%)
(75% 2-HPA, 25% 1-Methyl-2-hydroxyethyl acrylate)

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

10.08.2005 (36)

Type :
Species : mouse
Sex : male
Strain : Swiss Webster
Route of admin. : inhalation
Exposure period : 31 days
Frequency of treatm. : 6 hours/day, 5 days/week, total of 21 exposures
Post exposure period :
Doses : 5 and 10 ppm (27 and 53 mg/m3)
Control group : yes, concurrent no treatment
NOAEL : = 5 ppm
LOAEL : = 10 ppm
Method : other: no data available
Year : 1983
GLP : no
Test substance : other TS

Method : Three groups of animals, each consisting of 2 male beagle dogs, 4 male New Zealand white rabbits, 10 male Sprague-Dawley rats and 20 Swiss-Webster mice were used in the study. The animals were exposed (whole body) to hydroxypropyl acrylate (HPA) vapors at 0 (unexposed control), 5 ppm (27 mg/m3) or 10 ppm (53 mg/m3). Exposures were 6 hours/day, 5 days/week for a total of 21 exposures for the mice. Food and water were available at all times except during exposure. Food and water were removed from the control animals for 6 hours on the first day of exposure only.

HPA vapor was generated by injection into a countercurrent vaporization column heated to approximately 140°C for the 5 ppm chamber and 180°C

for the 10 ppm chamber. Air flow was maintained at 1.0 liter/minute in the 3.7 cubic meter chambers. The concentration of the vapor was determined 3-6 times daily by gas chromatography. Both isomers eluted in a single peak that was used for quantitation.

Animals were observed for signs of toxicity and irritation throughout the study. Body weights were recorded 3-4 times weekly.

A necropsy was performed on all animals. The liver, kidneys and testes were weighed. The following organs were retained in fixative: adrenal glands, parathyroid glands, thyroid glands, aorta, sternum, bone marrow, kidneys, urinary bladder, prostate, accessory sex glands, epididymides, testes, urethra, brain, pituitary gland, spinal cord, peripheral nerve, large intestine, small intestine, esophagus, salivary gland, stomach, pancreas, liver, lung, skin, larynx, trachea, nasal turbinates, heart, lymph nodes, spleen, thymus, skeletal muscle, mammary tissue, gall bladder, eyes, gross lesions.

Histologic examination of the tissues listed above was conducted for five mice/group.

Statistical analyses of body weight data were carried out using an analysis of variance and Dunnett's test ($p<0.05$).

Result : No mortality was observed during the study. Three of 20 mice exposed to 10 ppm, but none exposed to 5 ppm showed signs of eye irritation. No compound-related statistically significant effects on mean body weights were found. However, the high dose mice showed a slight weight loss during weeks 1, 3 and 4 of exposure (maximum loss of 4.5% in week 1) which was recovered during the weekend without treatment. High dose mice had a significantly lower absolute mean liver weight and higher relative testes weight which was regarded as secondary by the decreased fasted body weight. No gross or histopathological changes related to exposure were observed.

The LOAEC was 10 ppm (53 mg/m3) based on minimal eye irritation observed in some animals. The NOAEC was 5 ppm (27 mg/m3).

Test substance : Hydroxypropyl acrylate (purity 97.09%)
(75% 2-HPA, 25% 1-Methyl-2-hydroxyethyl acrylate)

Reliability : (2) valid with restrictions
08.08.2005 (36)

Type :
Species : rabbit
Sex : male
Strain : New Zealand white
Route of admin. : inhalation
Exposure period : 30 days
Frequency of treatm. : 6 hours/day, 5 days/week, total of 20 exposures
Post exposure period :
Doses : 5 and 10 ppm (27 and 53 mg/m3)
Control group : yes, concurrent no treatment
NOAEL : < 5 ppm
LOAEL : = 5 ppm
Method : other: no data available
Year : 1983
GLP : no
Test substance : other TS

Method : Three groups of animals, each consisting of 2 male beagle dogs, 4 male New Zealand white rabbits, 10 male Sprague-Dawley rats and 20 Swiss-Webster mice were used in the study. The animals were exposed (whole

body) to hydroxypropyl acrylate (HPA) vapors at 0 (unexposed control), 5 ppm (27 mg/m3) or 10 ppm (53 mg/m3). Exposures were 6 hours/day, 5 days/week for a total of 20 exposures for the rabbits. Food and water were available at all times except during exposure. Food and water were removed from the control animals for 6 hours on the first day of exposure only.

Animals were observed for signs of toxicity and irritation throughout the study. Body weights were recorded 3-4 times weekly. Hematology determination, including red cell counts, white cell counts, differential white cell counts, hemoglobin concentration, and packed cell volume were conducted on all animals before exposure and at termination. Clinical chemistry determinations were also made including BUN, glucose, SGPT, SGOT and alkaline phosphatase.

A necropsy was performed on all animals. The brain, heart, liver, kidneys and testes were weighed. The following organs were retained in fixative: adrenal glands, parathyroid glands, thyroid glands, aorta, sternum, bone marrow, kidneys, urinary bladder, prostate, accessory sex glands, epididymides, testes, urethra, brain, pituitary gland, spinal cord, peripheral nerve, large intestine, small intestine, esophagus, salivary gland, stomach, pancreas, liver, lung, skin, larynx, trachea, nasal turbinates, heart, lymph nodes, spleen, thymus, skeletal muscle, mammary tissue, gall bladder, eyes, gross lesions.

Histologic examination of the tissues listed above was conducted for all animals.

Statistical analyses of hematological, biochemical and body weight data were carried out using an analysis of variance and Dunnett's test ($p<0.05$).

Result : No mortality was observed during the study. All rabbits exposed to 10 ppm and 2 of 4 animals exposed to 5 ppm developed slight rhinitis and eye irritation (moderate conjunctivitis). No treatment-related effects on mean body weight were observed and all groups gained a similar amount of weight during the study. The absolute and relative organ weights were not affected. Hematological investigations and clinical chemistry indicated no treatment-related effects.

Gross and histopathological changes related to exposure were found in the upper respiratory system (rhinitis, squamous metaplasia, ulcerations), trachea and lungs (subacute bronchitis, focal pneumonitis) of both HPA exposure groups. The tracheal changes varied from no effect in some low dose animals to focal ulceration, squamous metaplasia and subacute tracheitis in the high dose group. The most marked effects were seen in the upper respiratory system of all rabbits, especially those in the 10 ppm group that were characterized by mucopurulent rhinitis with squamous metaplasia and ulceration of the nasal turbinate mucosa.

The LOAEC was 5 ppm (27 mg/m3) based on the irritation in the upper respiratory tract.

Test substance : Hydroxypropyl acrylate (purity 97.09%)
(75% 2-HPA, 25% 1-Methyl-2-hydroxyethyl acrylate)

Reliability : (2) valid with restrictions
29.12.2004 (36)

Type :
Species : dog
Sex : male
Strain : Beagle
Route of admin. : inhalation

Exposure period	:	30 days
Frequency of treatm.	:	6 hours/day, 5 days/week, total of 20 exposures
Post exposure period	:	
Doses	:	5 and 10 ppm (27 and 53 mg/m3)
Control group	:	yes, concurrent no treatment
NOAEL	:	< 5 ppm
LOAEL	:	= 5 ppm
Method	:	other: no data available
Year	:	1983
GLP	:	no
Test substance	:	other TS

Method : Three groups of animals, each consisting of 2 male beagle dogs, 4 male New Zealand white rabbits, 10 male Sprague-Dawley rats and 20 Swiss-Webster mice were used in the study. The animals were exposed (whole body) to hydroxypropyl acrylate (HPA) vapors at 0 (unexposed control), 5 ppm (27 mg/m3) or 10 ppm (53 mg/m3). Exposures were 6 hours/day, 5 days/week for a total of 20 exposures for the dogs. Food and water were available at all times except during exposure. Food and water were removed from the control animals for 6 hours on the first day of exposure only.

HPA vapor was generated by injection into a countercurrent vaporization column heated to approximately 140°C for the 5 ppm chamber and 180°C for the 10 ppm chamber. Air flow was maintained at 1.0 liter/minute in the 3.7 cubic meter chambers. The concentration of the vapor was determined 3-6 times daily by gas chromatography. Both isomers eluted in a single peak that was used for quantitation.

Animals were observed for signs of toxicity and irritation throughout the study. Body weights were recorded 3-4 times weekly. Hematology determination, including red cell counts, white cell counts, differential white cell counts, hemoglobin concentration, and packed cell volume were conducted on all animals before exposure and at termination. Urine was collected from all dogs and specific gravity, pH, glucose, protein, and the presence or absence of ketones, bilirubin and blood were determined. Clinical chemistry determinations were also made for all animals including BUN, glucose, SGPT, SGOT and alkaline phosphatase.

A necropsy was performed on all animals. The brain, heart, liver, kidneys, adrenals and testes were weighed. The following organs were retained in fixative: adrenal glands, parathyroid glands, thyroid glands, aorta, sternum, bone marrow, kidneys, urinary bladder, prostate, accessory sex glands, epididymides, testes, urethra, brain, pituitary gland, spinal cord, peripheral nerve, large intestine, small intestine, esophagus, salivary gland, stomach, pancreas, liver, lung, skin, larynx, trachea, nasal turbinates, heart, lymph nodes, spleen, thymus, skeletal muscle, mammary tissue, gall bladder, eyes, gross lesions.

Histologic examination of the tissues listed above was conducted for all animals.

Statistical analyses of hematological, biochemical and body weight data were carried out using an analysis of variance and Dunnett's test ($p<0.05$).

Result : No mortality was observed during the study. During the exposure period, both dogs exposed to 10 ppm HPA exhibited nasal irritation characterized by exudative rhinitis, and eye irritation characterized by bilateral corneal cloudiness, slight corneal edema and bilateral suppurative conjunctivitis. One dog in the 5 ppm group developed slight rhinitis approximately half way through the exposures. Loss of body weight (from 2 to 10%) was apparent in animals exposed to 10 ppm HPA that showed partial recovery over the weekends. No effects on absolute and relative body weights at 5

ppm occurred. No treatment-related effects in hematological, clinical chemistry or urinalysis measurements occurred.

Treatment-related findings at necropsy were found in the upper respiratory system of all exposed dogs and in the trachea and lungs of the high exposure dogs. These changes were characterized by exudative rhinitis, tracheitis, and suppurative bronchopneumonia.

Microscopic lesions occurred in the upper respiratory system of all dogs and included suppurative rhinitis, squamous metaplasia and hyperplasia of the lining epithelium with focal areas of ulceration in the nasal turbinate mucosa. The trachea of the high exposure dogs showed changes similar to the upper respiratory system with extension to the lungs resulting in bronchopneumonia. No tracheal changes were present in the 5 ppm exposed dogs. Focal foreign body pneumonia resulting from aspirated food particles was present in one dog from each exposure group that was considered secondary to the upper respiratory irritation. Dogs exposed to 10 ppm HPA had treatment-related pneumonic changes in the lung.

The LOAEC was 5 ppm (27 mg/m3) based on the irritation in the upper respiratory tract.

Test substance : Hydroxypropyl acrylate (purity 97.09%)
(75% 2-HPA, 25% 1-Methyl-2-hydroxyethyl acrylate)

Reliability : (2) valid with restrictions
29.12.2004 (36)

Type : Sub-chronic
Species : rat
Sex : male
Strain : Sherman
Route of admin. : inhalation
Exposure period : 28 days (up to 21 exposures)
Frequency of treatm. : 7 hours/day and 5 days/week
Post exposure period : up to 14 days
Doses : Control, 5, 10 or 25 ppm (0, 24, 48 and 120 mg/cubic meter)
Control group : yes, concurrent no treatment
LOAEL : = 5 ppm
Method : other: dynamic exposure
Year : 1970
GLP : no data
Test substance : other TS

Method : METHOD FOLLOWED: dynamic exposure
STATISTICAL METHODS: Means and standard deviations and t-test for significance (Steel, R.G.D. and Torrie, J.H. (1960). Principles and Procedures of Statistics. McGraw-Hill, New York, New York.

Result : LOAEL: 5 ppm
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
-Mortality and time to death: One animal in the 10 ppm group died after 15 exposures. In the 25 ppm group, a total of 8 animals died during the 10 exposure days and following the termination of exposures after exposure day 10, an additional 9 animals died. Only 3 animals survived and recovered from the exposures.
-Clinical signs: The 5 ppm group showed no adverse effects. Animals in the 10 ppm group exhibited mild nasal irritation and discharge and after seven exposures, some animals acquired lung rattles. The animals in the 25 ppm group were observed with eye and nasal irritation followed by dypsnea and a bloated stomach which were indicative of an upper respiratory tract irritant. These conditions became more severe as the exposures continued.
-Organ to body weight ratios: Organ to body weight ratios of liver and kidneys were significantly higher for rats exposed to 10 ppm HEA. Similar

elevation of liver to body weight ratio was also seen at 5 ppm. In contrast, heart to body weight ratios for the animals in the 5 ppm group were significantly lower. No changes occurred in the relative testes weight of HEA treated rats when compared to controls.
-Body weights: The 5 ppm group showed no adverse effects. At 10 ppm, mean body weights decreased during the five exposure days of the week but showed a rapid recovery or a gain during the two no-exposure days of the weekend. At termination, mean body weight of rats exposed to 10 ppm for 20 days was significantly lower than controls. For the 25 ppm group, body weights rapidly decreased during the exposure period but after the exposures were discontinued on study day 12 the surviving animals quickly gained body weight over the recovery period. No changes occurred in the relative testes weight of HEA treated rats when compared to the controls.

-Terminal organ and body weights (10 exposure group)-

Nominal Concentration (ppm)	0	5	10
Body Wt. (g, Mean+/-SD)	365+/-29	354+/-18	316+/-48

Nominal Concentration (ppm)	0	5	10
Relative Organ Wt. (g/100 g BW, Mean+/-SD)			
Heart	0.38+/-0.08	0.34+/-0.02	0.36+/-0.03
Liver	2.81+/-0.27	2.86+/-0.16	2.87+/-0.38
Kidney	0.57+/-0.05	0.57+/-0.18	0.64+/-0.07
Spleen	0.18+/-0.03	0.17+/-0.02	0.18+/-0.02
Testes	0.89+/-0.06	0.95+/-0.08	0.96+/-0.35

-Terminal organ and body weights (20/exposure group)-

Nominal Concentration (ppm)	0	5	10
Body Wt. (g, Mean+/-SD)	377+/-32	362+/-27	325+/-46
(t value)			2.851
Relative Organ Wt. (g/100 g BW, Mean+/-SD)			
Heart	0.35+/-0.02	0.33+/-0.03	0.37+/-0.08
(t value)		2.245	
Liver	2.56+/-0.16	2.84+/-0.09	2.85+/-0.30
(t value)		4.579	2.678
Kidney	0.58+/-0.03	0.61+/-0.05	0.65+/-0.03
(t value)			4.813
Spleen	0.18+/-0.03	0.15+/-0.02	0.17+/-0.02
Testes	0.94+/-0.14	0.94+/-0.09	1.00+/-0.11

t-values are shown for comparisons that were significant.
t-test for significance: 95% level t=2.110 d.f.=17
99% level t=2.898 d.f.=17

-In-life Body Weights (g, Mean)

Nominal Concentration (ppm) (ppm)	0	5	10	25
Study days				
1	269	313	278	280
3	273	308	279	265
4			279	
5	275	310		240
7			286	
8		315		225
9	290		283	

10		317		201
11			284	
12	302	318		190a
14	303		294	201
15		320		
16	305		292	227
17		321		
18	310		284	235
19		322		
21			303	
22		330		
23	325		302	258
24		335	300	
25	327			269
26		336		
28	338		313	
29	348	347		

a- exposure terminated because of high mortality

-Pathology findings: HEA produced ulcerative keratitis and chronic-active tracheitis at 5, 10 and 5 ppm. Focal ulcerative rhinitis and chronic-active laryngitis resulted from HEA exposure at 10 and 25 ppm. Lesions at the 25 ppm level were more severe than those at 10 and 5 ppm. Bronchopneumonia and severe upper respiratory lesions were responsible for the spontaneous deaths at the 25 ppm exposure. The 14-day recovery period did not significantly reduce the number of lesions observed, except for the absence of ulcerative rhinitis.

-Gross Lesions:

				Gross Lesions			
ppm	# of Exp.	Days Post-Exp.	# of rats	Focal Pneumonia	Corneal Lesions	Rhinitis	Cachexia
0	5	0	5	1			
25	5	0	5	2	4	3	
0	10	14	5				
25	10	14	3	2			
Spontaneous Deaths at 25 ppm							
	5-10	1-3	16	2	9	14	5
10	8	1	5	2			
5	9	1	5				
0	21	1	5				
10	20	2	10	2		1	
5	21	1	10	4			
0	21	14	10	2			
10	20	14	9a	5			
5	21	14	9b	4			

a- One rat died after the 14 exposure due to diffuse pneumonia.
b- One rat was euthanized after the 15th exposure due to otitis media.

-Microscopic Lesions:

					Microscopic Lesions	
ppm	# of Exp.	Days Post-Exp.	# of rats	Chronic Murine Pneumonia	Focal Acute Bronchopneumonia	Focal Acute Bronchitis
0	5	0	5	4		
25	5	0	5	2	1	
0	10	14	5	5		2
25	10	14	3	3	1	1
Spontaneous Deaths at 25 ppm						
	5-10	1-3	9	1	5	3

10	8	1	5	5		1
5	9	1	5	5		1
0	21	1	5	5		2
10	20	2	10	10	1	5
5	21	1	10	10	1	8
0	21	14	10	10	2	8
10	20	14	9	9a	2	5
5	21	14	9	9b		4

a- One rat died after the 14 exposure due to necrotizing bronchopneumonia.
b- One rat was euthanized after the 15th exposure, the lesions observed were purulent otitis media, pneumonia and tracheitis.

Microscopic Lesions (Cont'd)

ppm	# of Exp.	Days Post-Exp.	# of rats	Chronic Tracheitis	Chronic Active Tracheitis
0	5	0	5	5	
25	5	0	5	2	3
0	10	14	5	5	
25	10	14	3	2	
Spontaneous Deaths at 25 ppm					
	5-10	1-3	9	2	3
10	8	1	5	3	2
5	9	1	5	4	1
0	21	1	5	2	
10	20	2	10	5	1
5	21	1	10	6	2
0	21	14	10	9	
10	20	14	9	6	1
5	21	14	9	4	3

Microscopic Lesions (Cont'd)

ppm	# of Exp.	Chronic Laryngitis	Chronic Active Laryngitis	Focal Ulcerative Rhinitis	Karatitis	Focal Myocarditis	Testicular Atrophy
0	5	3					
25	5	3	2	4	3	1	
0	10					1	
25	10	1	1		3		
Spontaneous Deaths at 25 ppm							
	5-10		4	3	8		
10	8	3	2	1	1		
5	9	1			1	1	
0	21	3	1		1	1	
10	20	5	2	3	4	1	1
5	21	7			2	1	
0	21	4	2				
10	20	5	2		1		
5	21	5				1	

Testicular atrophy was observed histopathologically in one of 9 rats exposed to 10 ppm HEA for 20 exposures. This was judged to be spontaneous and not related to HEA exposure and consistent with an absence of testicular effects in a chronic toxicity/carcinogenicity study conducted by the inhalation route (Rampy L.W. et al. (1978) Toxicol. Appl. Pharmacol., 45:310).

Test condition : TEST ORGANISMS
-Age: no data
-Weight at study initiation: mean values ranged from 268-314 grams
-Number of animals: 15-20 animals/group (5-10 animals/group for 10 day

interim sacrifice)
ADMINISTRATION/EXPOSURE
-route: inhalation; whole body exposure
SATELITE GROUPS AND REASONS THEY WERE ADDED: An interim sacrifice group of 5- 10 animals were exposed at the same concentrations for 7 hours/day for 10 days.
CLINICAL OBSERVATIONS AND FREQUENCY: During exposures animals were observed closely for signs of irritation and toxicity.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
-Macroscopic: organ weight: lung, liver, spleen, kidney and testes
-Microscopic: yes

Test substance : 2-hydroxyethyl acrylate (CAS RN 818-61-1); no purity information provided

Conclusion : The LOAEL was 5 ppm. In the 5 ppm group, only irritation of the corneas was observed. Ulcerative corneal changes, nasal irritation and decreased body weight were found in the 10 ppm group; however, the animals were able to recover weight during the un-exposed weekend. Exposures of animals to 25 ppm resulted in considerable nasal irritation and severe respiratory distress within two days. Thereafter, the animals exhibited drastic loss of body weight and died of respiratory failure. These data indicate that the respiratory system and the eyes are the only systems likely to be affected by vapor exposure. Based on these results it is suggested that when worker's exposures are prolonged and repeated, the workroom concentrations be kept below 5 ppm and that the time weighed average of all exposures not exceed 1 ppm.

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well-documented and acceptable for assessment.

03.01.2005 (32)

Type : Sub-acute
Species : rabbit
Sex : male/female
Strain : New Zealand white
Route of admin. : dermal
Exposure period : 28 days
Frequency of treatm. : 5 days/week
Post exposure period :
Doses : 100, 500, 2000 mg/kg bw/d
Control group : yes, concurrent no treatment
Method : other: 28-day subacute dermal toxicity study in albino rabbits
Year : 1992
GLP : no
Test substance :

Method : Male and female New Zealand white rabbits (2-3 kg body weight) were treated percutaneously with the test substance at 0, 100, 500, or 2000 mg/kg/day (two animals/sex/group) once per day, five days per week for 20 applications. Twenty-four hours prior to the first dose, the back of each rabbit was shaved. The shaving procedure was repeated at least once a week or as necessary. Just prior to the first application, the shaved skin of one animal/sex/group was abraded . Animals were fitted with collars to prevent oral ingestion and no occlusion was used. The test substance was applied undiluted to approximately 5-20% of the total body surface area. The controls did not receive any applications but were treated similarly in all other respects.

Observations for mortality, behavioral changes, and skin reactions were made daily. Body weights were measured on days -14, -7, 0, 7, 14, 21, and 28. A gross pathological examination was conducted on all animals.

Result : All animals in the high dose group died after 1 or 2 applications of HPA. All of the animals in the mid dose group died after 8 - 10 applications and one

animal died at the low dose after 9 applications. Hypoactivity, muscular weakness, ataxia and prostration were observed in all animals prior to death. The test compound was severely irritating to the skin. One rabbit of the low dose group, and three rabbits of the mid dose group lost body weight prior to death. Pathological examination revealed hemorrhaging and hyperemia of the lungs in all dead rabbits. No gross pathological alterations were noted in the surviving animals except for local skin reactions (red erythema, severe edema, hemorrhaging, fissuring, 2nd and 3rd degree burns).

Test substance : UV Curable Industrial Coating CNF 427, containing:
(1) acrylic acid, monoester with 1,2 propanediol,
(2) 2,4-diisocyanato-1-methylbenzene,
(3) isocyanatobenzene (M&T Chemicals Inc.)

Reliability : (3) invalid
Proportion of mixture unknown. Toxicity could not be reliably ascribed to HPA.

07.01.2004 (5)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Salmonella typhimurium reverse mutation assay
System of testing : Salmonella typhimurium TA 1535, TA 1537, TA 98, TA 100
Test concentration : 10.0; 33.3; 100.0; 333.3; 1000.0; 2500.0; 5000.0 ug/plate
Cycotoxic concentr. : 2500 ug/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year : 1995
GLP : yes
Test substance : other TS

Method : A preliminary experiment (plate incorporation test) was conducted to evaluate the toxicity of the test article to strains TA 98 and TA 100. Based on the results of this study, the following concentrations were chosen for the main study (plate incorporation assay) and confirmatory assay (pre-incubation assay): 10, 33.3, 100, 333.3, 1000, 2500 and 5000 ug/plate. Solvent control (distilled water), untreated control and positive control groups were also included. The positive control substances utilized for tests without metabolic activation were: sodium azide for tester strains TA 1535 and TA 100) and 4-nitro-o-phenylene-diamine (4-NOPD) for tester strains TA 1537 and TA 98. 2-Aminoanthracene (2-AA) was the positive control substance utilized for tests with metabolic activation (all tester strains).

The S9 liver microsomal fraction was obtained at the testing facility from the livers of 8-12 week old male Wistar rats which received a single i.p. injection of 500 mg/kg b.w. Aroclor 1254 in olive oil five days previously. The protein concentration in the S9 preparation was 30.6 mg/ml. Before the experiment, an appropriate quantity of S9 supernatant was thawed and mixed with S9 co-factor solution.

In the pre-incubation assay (confirmatory assay), 100 ul test solution, 500 ul S9 mix or S9 mix substitution buffer and 100 ul bacterial suspension were mixed in a test tube and incubated at 37 degrees C for 60 minutes. After pre-incubation, 2.0 ml overlay agar was added to each tube. The mixture was poured on minimal agar plates. After solidification, the plates were incubated upside down for at least 48 hours at 37 degrees C in the dark. Colonies were counted using an automatic counter.

A test article was considered positive if either a dose-related and

reproducible increase in the number of revertants occurred, or a significant and reproducible increase for at least one test concentration is induced. A test article producing neither a dose-related and reproducible increase in the number of revertants nor a significant and reproducible positive response at any one of the test points was considered non-mutagenic in this test system.

A significant response is described as follows:
A test article is considered mutagenic if in strain TA 100 the number of reversions is at least twice as high as the spontaneous reversion rate and in strains TA 1535, TA 1537 and TA 98 at least three times higher than the spontaneous reversion rate (represents the laboratory historical control range).

Range of Spontaneous Reversion Frequencies:
TA1535 = 10-29;
TA 1537 = 5-28;
TA 98 = 15-57; and
TA 100 = 77-189

Also, a dose-dependent and reproducible increase in the number of revertants is regarded as an indication of possibly existing mutagenic potential of the test article whether or not the highest dose induced the above-described enhancement factors.

Result : In the preliminary toxicity test with TA 100 and TA 98, a clear dose-related reduction in spontaneous revertants was observed with and without metabolic activation at 2500 and 5000 ug/plate although there was no evidence of changes in normal background growth. In the definitive assays, a similar decrease in spontaneous revertants was observed at the two highest concentrations and the background growth was reduced at these concentrations in the confirmatory, pre-incubation assay. No relevant increases in the revertant colony numbers were observed in either assay with or without metabolic activation. The positive control substances produced the required response in all strains and conditions. Under the conditions of this assay, hydroxypropyl acrylate was not mutagenic.
Test condition : Two trials with 3 replicates each were performed.
Test substance : Hydroxypropyl acrylate (purity 97.05%)
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
29.12.2004 (41)

Type : Chromosomal aberration test
System of testing : Chinese Hamster Ovary cells
Test concentration : See methods
Cycotoxic concentr. : See results
Metabolic activation : with and without
Result : positive
Method : OECD Guide-line 473
Year : 1999
GLP : yes
Test substance : other TS

Method : Two assays for chromosomal damage were performed. In the first assay, concentrations of 39.1, 78.1, 156, 313, 625, 1250, 2500, 5000 ug/ml were used with and without metabolic activation. In the absence of metabolic activation, all concentrations showed severe cytotoxicity with almost complete cell death at concentrations of 156 ug/ml and higher. In the presence of S9, metabolism, severe toxicity was observed at 313 ug/ml and higher. Therefore, a second study was conducted at concentrations of 7.5, 15, 30, 45, 60 and 120 ug/ml without metabolic activation and 100, 120, 140, 160, 180, 200, 220, and 240 ug/ml with metabolic activation.

The S9 liver microsomal fraction was prepared from the livers of 8-12 week old male Sprague-Dawley rats that had received prior treatment with phenobarbital and betanaphthoflavone . The efficacy of the S9 mix was verified in an Ames test with 2-aminoanthracene prior to use.

The test substance was found to be directly soluble in culture medium (Ham's F10) at a concentration of 500 mg/ml. Mitomycin-C without metabolic activation and cyclophosphamide with activation were used as the positive control substances.

The cells were treated for three hours with the test substance and positive control and were harvested after 20 hours. Two replicates were used at each concentration. The concentrations selected for scoring were 15, 30 and 45 ug/ml without metabolic activation and 100, 140 and 160 ug/ml with metabolic activation. When possible, one hundred metaphase spreads were scored for chromosomal aberrations from each culture. For cultures where the number of aberrant metaphases , excluding gaps, was more than 50%, scoring was terminated at 50 metaphases.

Result : In the second experiment, reduced cell counts were observed at all concentrations (3 to 75% of control) with relative cell counts for the 15, 30 and 45 ug/ml scored groups of 78, 62, and 45%, respectively for the non-activated cultures and 73, 70 and 58% for the 100, 140 and 160 ug/ml cultures with metabolic activation. An approximate 5-fold and 10-fold increase in chromosomal aberrations was observed at 30 and 45 ug/ml, respectively in the non-activated cultures. An approximate 10-fold increase occurred at 140 ug/ml (but no change was observed at 100 or 160 ug/ml) with metabolic activation.

The positive control substances produced the expected increase in chromosomal aberrations.

It was concluded that HPA induced chromosomal aberrations under the conditions of this study.

The positive response in this study should be considered in light of the cytoxicity observed. No concentrations used in the study were without reductions in cell viability. Cytotoxicity may contribute to the observed increase in chromosomal aberrations.

Test substance : 2-hydroxypropyl acrylate (purity not stated)
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
04.01.2005 (42)

Type : Mammalian cell gene mutation assay
System of testing : Chinese hamster V79 cells
Test concentration : See methods
Cycotoxic concentr. : 30 ug/ml without activation
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 476
Year : 1995
GLP : yes
Test substance : other TS

Method : A preliminary toxicity experiment using the XTT-Assay at concentrations ranging from 3.0 to 1300 ug/ml with and without metabolic activation (S9 mix) was conducted to determine the appropriate concentration range for the mutagenicity assay. Based on the results of this study, The assay was performed in two independent experiments with the following concentrations (ug/ml):

Experiment I:
without S9 mix: 1, 3, 10*, 13, 17 and 20 ug/ml
with S9 mix: 3, 10*, 30, 60*, 100 and 150 ug/ml

Confirmatory, Experiment II:
without S9 mix: 1, 10*, 20, 30, 50, 70** and 100** ug/ml
with S9 mix: 3, 30*, 60, 100 and 150 ug/ml respectively.

* = not evaluated, culture not continued
** = not able to evaluate, toxic effects.

Solvent control (distilled water), untreated control and positive control groups were also included. The positive control substance utilized for tests without metabolic activation was ethylmethanesulfonate. 7,12-dimethylbenz(a)anthracene was the positive control substance utilized for tests with metabolic activation.

The S9 liver microsomal fraction was obtained at the testing facility from the livers of 8-12 week old male Wistar rats which received a single i.p. injection of 500 mg/kg b.w. Aroclor 1254 in olive oil five days previously. The protein concentration in the S9 preparation was 33.2 mg/ml. Before the experiment, an appropriate quantity of S9 supernatant was thawed and mixed with S9 co-factor solution.

Three-day old exponentially growing stock cultures were used. Approximately 500 cells for toxicity or 1.5 E06 cells for mutation rate were seeded. After 24 hours (Day 1), the medium was replaced with serum-free medium containing the test article with or without S9 mix. After 4 hours, the medium was replaced with untreated medium. The flasks were subcultured and incubated at 37°C (4.5% carbon dioxide) for 16 (toxicity) or 18 (mutation rate) days. At termination, the cells were fixed and stained with 10% methylene blue in 0.01% KOH. The stained colonies with more than 50 cells were counted.

A test article was considered positive if it induced either a concentration-related increase of the mutant frequency or a reproducible and positive response for one of the test points. A test article producing neither a concentration-related increase of the mutant frequency nor a reproducible positive response at any of the test points was considered non-mutagenic in this system.

A significant response is described as follows:
A test article was considered mutagenic if it induced a reproducible mutation frequency that is at least three times higher than the spontaneous mutation frequency in the experiment at one or more of the concentrations. The test article is classified as mutagenic if there is a reproducible concentration-related increase of the mutation frequency regardless of whether the 3-fold increase was observed. However, if there is a low spontaneous mutation rate in the normal range for the negative control, this is taken into account in determining whether the test substance is mutagenic in this system.

Result : In the pre-test toxicity experiment, reduced cell viability was observed at concentrations greater than 10 ug/ml without metabolic activation and greater than 100 ug/ml with metabolic activation. In the first experiment, the number of mutant colonies was similar across the solvent control (20.8 mutants/1E06 cells) and treated (with or without metabolic activation) groups. In the second experiment the values of the controls were exceeded at some concentrations both with and without activation. This "effect," however, was due to a low number of spontaneous mutant colonies in the solvent controls (4.3 mutants/1E06 cells) and did not indicate a mutagenic effect of the test article. The absolute number of mutant colonies (range in both experiments of 3.1 to 24.9 mutants/1E06

cells) was well within the historical control range for all concentrations tested.

The positive control agents produced the expected increase in mutations.

It was concluded that, under the conditions of this study, HPA was not mutagenic.

Test substance : Hydroxypropyl acrylate (97.05% pure)
Reliability : (1) valid without restriction
29.12.2004 (39)

Type : Cytogenetic assay
System of testing : Chromosome aberration assay in chinese hamster V79 cells
Test concentration :
Cycotoxic concentr. :
Metabolic activation : with and without
Result : positive
Method : OECD Guide-line 473
Year : 1995
GLP : yes
Test substance : other TS

Remark : This study was repeated. The repeat study is considered to be the definitive and critical study for SIDS evaluation.
Result : The mitotic indices were distinctly reduced after treatment at the highest concentration. The test article reproducibly induced structural chromosomal aberrations in V79 cells.
Test condition : The concentration range of the test article was determined in a pre-test (XTT-assay). After treatment with 30-1300ug/ml (without S9 mix) and 300-1300 ug/ml (with S9 mix), toxic effects could be observed. The following concentrations were used in the main test:

Without S9 mix: I, II (18 h): 1.0; 5.0; 10.0 ug/ml,
II (28 h): 10.0 ug/ml,
With S9 mix: I, II (18 h): 10.0; 50.0; 100.0 ug/ml,
II (28 h): 100.0 ug/ml.

The treatment interval was 4 h with metabolic activation, and 18 and 28 h without. The three lowest concentrations were evaluated after 18 h, and the highest 28 h after initiation of the test.

Test substance : Hydroxypropyl acrylate (purity 97.05%)
Reliability : (1) valid without restriction
Guideline study
04.01.2005 (40)

Type : Ames test
System of testing : Salmonella typhimurium TA 100
Test concentration : I: 75, 250, 750, 2500, 7500 nl/plate
II: 100, 250, 500, 750, 1000 nl/plate

Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: no data available
Year : 1982
GLP : yes
Test substance :

Result : Inhibition of growth was seen at concentrations as low as 500 nl/plate with activation and 500 nl/plate and above

without activation. No mutagenic activity was observed in strain TA100.

Test substance : Rocryl 430 (Hydroxypropyl acrylate, purity 97%)
Reliability : (2) valid with restrictions
Only basic data are given (summary of test results)

05.03.2003 (43)

Type : Bacterial reverse mutation assay
System of testing : Salmonella typhimurium TA102, TA2638 and E. coli WP2/pKM101 and WP2 uvrA/pKM101
Test concentration : 0, 156, 313, 625, 1250, 2500 and 5000 ug/plate
Cycotoxic concentr. : 5000 ug/plate
Metabolic activation : with
Result : positive
Method : other: plate incorporation method
Year : 1996
GLP : no data
Test substance : other TS

Method : Cultures were used for the mutagenicity assay as follows: 0.1 ml of a culture, 0.1 ml of a solution of the test chemical, 0.5 ml of S9 mix and 2 ml of the amino-acid-supplemented molten soft agar were mixed uniformly and overlaid on a minimal glucose agar plate. For metabolic activation, an S9 mix was used which contained 10% of S9 fraction which was prepared from livers of Sprague-Dawley rats induced by phenobarbital and 5,6-benzoflavone. The plates were incubated at 37 degrees C for 48 hours and colonies counted by automatic colony counters and or manually. The chemical was tested in at least two independent experiments using five dose levels and three plates per dose, and the tests were performed in two laboratories per chemical to assess reproducibility. A dose of 5000 ug/plate was used as the highest dose. Positive controls were included in each experiment. Mitomycin C (MMC) was tested in the S. typhimurium strains without metabolic activation at a dose level of 0.05 ug/plate (TA102) or 0.1 ug/plate (TA2638). 2-(2-Furyl)-3(5-nitro-2-furyl) acrylamide was tested in the E. coli strains without metabolic activation at a dose of 0.1 ug/plate (WP2/pKM101)or 0.01 ug/plate (WP2 uvrA/pKM101). 2-Aminoanthracene was used at a dose level of 5 ug/plate (TA102) or 10 ug/plate (TA2638 and WP2/pKM101) or 1 ug/plate (WP2 uvrA/pKM101) with metabolic activation. The results were analyzed for statistical significance using a linear regression test ($p<0.01$).
Result : The test was negative in the S. typhimurium strains but positive in both E. coli strains (WP2/pKM101 and WP2/uvrA/pKM101) in both laboratories.
Test substance : Acrylic acid, 2-hydroxypropyl ester from Wako of the highest purity available.
The same lot of test chemical was used for all experiments in two laboratories.
Reliability : (2) valid with restrictions
Well documented study - comparable to guideline study except: only two S. typhimurium strains used and only with metabolic activation.

29.12.2004 (56)

Type : other: in vitro cytotoxicity
System of testing : HeLa S3 cells
Test concentration :
Cycotoxic concentr. :
Metabolic activation : no data
Result :
Method : other
Year : 1997
GLP : no data
Test substance : other TS

Method	:	The 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H tetrazorium bromide (MTT) assay was used to evaluate the cytotoxicity of monomers. HeLa S3 cells were plated at 200,000 cells in 1 mL of Eagles' MEM with 10 vol % of fetal bovine serum and L-Glutamin (0.292 g/l) in a 12-well dish and incubated at 37 degrees C in 5% carbon dioxide and 100% relative humidity. After a 24-hour incubation, the culture medium was removed from each well and 1 ml of HPA solution was added. The control was serum-free medium. After cells were exposed to HPA for 24 hours, the medium was removed and cells were washed with phosphate buffered solution (PBS). After removing the PBS, 1 ml of serum-free medium and 0.1 ml of MTT solution were added to each well. After four hours of incubation, 1.5 ml of acid isopropanol was added to each well, the optical densities of formazan production were measured at 570 nm (OD570) and 630 nm (OD630). Relative cell viability was calculated by the following equation: relative cell viability (% of control) = (OD570 - OD630 of treated wells/OD570-OD630 of control) x 100. A dose-response curve of relative cell viability was plotted to delineate the concentrations of the monomer that depressed MTT-formazan production by 50% (IC50 value).
Result	:	IC50 = 0.58 mmol/l
Test substance	:	2-hydroxypropyl acrylate; Purity not provided.
Reliability	:	(2) valid with restrictions

29.12.2004 (58)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	NMRI
Route of admin.	:	gavage
Exposure period	:	Single administration
Doses	:	100, 300, 600 mg/kg b.w.
Result	:	negative
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	2000
GLP	:	yes
Test substance	:	other TS

Method	:	Groups of 10 mice (5 of each sex) were administered a single p.o. dose of the test substance orally at concentrations of 100, 300 and 600 mg/kg body weight. The test substance was prepared in carboxymethylcellulose. The volume administered was 33.3 ml/kg body weight. Two additional groups of mice (5/sex/group) were used as the negative control and positive control. The negative control group received carboxymethylcellulose by gavage. The positive control group animals received a single i.p. injection of 10 ml/kg cyclophosphamide in 0.9% NaCl at 30 mg/kg b.w. Five males and five females from each group were sacrificed 24 hours after dosing. Forty eight hours after dosing five animals per sex from the 600 mg/kg dose level were killed. One bone marrow smear was prepared per animal from the tissue cleared from each femur. Stained smears were examined by light microscopy for incidence of micronucleated cells per 2000 polychromatic erythrocytes per animal. To describe a cytotoxic effect, the ratio of polychromatic to normochromatic erythrocytes was assessed by the examination of at least 1000 erythrocytes. Evaluation of Results: Cells were evaluated for large (aneugenic effects) and small (clastogenic effects) micronuclei. The test substance was classified as mutagenic if it induced either a statistically significant (Mann-Whitney test), dose-related increase in the number of micronucleated

polychromatic erythrocytes or a reproducible, statistically significant positive response for at least one of the test points.

Remark : An initial experiment to determine the toxicity of the test substance was conducted. Three male and three female mice were administered the test substance orally at 1000 mg/kg b.w. This dose resulted in only slight toxicity and was therefore chosen as the top dose. In the main experiment, two animals died within the first 6 hours of dosing at 1000 mg/kg b.w. so a dose of 600 mg/kg b.w. was chosen as the highest dose that could be used for analysis of micronuclei. All 10 mice at 1000 mg/kg b.w. died within 24 hours of dosing.

Result : The ratio of normochromatic to polychromatic erythrocytes was slightly affected by the treatment with 2-hydroxypropylacrylate at a dose of 600 mg/kg b.w (at 24 and 48 hours in male mice and at 48 hours in female mice). At this dose level, only slight toxic effects, as evidenced by reduced spontaneous reactivity, were obtained up to 6 hours after dosing. There was no increase in the frequency of micronuclei at any dose level at either 24- or 48-hours after dosing compared to the negative control group.
The positive control compound, cyclophosphamide, produced significantly increased frequencies of micronucleated polychromatic and normochromatic erythrocytes.
Following are the results:

Males sacrificed at 24 hours:

	Mean Micronuclei/2000 PCE		
Dose group	All (%)	Small (%)	Mean PCE/NCE
Negative control	3.2 (0.16)	2.8 (0.14)	1000/873.6
600 mg/kg	4.4 (0.22)	3.8 (0.19)	1000/1056.8
300 mg/kg	5.4 (0.27)	5.4 (0.27)	1000/1177.6
100 mg/kg	4.8 (0.24)	3.8 (0.19)	1000/974.6
Positive control	20.2 (1.01)	18.8 (0.94)	1000/739.6

Females sacrificed at 24 hours:

	Mean Micronuclei/2000 PCE		
Dose group	All (%)	Small (%)	Mean PCE/NCE
Negative control	3.2 (0.16)	2.8 (0.14)	1000/737.4
600 mg/kg	2.8 (0.14)	2.0 (0.10)	1000/854.6
300 mg/kg	5.2 (0.26)	4.8 (0.24)	1000/773.8
100 mg/kg	3.2 (0.16)	2.8 (0.14)	1000/918.8
Positive control	19.6 (0.98)	18.4 (0.92)	1000/688.6

Males and Females sacrificed at 48 hours:

		Mean Micronuclei/2000 PCE		
Dose group	Sex	All (%)	Small (%)	Mean PCE/NCE
600 mg/kg	Male	2.2 (0.11)	2.0 (0.10)	1000/986.2
600 mg/kg	Female	2.2 (0.11)	1.8 (0.09)	1000/1065.4

It was concluded that 2-Hydroxypropyl acrylate is considered to be non-mutagenic in this micronucleus test.

Test substance : 2-Hydroxypropylacrylate (purity 97.8%) - Batch No. 790201167; Lot No. 32114707.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

29.12.2004 (25)

5.7 CARCINOGENICITY

Species : rat

Sex : male/female

Strain : Sprague-Dawley

Route of admin. : inhalation

Exposure period	:	18 months
Frequency of treatm.	:	6 hours/day; 5 days/week
Post exposure period	:	5 months (males); 6 months (females)
Doses	:	0 ppm, 0.5 ppm (2.4 mg/cubic meter), and 5.0 ppm (24 mg/cubic meter)
Result	:	negative
Control group	:	yes
Method	:	other
Year	:	1979
GLP	:	no
Test substance	:	other TS: 96% HEA

Test condition :

TEST ORGANISMS:
Age: not specified
Weight at study initiation: Male group means ranging from 287-300 g; Female group means ranging from 217-224 g
Number of animals: 99 or 100 animals/sex/exposure level

ADMINISTRATION/EXPOSURE:
Duration of test/exposure: 18 months
Type of exposure: Whole body
Post exposure period: Males: 5 months, Females: 6 months
Vehicle: none/not applicable
Target Exposure Concentrations: 0, 0.5 and 5 ppm vapor
Actual Analytical Mean +/- S.D. Exposure Concentrations:
0, 0.56 +/- 0.39 ppm, 3.66 +/- 1.65 ppm.

CLINICAL OBSERVATIONS AND FREQUENCY:
Body weights: All animals weighed on the following study days:
0,5,7,12,19.26,33,40,54,68,96,131,159,194,223,251,286,
314,342,377,405,433,468,496,532,552,585,620,648,675,702,723

Clinical signs: animals examined at "frequent intervals" for mortality/morbundity

Hematology: 12 months, 5 rats/sex/exposure level; and at end of 5 or 6 month post-exposure period, 10 rats/sex/exposure level. Packed cell volume, erythrocyte count, hemoglobin concentration, total and differential leukocyte count.

Cytogenetic evaluation: 12 months, 4 rats/sex/exposure level; chromosomal aberations, breaks

Clinical Chemistry: 12 months, 5 rats/sex/exposure level, Blood urea nitrogen, alkaline phosphatase, glutamic pyruvic transaminase

Urinalysis: 12 months, 5 rats/sex/exposure level; and at end of 5- or 6-month post-exposure period, 10 rats/sex/exposure level. Specific gravity, pH, glucose, protein, ketones, bilirubin and blood.

ORGANS EXAMINED AT NECROPSY:
Macroscopic:
At 12-month interim sacrifice: all organs, weight of brain, heart, liver, kidneys, testes, 5 rats/sex/exposure level.
At terminal sacrifice: all organs, all surviving animals. The weights of brain, heart, liver, kidneys, testes were recorded at the terminal sacrifice for 9-19 animals per sex/exposure level.

Microscopic:
Control and 5 ppm, at interim and terminal sacrifice: brain, heart, liver kidneys, testes, lungs, thoracic and/or mesenteric lymph nodes, salivary glands, pancreas, adrenals, spleen, thymus, aorta, skeletal muscle, small

intestine, large intestine, thyroid gland, trachea, spinal cord, peripheral nerve, pituitary gland, epididymides, urinary bladder, accessory sex glands, adipose tissue, ovaries, uterus, nasal turbinates, and any gross lesion suggestive of a pathologic process or with tumor formation.

At 0.5 ppm terminal sacrifice lungs, livers, kidneys, lymph nodes tracheas and grossly visible lesions from all surviving animals; at interim sacrifice grossly visible lesions or tissues where lesions seen at 5 ppm.

Rats dying or culled during the course of the study, complete necropsy and microscopic exam as described above (except when autolysis precluded evaluation) and the presence and absence of neoplasms recorded.

STATISTICAL METHODS:
Hematology, clinical chemistries, body weights, absolute and relative organ weights were analyzed using analysis of variance and Dunnett's Test. Cumulative mortality data were analyzed using Fisher's Exact Probability Test. In both cases, p values of less than 0.05 considered statistically significant.

Gross and microscopic pathology data were analyzed using Fisher's Exact Probability Test ($p<0.05$) as follows: Gross necropsy: the total collated data from each of the high and low exposure groups were compared with the data of the control group. Each sex was compared separately. Microscopic observations: the incidence of lesions in tissue for each sex from highest exposure group (5 ppm) was compared with the data from controls. At the terminal sacrifice, data from the lower exposure group (0.5 ppm) were analyzed statistically when the number of tissues examined was similar to the controls. The incidence rate for each type of neoplasm was compared separately for each sex between the high exposure group and controls. For the lower exposure (0.5 ppm), statistical evaluation was conducted for neoplasms in those organs upon which microscopic exam was conducted to the degree comparable to the controls and highest exposure group (liver, kidney, lung and lymph nodes and subcutaneous masses/nodules).

To examine the possibility that neoplasms appeared earlier in treated vs. control rats the following parameters were compared for 6 month time periods using Fisher's Exact Probability Test and the Mantel-Haenzel Test with $p<0.05$:
1) Total number of rats bearing tumors, 2) Number of rats with benign tumors, 3) Number of rats with malignant neoplasms, and 4) Number of rats bearing subcutaneous masses/nodules.

Remark : The statistically significant increase in the incidence of fibrinoid degeneration of the vascular channels in the testes of male rats exposed to 5 ppm was known to be a local vascular manifestation of mesenteric periarteritis syndrome observed as age-related lesion in this rat strain (Sprague-Dawley, Spartan substrain). The laboratory conducting this study commonly observed this lesion in control aging rats of this strain at similar incidence as was observed in this study during it's period of use in the mid to late '70s (the incidence in historical controls in this period ranged from approximately 37 to 85% for seven chronic toxicity/oncogenecity studies).

Polyarteritis (polyarteritis or periarteritis nodosa) is the most conspicuous inflammatory lesion of the blood vessels of rats. The etiology is unknown and the indidence varies among strains and colonies (Mitsumori, K. (1990) Chapter 29 in Pathology of the Fischer Rat. Eds: Boorman et al., Academic Press, Inc. p 477). A common site in male rats are the arteries of the testicle and to a lesser extent the arteries of the spermatic cord (Burek, J.D. (1978) Pathology of the Aging Rat, CRC Press p. 87). Carlton and Engelhardt (Polyarteritis, In: Cardiovascular and Musculoskeletal Systems Eds: Jones, T.C., Mohr, U. and Hunt, R.D., Springer-Verlag, 1991, p 71) also indicate that this lesion can be present in spermatic arteries.

Result : MORTALITY AND TIME TO DEATH: The cumulative mortality for male rats exposed to 5 ppm HEA was statistically increased from controls in the 16th month of the study only. This correlated with the onset of chronic murine pneumonia which initially affected this group and subsequently spread to the other exposure and control groups. Mortality of exposed females was comparable to controls except for a statistical increase in the 17th month at 5 ppm and in the 15th month at 0.5 ppm. Overall the cumulative mortality data were not markedly different between exposed and control groups indicating an absence of a treatment-related effect with the possible exception of the initial increased mortality associated with the onset of chronic murine pneumonia in rats exposed to 5 ppm (Tables 1 and 2).

CLINICAL SIGNS: The haircoat of rats exposed to 5 ppm had a characteristic yellow staining as well as an increased incidence and severity of chronic murine pneumonia. These effects were not observed in rats exposed to 0.5 ppm.

BODY WEIGHTS: A statistically significant decrease in body weights was observed for male rats at 0.5 and 5.0 ppm at 12 months but not at terminal sacrifice (Tables 3 and 4). The difference in body weight at 12 months was not concentration dependent; the 0.5 ppm group having a lower mean weight than the 5 ppm group.

FOOD/WATER CONSUMPTION: No data collected

OPHTHALMIC EXAMINATION: No treatment-related effect observed at necropsy using a glass microscope slide on the surface of the eye for magnification and examination of the interior of the eye.

CLINICAL CHEMISTRY: There were no significant differences between control and exposed groups in regard to blood urea nitrogen, or SGPT and AP activities either at the interim or terminal sacrifice.

HEMATOLOGY: At the interim sacrifice, no statistical differences were observed for male rats. Females at 5 ppm had statistically significant elevation of the mean hemoglobin concentration and statistically lower total leukocyte count. At the terminal sacrifice, there were no statistical differences from controls with the exception of a increase in red blood cell count in male rats exposed to 5 ppm.

URINALYSIS: No treatment-related effects were observed at either the interim or terminal sacrifice.

ORGAN WEIGHTS: At the interim sacrifice, there were no statistically significant differences in absolute organ weights; the relative brain and testes weight for males exposed to 0.5 ppm were significantly increased relative to controls secondary to a statistically significant decrease in the terminal body weights. There were no significant differences from either absolute or relative control organ weights for females exposed to HEA for twelve months, consistent with the absence of an effect on body weight in females.

At the terminal sacrifice, there were no statistically significant differences from controls in body weight, or the absolute or relative organ weights for HEA exposed rats with the exception of a decrease in the absolute weight of the brain for males at 0.5 ppm and of the heart for females exposed to 5 ppm. These observations were considered of no toxicologic significance in view of no change in the relative weight. In addition for the females, the inclusion of one "inordinately low" heart weight from one animal also had impact on the differences.

Mean organ weight data for interim and terminal sacrifices (Tables 3 and 4,

respectively).

GROSS PATHOLOGY: A statistically significant number of both male and female rats exposed to 5 ppm HEA had a distinctive grossly visible yellow staining of the haircoat that persisted into the post-exposure portion of the study. The yellow staining was judged to be a result of the contact of the HEA vapor with the haircoat and was not observed in rats exposed to 0.5 ppm HEA. Chronic murine pneumonia caused by Mycoplasma sp. was observed in all groups as evidenced by pulmonary consolidation and mucopurulent inflammation along the tracheobronchial system. This sometimes included abscess formation, pleuritis, pericarditis, rhinitis and/or tracheitis. An increase in the incidence of numerous gross or microscopically visible lesions occurring as part of or secondary to the chronic murine pneumonia was observed in both male and female rats exposed to 5 ppm HEA.

An increase was observed in the incidence of female rats having a total of 3 grossly-visible subcutaneous masses in the groups exposed to 5 or 0.5 ppm HEA. However, this was not the case with female rats of either exposure group that had 1,2,4, or 5 subcutaneous masses.

HISTOPATHOLOGY: Statistical differences between control and HEA exposed rats in the respiratory tract lesions related to chronic murine pneumonia were observed. Specifically, at 5 ppm, an increase in the incidence and severity of the lesions associated with chronic murine pneumonia was observed.

Lymphoreticular System: Statistical increases in the incidence of edema, inflammation and reactive lymphoid hyperplasia of the thoracic lymph nodes in females at 5 and 0.5 ppm, secondary to chronic murine pneumonia were observed; an increased incidence of edema in mesenteric lymph nodes was also present in females at 0.5 ppm.

Liver: At the terminal sacrifice a statistically significant increase as compared to controls was observed in the focal areas of swollen hepatocytes and focal aggregates of mononuclear cells in males exposed to 5 ppm. A statistically significant increase as compared to controls in the incidence of focal bile duct proliferation in female rats exposed to 5 ppm HEA was also observed.

Female reproductive organs: At the terminal sacrifice only, a statistically significant increase in the incidence of inflammation of the uterus of female rats exposed to 5 ppm was observed (Table 5). No other statistically significant differences for histopathologic observations of the female reproductive organs were found. Specifically, there were no histopathological effects in the ovaries of 2-HEA exposed rats that were considered treatment-related. In addition, at the interim sacrifice, no treatment-related histopathological effects were noted in female reproductive organs of five animals evaluated immediately after 12 months of 2-HEA exposure at 5 ppm.

Male reproductive organs: At the terminal sacrifice only, there was a statistically significant increase in the incidence of fibrinoid degeneration of the vascular channels (local vascular manifestation of mesenteric periarteritis syndrome observed as age-related lesion in this rat strain) in the testes of male rats exposed to 5 ppm (8/14 or 57% in controls; 17/19 or 89% in the 5 ppm group) (Table 6A). The laboratory conducting this study commonly observed this lesion in control aging rats of this strain at similar incidence as was observed in this study during its use in the mid to late '70s (historical control values from seven chronic toxicity/oncogenicity studies ranged from 37 to 85%). Periarteiris of the mesenteric blood vessels was also common in the control and DEA exposed rats (Table 6B).

No other statistically significant differences were found in the histopathologic observations of the male reproductive organs. Specifically, there was no difference between treated and control groups in spermatogenesis in the testes or in the morphology and secretory content of the male accessory sex glands. In addition, at the interim sacrifice, no treatment-related histopathological effects were noted in male reproductive organs of five animals evaluated immediately after 12 months of 2-HEA exposure at 5 ppm.

Stomach: An increase in the incidence of microscopically visible dilatation of gastric pits in male rats exposed to 5 ppm HEA was observed.

Cardiovascular system: An increase in the incidence of microscopically visible degeneration of myocardial blood vessels in female rats exposed to 5 ppm was observed (Table 7).

OTHER: CYTOGENETIC EVALUATION - Bone Marrow: There were no indications of alterations related to HEA exposure that were observed in the cytogenetic evaluation.

TIME TO TUMORS: Statistical analyses revealed no increases in the incidence of HEA exposed rats bearing benign neoplasms, malignant neoplasms or all types of neoplasms as compared to controls nor were there differences as compared to controls in the temporal occurrence of neoplasms.

Attached document : Tables 1-7.

Table 1

CUMULATIVE PERCENT MORTALITY FOR MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE 5 DAYS/WEEK FOR 18 MONTHS FOLLOWED BY A 5 MONTH OBSERVATION PERIOD

Months on Study	Exposure Level: Control No. Dead (% Dead)	5 PPM No. Dead (% Dead)	0.5 PPM No. Dead (% Dead)
No. Rats Alive on Day 0[a]	91	91	91
1	0 (0)	0 (0)	1 (1)
2	1 (1)	0 (0)	2 (2)
3	1 (1)	0 (0)	2 (2)
4	1 (1)	1 (1)	3 (3)
5	1 (1)	1 (1)	5 (5)
6	1 (1)	1 (1)	5 (5)
7	2 (2)	1 (1)	6 (7)
8	2 (2)	1 (1)	7 (8)
9	2 (2)	1 (1)	7 (8)
10	2 (2)	1 (1)	8* (9)
11	3 (3)	1 (1)	8 (9)
12	4 (4)	2 (2)	8 (9)
13	5 (5)	5 (5)	9 (10)
14	7 (8)	7 (8)	9 (10)
15	8 (9)	11 (12)	10 (11)
16	8 (9)	28* (31)	13 (14)
17	37 (41)	42 (46)	24* (26)
18	53 (58)	44 (48)	44 (48)
19	57 (63)	48 (53)	54 (59)
20	66 (73)	49* (54)	64 (70)
21	70 (77)	56* (62)	71 (78)
22	74 (81)	60* (66)	80 (88)
23	77 (85)	70 (77)	82 (90)
Beginning of 24	77 (85)	72 (79)	82 (90)
Terminal Kill	14	19	9
12 Month Interim Kill	5	5	5
12 Month Kill for Cytogenetics	4	4	4
Total Rats In Study	100	100	100

[a] Excludes those rats used in interim kill (5/sex/dose), and used for cytogenetic examination (4/sex/dose).

* Statistically different from control data when analyzed using Fisher's Exact Probability test, $p<0.05$.

Table 2

CUMULATIVE PERCENT MORTALITY FOR FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE 5 DAYS/WEEK FOR 18 MONTHS FOLLOWED BY A 6 MONTH OBSERVATION PERIOD

Months on Study	Exposure Level: Control No. Dead (% Dead)	5 PPM No. Dead (% Dead)	0.5 PPM No. Dead (% Dead)
No. Rats Alive on Day 0[a]	91	91	91
1	0 (0)	0 (0)	1 (1)
2	0 (0)	0 (0)	1 (1)
3	0 (0)	0 (0)	1 (1)
4	0 (0)	0 (0)	1 (1)
5	0 (0)	0 (0)	1 (1)
6	0 (0)	0 (0)	1 (1)
7	0 (0)	0 (0)	1 (1)
8	2 (2)	1 (1)	1 (1)
9	3 (3)	3 (3)	2 (2)
10	3 (3)	4 (4)	3 (3)
11	4 (4)	4 (4)	5 (6)
12	4 (4)	5 (5)	7 (8)
13	4 (4)	8 (9)	9 (10)
14	5 (5)	9 (10)	12 (13)
15	5 (5)	10 (11)	13* (14)
16	5 (5)	16 (18)	16 (18)
17	16 (18)	28* (31)	21 (23)
18	23 (25)	34 (37)	27 (30)
19	28 (31)	39 (43)	35 (39)
20	37 (41)	42 (46)	41 (46)
21	43 (47)	46 (51)	46 (51)
22	53 (58)	56 (62)	59 (66)
23	62 (68)	61 (67)	65 (72)
24	70 (77)	64 (70)	70 (78)
Terminal Kill	21	27	20
12 Month Interim Kill	5	5	5
12 Month Kill for Cytogenetics	4	4	4
Total Rats In Study	100	100	99

[a] Excludes those rats used in interim kill (5/sex/dose), and used for cytogenetic examination (4/sex/dose).

* Statistically different from control data when analyzed using Fisher's Exact Probability test, $p<0.05$.

Table 3. BODY WEIGHTS, ORGAN WEIGHTS, AND ORGAN/BODY WEIGHT RATIOS FOR MALE AND FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE 5 DAYS/WEEK FOR 12 MONTHS

Exposure level PPM	Sex		Body Weight g	Organ Weights (g and g/100 g Body Weight)									
				Brain		Heart		Liver		Kidneys		Testes	
				g	g/100 g	g	g/100g	g	g/100 g	g	g/100g	g	g/100g
0	M	Mean	621	1.97	0.32	1.64	0.26	15.14	2.42	3.95	0.63	3.87	0.62
		±S.D.	37	0.03	0.02	0.07	0.01	2.75	0.32	0.62	0.07	0.76	0.12
5.0	M	Mean	565[a]	1.93	0.34	1.59	0.28	14.98	2.64	3.77	0.66	4.08	0.72
		±S.D.	24	0.08	0.01	0.12	0.02	3.17	0.46	0.79	0.12	0.18	0.02
0.5	M	Mean	549[a]	1.98	0.36[a]	1.55	0.28	12.92	2.35	3.30	0.60	4.38	0.80[a]
		±S.D.	40	0.06	0.03	0.17	0.02	1.32	0.13	0.15	0.06	0.24	0.03
0	F	Mean	317	1.85	0.59	1.05	0.33	7.36	2.32	2.16	0.68		
		±S.D.	16	0.05	0.04	0.02	0.02	0.41	0.18	0.21	0.08		
5.0	F	Mean	342	1.80	0.53	1.13	0.33	7.87	2.30	2.31	0.68		
		±S.D.	26	0.07	0.04	0.07	0.02	0.63	0.12	0.27	0.04		
0.5	F	Mean	347	1.87	0.54	1.11	0.32	9.18	2.63	2.17	0.63		
		±S.D.	15	0.04	0.02	0.13	0.03	2.05	0.46	0.14	0.02		

[a] Statistically significant difference from control mean by analysis of variance and Dunnett's test $p < 0.05$.

Table 4. BODY WEIGHTS, ORGAN WEIGHTS, AND ORGAN/BODY WEIGHTS OF MALE AND FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE 5 DAYS/WEEK FOR 18 MONTHS FOLLOWED BY A 5 MONTH (males) or 6 MONTH (females) OBSERVATION PERIOD

Exposure level PPM	Sex		Fasted Body Weight g	Organ Weights (g and g/100 g Body Weight)									
				Brain		Heart		Liver		Kidneys		Testes	
				g	g/100 g	g	g/100g	g	g/100 g	g	g/100g	g	g/100g
0	M	Mean	478	1.99	0.43	1.72	0.36	16.88	3.49	5.38	1.13	3.81	0.80
		±S.D.	93	0.06	0.09	0.38	0.06	4.62	0.51	1.56	0.23	0.90	0.13
5.0	M	Mean	485	1.98	0.42	1.71	0.36	16.30	3.39	4.73	0.98	3.48	0.71
		±S.D.	77	0.08	0.06	0.20	0.04	2.01	0.32	0.91	0.16	1.16	0.19
0.5	M	Mean	480	1.91[a+]	0.41	1.81	0.39	15.53	3.26	4.48	0.95	3.11	0.64
		±S.D.	96	0.12	0.09	0.32	0.09	2.91	0.38	1.02	0.21	1.22	0.21
0	F	Mean	367	1.80	0.51	1.32	0.38	12.13	3.35	2.84	0.82		
		±S.D.	81	0.07	0.10	0.12	0.09	2.31	0.52	0.44	0.26		
5.0	F	Mean	319	1.80	0.58	1.12[a]	0.36	10.21	3.23	2.57	0.82		
		±S.D.	53	0.08	0.09	0.13	0.05	1.57	0.43	0.35	0.16		
0.5	F	Mean	440	1.82	0.47	1.28	0.32	12.61	2.88	2.68	0.67		
		±S.D.	167	0.04	0.16	0.07	0.11	5.47	0.55	0.35	0.21		

[a] Statistically significant difference from control mean by analysis of variance and Dunnett's test, $p<0.05$
+ {[mean + T value =2.07] [mean – T value = 1.92]}

Table 5

MICROSCOPIC OBSERVATIONS ON FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE

(Terminal Kill After Month 24)

Dose in ppm	0	5	0.5
Number of rats per group[a]	21	27	20
Number of rats in study	100	100	99
REPRODUCTIVE SYSTEM (Continued)			
Uterus			
Multiple areas of cystic endometrial hyperplasia	14/21/21	20/27/27	1/3/20
Sclerosing carcinoma of uterus with metastasis to lungs	0/21/21	0/27/27	1/3/20
Uterine inflammation	2/21/21	11/27/27[b]	1/3/20
Adenomatous polyp formation in uterus	4/21/21	9/27/27	0/3/20
Squamous keratinization of uterus	0/21/21	1/27/27	0/3/20
Fibrotic polyp of uterus	0/21/21	0/27/27	1/3/20
Hematogenous pigment within uterus	2/21/21	6/27/27	1/3/20
Cyst formation within endometrium	3/21/21	8/27/27	0/3/20
Uterine polyp formation	1/21/21	0/27/27	0/3/20
Adenocarcinoma of uterus	1/21/21	1/27/27	0/3/20
Abscess of uterus	1/21/21	2/27/27	0/3/20
GASTROINTESTINAL SYSTEM			
Stomach			
Dilatation of gastric pits	7/21/21	11/27/27	0/1/20

Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/ number of animals examined grossly.

[a]Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group.

[b]Statistically different from control by the Fisher Exact Probability Test, $p<0.05$.

Table 6A

MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE

(Terminal Kill During Month 24)

Dose in ppm	0	5	0.5
Number of rats per group[a]	14	19	9
Number of rats in study	100	100	100
URINARY SYSTEM (Continued)			
Urogenital Tract			
Diffuse hyperplasia of urinary bladder mucosa	2/14/14	0/19/19	0/0/9
Organized plug within lumen of urinary bladder	3/14/14	1/19/19	0/0/9
REPRODUCTIVE SYSTEM			
Testis			
Decreased spermatogenesis, one testis	1/14/14	0/19/19	0/0/9
Decreased spermatogenesis, both testes	2/14/14	1/19/19	0/0/9
Focal atrophy of seminiferous tubules	9/14/14	7/19/19	0/0/9
Vascular fibrinoid degeneration in the testes	8/14/14	17/19/19[b]	0/0/9
Focal interstitial fibrosis of testicle	3/14/14	5/19/19	0/0/9
Interstitial cell tumor of testicle	0/14/14	1/19/19	0/0/9
Diffuse testicular atrophy	1/14/14	2/19/19	0/0/9
Accessory Sex Glands			
Decreased secretory content of accessory sex glands	11/14/14	10/19/19	0/0/9
Atrophy of accessory sex glands	2/14/14	5/19/19	0/0/9

Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/ number of animals examined grossly.

[a]Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group.

[b]Statistically different from control by the Fisher Exact Probability test, $p<0.05$.

Table 6B

MICROSCOPIC OBSERVATIONS ON MALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE

(Terminal Kill During Month 24)

Dose in ppm	0	5	0.5
Number of rats per group[a]	14	19	9
Number of rats in study	100	100	100
CARDIOVASCULAR SYSTEM			
Heart			
Focal myocardial degeneration and inflammation - slight	8/14/14	11/19/19	0/0/9
Focal myocardial degeneration and inflammation - moderate	3/14/14	5/19/19	0/0/9
Focal myocardial degeneration and inflammation - pronounced	1/14/14	0/19/19	0/0/9
Myocardial mineralization	1/14/14	0/19/19	0/0/9
Aorta			
Aortic mural mineralization	0/14/14	4/19/19	1/8/9
Thickening of endothelial lining of aorta	2/14/14	3/19/19	0/8/9
Blood Vessels			
Degeneration of myocardial blood vessels	10/14/14	14/19/19	0/0/9
Periarteritis and sclerosis of mesenteric blood vessels	6/14/14	7/19/19	2/2/9
Thrombosis and hematoma formation associated with mesenteric periarteritis	1/14/14	0/19/19	1/2/9
Mineralization of selected blood vessels	1/14/14	2/19/19	0/2/9
Hyalinization and thickening of mesenteric blood vessels	2/14/14	6/19/19	0/2/9
Congestion of myocardial vessels	1/14/14	0/19/19	0/0/9

Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/ number of animals examined grossly.

[a]Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group.

Table 7

MICROSCOPIC OBSERVATIONS ON FEMALE RATS EXPOSED TO VAPORS OF 2-HYDROXYETHYL ACRYLATE

(Terminal Kill After Month 24)

Dose in ppm	0	5	0.5
Number of rats per group[a]	21	27	20
Number of rats in study	100	100	99
CARDIOVASCULAR SYSTEM			
Heart			
Focal myocardial degeneration and inflammation - slight	7/21/21	12/27/27	0/1/20
Focal pericarditis	0/21/21	1/27/27	0/1/20
Aorta			
Aortic mural mineralization	1/19/21	1/27/27	0/16/20
Thickening of endothelial lining of aorta	3/19/21	7/27/27	2/16/20
Blood Vessels			
Degeneration of myocardial blood vessels	1/21/21	11/27/27[b]	0/1/20
Periarteritis and sclerosis of mesenteric blood vessels	4/21/21	2/27/27	0/1/20
Mineralization of selected blood vessels	1/21/21	0/27/27	0/20/20
Fibrosis around blood vessel in thoracic adipose tissue	1/21/21	0/27/27	0/18/20

Data listed as number of observations/total number of tissues, organs, or masses examined microscopically/ number of animals examined grossly.

[a]Microscopic examination of all major organs limited to control and top dose group. Liver, kidney, lungs, nasal turbinates, thoracic lymph nodes, and all lesions grossly suggestive of tumor formation were examined from the low dose group.

[b]Statistically different from control by the Fisher Exact Probability Test, $p<0.05$.

Conclusion : The results of this study indicate that chronic inhalation of 2-HEA by rats produced only a minimal degree of toxicity at 5 ppm (haircoat staining and increased incidence and severity of chronic murine pneumonia). Female rats in the 5 ppm group at the terminal sacrifice showed an increased incidence of uterine inflammation as compared to the control animals. However, no other statistically significant differences for histopathological observations of the female reproductive organs were found, including the ovaries. An evaluation of the histopathological data from the male animals exposed to 5 ppm indicated an increased incidence of fibrinoid degeneration in the vascular channels of the testes which was a local

vascular manifestation of mesenteric periarteritis syndrome observed as age-related lesion in this rat strain. This effect was also present in the control rats. In a recent review of the histopathological findings in male and female reproductive organs by the study pathologist and principal author, the fibrinoid degeneration in the testes was not considered to be a substance-specific toxic effect of HEA and the effects in the uterus were not considered indicative of a reproductive toxicity potential for 2-HEA. In summary, the NOAEL was 0.5 ppm and there was no evidence in this study that 2-HEA has the potential for reproductive toxicity or an oncogenic effect in either of the exposure groups.

Test substance : SOURCE: Texas Division of The Dow Chemical Company

PURITY: 96.3% 2-hydroxyethyl acrylate by vapor phase chromatography

IMPURITIES:

Acrylic acid	0.91%
Water	0.06%
Ethylene oxide	0.43%
Hydroxyethyl acetate	0.82%
Hydroxyethyl methacrylate	0.1%
Ethylene diacrylate	0.11%
Diethylene glycol nitroacrylate	1.11%
2-Hydroxyethyl ester of diacrylic acid	0.19%
methyl ethyl hydroquinone (ppm)	475

COMMON NAME: 2-hydroxyethyl acrylate

LOT NUMBER: TB-08153

Reanalysis 14 months from the initial analysis showed the test material to be stable.

Source : HEA/HPA Consortium

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards, well-documented and acceptable for assessment.

The number of animals per group at the start of the study was twice the number specified in current guidelines for chronic toxicity/carcinogenicity studies.

Flag : Critical study for SIDS endpoint

10.08.2005 (31)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 6 hours/day
Frequency of treatm. : daily on days 6-20 of gestation
Duration of test : gestation day 21
Doses : 0, 1, 5 and 10 ppm (0, 5.3, 26.5, 53 mg/cubic meters)
Control group : yes, concurrent vehicle
NOAEL maternal tox. : = 1 ppm
NOAEL teratogen. : > 10 ppm

NOAEL Fetotoxicity : > 10 - ppm
Result : not selectively toxic to the embryo or fetus
Method : other: consistent with OPPTS 870.3700 with minor exceptions
Year : 1999
GLP : no data
Test substance : other TS

Remark : The developmental toxicity of seven acrylates were studied in Sprague-Dawley rats after inhalation exposure for 6 h/day, during 6 to 20 days of gestation. The exposure concentrations were 0, 1, 5 and 10 for hydroxypropyl acrylate. Dose groups consisted of 20-22 pregnant females.

Result : MATERNAL TOXIC EFFECTS BY DOSE LEVEL:
-Mortality and day of death: none
-Body weight/body weight gain: Maternal weight gain was significantly less than controls during the first half of the exposure at 10 ppm and absolute weight gain was reduced at 5 and 10 ppm.

Exp. Conc.	# of Dams	BW GD 6	BW gain (g) on GD 6-13	13-21	6-21	Absolute wt gain(g)
0	21	266±16	28±6	99±19	126±22	27±13
1	20	272±15	26±6	99±19	125±20	27±9
5	22	271±13	25±7	93±30	118±33	19±11*
10	21	272±15	22±8*	92±21	114±26	16±12**

*,** Significant differences from control (0 ppm) value, p<0.05, and p<0.01, respectively.

-Food consumption: Food consumption was slightly reduced during treatment at 10 ppm.

Exp. Conc.	# of Dams	Food consumption (g/dam/day) on GD 0-6	6-13	13-21	6-21
0	21	22 ± 2	21 ± 2	26 ± 2	24 ± 2
1	20	23 ± 2	21 ± 2	26 ± 2	24 ± 2
5	22	22 ± 1	21 ± 2	25 ± 3	23 ± 2
10	21	22 ± 2	20 ± 2*	24 ± 2*	22 ± 2*

* Significant differences from control (0 ppm) value, p<0.05, and p<0.01, respectively.

-Implantations and resorptions: There were no significant differences in the numbers of implantation sites and live fetuses, in the incidence of non-live implants and resorptions, or in the fetal sex ratio.

Litters with implants

Exp. Conc.	# of females	# of litters	# of implant sites/ litter	% of non-live implants/ litter@	% of resorp. sites/ litter
0	24	21	14.48±3.06	6.10±8.37	6.10±8.37
1	23	20	14.40±2.23	9.76±15.58	9.76±15.58
5	24	22	14.27±4.09	10.83±21.79	10.83±21.79
10	23	21	14.52±3.74	6.70±5.90	6.70±5.90

@ Resorptions plus dead fetuses.

FETAL DATA:
-Fetal body weights: There were no effects on fetal body weights at any exposure level.

Litters with Live Fetuses
# of live

Exp. Conc.	# of lit.	fetuses/ litter	Average Fetal Body Weight (g)/litter All	Males	Females
0	21	13.62 ±3.29	5.48 ±0.21	5.65 ±0.22	5.31 ±0.25
1	20	13.00 ±2.90	5.61 ±0.29	5.74 ±0.30	5.47 ±0.33
5	21	14.00 ±3.22	5.58 ±0.33	5.74 ±0.35	5.43 ±0.34
10	21	13.57 ±3.70	5.48 ±0.27	5.61 ±0.32	5.35 ±0.27

Litters with live fetuses

Exp. Conc.	# of lit.	Fetal sex ratio M:F
0	21	1.01
1	20	1.03
5	21	0.93
10	21	0.80

-Fetal malformations: Single occurrences of visceral malformations were seen in the control and in the 5 ppm-exposure groups. There were no external variations observed in any group. The incidences of visceral and skeletal variations were scattered, with no indication of adverse effects in any of the exposed groups when compared to controls.

Incidence of Malformations and Variations in Fetuses (a)

Exp. Conc. (ppm):	0	1	5	10
Total # fetuses (litters) examined				
External	286 (21)	260 (20)	294 (21)	285 (21)
Visceral	143 (21)	130 (20)	147 (21)	143 (21)
Skeletal	143 (21)	130 (20)	147 (21)	142 (21)

Malformations:

Exp. Conc. (ppm):	0	1	5	10
Microphthalmia (bilateral)	0	0	1 (1)	0
Diaphragmatic hernia	1 (1)	0	0	0
# (%)fetuses with any malformations	1 (0.3)	0	1 (0.3)	0
# (%) litters with any malformations	1 (4.8)	0	1 (4.8)	0
Mean % fetuses with any malformations/litter (b)	0.4±2.0	0	0.3±1.2	0

External variations

Exp. Conc. (ppm):	0	1	5	10
# (%) fetuses with external variations	0	0	0	0
# (%) litters with external variations	0	0	0	0
Mean % fetuses with external variations/litter	0	0	0	0

Visceral variations

Exp. Conc. (ppm):	0	1	5	10
Subclavian branching variation	0	1 (1)	1 (1)	0
Dilated renal pelvis	0	0	2 (2)	0
Distended ureter	5 (4)	8 (5)	10 (5)	7 (7)
# (%) fetuses with visceral variations	5 (3.5)	9 (6.9)	11 (7.5)	7 (4.9)

# of litters with visceral variations
4 (19.0) 6 (30.0) 6 (28.6) 7 (33.3)
Mean % fetuses with visceral variations per litter
5±12 7±13 8±13 5±7

Skeletal variations
Exp. Conc. (ppm): 0 1 5 10
Sternebra(e)
5th incomplete ossification or unossified (c)
5 (4) 2 (2) 0 5 (4)
1st and 2nd, fused
0 1 (1) 0 0
Rib(s)
Cervical, rudimentary
4 (4) 0 1 (1) 1(1)
14th, supernumerary
4 (4) 11 (6) 18 (8) 4 (3)
11 and 12th, wavy
0 0 1 (1) 0
Thoracic vertebral centra,
incomplete ossification (one to three)
3 (3) 3 (2) 15 (8) 1 (1)
(%) fetuses with skeletal variations
16 (11.2) 17 (13.1) 33 (22.4) 11 (7.7)
(%) litters with skeletal variations
11 (52.4) 9 (45.0) 16 (76.2) 9 (42.9)
Mean % fetuses with skeletal variations/litter
10±11 12±19 24±29 7±9

Exp. Conc. (ppm) 0 1 5 10
(%) fetuses with any variations
21 (7.3) 26 (10.0) 44 (15.0) 18 (6.3)
(%) litters with any variations
13 (61.9) 13 (65.0) 17 (80.9) 13 (61.9)
Mean % fetuses with any variations /litter
8±9 10±11 16±18 6±6

(a) The incidence of individual defect is presented as number of fetuses (number of litters). Only live fetuses were examined. A single fetus may be represented more than once in listing individual defects.
(b) Mean +/-SD
(c) Unossified: alizarin red S negative

No evidence of developmental toxicity was observed after inhalation exposure to hydroxypropyl acrylate even at concentrations which produced maternal effects.

Source : Rohm and Haas Company Spring House

Test condition : Test Conditions:
TEST ORGANISMS
-Age: Young, nulliparous females
-Weight at study initiation: 200-220g
-Number of animals: groups of 23-24 bred female rats (20-22 pregnant)
ADMINISTRATION/EXPOSURE
-Route: inhalation
-Concentrations: The analytical concentrations were 1.0+/-0.1, 5.1+/-0.3 and 10.3+/-0.8 for the 1, 5 and 10 ppm groups as measured by gas chromatography. Control animals were exposed concurrently to filtered room air in an adjacent chamber with characteristics identical to those of the treatment groups.
-Exposures: Exposures were conducted in 200-L glass/stainless-steel inhalation chambers with dynamic and adjustable laminar air flow (6-20m3/hour). Hydroxypropyl acrylate was delivered with an infusion pump, a

constant rate of liquid chemical from the top of a heated glass column filled with glass beads. Compressed air heated by a glass heater was introduced at the bottom of the glass column in a countercurrent fashion to the liquid flow. Concentrations were monitored continuously with a gas-chromatograph equipped with a flame ionization detector and an automatic gas-sampling valve. In addition, exposure levels were determined once during each 6-hour exposure period by collecting atmosphere samples through glass tubes packed with activated charcoal. Samples were then desorbed with dichloromethane and analyzed by gas chromatography.

MATING PROCEDURES: Females were housed overnight with adult males (one male:two or three females) from the same strain and supplier. The day that vaginal smears were found to be sperm-positive was considered day 0 of gestation.
PARAMETERS ASSESSED DURING STUDY:
-Body weight/body weight gain: Maternal body weights were recorded on GD 0, 6, 13 and 21.
-Food consumption: Food consumption was recorded on GD 0-6, 6-13 and 13-21.
-Clinical observations performed and frequency:
Parent: no data
Fetus: no data
-Examination of uterine content: Uteri were removed and weighed, and the number of implantation sites, resorptions, and dead and live fetuses were recorded. Uteri which had no visible implantation sites were stained with ammonium sulfide to detect very early resorptions.
-Examination of fetuses: Live fetuses were weighed, sexed, and examined for external anomalies including those of the oral cavity. Half of the live fetuses from each litter were preserved in Bouin's solution and examined for internal soft tissue changes. The other half were fixed in ethanol, eviscerated, and then processed for skeletal staining with alizarin red S for subsequent skeletal examination.
-Organs examined at necropsy:
Parent: none
Fetus: see results table
STATISTICAL METHODS: Data were presented as mean +/-SD. The number of implantation sites and live fetuses and the various body weights were analyzed by one-way analysis of variance (ANOVA), followed by Dunnett's test if differences were found. The percentages of non-live implants and resorptions and the proportions of fetuses with alterations in each litter were evaluated by using the Kruskal-Wallis test, followed by the Dixon-Massey test where appropriate. Rates of pregnancy, fetal sex ratio, and percentage of litters with malformations or external, visceral, or skeletal variations were analyzed by using Fisher's test. Where applicable, least-squares analysis was carried out. For all statistical tests, the level of significance was set a priori at alpha=0.05.

Test substance : hydroxypropyl acrylate; purity 97.5%, GC, mixture of isomers

Conclusion : Exposure to 5 and 10 ppm HPA caused overt maternal toxicity. This was evidenced by a decrease in body weight changes (10 ppm only) and a decrease in absolute weight gain. There were no effects in maternal toxicity in animals exposed to 1 ppm HPA; therefore, the NOAEC for maternal toxicity was 1 ppm. There was no increase in incidence of malformations or variations at any dose level; therefore, the NOAEC for teratogenicity > 10 ppm for HPA.

Reliability : (2) valid with restrictions
Meets generally accepted scientific standards and is described in sufficient detail.

Flag : Critical study for SIDS endpoint

29.12.2004 (46)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience : other: Allergic contact dermatitis.

Remark : Three dental nurses and three dentists developed allergic contact dermatitis from a dentin adhesion promoter system. These persons were tested with a (meth)acrylate series, a dental series, and their "own" components. Each patient's patch test (48 h exposure) reaction to 2-Hydroxyethyl methacrylate and their "own" components of the dentin adhesion promoter system were positive. The standardized acrylate series included testing with 2-hydroxypropyl acrylate. Neither of the two female patients (dental nurses, age: 36 and 49) tested with 0.1 % (wt/wt) 2-Hyxdroxypropyl acrylate showed reactions.

13.01.2003 (28)

Type of experience : other: Allergic contact dermatitis.

Remark : A worker (maintenance fitter, wearing protective clothing), who cleaned the tube valve in the manufacturing process of an acrylate chemical, was exposed to hydroxypropyl acrylate. After 6-12 hours, he developed symptoms (on his right foot) of a contact allergy. 6 month later, signs of allergic contact dermatitis were evident first after a working day in the plant and later without working. In a patch test, the worker was found to be sensitized to HPA (++), HPMA (+) and HEMA (+). 150 other workers employed in the same plant have not developed allergic contact dermatitis from acrylates. However, three other maintenance fitters and 8 process operatives developed irritation immediately after contact with HPA. Blistering occurred in two workers 5-6 h after exposure in absence of immediate sensation of irritation.

13.01.2003 (33)

Type of experience : other: Allergic contact dermatitis.

Remark : A 44-year-old man developed recurrent dermatitis on the dorsa of the hands and the sides of fingers after 6 months of work in the factory. The patient developed gastro-intestinal symptoms. Patch testing was done with different working materials. He was found to be sensitized to 2-hydroxyethyl-acrylate and reacted to 2-hydroxypropyl acrylate which was tested simultaneously. The systemic symptoms, however, were not reproduced by patch testing.

13.01.2003 (34)

Type of experience : other: Allergic patch test reactions from acrylics.

Remark : A female dentist specialized in orthodontics repeatedly developed symptoms of pharyngitis at work. A chamber provocation test indicated that her symptoms were caused by acrylics. Prick tests with acrylics were negative, while patch tests were strongly positive although the patient had

never had skin symptoms. In the patch test with 1 % (w/w) 2-Hydroxypropyl acrylate (2-HPA; 6-day reading), an allergic test reaction of 3+ (=abundant) was determined.

13.01.2003 (29)

Type of experience : other: Cross-sensitisation in acrylate allergies.

Remark : Five persons developed allergic contact dermatitis to one or more acrylate components used in a commercial adhesive tape. Patch testing to acrylic monomers was performed to examine their cross-reaction patterns. 3 of the 5 patients did not respond to hydroxypropyl acrylate. 2 Patients were strongly positive to hydroxypropyl acrylate and did react to hydroxypropyl methacrylate. If, for discussion purposes, methacrylate and acrylate allergies are basically distinct, then some alkyl side chains, being more reactive with protein than others, could possibly obscure or override the normal haptenic distinctions between methacrylates and acrylates, so that cross-reactions may occur.

13.01.2003 (26)

Type of experience : other: Skin sensitization, case report

Remark : A 31-year-old woman became sensitized to Ethyl acrylate, 2-Hydroxyethyl acrylate and 2-Hydroxypropyl acrylate. This was confirmed on retesting but on day 13, after retesting, the patient developed further positive acrylate and methacrylate patch reactions indicating that the second patch test session sensitized her - at least Ethyl methacrylate and Triethyleneglycol diacrylate.

Reliability : (2) valid with restrictions

03.02.2003 (27)

Type of experience : other: Skin sensitization, case report

Remark : 5 (1.4 %) of 377 patiens tested in German dermatological clinics for possible contact allergy to Hydroxypropyl acrylate showed a positive reaction.

Reliability : (2) valid with restrictions

13.01.2003 (49)

5.11 ADDITIONAL REMARKS

Type : Metabolism

Method : The disposition of 14C-hydroxyethyl acrylate (HEA) was determined following a single dose administration via the oral, intraperitoneal, dermal, and inhalation routes of exposure. Four male Fischer 344 rats (approx. 200g) were utilized per dose and route of exposure. Doses selected for the oral and IP studies were 2.5 and 50 mg/kg, respectively, which were prepared in distilled deionized water. The radiotracer was diluted with non-radiolabeled HEA to obtain a target radioactivity and concentration of 20 uCi and 1.75 and 36.7 mg/ml of dosing solution. The dose applied dermally was 12.5 mg/kg and each animal received approximately 15-20 uCi of activity. The dermal site was clipped of hair and a frame was attached to the skin with adhesive. The dermal dosing solution prepared in water was then applied to the skin and immediately covered with a piece of Teflon film. The dosed area was then wrapped with tape. The nose-only inhalation exposure concentration was 8 ppm 14C-HEA for a 6-hour period under dynamic flow-through conditions. Exposure HEA concentrations and

radioactivity were monitored over the exposure period.

After administration or termination of exposure to 14C-HEA, rats from all groups were housed in metabolism cages. Urine and cage rinse was collected at 0-12, 12-24 and 24-48 hr, post-dosing or post-exposure. Feces were collected at 24-hr intervals for up to 48 hr post-dosing or post-exposure. Expired organics and 14CO2 were collected at 0.25,0.5,1,2,4,8, and 12 hr post administration and then at 12-hr intervals thereafter. All of the above samples were analyzed for radioactivity. Urine and feces were also collected from individual rats during the inhalation exposure. In addition, the combined 14CO2 released into the inhalation chamber from the expired air of all 4 rats was trapped and analyzed after scrubbing 14C-HEA from the chamber exhaust. Selected samples of urine were analyzed by HPLC to determine 14C metabolic profiles.

Blood concentration-time profiles were obtained from separate groups of animals so that expired 14CO2 would not be lost while blood was collected from the animals in the metabolism cages. Blood samples for the 14C-plasma and red blood cell time course were collected at 0.25,0.5,1,2,4,6,8,12,16,24,30 and 48 hr after the administration of 14C-HEA by the oral, IP and dermal routes. During the inhalation exposure, blood samples were collected at 0.25,0.5,1,2,4 and 6 hr, and 0.5,1,2,4,8,20,30 and 48 hr post inhalation exposure. Plasma and red blood cells were analyzed for radioactivity.

The rats were sacrificed 48 hr after administration or exposure to 14C-HEA, and the radioactivity remaining in samples of blood, skin, and the carcass was quantified. For the dermal route of administration, the radioactivity associated with the skin at the dose site and all bandage material was also determined.

The half-lives for the CO2 excretion and the plasma radioactivity were determined from the slope of the line by regression analysis of the excretion time-course obtained from each treatment group. Statistical analysis of the data was limited to the calculation of means and standard deviations were appropriate. Pharmacokinetic analyses (calculation of half-lives, AUC's etc.) were carried out using standard methodologies.

Result **:** Once systemically available, 2-HEA was rapidly metabolized and eliminated from the body. The in vitro half-life of HEA in rat blood was approximately 100 seconds. In vivo, greater than 70% of the administered dose of [14C]-HEA was excreted by 12 hours post-dosing or post-exposure as urinary metabolites and as [14C]-CO2 in the expired air for the oral, i.p. and inhalation routes.

Following the 2.5 mg/kg dose via the oral and IP routes, 43-47% of the dose was excreted in urine and 35-36% as expired 14CO2. At 50 mg/kg dose via the oral and IP routes, there was some evidence of saturation kinetics, with 33-36% excreted in the urine and 40-45% expired as 14CO2. The rate of absorption of HEA appeared to be route-dependent and was complete within 4 hours or less when given by oral or i.p. routes.

Following dermal administration of a dose of 12.5 mg/kg, 66% of the applied dose was slowly absorbed within 48 hours with the remaining 33% being associated with the application site. Once absorbed, 27% was excreted in the urine and 27% was expired as 14CO2.

Following inhalation exposure to 8 ppm HEA for 6 hours, 39% of the radioactivity recovered at 48 hr was eliminated
in the urine as metabolites of HEA and 41% was expired as 14CO2.

For all routes 9-16% of the dose or recovered radioactivity was found in the tissues and carcass and less than 3% in the feces. The half-lives of

elimination of radioactivity in the urine and expired 14CO2 were approximately 14 hours and 17 hours, respectively. The half-life of elimination of radioactivity in the plasma was determined to be approximately 26 hours and did not represent parent chemical. No qualitative differences in urinary metabolites between routes were observed, indicating no marked route-dependent differences in the metabolic fate of HEA.

Test substance : 2-hydroxyethyl acrylate (HEA; CAS RN 818-61-1)

Uniformly labeled 14C-HEA had a specific activity of 6.3 mCi/mmol and a radiochemical purity of 100% as determined by HPLC. Radiochemical purity was evaluated throughout the study and ranged from 100% to 87% (lower purity for inhalation study only).

Non-radiolabeled HEA had a molar purity of 98.3% as determined by GC and IR.

Reliability : (1) valid without restriction
1d

02.01.2004 (15)

Type : other: Hydrolysis in simulated saliva

Method : CS/PM/1025 according to a CEC standard method

Result : In a test with simulated (human) saliva, the degree of hydrolysis of HPA was very low following incubation for 4 h at 37 degree C. The percentage loss of the initial concentration was given with 6 +/- 3 %.

Test substance : 2-Hydroxypropyl acrylate (PM / ref. no. 11530)

Reliability : (2) valid with restrictions
Acceptable, well documented study report, meeting basic scientific principles

03.02.2003 (13)

(1) Anonymous (undated):
Ermittlung der minimalen Hemmstoffkonzentrationen von
Acrylaten der Firma BMC Acryl-Chemie, 7p.

(2) Anonymous (undated): Ermittlung der minimalen Hemmstoffkonzentrationen von
Acrylaten der Firma BMC Acryl-Chemie, 7p.

(3) Bjoerkner, B. (1984):
Contact allergy to 2-Hydroxypropyl-Methacrylate (2-HPMA) in
an ultraviolet curable ink, Acta Derm.-Venerol. 64 (3), 264-267

(4) BP Chemicals Inc.: Initial Submission: Irritation and
Mutagenicity tests of Hydroxyethyl methacrylate and related
studies with cover letter dated 082892; Microfiche No.:
OTS0556083; Carpanini Dr. F.M.B., date produced: 03/10/81

(5) Calandra, J.C. (1974). 28-Day Subacute Dermal Toxicity Study with "UV Curable
Industrial Coating CNF 427" in Albino Rabbits. Industrial Bio-Test Report 601-05499.

(6) Canadian Environmental Modelling Centre. 1999. Level I Model Version 2.11; Computer
Software Available from www.trentu.ca

(7) Carreon, R.E., J.T. Young and J.M. Wall. 1981. Hydroxypropyl acrylate: Acute
percutaneous absorption potential. Unpublished report. Toxicology Research Laboratory,
Dow Chemical, Midland, MI, USA.

(8) Ciba-Geigy (1976):
Eye Irritation in the rabbit of TK 12116,
Ciba-Geigy Limited, Basle, Switzerland, 4p.

(9) Ciba-Geigy (1976):
Eye Irritation in the rabbit of TK 12117,
Ciba-Geigy Limited, Basle, Switzerland, 4p.

(10) Ciba-Geigy (1976):
Skin irritation in the rabbit after single application of
TK 12116, Ciba-Geigy Limited, Basle, Switzerland, 4p.

(11) Ciba-Geigy (1976):
Skin irritation in the rabbit after single application of
TK 12117, Ciba-Geigy Limited, Basle, Switzerland, 4p.

(12) Clemmensen, S. (1984): Cross-reaction patterns in guinea pigs sensitized to acrylic
monomers, Drug and Chemical Toxicology, 7 (6), 527-540

(13) Cooper, I. (1992):
Research report: Hydrolysis studies on 2-Hydroxypropyl
acrylate (HPA) and 2-hydroxypropyl methacrylate (HPMA) in
simulated saliva, BP Chemicals, Ref.: RJ/111/083/SC

(14) DIPPR (The Design Institute for Physical Properties) (2000). The DIPPR Information and
Data Evaluation Manager, Version 1.5.0, Copyright BYU-TPL2000.

(15) Domoradzki, J.Y., Freshour, N.L., Dryzga, M.D., Hiser, M.F., Smith, F.A., and Waechter,
Jr., J.M. (1992). 2-Hydroxyethyl Acrylate: Pharmacokinetics in Male Fischer 344 Rats
Following Administration by Four Routes. R & D report of The Dow Chemical Company.

(16) Dow (1964): Results of Range-Finding Toxicological Test on 2-Hydroxypropyl Acrylate.
Unpublished report, February 19, 1964. The Dow Chemical Company, 5p.

(17) DOW (1970). Guinea pig skin sensitization study on 2-hydroxypropyl acrylate. Unpublished report, June 30, 1970. The Dow Chemical Company Biochemical Research Laboratory, 1p.

(18) Dow (1973). DOT Test for Corrosiveness Conducted on: Hydroxypropyl Acrylate. Unpublished report, March 14, 1973. Dow Chemical, USA, 1p.

(19) Dow (1981). DOT (Department of Transportation) Test for Corrosiveness to the Skin of 2-Hydroxypropyl Acrylate. Unpublished report, Lab No. 485, September 1, 1981. Dow Chemical, USA, 1p.

(20) Dow (1992):
2-Hydroxypropylacrylate, Acute toxicity to Daphnia magna, Unpublished report, Project No. 44/991, Safepharm Laboratories Limited, U.K., Sponsor: Dow Europe S.A., 22p.

(21) Dow Chemical Company. 1975. The pollutional evaluation of compounds. Unpublished report, February 26, 1975. Dow Chemical Company, USA, 5 p.

(22) Dow Product Stewardship Manual (October 2002)

(23) Geiger, D.L., S.H. Poirier, L.T. Brooke and D.J. Call (Eds.) (1986): Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas), Volume III. Center for Lake Superior Environmental Studies, University of Wisconsin-Superior, ISBN 0-9614968-2-7.

(24) Gonsior, S.J., Goodwin, P.A. and Tryska, T.J. (1997). Hydrolysis of Hydroxyethyl Acrylate (HEA), Hydroxypropyl Acrylate (HPA) in Buffered Solutions. R & D report of The Dow Chemical Company.

(25) Hamann, U. 2000. Mammalian Micronucleus Test of Murine Bone Marrow Cells with 2-Hydroxypropylacrylate. BSL Bioservice Project No.: 001524 A. BSL Bioservice Scientific Laboratories GmbH, Planegg/München, Germany.

(26) Jordan, W.P. (1975):
Cross-sensitization patterns in acrylate allergies,
Contact Dermatitis 1, 13-15

(27) Kanerva L., Estlander T., Jolanki R.: Double active sensitization caused by acrylics; American Journal of Contact Dermatitis 3(1): 23 - 26 (1992)

(28) Kanerva, L. et al. (1991):
Occupational allergic contact dermatitis caused by 2-Hydroxyethyl methacrylate (2-HEMA) in a new dentin adhesive, Am. J. Cont. Derm 2(1), 24-30

(29) Kanerva, L. et al. (1992):
Occupational pharyngitis associated with allergic patch test reactions from acrylics, Allergy 47 (5), 571-573

(30) Kanerva, L.; Estlander, T.; Jolanki, R. (1988): Sensitization to patch test acrylates. Contact Dermatitis 18, 10-15

(31) Kociba, R.J., Keyes, D.G., Schuetz, D.J., Yakel, H.O., Balmer, M.F. and Rampy, L.W. (1979) Results of a Two-Year Inhalation Toxicity Study of 2-Hydroxyethyl Acrylate (HEA) in Rats. Unpublished Report of The Dow Chemical Company.

see also:

Rampy L.W. et al. (1978) Toxicol. Appl. Pharmacol., 45: 310.

(32) Leong, B.K.J. and Trice, V.R. (1970). Effects of Repeated Inhalation Exposures of Rats and Single Exposure of Humans to Vapours of Hydroxy Ethyl Acrylate. R & D report of The Dow Chemical Company.

(33) Lovell, C.R. et al. (1985):
Contact dermatitis from the irritancy (immediate and delayed) and allergenicity of hydroxypropyl acrylate,
Contact Derm. 12, 117-118

(34) Peters, K.; Andersen, K.E. (1986):
Allergic hand dermatitis from 2-hydroxyethyl-acrylate in contact lenses, Contact Dermatitis 15, 188-189

(35) Properties of Flammable Liquids, Gases, Solids. Page 325M-83. in: Fire Protection Guide on Hazardous Materials, 9th edition. National Fire Protection Association, Quincy, MA, USA.

(36) Quast, J.F. and Rampy, L.W. (1983). Repeated Inhalation Toxicity of Hydroxypropyl Acrylate. Dow Chemical, USA; Final Report, July 7, 1983; 35p.

(37) Rao, K.S.; Betso, J.E.; Olson, K.J. (1981):
A collection of guinea pig sensitization test results - grouped by chemical class, Drug and Chemical Toxicology, 4 (4), 331-351

(38) Results
BOD= 83%
TOC = 93%
HPLC = 100%

readily biodegradable

(39) Roehm (1995):
Gene Mutation Assay in Chinese Hamster V79 Cells in Vitro (V79/HPRT) with Hydroxypropyl acrylate, CCR Robdorf, Unpublished report, Project no. 517703, Roehm GmbH, Chemische Fabrik, Darmstadt, 29p.

(40) Roehm (1995):
In vitro chromosome aberration assay in chinese hamster V79 cells with Hydroxypropyl acrylate,
Roehm GmbH, Chemische Fabrik, Darmstadt, 29p.

(41) Roehm (1995):
Salmonella typhimurium reverse mutation assay with Hydroxypropylacrylat, CCR Robdorf, Unpublished report, Project no. 517701, Roehm GmbH, Chemische Fabrik, Darmstadt, 30p.

(42) Roehm (2000):
2-Hydroxypropyl Acrylate chromosome Aberrations in Chinese Hamster Ovary Cells in Vitro. Unpublished report. RTC Report no. 7384-M-04899 Roehm GmbH, Chemische Fabrik, Darmstadt, 26p.

(43) Rohm and Haas (1982):
Results, Microbial Mutagen Assay (Ames): Rocryl 430 (HPA).
Rohm and Haas, Spring House, 3p.

(44) Rohm and Haas (1983):
Toxicity report. Unpublished report no. 82R 0224. Rohm and Haas, toxicology department, Spring House, PA, 16p.

(45) Russom, C.L.; Drummond, R.A.; Hoffman, A.D. (1988): Acute toxicity and behavioural effects of acrylates and methacrylates to juvenile fathead minnows. Bull. Environ. Contam. Toxicol., 41, 589-596.

(46) Saillenfait A, et al. Relative Developmental Toxicities of Acrylates in Rats Following Inhalation Exposure. Toxicological Sciences 48: 240-245, (1999).

(47) Schaefer, E. (1995). Chemical Oxygen Demand and Biochemical Oxygen Demand Test Results. Wildlife International LTD. Project Number: 408E-101.

(48) Scheerbaum, D. (2004). Hydroxypropyl Acrylate (HPA): Alga, Growth Inhibition Test with Pseudokirchneriella subcapitata, 96 H (formerly Selenastrum capricornutum). Project-No. 031022HH from Dr. U. Noack-Laboratorien, Sarstedt, Germany for HEA/HPA Consortium, 941 Rhonda Place SE, Leesburg, VA 20175, USA.

(49) Schnuch A.: Allergien gegen Hydroxyethylmethacrylat, Hydroxypropylmethgacrylat, Hydroxyethylacrylat und Hydroxypropylacrylat; personnel communication to Dr. Mullerschon and Dipl.-Ing. G. Ritz, Rohm GmbH; Informationsverband Dermatologischer Kliniken, Gottingen (1997)

(50) Tanii, H,; Hashimoto, K. (1982): Structure-toxicity relationship of acrylates and methacrylates. Toxicology Letters, 11, 125-129

(51) U. S. EPA (U.S. Environmental Protection Agency). 2000. EPI Suite, Version 3.11; WSKOWWIN Program, Version 1.40; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

(52) U.S. EPA (U.S. Environmental Protection Agency). 2000. EPI Suite, Version 3.11; AOPWIN Program, Version 1.91; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

(53) U.S. EPA (U.S. Environmental Protection Agency). 2000. EPI Suite, Version 3.11; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

(54) Union Carbide Corporation. 1967. 2-Hydroxypropyl Acrylate Range Finding Toxicity Studies. Unpublished report. Chemical Hygiene Fellowship, Mellon Institute, Industrial Fellowship 274-30.

(55) Union Carbide Corporation. 1971. Hydroxypropyl Acrylate Range Finding Toxicity Studies. Unpublished report no. 34-3. Chemical Hygiene Fellowship, Mellon Institute, Carnegie-Mellon University, PA. Submission with cover letter dated July 29, 1992, US EPA Doc. # 88-920004579.

(56) Watanabe, K., K. Sakamoto and T. Sasaki. (1996) Comparisons on chemically-induced mutagenicity among four bacterial strains, Salmonella typhimurium TA102 and TA2638, and Escherichia coli WP2/pKM101 and WP2 uvrA/pKM101: Collaborative study I. Mutation Research 361: 143-155.

(57) Wu, H. 1996. Determination of ready biodegradability: Closed bottle test, Ethyl Acrylate (EA), Methyl Acrylate (MA), Hydroxyethyl Acrylate (HEA), Hydroxypropyl Acrylate (HPA), Butyl Acrylate (BA). Unpublished report Weston Study No. 96-016. Roy F. Weston, Inc., Lionville, PA, USA.

(58) Yoshii, E. 1997. Cytotoxic effects of acrylates and methacrylates: Relationships of monomer structures and cytotoxicity. J. Biomed. Mater. Res. 37:517-524.