FOREWORD INTRODUCTION

GLUCIDYL METHACRYLATE

CAS N°: 106-91-2

COVER PAGE
SIDS Initial Assessment Report
for
10th SIAM

(Japan, March 15-17, 2000)

Chemical Name: Glycidyl methacrylate
CAS No: 106-91-2
Sponsor Country: Japan and United States

National SIDS Contact Point in Sponsor Country: Mr. Kazuhide Ishikawa
Ministry of Foreign Affairs, Japan
Mr. Oscar Hernandez
US EPA

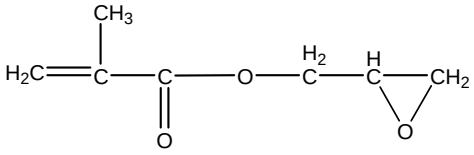
HISTORY:

SIDS Testing Plan were reviewed in SIDS Review Process, where the following SIDS Testing Plan was agreed:

no testing ( )
testing (X) Water solubility, Vapour pressure, Octanol/water partition coefficient, Stability in water, Biodegradation
Chronic toxicity to daphnia
Combined repeat dose and reproductive toxicity,
Chromosomal aberration test in vitro, Micronucleus test in vivo

Deadline for circulation: November 30, 1999
Date of Circulation: December 20, 1999
(To all National SIDS Contact Points and the OECD Secretariat)

SIDS INITIAL ASSESSMENT PROFILE

CAS NO.	106-91-2
CHEMICAL NAME	Glycidyl methacrylate
STRUCTURAL FORMULA	

RECOMMENDATION

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health Hazards

Acute lethal toxicity of glycidyl methacrylate is low via the oral administration route. No mortality was observed in rats following inhalation exposure up to 2,394 mg/m^3, the highest practically attainable vapor concentration. This chemical is considered both highly irritating (including necrosis, degeneration and hyperplasia) to the skin, eyes and respiratory tracts and a skin sensitizer. In an oral (via gavage) OECD combined repeat dose and reproductive/ developmental screening toxicity test (TG 422) in rats at doses of 10, 30, 100 mg/kg/day, squamous hyperplasia in forestomach was induced at 30 and 100 mg/kg/day. Thus, the NOAEL was 10 mg/kg/day. In many repeated inhalation studies, the changes were observed only in respiratory tract (necrosis, inflammation etc. in nasal tissues), and were likely due to irritation. The lowest NOAEL was 0.5 ppm (equivalent to 0.26 mg/kg/day) in a rabbit study. In the OECD combined study (TG 422), the NOAEL for reproductive toxicity was considered to be 30 mg/kg/day, based on a decrease in the fertility index (number of delivered animals/ number of mated animals) at 100 mg/kg. In developmental toxicity studies, teratogenic effect**s** were not induced either by oral administration at 108 mg/kg for rats or inhalation at 291 mg/m^3 for rabbits. Most *in vitro* genotoxicity studies showed positive results. In an *in vivo* micronucleus test, oral administration of glycidyl methacrylate increased the frequency of micronucleated polychromatic erythrocytes only at the highest dose (750 mg/kg in males and 1000 mg/kg in females), although mostly negative results were shown in other *in vivo* genotoxicity studies including micronucleus tests by intraperitoneal administration. Therefore, the genotoxic potential of this chemical can not be ruled out. There was no available data on carcinogenicity of this chemical.

Hazards to the Environment

Glycidyl methacrylate is readily biodegradable (OECD 301C: 100 % after 28-d) and readily hydrolyzed ($T_{1/2}$ = 3.66 days at pH 7). This chemical has a low bioaccumulative potential judging from the low log Pow value, 0.96 at 25 °C.

The lowest acute and chronic aquatic toxicity data reported were 14d LC_{50} (1.9 mg/l) of fish (Medaka; *Oryzias latipes*) and 21d NOEC (1.02 mg/l) of *Daphnia magna*, respectively. An assessment factor of 100 was chosen and applied to the chronic toxicity data to determine PNEC, which is 0.01 mg/l.

Exposure

About 3,000 tones/year of glycidyl methacrylate is produced as intermediate for resins in the closed system in Japan, and ca. 3.3 tones (ca. 0.1%)/ year is released into rivers. Release to air phase is negligible. A generic fugacity model (Mackey level III) shows this chemical will be distributed mainly to water phase (99.1%) when it is discharged into water.

NATURE OF FURTHER WORK RECOMMENDED

There is a need for limiting the risk; risk reduction should be taken into account because of the high irritation, sensitization, and the genotoxic potential.

Occupational exposure information should be collected by individual member countries.

FULL SIDS SUMMARY

CAS NO: 106-91-2		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			< -10 °C
2.2	Boiling Point			196.8 – 197.9 °C
2.3	Density			
2.4	Vapour Pressure		OECD TG104	4.2 x 10^2 Pa at 25 °C
2.5	Partition Coefficient (Log Pow)		OECD TG 107	0.96
2.6 A.	Water Solubility		OECD TG 105	Ca. 50 g/L at 25 °C
B.	PH			
	PKa			
2.12	Oxidation: Reduction Potential			
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation			
3.1.2	Stability in Water		OECD TG 111	$T_{1/2}$ = 2.83 day at pH4 at 25 °C $T_{1/2}$ = 3.66 day at pH7 at 25 °C $T_{1/2}$ = 2.22 day at pH9 at 25 °C
3.2	Monitoring Data			In surface water = not detected In soil/sediment = not detected
3.3	Transport and Distribution		Calculated (Fugacity Level III type)	Release: 100% to Water In Air 0.4 % In Water 99.1% In Sediment 0.0 % In Soil 0.4 %
			(local exposure)	0.21 mg/L (Japan A) 8.9 x 10^{-3} mg/L (Japan B)
3.5	Biodegradation		OECD 301C	Readily biodegradable 94%(BOD,TOC), 100%(GC) in 28 days
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oryzias latipes*	OECD TG 203	LC_{50} (24hr) = 12.9 mg/l LC_{50} (48hr) = 5.7 mg/l LC_{50} (72hr) = 3.7 mg/l LC_{50} (96hr) = 2.8 mg/l LC_{50} (14d) = 1.9 mg/l
4.2	Acute Toxicity to Aquatic Invertebrates *Daphnia*	*Daphnia magna*	OECD TG 202	EC_{50}(24hr): 42.3 mg/l EC_{50}(48hr): 24.9 mg/l
4.3	Toxicity to Aquatic Plants e.g. Algae	*Selenastrum capricornutum*	OECD TG 201	EC_{50}(72hr) = 14.6 mg/l NOEC = 3.2 mg/l

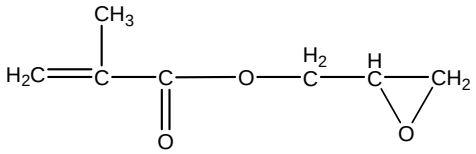
CAS NO: 106-91-2		SPECIES	PROTOCOL	RESULTS
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	OECD TG 202	EC_{50}(21d, Repro)= 3.2 mg/l NOEC(21d, Repro)= 1.0 mg/l
4.6.1	Toxicity to Soil Dwelling Organisms			None
4.6.2	Toxicity to Terrestrial Plants			None
4.6.3	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)			None
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	Other (unknown)	LD_{50} = 597 mg/kg
5.1.2	Acute Inhalation Toxicity	Rat	OECD TG 403	LC_0 = 2,394 mg/m^3/4hr
5.1.3	Acute Dermal Toxicity	Rabbit	Other (unknown)	LD_{50} = 480 mg/kg
5.2.1	Skin Irritation/Corrosion	Rabbit	Other (unknown)	Highly irritating
5.2.2	Eye Irritation/Corrosion	Rabbit	Other (unknown)	Highly irritating
5.3	Sensitisation	Guinea pig	Other (unknown)	Strongly sensitising
5.4	Repeated Dose Toxicity	Rat	OECD TG 422 (oral)	NOAEL = 10 mg/kg/day
		Rat	Other (inhalation)	NOAEL = 12 mg/m^3 (1.46 mg/kg/day)
		Rabbit	Other (inhalation)	NOAEL = 2.9 mg/m^3 (0.26 mg/kg/day)
5.5	Genetic Toxicity In Vitro			
A.	Bacterial Test (Gene mutation)	S. typhimurium	Other	+ (With metabolic activation) + (Without metabolic activation)
B.	Non-Bacterial In Vitro Test (Chromosomal aberrations)	Chinese hamster lung (CHL/IU) cells	Japanese TG and OECD TG 473	+ (With metabolic activation) + (Without metabolic activation)
5.6	Genetic Toxicity In Vivo (Micronucleus)	Mouse	Japanese TG and OECD TG 474	+ (Oral)
		Mouse	Other	- (Intraperitoneal)
5.8	Toxicity to Reproduction	Rat	OECD TG 422	NOAEL = 30 mg/kg/day
5.9	Developmental Toxicity/ Teratogenicity	Rat	Other (oral)	No teratogenic
		Rabbit	Other (inhalation)	No teratogenic
5.11	Experience with Human Exposure		Patch test	Sensitising

SIDS INITIAL ASSESSMENT REPORT

Glycidyl methacrylate (**CAS No. 106-91-2**)

1. IDENTITY

- OECD Name: Glycidyl methacrylate
- Synonym: 2,3-Epoxypropyl methacrylate; Glycidyl alpha-methylacrylate; 1-Propanol, 2,3-epoxy-, methacrylate
- CAS Number: 106-91-2
- Empirical Formula: $C_7H_{10}O_3$
- Structural Formula:



- Degree of Purity: 97.9 %
- Major Impurity: None
- Essential Additives: None
- Physical-chemical properties
  - Melting Point: < -10 °C
  - Vapour pressure: 4.2 x 10^2 Pa at 25 °C
  - Water solubility: Ca. 50 g/L
  - Log Pow: 0.96

2. GENERAL INFORMATION ON EXPOSURE

2.1 Production and import

The production volume of glycidyl methacrylate in Japan is 3,128 tonnes/year in 1995.

2.2 Use pattern

All of glycidyl methacrylate produced in Japan is used as monomer unit of paint resin and as intermediate of chemical products, and no consumer use is reported.

HSDB (Hazardous Substances Database) states that the chemical is a diluent in epoxy resins and a paper by Matura et al (1995) states that it is used in emulsions to impregnate paper and textile materials. It is also listed as an epoxy resin additive used in paint coating formulations and adhesive applications.

2.3 Other information

None

3. ENVIRONMENT

3.1 Environmental Exposure

3.1.1 General Discussion

Glycidyl methacrylate is readily biodegradable (OECD 301C: 100 % after 28d) and readily hydrolyzed ($T_{1/2}$ = 2.83, 3.66 and 2.22 day at pH 4,7,and 9, respectively). Direct photodegradation is not expected because glycidyl methacrylate has not absorption band in UV and VIS region.

Glycidyl methacrylate is low bioaccumulative based on Log Pow (0.96 at 25 °C).

The potential environmental distributions of glycidyl methacrylate obtained from a generic Mackay level III fugacity model is shown in Table 1. Parameters used for this model are shown as Annex to this report. The results show that, if glycidyl methacrylate is released into water or soil, it is unlikely to be distributed into other compartments. If glycidyl methacrylate is released into air, it is likely to be distributed in other compartments.

Table 1 Environmental distribution of glycidyl methacrylate
Using a generic level III fugacity model.

Compartment	Release 100% to air	Release 100% to water	Release 100% to soil
Air	77.0 %	0.4 %	0.4 %
Water	15.2 %	99.1 %	9.0 %
Soil	7.7 %	0.0 %	90.6 %
Sediment	0.1 %	0.4 %	0.0 %

As this chemical is used in closed system as a monomer unit of paint resin or an intermediate of chemical products and is not included in consumer products, its release to the environment may occur only from the production site.

3.1.2 Predicted Environmental Concentration

As glycidyl methacrylate is produced under the well-controlled closed system, amount of release to air phase is negligibly small. The waste of glycidyl methacrylate from the production system is released to water phase after treated its own wastewater treatment plant. Therefore, Predicted Environmental Concentration (PEC) will be calculated only for the water environment.

Regional exposure

(a) According to report from a Japanese manufacturer (A), 3.3 tonnes/year (measured) of glycidyl methacrylate are released with 5.35 x 10^9 L/year of effluent into river. Local Predicted Environmental Concentration (PEC_{local}) is calculated to be 6.2 x 10^{-3} mg/L as a worst case scenario, employing the following calculation model and dilution factor of 100.

$$\frac{\text{Amount of release } (3.3 \times 10^9 \text{ mg/y})}{\text{Volume of effluent } (5.35 \times 10^9 \text{ L/y}) \times \text{Dilution Factor } (100)}$$

(b) According to report from a Japanese manufacturer (B), 1.62 tonnes/year (measured) of glycidyl methacrylate are released with 9.1 x 10^9 L/year of effluent into river which has flow rate of 1.82 x 10^{11}L/year at dry season. Local Predicted Environmental Concentration (PEC_{local}) is calculated to be 8.9 x 10^{-3} mg/L as a worst case scenario, employing the following calculation model and dilution factor of 20.

$$\frac{\text{Amount of release } (1.62 \times 10^9 \text{ mg/y})}{\text{Volume of effluent } (9.1 \times 10^9 \text{ L/y}) \times \text{Dilution Factor } (20)}$$

3.2 Effects on the Environments

3.2.1 Effects on aquatic organisms

Acute and chronic toxicity data of glycidyl methacrylate to aquatic organisms are summarized in Table 2. All tests were conducted by a GLP-laboratory. As the lowest acute and chronic toxicity data, 14d LC_{50} of *O. latipes* and 21 d NOEC (reproduction) of *D. magna* were selected, respectively (Table 2). An assessment factor of 100 was chosen and applied to the chronic toxicity data to determine PNEC, because chronic toxicity data for fish were not available. Thus, PNEC of gycidyl methacrylate is 0.01 mg/l.

Table 2. Acute and chronic toxicity data of glycidyl methacrylate to aquatic organisms at different trophic levels.

Species	Endpoint	Conc. (mg/l)	Remarks
Selenastrum capricornutum (algae)	Bms 72h EC50	14.6	a, 1)
	Do. 72h NOEC	3.2	c, 1)
Daphnia magna (Water flea)	Imm 24h EC50	42.3	a, 1)
	Imm 48h EC50	24.9	c, 1),
	Rep 21d EC50	3.2	c, 1)
	Rep 21d NOEC	1.0	c, 1), C
Oryzias latipes (fish, Medaka)	Mor 24h LC50	12.9	a, 1)
	Mor 48h LC50	5.7	a, 1)
	Mor 72h LC50	3.7	a, 1)
	Mor 96h LC50	2.8	a, 1),
	Mor 14d LC50	1.9	a, 1), A

Notes: Bms; growth measure by biomass change, Imm; immobilization, Mor; mortality, Rep; reproduction,

1); reference number, A), C); the lowest values of the acute (a) or chronic (c) toxicity data among algae, cladocera (water flea) and fishes.

References; 1) Environment Agency of Japan (1997)

3.2.2 Terrestrial effects

No data available

3.2.3 Other effects

No data available

3.3 Initial Assessment for the Environment

Glycidyl methacrylate is readily biodegradable and readily hydrolyzed. This chemical seems to have a low bioaccumulation potential judging from a low log P_{ow} value. The lowest acute toxicity

value was 1.9 mg/l (14d LC_{50} of fish Medaka; *O. latipes*) and 1.0 mg/l (21 d NOEC of *D. magna*), respectively.

4. HUMAN HEALTH

4.1 Human Exposure

4.1.1 Occupational exposure

Glycidyl methacrylate is produced in closed systems and used for resin synthesis. The occupational exposures are expected through inhalation and dermal route. The atmospheric concentration was measured at two production sites. The average concentrations, working schedules and EHEs for each operation were shown in the Table. Dermal exposure was also calculated, based on EASE model. The duration of dermal exposure was assumed to be 5 minutes. If a single worker (body weight; 70 kg, respiratory volume; 1.25 m^3/hr) is assigned to implement all daily operation without protection, the highest daily intake (combined EHE) is calculated as 0.22 mg/kg/day as the worst case. Practically, workers always wear protective gloves and respiratory protective equipment (mask) during the operation.

	Frequency Times/day	Duration hr	Working hr/day	Average Concentration mg/m^3	Average EHE mg/kg/day	Combined EHE mg/kg/day
Case 1						
Sampling	1/30	0.03	0.001	<2.3	0.00005	
Maintenance	1/30	0.17	0.006	<2.3	0.00023	
Can Filling	1/7	6.00	0.800	2.3	0.03316	
Dermal			0.083	0.1*	0.00625	0.040
Case 2						
Sampling	3	0.08	0.250	<2.3	0.01036	
Filtration	3	0.08	0.250	2.3	0.01036	
Analysis	3	0.08	0.250	<2.3	0.01036	
Sluge Removal	3	0.50	1.500	<2.3	0.06218	
Transfer	3	0.50	1.500	<2.3	0.06218	
Waste Treatment	3	0.50	1.500	<2.3	0.06218	
Dermal			0.083	0.1*	0.00625	0.220

* Dermal exposure; mg/cm^2/day
EHE: Estimated Human Exposure
<: Concentrations were below determination limit. Figure is lower determination limit used for EHE calculation.

The data shown were essentially personal monitoring data. Two air samplers were kept on both sides of the operator's face approximately 20 cm away.

Analytical method:
Sampling: XAD2 tube, Air flow rate: 1 liter/min, Air volume: 3 liter
Desorption: Butyl acetate
Determination: Gas chromatograph with FID
Date of Sampling: October 1998

Activity of operator:
Sampling: Take ca. 100 ml of GM from the sampling nozzle in a glass bottle, just like taking water from faucet.

Maintenance: Replace a strainer to trap polymeric by-products with a new one. The strainer housing was isolated from the flow line, but the housing was filled with glycidyl methacrylate during this operation.

Can filling: Filling 18-liter cans using semi-automatic instrument. Operator removed the cap of the can, and placed the can under the nozzle after filling replace the cap. Filled can was transferred by a conveyer.

Analysis: Analyze the quality control sample with GC.
Operator takes a neat sample by a micro-syringe from the bottle in a hood, and injects it to GC.

Sludge removal: Remove residue of distillation vessel manually after residual glycidyl methacrylate was removed by vacuum.

In following operation, operator did not handle glycidyl methacrylate directly.

Transfer: Transfer the product to storage tank using pump.
Waste treatment: The crude product is washed with water to remove sodium chloride.
Waste water is transferred to treatment plant.

4.1.2 Consumer exposure

Glycidyl methacrylate produced in Japan is used as monomer unit of paint resin and as intermediate of chemical products. As the detailed information could not be given in Japan, one report indicates it is used as paints in the product concentrations of 1 to 5 % and the other shows it is mainly used as car coating paints in car industry. Therefore consumer exposure might be low.

4.1.3 Indirect exposure via the environment

Although glycidyl methacrylate is readily biodegradable and low bioaccumulative, the exposure to the general population via the environment would be possible through drinking water processed from surface water and through fish which may accumulate this chemical.

The concentration in drinking water should be estimated to be equal to PEC calculated in Section 3.1, i.e. 8.9×10^{-3} mg/l. The daily intake through drinking water is calculated as 2.97×10^{-4} mg/kg/day (2 l/day, 60 kg b.w.).

Using the bioconcentration factor of 1.0 estimated from logPow (0.96), the concentration of this chemical in fish can be calculated as follows:

$$PEC_{fish} = (8.9 \times 10^{-3}\ mg/l) \times 1.0 = 8.90 \times 10^{-6}\ mg/g\text{-wet}$$

As a daily intake of fish in Japan is estimated to be 90 g for 60 kg body weight person, a daily intake of this chemical will be 1.34×10^{-5} mg/kg/day.

4.2 Effects on Human Health

a) Motion of action of the chemical, toxicokinetics and metabolism

Toxicokinetics of glycidyl methacrylate were investigated in rabbits. After an intravenous injection at 200 mg/kg, over 95 % of the parent compound disappeared from the blood within 10 minutes according to two-compartment open model. Following a subcutaneous injection at 800 mg/kg, the toxicokinetics appeared to fit a first-order absorption one-compartment open model. This chemical was metabolized by incubation with whole blood, plasma, erythrocyte suspension, and homogenates of various tissues. The subcutaneous co-administration of tri-o-cresyl-phosphate (a carboxylesterase inhibitor) with this chemical resulted in about a ten-fold increase in the maximum blood concentrations, compared to those of animals dosed with this chemical alone. (Shi Tao *et al.*: 1988)

The metabolism of glycidyl methacrylate in mammals will likely proceed by at least two different and competing enzyme systems, epoxide hydratase and non-specific carboxylesterases. Species differences in the activity of these enzymes suggest that the carboxylesterase route of metabolism may predominate in the nasal tissue of rabbits (yielding glycidol and methacrylic acid) whereas the epoxide hydratase route would likely predominate in rats and humans (producing glycerol methacrylate, then glycerol and methacrylic acid by carboxylesterase). (Bogdanffy *et al.*: 1987, Dahl *et al.*: 1987, Glatt *et al.*: 1984, Mattes and Mattes: 1992, Pacifici *et al.*: 1981)

b) Acute toxicity

[SIDS data] Oral LD_{50} value for glycidyl methacrylate was 597 mg/kg b.w. for rat (Zdravko *et al.*: 1985). In inhalation toxicity study by OECD TG 403, there was no mortality observed in rats exposed for 4 hours at 2,394 mg/m^3, the highest practically attainable vapor concentration. Change of respiration (labored breathing) and eyes (irritation and corneal opacity), and decrease in body weight were induced even at the lowest concentration of 1,563 mg/m^3. (Nitschke *et al.*: 1990) Dermal LD_{50} for rabbits was 480 mg/kg b.w. (Smyth *et al.*: 1969).

In another inhalation toxicity study, acute exposure to rats with saturated vapour of this chemical resulted in a maximum survival time of 2 hours (Smyth *et al.*: 1969). It was reported that saturated vapour of glycidyl methacrylate at 20 °C was 474 ppm (2,754 mg/m^3) (Draft Workplace Environmental Exposure Level Guide: 1999).

Routes	Strain	Type	Values	Reference
Oral	Rats	LD_{50}	597 mg/kg	Zdravko *et al.*: 1985
	Rats	LD_{50}	about 700 mg/kg	Olson: 1960 Smyth *et al.*: 1969
	Rats*	LD_{50}	451 mg/kg	EPA/OTS: 1992
	Mice	LD_{50}	390 mg/kg	Zdravko *et al.*: 1985
	Mice	LD_{50}	1,050 mg/kg	Smyth *et al* : 1969
	Guinea pigs	LD_{50}	697 mg/kg	Zdravko *et al.*: 1985
Inhalation	Rats	LC_0	2,394 mg/m^3/4hr	Nitschke *et al.*: 1990
	Rats**	LCL_0	1,400 mg/m^3/6hr	Haag: 1953
	Rabbits**	LCL_0	1,400 mg/m^3/6hr	Haag: 1953
	Guinea pigs**	LCL_0	1,400 mg/m^3/6hr	Haag: 1953
	Dogs**	LCL_0	1,400 mg/m^3/6hr	Haag: 1953

Dermal	Rabbits	LD_{50}	480 mg/kg	Smyth *et al.*: 1969
Intraperitoneal	Rats	LD_{50}	290 mg/kg	Petrov: 1973
	Mice	LD_{50}	350 mg/kg	Petrov: 1973

* as a mixture of glycidyl methacrylate (97.8 %), epichlorohydrin (0.3 %) and dichlorohydrin (0.6 %)
** Changes in lungs, thorax, respiration, *etc*. were observed.

c) Irritation

Skin irritation
Glycidyl methacrylate induced high irritation to the skin of rabbits (Ou-Yang *et al*.: 1988). The 0.1 ml applied area showed red, swelled and blistered after one or two days, subdermal bleeding and ulcers after three days, and hard, thicker, cracked, pigmentation after five days. The pathological changes were degeneration and necrosis of surface skin cells, disappearance of cellular boundaries, displaying pink staining material, bleeding in the corium cells and lymph cell infiltration with accompanying formation of abscesses.

There were other data on skin irritation of glycidyl methacrylate. A single covered topical application to the skin of albino rabbits for four hours induced moderate to severe skin irritation including necrosis with slight to moderate edema (Olson: 1960). A 10% solution (aqueous) produced slight redness and edema after 1 application (for 4 hours) and a moderate burn after 2 applications (Olson: 1960). In DOT standard test (equivalent to OECD Test Guideline 404), corrosiveness occurred by 4 hours exposure but not 1-hour exposure (Lockwood: 1991). However, there was no more information on these studies.

Eye irritation
Direct instillation of undiluted glycidyl methacrylate to the eye of albino rabbits induced moderate to severe irritation and corneal damage. Corneal damage did not heal within 7 days post-dosing. This ocular damage was prevented by washing with water within 30 seconds. (Olson: 1960, Smyth: 1969)

In inhalation study using rats, eye irritation was also induced. Acute exposure for 4 hours induced eye irritation at 1,563 mg/m^3 and 2,394 mg/m^3. Corneal opacity was also observed slightly at 610 mg/m^3, and moderately at 1,563 mg/m^3 and 2,394 mg/m^3. These changes did not heal within 14 days post-exposure. (Nitschke *et al.*: 1990) In subacute study, rats were exposed at 58.2, 223 and 931 mg/m^3, 6 hours/day, 5 days/week for 2 weeks. As a result, eye irritation and corneal clouding were observed at 931 mg/m^3. (Landry *et al*.: 1991)

Respiratory irritation
Labored breathing was induced in rat by acute inhalation exposure for 4 hours at 1,563 mg/m^3 and 2,394 mg/m^3 (Nitschke *et al*.: 1990). In another acute inhalation study, changes in lungs, thorax, respiration, *etc*. were observed in rats, rabbits, guinea pigs and dogs. In this study, exposure was conducted at 1,400 mg/m^3 for 6 hours (Haag: 1953). These changes may be resulted from respiratory irritation of this chemical.

In inhalation repeated dose toxicity studies, there were also many changes in respiratory tract, such as noisy and difficult respiration (mouth breathing), and hyperplasia, necrosis and inflammation in nasal tissues. In one subacute toxicity study, rabbits were exposed at 2.9, 12, 29 or 60 mg/m^3 6 hours/day, daily for 13 consecutive days. Treatment-related degeneration of the nasal olfactory epithelium was observed at 12 mg/m^3. At 29 and 60 mg/m^3, there were olfactory epithelial degeneration, and the hyperplasia, erosions, ulcers and inflammation of the nasal epithelium. After

4-week recovery period, there was complete reversibility of these changes except for olfactory epithelial degeneration observed at 29 and 60 mg/m^3, which showed only partial reversibility. At 12 mg/m^3, nasal tissue was indistinguishable from controls at one month post-exposure. (Cieszlak *et al.*, 1996)

In European labelling and classification, this chemical is listed as R36/38, irritating to eyes and skin.

Based on these data, it is considered that glycidyl methacrylate irritates to the skin, eyes and respiratory tract. The irritation of this chemical is likely strong.

d) Sensitisation

Guinea pigs received three topical applications with 0.4 ml of 10 or 25 % glycidyl methacrylate in dipropylene glycol monomethyl ether during the three-week induction phase. The single challenge application induced slight erythema in these animals (7/10). (The Dow Chemical Company: 1992)

Ou-Yang *et al*. (1988) reported on delayed and rapid allergy reaction tests in guinea pigs. In delayed allergy reaction test, localized smear applications or intradermal injection with 0.1 ml of 1 % glycidyl methacrylate in acetone induced hyperemia, edema, scleroma and necrosis. Those changes belong to the strong allergenic category. As for rapid allergic reaction test, two tests by active and passive stimulation were conducted. In the active stimulation, 0.5 % glycidyl methacrylate with homologous serum albumin was injected intradermally and the challenge was conducted intravenously. Breathing difficulties, wheezing, increased mouth and nose secretions, spasms and death were observed, belonging to the strong allergic category. In the passive stimulation, firstly, the diluted serum given from the sensitized guinea pig was injected subcutaneously to other animals and one hour later, 0.5 ml of 0.1 % glycidyl methacrylate with homologous serum albumin was injected intravenously to the same animals. Blue circles or spots observed belonged to the strong allergic category. Both the delayed and rapid allergy test results showed that glycidyl methacrylate was a strong sensitizer. The author reported that this might be the reason that the epoxy radical of glycidyl methacrylate easily combined with protein.

There were two data on human patch test.

Three cases of allergic contact hypersensitivity to glycidyl methacrylate used in adhesive sealant manufacturing were reported. Both closed and open patch testing with 1 % glycidyl methacrylate solution in petrolatum was positive in all 3 cases. Symptoms included erythema, edema, and vesiculation and a strong 2+ reaction as scored according to the International Contact Dermatitis Research Group classification. (Dempsey: 1982)

Patch test was conducted for a 31-year-old non-atopic woman, who had worked as a chemist and mixed emulsions used to impregnate paper and textile materials to make them oil and water resistant. In this work, she had been in contact with acrylate derivatives (glycidyl methacrylate, ethoxyethyl acrylate, etc.). In relation to this work, she had a history of recurrent acute vesiculopapular hand dermatitis with severe itching and burning mainly on the fingertips, palmar and dorsal aspects of the fingers, and both palms. As a result of patch test, she reacted only to nickel, glycidyl methacrylate (0.01 and 0.05 % acet.) and ethoxyethyl acrylate among the European standard series and (meth) acrylate series. This reaction to nickel was relevant to her jewely intolerance. (Matura *et al.*: 1995)

In European labelling and classification, this chemical is classified as R43, may cause sensitisation by skin contact

Based on these data, glycidyl methacrylate is considered to be a skin sensitizer.

e) Repeated toxicity

[SIDS data] Oral toxicity study of glycidyl methacrylate was performed in SD (Crj: CD) rats by an OECD combined repeated dose and reproductive/developmental toxicity screening test (OECD TG 422). Administration was conducted at doses of 10, 30 and 100 mg/kg/day by gavage for 45 days in males and from 14 days before mating to day 3 of lactation in females. (MHW, Japan: 1997)

Salivation was observed at 30 mg/kg (5/12) and 100 mg/kg (12/12) in males. In males, there was an increase in absolute and relative kidney and adrenal weights at 100 mg/kg. In blood chemistry of males, increase in total protein and albumin was observed. These changes were not considered as adverse effects. In histological examination, squamous hyperplasia in forestomach was observed at 30 and 100 mg/kg in males and cellular infiltration in forestomach at 100 mg/kg in females. These histological changes were considered to be due to the irritation of glycidyl methacrylate. NOAEL for oral repeat toxicity was considered to be 10 mg/kg/day for males and 30 mg/kg/day for females.

Two other orally repeated toxicity studies were reported.

One-year study is very limited (Hadidian *et al.*, 1968). Rats (3 males and 3 female) were dosed 5 days/week by gavage at 0.1 mg/kg. Groups of 15 male and 15 female rats were also dosed at 0.3 mg/kg. The authors concluded that no tissue effects related to the treatment were found. These dosages are considered to be too low.

In another study, five male and female rabbits were given orally at 50 mg/kg daily for 15 days (Ou-Yang *et al.*: 1988). Some animals showed slow reactions, head shaking and prostration, and two animals died. There were several hematological and pathological changes including bleeding, necrosis and so on in heart, liver, kidneys and stomach.

This study can not be adapted to hazard assessment because of unreliability such as no Test Guideline, no GLP, only single dose and unlikely severe systemic toxicity compared to other reliable oral and inhalation toxicity studies using rats and rabbits, and insufficient information on protocol and data analysis including purity of chemical and pathological data.

Subacute inhalation toxicity studies were performed in rats and rabbits.

Rats were exposed to glycidyl methacrylate at concentrations of 58.2, 233 or 931 mg/m^3 for 2 weeks (6 hours/day, 5 days/week) (Landry *et al.*: 1991). These three concentrations were calculated as 7.09, 28.4 or 113 mg/kg/day. Decrease in body weight was observed at 233 and 931 mg/m^3. At 931 mg/m^3, general debilitation with noisy and difficult respiration (mouth breathing), eye irritation, corneal clouding and distended abdomen (day 4) were observed. The animals at 931 mg/m^3 were terminated early on day 4 because of the severity of the respiratory and ocular effects. Microscopically, there was severe multifocal necrosis and inflammation of the olfactory epithelium in the nasal cavity. At 233 mg/m^3, there were slight to moderate multifocal necrosis, and inflammation of the respiratory and olfactory nasal epithelium. At 58.2 mg/m^3, microscopically there was very slight multifocal necrosis of individual respiratory epithelial cells in 3 of 5 males and in 2 of 5 females. These changes in respiratory tract were considered due to irritation of glycidyl methacrylate. There were no histopathological changes in any other tissues. Therefore, 58.2 mg/m^3 (7.09 mg/kg/day) was considered to be LOAEL because of tissue damages in respiratory tract.

Rabbits were exposed at 2.91, 11.6, 29.1, 58.2 mg/m^3 6 hours/day, daily for 13 consecutive days. (Cieszlak *et al.*, 1996) Treatment-related degeneration of the nasal olfactory epithelium was observed at 11.6 mg/m^3. At 29.1 and 58.2 mg/m^3, there were olfactory epithelial degeneration, and the hyperplasia, erosions, ulcers and inflammation of the nasal epithelium. After 4-week recovery period, there was complete reversibility of these changes except for olfactory epithelial degeneration observed at 29.1 and 58.2 mg/m^3, which showed only partial reversibility. At 11.6 mg/m^3, nasal tissue was indistinguishable from controls at one month post-exposure. 2.91 mg/m^3 (0.26 mg/kg/day) was considered to be NOAEL. Unfortunately purity of chemical and GLP were not mentioned.

Subchronic inhalation toxicity study was conducted in rats at concentrations of 2.9, 12 or 87 mg/m^3 for 13 weeks (6 hours/day, 5 days/week) (Landry *et al.*: 1996). These three doses were calculated as approximately 0.35, 1.46 or 10.6 mg/kg/day, respectively. There were no treatment related in-life observations, and no significant treatment-related effects on body weight, urinalysis, clinical chemistry or hematology parameters, as well as gross pathologic changes or organ weights at any exposure level. Treatment-related effects were limited to hyperplasia of respiratory epithelium of the nasal tissues in all animals at 87 mg/m^3. In all affected animals, the hyperplastic respiratory epithelium was approximately two to three times as thick as in control animals, and was located in the anterior portions of the nasal passages, involving the tips of the turbinates and the lateral walls of the nasal passages. These changes were considered to be resulted from reparatory irritation. Therefore, NOAEL was considered 12 mg/m^3 (1.46 mg/kg/day) for both sexes.

There was 26 weeks inhalation toxicity study at concentrations of 15.3 and 206 mg/m^3 in rats and rabbits (Ouyang Guoshun *et al.*: 1990). A wide range of toxic effects, such as lesion in central nervous system, cardiovascular system, liver and kidney, were observed in both species at the low and high doses. However, because of the higher vapor pressure and lower purity, the author suggested that the test material used in this study contained components other than glycidyl methacrylate, which may have contributed to the toxicity observed. Therefore these systemic toxicities observed in the studies are questionable.

Based on all above information, the major toxicity was tissue damages in the first exposure sites such as forestomach by oral administration and respiratory tract by inhalation, due to the irritation of chemical and NOAELs were 10 mg/kg for rat oral, 12 mg/m^3 for rat inhalation and 2.91 mg/m^3 for rabbit inhalation.

f) Reproductive/developmental toxicity

Reproductive toxicity

[SIDS data] Oral toxicity study was performed in SD (Crj: CD) rats by an OECD combined repeated dose and reproductive/developmental toxicity screening test (OECD TG 422). Administration was conducted by gavage at doses of 10, 30 and 100 mg/kg/day from 14 days before mating to 14 days after mating in males and from 14 days before mating to day 3 of lactation in females. (MHW, Japan: 1997)

The fertility index (number of delivered animals/ number of mated animals) decreased significantly at 100 mg/kg. There were no effects on the estrous cycle, copulation index, or gestation length. No significant changes in the numbers of corpora lutea, implants, pups born and live pups as well as the implantation and delivery indices were observed. There were no significant differences in the gestation index, live birth index or viability index on day 4. Histopathological analysis of the gonads showed no significant effect considered to cause infertility in all treatment groups. No change in the number of gonocyte per Sertoli cell was observed in epithelium of seminiferous

tubule (stage VIII) of all survival males at 100 mg/kg. No abnormalities attributable to the administration of this chemical were noted in the body weights of live pups or on necropsy of pups in any treated group. Therefore, NOAELs for reproductive performance of parents and pup development were considered to be 30 mg/kg/day and 100 mg/kg/day, respectively.

Male mice injected i.p. with 5 consecutive daily doses of 0, 25, 50 or 100 mg/kg/day showed an increase in the percentage of abnormal sperm and decrease in the number of sperm (Xie *et al.*: 1990). These results were confirmed in a subsequent study where mice were dosed i.p. with 0, 5, 25 or 100 mg/kg for five consecutive days (Vedula *et al.,* 1994). At 100 mg/kg, mice had decreased caudal epididymal weights, slightly lower testicular weights, decreased sperm counts and increased abnormal sperm. Mice given 25 mg/kg/day showed decreased sperm counts and increased abnormal sperm. These results might support the decreased fertility index of rat study at 100 mg/kg/day.

Developmental toxicity

Glycidyl methacrylate was administered by gavage to rats during day 5 to day 15 of gestation at doses of 5.38, 10.76, 21.52 and 108.0 mg/kg/day. The animals were sacrificed on day 19 of pregnancy. (OuYang *et al.*: 1988)

As maternal toxicity, there was significant decrease in body weight gain at 108.0 mg/kg. There was a statistically significant increase in the fetal resorption rate at the 108.0 mg/kg. The percentage of pups stillborn was somewhat higher than control at all dose levels. However, because this change was not dose-dependent and statistically significant change was only at 10.76 mg/kg, this was not considered to be chemical-related change. Neither birth defects nor fetal abnormalities were noted in rats treated with this chemical. There was also no significant difference in fetal body weight from the control. Therefore, NOAELs were considered to be 21.52 mg/kg/day for maternal toxicity and 108.0 mg/kg/day for teratogenicity.

There were two inhalation tests on developmental toxicity.

Rabbits were exposed to glycidyl methacrylate at concentrations of 29.1, 58.2 and 291 mg/m^3, 6 hours/day, daily during day 7 to day 19 of gestation (Vedula *et al.*: 1995). Daily intake is calculated as 2.62, 5.24 and 26.2 mg/kg/day. Respiratory distress and decrease in feed consumption was observed at 291 mg/m^3. Less severe signs of ocular and respiratory irritation consisting of reddened eyes, wet muzzle and sneezing after exposure were observed at 58.2 mg/m^3. Treatment-related histopathologic alterations of the nasal tissues (hyperplasia, necrosis, etc.) were present in all animals treated with this chemical. Because of respiratory distress, animals at 291 mg/m^3 were removed early from study after the third exposure. Therefore, evaluation of reproductive and embryonal/fetal parameter was precluded. There was no adverse effect on any reproductive and embryo/fetal parameter at 29.1 and 58.2 mg/m^3. LOAEL for maternal toxicity was 29.1 mg/m^3 (2.62 mg/kg/day) and NOAEL for teratogenicity was 58.2 mg/m^3 (5.24 mg/kg/day).

Rabbits were also exposed to glycidyl methacrylate at concentrations of 2.91, 11.6 and 58.2 mg/m^3, 7 hours/day, daily during day 7 to day 19 of gestation (Vedula *et al.*: 1995). Daily intake is calculated as 0.31, 1.22, 6.11 mg/kg/day. The principal indication of maternal toxicity was inflammation of the nasal olfactory and respiratory epithelium at the 11.6 and 58.2 mg/m^3. There was no adverse effect on any reproductive and embryo/fetal parameter at any doses. Therefore, NOAEL for maternal toxicity was 2.91 mg/m^3 (0.31 mg/kg/day) and NOAEL for teratogenicity was 58.2 mg/m^3 (6.11 mg/kg/day).

As three reliable developmental studies by two different routes, oral and inhalation, indicated no teratogenicity even at the highest doses which showed the maternal toxicity, glycidyl methacrylate is not considered to have developmental toxicity.

g) Genetic toxicity

Bacterial test

[SIDS data] Glycidyl methacrylate was mutagenic to *Salmonella typhimurium* TA97, TA100, TA1535 with and without metabolic activation but not to TA98 (Dorothy *et al*.: 1986, The Goodyear Tire & Rubber Company: 1981, OuYang *et al.*: 1988).

Glycidyl methacrylate was mutagenic to *Klebsiella pneumoniae* without metabolic activation (Voogd *et al*.: 1981). In *Escherichia coli*, this chemical induced SOS repair with and without metabolic activation (von der Hude *et al.*: 1990). This chemical was shown to react with the DNA of the gene governing tetracycline resistance in the plasmid pBR322. The modified DNA was transferred to a receptor cell (*Escherichia coli* HB 101) to screen for mutations based on alterations in phenotypic changes. Results showed the mutations caused by reactions of glycidyl methacrylate with the plasmid were stable and heritable (Xie *et al*.: 1990a).

Non-bacterial test *in vitro*

[SIDS data] In chromosomal aberration test of glycidyl methacrylate, using cultured Chinese hamster lung (CHL/IU) cells, both structural abnormality and polyploidy were induced with and without metabolic activation. However, a trend test showed no dose-dependency for the induction of polyploidy with the 24 hours continuous treatment and the short-term treatment with the metabolic activation system. (MHW, Japan: 1997)

In cell cultures, glycidyl methacrylate induced hypoxanthine-guanine-phosphoribosyl transferase forward gene mutation with metabolic activation in Chinese hamster ovary cell (Linscombe and Engle: 1995), very slight increase of unscheduled DNA synthesis in lymphocytes of human and/or rat (Xie *et al.*: 1990b), non-reverse type inhibition of the DNA replication in lymphocytes of human and/or rat (Xie *et al*.: 1989), sister-chromatid exchange without metabolic activation in Chinese hamster V79 cells (von der Hude *et al*.: 1991), transformation of Syrian hamster embryonic cells (SHE) (Xie *et al.*, 1992) and transformation in diploid golden Syrian hamster embryo (SHE) cells (Yang *et al*.; 1996). This chemical was strongly and covalently bound with calf thymus DNA *in vitro* (Xie *et al*.: 1990b).

in vivo test

[SIDS data] In micronucleus assay, mice was administered by gavage with glycidyl methacrylate at a single dose of 188, 375 and 750 mg/kg in males and 250, 500 and 1000 mg/kg in females. The frequency of micronucleated polychromatic erythrocytes in both sexes was significantly increased only at the highest doses 48 hour after administration. (MHW, Japan: 1997)

There were many data on the in vivo genotoxic potential of glycidyl methacrylate. Three of them were mouse bone marrow micronucleus tests by intraperitoneal administration. In one study, this chemical produced an increase in the number of cells with micronuclei at doses of 25, 50 and 100 mg/kg, although the increase was very slight and showed an inversed dose-response (Ou-Yang *et al*., 1988). On the other hands, this chemical did not cause an increase in the number of cells containing micronuclei in two other studies with doses of 75, 150, and 300 mg/kg (Lick *et al*., 1995) or doses of 42.2, 133, 422, and 464 mg/kg (INBIFO: 1979).

This chemical increased unscheduled DNA synthesis in germ cell of male mice but this effect was very slight and not dose-related (Xie *et al.*: 1990b). In inhalation gene mutation assay using transgenic Big Blue® Fischer 344 rats with the *lacI* locus, there were no statistically significant increases in the frequencies of *lacI* mutants in either the olfactory or respiratory epithelium at 145.5 mg/cm^3 (17.7 mg/kg/day) (No reference in Draft Workplace Environmental Exposure Level Guide (1999))

Most genotoxicity studies *in vitro* showed positive results. In micronucleus test *in vivo*, oral administration increased the frequency of micronucleated polychromatic erythrocytes at the highest dose, although mostly negative results were shown in other *in vivo* genotoxicity studies including micronucleus tests by intraperitoneal administration. Therefore, genotoxic potential of this chemical can not be ruled out.

g) Carcinogenicity

There was no available data.

h) Any other human health related information that is available

1: Specific toxicities

Neurotoxicity

Fischer 344 rats were exposed by inhalation to glycidyl methacrylate at approximately 0.5, 2 or 15 ppm (2.9, 12, 87 mg/m^3), 6 hours/day, 5 days/ week for 13weeks (calculated daily dose: 0.35, 1.46, 10.59 mg/kg/day). At week 4, there was a low incidence of rat with nasal discharge and enlarged nostrils at 2 and 15 ppm. There were no other treatment-related effects. A functional observation battery (FOB) and motor activity (MA) were conducted preexposure and at the end of each month of exposure. In addition, the postexposure neurotoxicity evaluation focused on evoked potential testing of the visual (FEP), auditory (ABR), somatosensory system (SEP), and caudal nerves (CNAP), and a comprehensive neuropathological examination. There was no evidence of neurotoxic effects at any exposure level. (Mattsson *et al.*: 1996)

2: Experience with human exposure

Two human patch test data and the evaluation are given at section d).

4.3 Initial Assessment for Human Health

Glycidyl methacrylate is produced in closed systems and used for resin synthesis. The occupational exposures are expected through inhalation and dermal route. Consumer exposure might be low because of no consumer use. Environmental exposure also might be low because of ready biodegradation and low bioaccumulation. Acute toxicity of glycidyl methacrylate is low via the oral administration or inhalation route. This chemical is considered both highly irritating to the skin, eyes and respiratory tracts and a skin sensitizer. In an oral repeat dose study, squamous hyperplasia in forestomach was induced at 30 and 100 mg/kg/day. In repeated inhalation study, necrosis and inflammation in nasal tissues were observed. The reproductive toxicity was only a decrease in the fertility index (number of delivered animals/ number of mated animals) at 100 mg/kg. In developmental toxicity study, teratogenic effects were not induced either by oral administration or inhalation route. Most *in vitro* genotoxicity studies showed positive results. In an *in vivo* micronucleus test, oral administration increased the frequency of micronucleated polychromatic erythrocytes at the highest dose, although mostly negative results were shown in other *in vivo*

genotoxicity studies including micronucleus tests by intraperitoneal administration. Therefore, genotoxic potential of this chemical can not be ruled out. Although there was no available data on carcinogenicity of this chemical, carcinogenic potential in nasal cavity is highly expected because whole toxicity profile of glycidyl methacrylate is very similar to that of formaldehyde (WHO/IARC: 1995).

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

Exposure

About 3,000 tones/year of glycidyl methacrylate is produced and used as intermediate for resins in the closed system in Japan, and ca. 3.3 tones (ca. 0.1%)/ year is released into rivers. Release to air phase is negligible. A generic fugacity model (Mackey level III) shows this chemical will be distributed mainly to water phase (99.1%) when it is discharged into water.

Hazards to the Environment

Glycidyl methacrylate is readily biodegradable (OECD 301C: 100 % after 28-d) and readily hydrolyzed ($T_{1/2}$ = 3.66 days at pH 7). This chemical has a low bioaccumulative potential judging from the low log Pow value, 0.96 at 25 °C. The lowest acute and chronic aquatic toxicity data reported were 14d LC_{50} (1.9 mg/l) of fish (Medaka; *Oryzias latipes*) and 21d NOEC (1.02 mg/l) of *Daphnia magna*, respectively. An assessment factor of 100 was chosen and applied to the chronic toxicity data to determine PNEC, which is 0.01 mg/l.

Human Health Hazards

Acute lethal toxicity of glycidyl methacrylate is low via the oral administration route. No mortality was observed in rats following inhalation exposure up to 2,394 mg/m^3, the highest practically attainable vapor concentration. This chemical is considered both highly irritating (including necrosis, degeneration and hyperplasia) to the skin, eyes and respiratory tracts and a skin sensitizer. In an oral (via gavage) OECD combined repeat dose and reproductive/ developmental screening toxicity test (TG 422) in rats at doses of 10, 30, 100 mg/kg/day, squamous hyperplasia in forestomach was induced at 30 and 100 mg/kg/day. Thus, the NOAEL was 10 mg/kg/day. In many repeated inhalation studies, the changes were observed only in respiratory tract (necrosis, inflammation etc. in nasal tissues), and were likely due to irritation. The lowest NOAEL was 0.5 ppm (equivalent to 0.26 mg/kg/day) in a rabbit study. In the OECD combined study (TG 422), the NOAEL for reproductive toxicity was considered to be 30 mg/kg/day, based on a decrease in the fertility index (number of delivered animals/ number of mated animals) at 100 mg/kg. In developmental toxicity studies, teratogenic effects were not induced either by oral administration at 108 mg/kg for rats or inhalation at 291 mg/m^3 for rabbits. Most *in vitro* genotoxicity studies showed positive results. In an *in vivo* micronucleus test, oral administration of glycidyl methacrylate increased the frequency of micronucleated polychromatic erythrocytes only at the highest dose (750 mg/kg in males and 1000 mg/kg in females), although mostly negative results were shown in other *in vivo* genotoxicity studies including micronucleus tests by intraperitoneal administration. Therefore, the genotoxic potential of this chemical can not be ruled out. There was no available data on carcinogenicity of this chemical.

5.2 Recommendations

Human health

There is a need for limiting the risk; risk reduction should be taken into account because of the high irritation, sensitization, and the genotoxic potential.

Occupational exposure information should be collected by individual member countries.

6. REFERENCES

WHO/IARC: Formaldehyde. IARC Monograph 62: 217-362 (1995)

Appendix 1

Method for Prediction of Environmental Concentration of Pollutant in Surface Water

1. Predicted environmental concentration in the local environment (PEC_{local}) with effluent release into river

When decomposition, precipitation and vaporization of pollutant can be ignored, it is used that simplified equation by complete mixing model shown with equation (1) to calculate predicted environmental concentration in the local environment (PEC_{local}) as for release effluent into river.

$$PEC_{local}\ (mg/L) = \frac{Co\ Q + Cs\ Qs}{Q + Qs} \quad (1)$$

Where

Co: Concentration of pollutant in upper stream of release point (mg/L)
Cs: Concentration of pollutant in effluent (mg/L)
Q: Flow rate of river (m^3/day)
Qs: Flow rate of effluent released into river (m^3/ day)

At the equation (1), when Co can be considered as 0, dilution factor of pollutant in the river (R) can be shown with following equation.

$$R = Cs/C = (Q + Qs) / Qs \quad (2)$$

As the worst case, it is used to employ a flow rate at dry season as flow rate of river (Q). When flow rate at dry season is indistinct, it is estimated using the following equation in Japan.

$$\text{Flow rate at dry season} = \text{mean flow late} / 2.5 \quad (3)$$

2. Predicted environmental concentration in the local environment (PEC_{local}) with effluent release into sea

For prediction of concentration of pollutant in the sea water with effluent, it is employed generally Joseph-Sendner's equation (4). This equation is one of analytic solution led under the following conditions from diffusion equation.

1 It is adopted large area of sea or lake.
2 The flow rate of effluent and concentration of pollutant in the effluent are constant, and distribution of concentration is able to regard as equilibrium state.
3 Effluent is distributed uniformly to vertical direction, and it spreads in a semicircle or segment to horizontal direction.
4 Diffusion coefficient of pollutant at the sea is in proportion to distance from release point of effluent.
5 There is not any effect of tidal current.
6 Decomposition of pollutant can be ignored.

$$C(x) = (C_s - C(r))\left(1 - \exp\left(-\frac{Q_s}{\theta\, d\, p}\left(\frac{1}{x} - \frac{1}{r}\right)\right)\right) + C(r) \quad (4)$$

Where

C (x): Concentration of pollutant at distance x (m) from release point
Cs: Concentration of pollutant in effluent
C (r): Concentration of pollutant at distance r (m) from release point
Qs: Flow rate of effluent (m^3/day)
θ: Opening angle of seacoast (rad.)
d: Thickness of diffusion layer (m)
P: Diffusion velocity (m/day) (1.0 ± 0.5 cm/sec)

When C(x) is 0 at $r = \infty$ and density stratification is ignored for simplification, Joseph-Sendner's equation (4) is simplified to equation (5)

$$C(x) = C_s\left(1 - \exp\left(-\frac{Q_s}{\theta\, d\, p\, x}\right)\right) \quad (5)$$

Because of $Q_s/\theta\, d\, p\, x \ll 1$ except vicinity of release point, dilution factor in distance x from release point R(x) can be shown with equation (6).

$$R(x) = C_s/C(x) = \theta\, d\, p\, x/Q_s \quad (6)$$

When it is employed following parameters in equation (6) as default, dilution factor R can be shown with equation (7).

P = 1 cm/sec (860 m/day)
θ = 3.14
d = 10 m
x = 1000 m

$$R = 2.7 \times 10^7/Q_s \quad (7)$$

Qs: volume of effluent (m^3/day)

Appendix 2

Sample of Risk Assessment for Environment and Human Health in Japan

1. Initial Risk Assessment for the Environment

PNEC of this chemical was calculated as 0.01 mg/l. PECs from the Japanese local exposure scenario, case A and case B, were calculated to be 6.2×10^{-3} and 8.9×10^{-3} mg/l, respectively.

Thus

PEC_{local} (case A/ PNEC = $(6.2 \times 10^{-3})/0.01 = 0.62 < 1$

PEC_{local} (case B/ PNEC = $(8.9 \times 10^{-3})/0.01 = 0.89 < 1$

PEC is close to PNEC.

2. Initial Risk Assessment for the Human Health

Occupational exposure

Glycidyl methacrylate is produced in a closed system at industries and workers wear protective gloves and respiratory protective equipment (mask) during the operation. The occupational exposures are expected through inhalation and skin in limited workers. The atmospheric concentration was measured at two production sites in Japan. Based on these values and exposure periods, the daily intake including dermal exposure is calculated as 0.24 mg/kg/day as the worst case. The lowest NOAEL of 0.26 mg/kg/day (rabbit inhalation study; Vedula *et al.*: 1995) was used to derive the margin of safety because the major exposure route at occupational place is expected to be inhalation.

$$0.26 \text{ mg/kg/day} / 0.24 \text{ mg/kg/day} = 1.08 < 100$$

Consumer exposure

Consumer exposure is expected to be low because of its use pattern.

Indirect exposure via environment (Japanese scenario)

As for indirect exposure via environment, PEC_{local} of 8.9×10^{-3} mg/l from local exposure scenario was used for the estimation. The daily intakes through drinking water and fish are calculated as 2.97×10^{-4} mg/kg/day and 1.34×10^{-5} mg/kg/day, respectively. The NOAEL of 10 mg/kg/day (rat oral study; MHW, Japan: 1997) was used to derive the margin of safety.

For drinking water

$$10 \text{ mg/kg/day} / 2.97 \times 10^{-4} \text{ mg/kg/day} = 3.36 \times 10^{4} > 100$$

For fish

$$10 \text{ mg/kg/day} / 1.34 \times 10^{-5} \text{ mg/kg/day} = 7.46 \times 10^{5} > 100$$

REVISED OECD HPV FORM 1

SIDS DOSSIER
ON THE HPV PHASE 5 CHEMICAL

Glycidyl methacrylate

CAS No. 106-91-2

Sponsor Country: Japan and United States

DATE: December 1, 1999

CONTENTS

2.10 EXPLOSIVE PROPERTIES
2.11 OXIDISING PROPERTIES
2.12 † OXIDATION: REDUCTION POTENTIAL
2.13 ADDITIONAL REMARKS
A. PARTITION CO-EFFICIENT BETWEEN SOIL/SEDIMENT AND WATER (Kd)
B. OTHER REMARKS

3. ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY
3.1.1 * PHOTODEGRADATION
3.1.2 * STABILITY IN WATER
3.1.3 STABILITY IN SOIL
3.2 * MONITORING DATA (ENVIRONMENT)
3.3 * TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS
3.3.1 TRANSPORT
3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)
3.4 MODE OF DEGRADATION IN ACTUAL USE
3.5 * BIODEGRADATION
3.6 BOD-5, COD OR RATIO BOD-5/COD
3.7 BIOACCUMULATION
3.8 ADDITIONAL REMARKS
A. SEWAGE TREATMENT
B. OTHER

4. ECOTOXICITY

4.1 * ACUTE/PROLONGED TOXICITY TO FISH
4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES
* A. DAPHNIA
B. OTHER AQUATIC ORGANISMS
4.3 * TOXICITY TO AQUATIC PLANTS e.g., ALGAE
4.4 TOXICITY TO BACTERIA
4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS
4.5.1 CHRONIC TOXICITY TO FISH
4.5.2 (*) CHRONIC TOXICITY TO AQUATIC INVERTEBRATES (e.g., DAPHNIA REPRODUCTION)
4.6 TOXICITY TO TERRESTRIAL ORGANISMS
4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS
4.6.2 TOXICITY TO TERRESTRIAL PLANTS
4.6.3 TOXICITY TO OTHER NON-MAMMALIAN TERRESTRIAL SPECIES (INCLUDING BIRDS)
4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)
4.8 BIOTRANSFORMATION AND KINETICS
4.9 ADDITIONAL REMARKS

5. TOXICITY

5.1 * ACUTE TOXICITY

Note: *; Data elements in the SIDS
†; Data elements specially required for inorganic chemicals

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

***A. CAS number** 106-91-2

B. Name *(IUPAC name)*

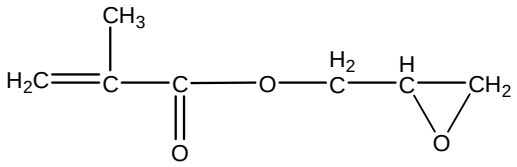
***C. Name** *(OECD name)* Glycidyl methacrylate

†D. CAS Descriptor

E. EINECS-Number 203-441-9

F. Molecular Formula $C_7H_{10}O_3$

***G. Structural Formula**



H. Substance Group

I. Substance Remark

J. Molecular Weight 142.15

1.02 OECD INFORMATION

A. Sponsor Country: Japan and United States

B. Lead Organisation:

Name of Lead Organisation: Ministry of Health and Welfare (MHW), Japan
Ministry of International Trade and Industry (MITI), Japan
Environmental Agency (EA), Japan
Ministry of Labour (MOL), Japan

Contact person: Mr. Kazuhide Ishikawa
Economic International Bureau
Second International Organization Division
Ministry of Foreign Affairs
Japan

Address:

Street: 2-2-1 Kasumigaseki, Chiyoda-ku, Tokyo 100 Japan
Tel: 81-3-3581-0018
Fax: 81-3-3503-3136

Name of Lead Organisation: United States Environmental Protection Agency

Contact person: Mr. Oscar Hernandez
Risk Assessment Division
Office of Pollution Prevention and Toxics
US-EPA (7403)

Address:
401 M Street S.W., Washington D.C. 20460 United States
Tel: 1-202-260-1832
Fax: 1-202-260-1283

C. Name of responder

Name: Same as above contact persons

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element **[ ]**; inorganic **[ ]**; natural substance **[ ]**; organic **[X]**; organometallic **[ ]**; petroleum product [ ]

B. Physical State *(at 20°C and 1.013 hPa)*

gaseous **[ ]**; liquid **[X]**; solid **[ ]**

C. Purity

97.9 %

1.2 SYNONYMS

2,3-Epoxypropyl methacrylate, CP-105; Glycidyl alpha-methylacrylate; 1-Propanol, 2,3-epoxy-, methacrylate

1.3 IMPURITIES

None

1.4 ADDITIVES

None

*1.5 QUANTITY

Remarks: 3,128 tonnes/year
Reference: MITI, Japan

1.6 LABELLING AND CLASSIFICATION

R20/21/22 Harmful by inhalation, in contact with skin and if swallowed.
R36/38 Irritating to eyes and skin.
R43 May cause sensitisation by skin contact.

*1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Intermediate
industrial	Intermediate in closed system
use	Intermediate for resins

Remarks: None
Reference: MITI, Japan

Chemical intermediate for polymer in hydrogel lenses and BIS-GMA dental resin
Reference Kirk-Othmer, Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26.New York, NY: John Wiley and Sons, 1978-1984., p.6-7(79)

1.8 OCCUPATIONAL EXPOSURE LIMIT

None

* 1.9 SOURCES OF EXPOSURE

In Japan, glycidyl methacrylate is produced in 3 companies.

Source: Media of release: River
Quantities per media: 115 tonnes/year
Remarks:
Reference: MITI, Japan

2. PHYSICAL-CHEMICAL DATA

*2.1 MELTING POINT

Value: < - 10 °C
Decomposition: Yes **[ ]** No **[X]** Ambiguous **[ ]**
Sublimation: Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Remarks:
Reference: MITI, Japan

*2.2 BOILING POINT

Value: 196.8 – 197.9 °C
Pressure: at 1.018 hPa
Decomposition: Yes **[ ]** No **[X]** Ambiguous **[ ]**
Method:

GLP: Yes **[ ]** No **[X]** ? **[ ]**
Remarks:
Reference: MITI, Japan

***2.4 VAPOUR PRESSURE**

Value: 4.2×10^2 Pa
Temperature: 25 °C
Method: calculated **[ ]**; measured **[X]**
OECD TG 104
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Remarks: purity: 98.2 %
Reference: MITI, Japan

***2.5 PARTITION COEFFICIENT $log_{10}P_{ow}$**

Log Pow: 0.96
Temperature: 25 °C
Method: calculated **[ ]**; measured **[X]**
OECD TG 107
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Remarks: purity: 98.2 %
Reference: MITI, Japan

***2.6 WATER SOLUBILITY**

A. Solubility

Value: not measurable
Ca. 50 g/L
Temperature:
Description: Miscible **[ ]**; Of very high solubility **[X]**;
Soluble **[ ]**; Slightly soluble **[ ]**; Of low solubility **[ ]**;
Of very low solubility **[ ]**; Not soluble **[ ]**
Method: OECD TG 105
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Remarks: hydrolysis
Reference: MITI, Japan

B. pH Value, pKa Value

No ionizable Functional Group

2.7 Flash point

Value: 84°C, open cup(HSDB, CHRIS), 83°C(NTP), 76 °C(Chemfinder, aldrich)
Reference: Kirk-Othmer, Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26.New York, NY: John Wiley and Sons, 1978-1984., p.15(81)

3. ENVIRONMENTAL FATE AND PATHWAYS

3.1 STABILITY

*3.1.2 STABILITY IN WATER

Type:	Abiotic (hydrolysis) **[X]**; biotic (sediment)**[ ]**
Half life:	2.83 days in pH 4 at 25 °C 3.66 days in pH 7 at 25 °C 2.22 days in pH 9 at 25 °C
Method:	OECD TG 111
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	purity: 98.2 %
Remarks:	
Reference:	MITI, Japan

*3.2 MONITORING DATA (ENVIRONMENTAL)

(a)
Type of Measurement: Background **[ ]**; At contaminated site **[ ]**; Other **[X]**
Media: Surface water (lake)
Results: ND (Detection limits: 0.0003 mg/l) in 1 area in Japan as of 1986
Remarks: ND: Not detected
Reference: Chemicals in the environment, EA, Japan (1987)

(b)
Type of Measurement: Background **[ ]**; At contaminated site **[ ]**; Other **[X]**
Media: Surface water (estuary)
Results: ND (Detection limits: 0.0003 mg/l) in 1 area in Japan as of 1986
Remarks: ND: Not detected
Reference: Chemicals in the environment, EA, Japan (1987)

(c)
Type of Measurement: Background **[ ]**; At contaminated site **[ ]**; Other **[X]**
Media: Surface water (sea)
Results: ND (Detection limits: 0.0003 mg/l) in 6 areas in Japan as of 1986
Remarks: ND: Not detected
Reference: Chemicals in the environment, EA, Japan (1987)

(d)
Type of Measurement: Background **[ ]**; At contaminated site **[ ]**; Other **[X]**
Media: Sediment (lake)
Results: ND (Detection limits: 0.04 mg/kg-dry) in 1 area in Japan as of 1986
Remarks: ND: Not detected
Reference: Chemicals in the environment, EA, Japan (1987)

(e)
Type of Measurement: Background **[ ]**; At contaminated site **[ ]**; Other **[X]**
Media: Sediment (estuary)
Results: ND (Detection limits: 0.04 mg/kg-dry) in 1 area in Japan as of 1986
Remarks: ND: Not detected

Reference: Chemicals in the environment, EA, Japan (1987)

(f)
Type of Measurement: Background **[ ]**; At contaminated site **[ ]**; Other **[X]**
Media: Sediment (sea)
Results: ND (Detection limit: 0.04 mg/kg-dry) in 6 areas in Japan as of 1986
Remarks: ND: Not detected
Reference: Chemicals in the environment, EA, Japan (1987)

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION

*3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

Media: Air-biota **[ ]**; Air-biota-sediment-soil-water **[X]**; Soil-biota **[ ]**; Water-air **[ ]**; Water-biota **[ ]**; Water-soil **[ ]**; Other **[ ]**
Method: Fugacity level I **[ ]**; Fugacity level II **[ ]**; Fugacity level III **[X]**; Fugacity level IV **[ ]**; Other (calculation) **[ ]**; Other (measurement)**[ ]**
Results:

Compartment	Release 100% to air	Release 100% to water	Release 100% to soil
Air	77.0 %	0.4 %	0.4 %
Water	15.2 %	99.1 %	9.0 %
Soil	7.7 %	0.0 %	90.6 %
Sediment	0.1 %	0.4 %	0.0 %

Remarks: Appendix 1
Reference: MITI. Japan

*3.5 BIODEGRADATION

Type: aerobic **[X]**; anaerobic **[ ]**
Inoculum: adapted **[ ]**; non-adapted **[X]**;
Concentration of the chemical: related to COD **[ ]**; DOC **[ ]**; test substance **[X]**
Medium: water **[X];** water-sediment **[ ];** soil **[ ];** sewage treatment **[ ]**
Degradation: 94 % by BOD after 28 days
96 % by TOC after 28 days
100 % by GC after 28 days
Results: readily biodeg. **[X];** inherently biodeg. **[ ]**; under test condition no biodegradation observed **[ ]**, other **[ ]**
Method: OECD TG 301C
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: purity: > 95.0 %
Reference: MITI, Japan

4. ECOTOXICITY

*4.1 ACUTE/PROLONGED TOXICITY TO FISH

(a)
Type of test: static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]** open-system **[ ]**; closed-system **[X]**
Species: Medaka (*Oryzias latipes*)
Exposure period: 96 h
Results: $LC_{50\ (24h)}$ = 12.9 mg/l
$LC_{50\ (48h)}$ = 5.7 mg/l
$LC_{50\ (72h)}$ = 5.7 mg/l
$LC_{50\ (96h)}$ = 3.7 mg/l
Analytical monitoring: Yes **[X]** No **[ ]** ? **[ ]**
Method: OECD TG 203 (1992)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4, purity: 97.9%
Remarks: Groups of ten Medaka were placed to nominal concentrations of 1.0, 2.0, 4.0, 8.0 and 16 mg/l, and dechlorinated tap water as control. Test water was exchanged with freshly prepared one every 24h. The measured concentrations were between 103 and 118% of the nominal concentrations throughout the test period. Toxicity data were calculated based on the nominal concentrations.
Reference: Environment Agency of Japan (1996)

(b)
Type of test: static **[ ]**; semi-static **[ ]**; flow-through **[X]**; other *(e.g. field test)* **[ ]** open-system **[ ]**; closed-system **[X]**
Species: Medaka (*Oryzias latipes*)
Exposure period: 14 d
Results: $LC_{50\ (14d)}$ = 1. 9 mg/l
Analytical monitoring: Yes **[X]** No **[ ]** ? **[ ]**
Method: OECD TG 203 (1992)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4, purity: 97.9 %
Remarks: Groups of ten Medaka were placed to nominal concentrations of 0.49, 1.20 and 3.0 mg/l, and dechlorinated tap water as control. The measured concentrations were between 83 and 106 % of the nominal concentrations throughout the test period. Toxicity data was calculated based on the nominal concentrations.
Reference: Environment Agency of Japan (1996)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

*A. Daphnia

Type of test: static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]**; open-system **[X]**; closed-system **[ ]**
Species: *Daphnia magna*.
Exposure period: 48 h
Results: EC_{50} (24 h) = 42.3 mg/l
EC_{50} (48 h) = 24.9 mg/l
Analytical monitoring: Yes **[X]** No **[ ]** ? **[ ]**
Method: OECD TG 202
GLP: Yes **[X]** No **[ ]** ? **[ ]**

Test substance: As prescribed by 1.1 - 1.4, purity: 97.9 %
Remarks: 20 daphnids (4 replicates of 5 organisms) were placed to nominal concentrations of 10, 18, 32, 56 and 100 mg/l, and dechlorinated tap water. The EC_{50} (48h) was determined based on the nominal concentrations. Measured concentrations at the start of exposure and after 48h were between 108-111% and between 88-90% of the nominal concentrations, respectively.
Reference: Environment Agency of Japan (1995).

*4.3 TOXICITY TO AQUATIC PLANTS, e.g. algae

Species: *Selenastrum capricornutum* ATCC 22662
Endpoint: Biomass **[X]**; Growth rate **[ ]**; Other **[ ]**
Exposure period: 72 h
Results: Biomass EC_{50} (72h) = 14.6 mg/l
(Endpoint) NOEC = 3.20 mg/l
Analytical monitoring: Yes **[X]** No **[ ]** ? **[ ]**
Method: OECD TG 201 (1984)
open-system **[X]**; closed-system **[ ]**
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: As prescribed by 1.1 - 1.4, purity: 97.9 %
Remarks: Static test. Biomass change (% inhibition) was measured in five nominal concentrations (1.6, 3.2, 6.4, 13.0, 25.0 and 50.0 mg/l). No solubilizer was used. EC_{50} was calculated based on the nominal concentrations irrespective of measured concentrations ranging from 50-57% of the nominal concentrations after 72 h. EC_{50} and NOEC calculated by the submitter using the time-weighted mean of measured concentrations are 9.2 and 2.4 mg/l, respectively.
Reference: Environment Agency of Japan (1995)

4.4 TOXICITY TO BACTERIA

No data

4.5 CHRONIC TOXICITY TO AQUATIC ORGANISMS

4.5.1 CHRONIC TOXICITY TO FISH

No data

(*)4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Type of test: static **[ ]**; semi-static **[X]**; flow-through **[ ]**; other *(e.g. field test)* **[ ]**; open-system **[X]**; closed-system **[ ]**
Species: *Daphnia magna*.
Endpoint: Mortality **[ ]**; Reproduction rate **[X]**; Other **[X]**
Results: Reproduction rate: EC_{50} (21 d) = 3.18 mg/l
(Endpoint) NOEC = 1.02 mg/l
LOEC = 3.18 mg/l
Analytical monitoring: Yes **[X]** No **[ ]** ? **[ ]**
Method: OECD TG 202 (1984)

GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	As prescribed by 1.1 - 1.4, purity: 97.9 %
Remarks:	40 daphnids (4 replicate; 10 daphnids per replicate) were placed to five nominal concentrations (0.50, 1.5, 3.5, 9.5, 25.0 mg/l) and dechlorinated tap water as control (pH: 7.6 to 8.1; Hardness: 65 mg/l). Solubilizer was not used. Concentrations measured after 2 or 3 days, when test water was renewed through 21d test, were between 25-70% of the nominal concentrations, thus, toxicity data were calculated based on the time-weighted mean of measured concentrations.
Reference:	Environment Agency of Japan (1995).

4.6 TOXICITY TO TERRESTRIAL ORGANISMS

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

No data

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

No data

4.6.3 TOXICITY TO OTHER NON MAMMALIAN TERRESTRIAL SPECIES (INCLUDING AVIAN)

No data

4.7 BIOLOGICAL EFFECTS MONITORING (INCLUDING BIOMAGNIFICATION)

No data

4.8 BIOTRANSFORMATION AND KINETICS

No data

4.9 ADDITIONAL REMARKS

None

5. TOXICITY

*5.1 ACUTE TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(a)

Type:	LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain:	Rats
Value:	597 mg/kg b.w.
Method:	Other
GLP:	Yes **[ ]** No **[ ]** ? **[X]**

Test substance: Purity: Unknown
Remarks:
Reference: Zdravko *et al.*: 1985

(b)
Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rats
Value: about 700 mg/kg b.w.
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Olson: 1960, Smyth *et al.*: 1969

(c)
Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Mice
Value: 390 mg/kg b.w.
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Zdravko *et al.*: 1985

(d)
Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Mice
Value: 1,050 mg/kg b.w.
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Smyth *et al.*: 1969

(e)
Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Guinea pigs
Value: 697 mg/kg b.w.
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Zdravko *et al.*: 1985

(f)
Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Albino rats
Value: 451 mg/kg b.w. (0.42 ml/kg b.w.)
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**

Test substance: Mixture of glycidyl methacrylate (97.8 %), epichlorohydrin (0.3 %) and dichlorohydrin (0.6 %)
Remarks:
Reference: EPA/OTS: 1992

5.1.2 ACUTE INHALATION TOXICITY

(a)
Type: LC_0 **[X]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[ ]**; Other **[ ]**
Species/strain: Rats/ Fischer 344
Exposure time: 4 hours
Value: See Remarks
Method: OECD TG 403 (5 males and 5 females at each dose level)
GLP: Yes **[X]** No **[ ]** ? **[ ]**
Test substance: Purity: 99.8 %
Remarks: The highest concentration was the maximum practically attainable concentration and lower concentrations were run due to eye effects observed at higher concentrations. At nominal concentrations of 412 ppm (2,394 mg/m^3) and 269 ppm (1,563 mg/m^3), weight losses up to 15 %, labored breathing and eye irritation was observed. At 105 ppm (610 mg/m^3), a 3 % decrease in body weight occurred. Corneal opacity was produced at all exposure concentrations (moderate at 412 and 269 ppm, slight at 105 ppm) and did not heal within 14 days post-exposure. There was no mortality observed at any concentration, including 412 ppm, the highest practically attainable vapor concentration.
Reference: Nitschke *et al.*: 1990

(b)
Type: LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[ ]**; Other **[X]**
Species/strain: Rats
Exposure time: See Remarks
Value: See Remarks
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: Maximum survival time of rats, exposed to saturated vapors of glycidyl methacrylate, was 2 hours.
Reference: Smyth *et al.*: 1969

(c)
Type: LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[X]**; Other **[ ]**
Species/strain: Rats
Exposure time: 6 hours
Value: 1,400 mg/m^3
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: Changes in lungs, thorax, respiration, *etc.*
Reference: Haag: 1953

(d)
Type: LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[X]**; Other **[ ]**
Species/strain: Rabbits
Exposure time: 6 hours
Value: 1,400 mg/m^3
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: Changes in lungs, thorax, respiration, *etc*.
Reference: Haag: 1953

(e)
Type: LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[X]**; Other **[ ]**
Species/strain: Guinea pigs
Exposure time: 6 hours
Value: 1,400 mg/m^3
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: Changes in lungs, thorax, respiration, *etc*.
Reference: Haag: 1953

(f)
Type: LC_0 **[ ]**; LC_{100} **[ ]**; LC_{50} **[ ]**; LCL_0 **[X]**; Other **[ ]**
Species/strain: Dogs
Exposure time: 6 hours
Value: 1,400 mg/m^3
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: Changes in lungs, thorax, respiration, *etc*.
Reference: Haag: 1953

5.1.3 ACUTE DERMAL TOXICITY

Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rabbits
Value: 480 mg/kg b.w. (450 µl/kg)
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Smyth *et al.*: 1969

5.1.4 ACUTE TOXICITY, OTHER ROUTES OF ADMINISTRATION

(a)
Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Rats
Route of Administration: i.m. **[ ]**; i.p. **[X]**; i.v. **[ ]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time:

Value: 290 mg/kg
Method: Unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Petrov: 1973

(b)
Type: LD_0 **[ ]**; LD_{100} **[ ]**; LD_{50} **[X]**; LDL_0 **[ ]**; Other **[ ]**
Species/strain: Mice
Route of Administration: i.m. **[ ]**; i.p. **[X]**; i.v. **[ ]**; infusion **[ ]**; s.c. **[ ]**; other **[ ]**
Exposure time:
Value: 350 mg/kg
Method: Unknown
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Petrov: 1973

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

(a)
Species/strain: Rabbits (domestic)
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[X]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[ ]**
Classification: Irritating **[ ]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: Other
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Purity: 92 %
Remarks: One piece of undamaged skin two by two centimetres on either side of the spine was chosen for the testing, one side for testing and the other for control (an equal amount of tap water). 0.1 ml of original concentration of glycidyl methacrylate was applied for five days. The localized skin reaction was observed daily. After the experiments, the skin was removed for microscopic examination.

After application for one or two days, the test areas turned red, swelled and blistered. After three days, there was subdermal bleeding and ulcers. After five days the skin turned hard, become thicker and cracked, and there was pigmentation. The tissue pathological changes included degeneration and necrosis of surface skin cells, disappearance of cellular boundaries, displaying pink staining material, bleeding in the corium cells and lymph cell infiltration with accompanying formation of abscesses.
Reference: Ou-Yang *et al.*: 1988

(b)
Species/strain: Albino rabbits

Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[X]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[ ]**
Classification: Irritating **[ ]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: A single covered topical application with glycidyl methacrylate was conducted to the skin of albino rabbits for four hours.

Moderate to severe skin irritation including necrosis was induced with slight to moderate edema.
Reference: Olson: 1960

(c)
Species/strain: Unknown
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[X]**; Slightly irritating **[ ]**; Not irritating **[ ]**
Classification: Irritating **[ ]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: A 10% solution (aqueous) produced slight redness and edema after 1 application (4 hours duration) and a moderate burn after 2 applications.
Reference: Olson: 1960

(d)
Species/strain: Unknown
Results: Highly corrosive **[ ]**; Corrosive **[X]**; Highly irritating **[ ]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[ ]**
Classification: Irritating **[ ]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: DOT standard test (equivalent to OECD Test Guideline 404)
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: Although 4 hours exposure induced corrosiveness, but not 1 hour exposure.
Reference: Lockwood: 1991

5.2.2 EYE IRRITATION/CORROSION

Species/strain: Albino rabbits
Results: Highly corrosive **[ ]**; Corrosive **[ ]**; Highly irritating **[X]**; Irritating **[ ]**; Moderate irritating **[ ]**; Slightly irritating **[ ]**; Not irritating **[ ]**
Classification: Irritating **[ ]**; Not irritating **[ ]**; Risk of serious damage to eyes **[ ]**
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown

Remarks: Undiluted glycidyl methacrylate was instillated directly into the eye of rabbits.

Moderate to severe irritation and corneal damage was induced. Corneal damage did not heal within 7 days post-dosing. This ocular damage was prevented by washing with water within 30 seconds.

Reference: Olson: 1960, Smyth: 1969

5.3 SKIN SENSITISATION

(a)

Type: Delayed allergy reaction test
Species/strain: Hartley guinea pigs (male)
Results: Sensitizing **[X]**; Not sensitizing **[ ]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**
Method: Modified Buehler method
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: 10 animals received three topical applications on the left side with 0.4 ml of 10 or 25 % glycidyl methacrylate in dipropylene glycol monomethyl ether (DPGME) during the three week induction phase. The animals with slight erythema on the dermal test site after the second application received the third application at lower concentration. The applications were removed after a six-hour exposure period. After a two-week rest period, the single challenge application was conducted to the right side of the animals in the same manner as the induction applications. The animals with slight erythema on the dermal test site after the third induction exposure received a 1 % solution of glycidyl methacrylate in DPGME. As positive control (10 animals), DER 331 epoxy resin in DPGME was used.

During the challenge phase, slight erythema at the application site was observed in 7/10 animals treated with glycidyl methacrylate. In positive control group, 8/10 animals showed the same change.

Reference: The Dow Chemical Company: 1992

(b)

Type: Delayed allergy reaction test
Species/strain: Guinea pigs
Results: Sensitizing **[X]**; Not sensitizing **[ ]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**
Method: Other
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Purity: 92 %
Remarks: The hair of animals was removed and a patch of skin two by two centimetres on either side of the spine was chosen for testing. One side for testing and the other for control. Localized smear application (to 10 animals) or intradermal injection (to 10 animals) with 0.1 ml of 1 % glycidyl methacrylate in acetone was conducted to the animals for

ten days, and after 21 days they were excited and the localized reactions were observed.

Hyperemia, edema, scleroma and necrosis were observed on the treated area and these changes reached a peak on the fourth day. But no obvious change was observed on the control area. Using the evaluation standards of rating the intensity of delayed reactions, the skin smear allergic intensity was 14 and the intradermal injection intensity was 13, both belonging to the strong allergenic category.

Reference: Ou-Yang *et al*.: 1988

(c)

Type: Rapid allergic reaction test (active stimulation)
Species/strain: Guinea pigs
Results: Sensitizing **[X]**; Not sensitizing **[ ]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**
Method: Other
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Purity: 92 %
Remarks: The hair of animals was removed and a patch of skin two by two centimetres was chosen for testing. Intradermal injection of 0.5 % glycidyl methacrylate solution with homologous serum albumin was conducted to 8 animals for ten days. After 21 days, the same solution was injected intravenously to 5 of these 8 animals and the reactions were observed. As control, homologous serum albumin with no antibodies was injected to 3 other animals.

Breathing difficulties, wheezing, increased mouth and nose secretions, spasms and death were observed in the test group, but no obvious changes in the control group. In accordance with the rapid allergic reaction strength category standards, the reaction intensity was evaluated as 13, which belongs to the strong allergic category.

Reference: Ou-Yang *et al*.: 1988

(d)

Type: Rapid allergic reaction test (passive stimulation)
Species/strain: Guinea pigs
Results: Sensitizing **[X]**; Not sensitizing **[ ]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**
Method: Other
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Purity: 92 %
Remarks: The blood of three animals, which were already allergic, was removed and placed in a centrifuge, and serum was extracted and diluted one part to three, one part to ten and one part to thirty with biological saline solution. The hair of other five animals was removed, and four pieces of skin two by two centimetres was chosen for testing. 0.1 ml of saline solution (control), or one to three solution, one to ten solution or one to thirty solution of serum saline solution was injected under the skin. One hour later, 0.5 ml of 0.1 % glycidyl methacrylate

homologous serum albumin solution and 0.4 ml of saline solution was injected intravenously, and the localized reactions were observed.

Blue circles or spots were observed most markedly in the one to three areas, followed by the one to ten area and in the one to thirty areas, and there were a few scattered blue spots. This showed that the reaction is related to the dosage. Evaluating these reactions in accordance with the rapid allergic reaction strength category standards, they belong to the strong allergic category.

Reference: Ou-Yang *et al*.: 1988

(e)
Type:
Species/strain: Guinea pigs
Results: Sensitizing **[X]**; Not sensitizing **[ ]**; Ambiguous **[ ]**
Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: 6 of 6 animals showed skin sensitization (e.g. contact dermatitis).
Reference: BIBRA working group: 1988

*5.4 REPEATED DOSE TOXICITY

(a)
Test Substance Glycidyl methacrylate
Produced by Japan Oil Ltd, Lot No. 50905Y, Purity: 99.93 %, Kept at cold and closed dark place until use

Method
Method: OECD TG 422
Test type: Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test
GLP: Yes
Year: 1997
Species: Rats
Strain: Cij; CD (SD)
Route of administration: Oral (by gavage)
Duration of test: Males; 46 days
Females; 40 - 47 days
Doses: 10, 30, 100 mg/kg/day (in corn oil)
Sex: Male/Female
Exposure period: Males; 45 days,
Females; from 14 days before mating to day 3 of lactation
Frequency of treatment: Daily
Control group and treatment: Concurrent vehicle
Post exposure observation period: 1 day
Statistical analysis: Multi-comparison analysis for continuous data and Fisher's exact test for quantal data
Test condition: Age at study initiation was 10 weeks old (males: 382-414 g, females: 245-282 g). Number of animals per sex per dose was 12. Functional

observation was not performed because the test was conducted by the Test Guideline adopted in 1990.

Results

NOAEL: 10 mg/kg/day for males, 30 mg/kg/day for females

LOAEL: 30 mg/kg/day for males, 100 mg/kg/day for females

Toxic effects: Male:

<u>At 30 mg/kg:</u>

Salivation at day 25 to day 40 of administration in 5 of 12 animals (This symptom disappeared within 10 minutes after the appearance)

Squamous hyperplasia in forestomach (0: 1/12, 10 mg/kg: 1/11, 30 mg/kg: 11/12, 100 mg/kg: 11/11)

<u>At 100 mg/kg:</u>

Salivation continuously after 19 days of administration in all animals (This symptom were observed immediately after administration and almost disappeared within 30 minutes)

Increase in absolute and relative kidney and adrenal weights

Increase in total protein and albumin

Squamous hyperplasia in forestomach

Female:

<u>At 100 mg/kg:</u>

Cellular infiltration in forestomach ((0: 0/12, 10 mg/kg: 2/12, 30 mg/kg: 3/12, 100 mg/kg: 4/12)

Remarks: Two males died at 10 mg/kg on day 21 of administration and at 100 mg/kg on day 26 of administration, respectively.

Although the reason of two males' death was not clear, authors concluded it might be no chemical-related.

Salivation and increased serum protein in males was not considered as adverse effects.

Histological change observed in forestomach was considered to be due to irritation of this chemical.

Conclusions Repeated dose toxicity in rats by oral administration is hyperplasia in forestomach and NOAEL is 10 mg/kg/day.

Data Quality Valid without restriction

Reference Ministry of Health and Welfare: Japan, *Toxicity Testing Reports of Environmental Chemicals* 5, 359-385 (1997)

Other September 16, 1999

(b)

Species/strain: Rats

Sex: Female **[ ]**; Male **[ ]**; Male/Female **[X]**; No data **[ ]**
Route of Administration: Oral (by gavage)
Exposure period: 1 year
Frequency of treatment: 5 days/week
Post exposure observation period:
Dose: 0.1, 0.3 mg/kg/day
Control group: Yes **[ ]**; No **[X]**; No data **[ ]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL: 0.3 mg/kg/day
LOAEL:
Results: No effects in all tissues were found, which could clearly be related to treatment. However, there were no more information.

In this study, the number of animals was 3 and 15 for each sex at 0.1 and 0.3 mg/kg/day, respectively.

. Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Reference: Hadidian *et al.*: 1968

(c)
Species/strain: Rabbits (domestic)
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Route of Administration: Oral
Exposure period: 15 days
Frequency of treatment: Daily
Post exposure observation period:
Dose: 50 mg/kg/day
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**; Vehicle: Peanut oil
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL:
LOAEL: Could not be evaluated
Results: Fifteen days after treatment, slow reactions and some head shaking was observed in the treated group. In addition, 2 of 10 animals succumbed to prostration and died. There were decrease in body weight, increase in relative weights of heart, liver and kidneys, and some hematological changes (increase in white blood cells, platelets and lymph cells, decrease in leukoplasts and intermediate cells). In pathological examination, there was heart bleeding, deterioration of the heart muscle fibers, widespread fatty changes in the liver with focal necrosis. In kidneys, extravasated blood and hemorrhaging were observed, and the upper part of the renal tubules was swollen. There was also red stained protein in the tubular cavity, cranial hemorrhaging, small focal necrosis of the gray matter, and ulceration and necrosis of the mucous membrane of the stomach. However, incidence of these changes was not reported.

. Method: Other
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Purity: 92 %
Reference: Ou-Yang *et al.*: 1988

(d)

Test Substance Glycidyl methacrylate
Supplied by the Dow Chemical Company, Identification # IL13016601, Purity: 99.5 %

Method

Method: Other
Test type: Thirteen-week vapor inhalation toxicity study
GLP: Yes
Year: 1996
Species: Rats
Strain: Fischer 344
Route of administration: Inhalation (vapor)
Duration of test: 13 weeks
Doses: 0.5, 2, 15 ppm (2.9, 12, 87 mg/m^3, calculated daily dose: 0.35, 1.46, 10.59 mg/kg/day)
Sex: Male/Female
Exposure period: 13 weeks
Frequency of treatment: 6 hours/day, 5 days/week
Control group and treatment: Concurrent vehicle
Post exposure observation period: 1 day
Statistical analysis: Statistical significance by Dunnett's test or Wilcoxon Rank-Sum test with a Bonferroni correction for multiple comparisons
Test condition: Age at study initiation was 8 weeks old. Number of animals per sex per dose was 10.

This study was conducted to meet the Standard Operating Procedures of the Toxicology Research Laboratory and many Good Laboratory Practice Standards. Permanent records of all data generated during the course of the study, the protocol, any addenda to the protocol and a copy of the final report were available for inspection by the Quality Assurance Unit of Health and Environmental Sciences, The Dow Chemical Company.

Results

NOAEL: 12 mg/m^3 (1.46 mg/kg/day)
LOAEL: 87 mg/m^3 (10.59 mg/kg/day)
Toxic effects: Male:

<u>At 87 mg/m^3</u>

Hyperplasia of respiratory epithelium of the nasal tissues, graded as very slight, in all animals. The hyperplastic respiratory epithelium was approximately two to three times as thick as that of control animals, and was located in the anterior portions of the nasal passages, involving the tips of the turbinates and the lateral walls of the nasal passages.

Female:

<u>At 87 mg/m^3</u>

Hyperplasia of respiratory epithelium of the nasal tissues, graded as very slight, in all animals. The hyperplastic respiratory epithelium was approximately two to three times as thick as that of control animals, and was located in the anterior portions of the

nasal passages, involving the tips of the turbinates and the lateral walls of the nasal passages.

Remarks: There were no treatment related in-life observations, and no significant treatment-related effects on body weight, urinalysis, clinical chemistry or hematology parameters, as well as gross pathologic changes or organ weights at any exposure levels.

The changes observed in respiratory tract were likely resulted from the irritation of glycidyl methacrylate.

Conclusions Repeated dose toxicity in rats by inhalation is hyperplasia in nasal tissues and NOAEL is 2 ppm (equivalent to 1.46 mg/kg/day).

Data Quality Valid with restriction because of unspecified Test Guideline and unpublished

Reference Landry, T. *et al.*, Unpublished report of The Dow Chemical Company (13-wk inhalation in rats) (1996)

Other October 1, 1999

(e)
Species/strain: Rats
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Route of Administration: Inhalation
Exposure period: 2 weeks
Frequency of treatment: 6 hours/day, 5 days/week
Post exposure observation period: 2 weeks
Dose: 35 ppm (204 mg/m^3, calculated daily dose: 24.9 mg/kg/day)
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**; Unknown
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL:
LOAEL: 204 mg/m^3 (24.9 mg/kg/day)
Results: Decrease in body weight gain, respiratory symptoms, and higher red blood cell count than that of control were observed. There were no histopathologic effects. No remaining exposure-related effects were observed at two weeks after exposure.
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Reference: DuPont Haskell Laboratory: 1982

(f)
Species/strain: Rats
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Route of Administration: Inhalation
Exposure period: 26 weeks
Frequency of treatment: 6 hours/day, 6 days/week
Post exposure observation period:
Dose: 15.3, 206 mg/m^3 (calculated daily dose: 2.24, 30.1 mg/kg/day)
Control group: Yes **[ ]**; No **[ ]**; No data **[X]**;

Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**

NOAEL:
LOAEL: 15.3 mg/m^3 (2.24 mg/kg/day)
Results: A wide range of chronic toxic effects, such as changes of liver and spleen weight, and enzyme (transaminase) levels in blood or tissue, and lesion in central nervous system, cardiovascular system, liver and kidney, were observed. At 206 mg/m^3, all the changes were more pronounced and the pathological lesions only got worsened after the exposure was ceased. On the other hands, the changes at 15.3 mg/m^3 were sparse and slight, and almost all vanished one month after the exposure was ended.

Because of the higher vapor pressure and lower purity, the author suggested that the test material used in this study contained components other than glycidyl methacrylate, which may have contributed to the toxicity observed.
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: 92 %
Reference: Ouyang Guoshun *et al*.: 1990

(g)
Test Substance Glycidyl methacrylate, Purity: Unknown

Method
Method: Other
Test type: Thirteen days inhalation toxicity study
GLP: Unknown
Year: 1996
Species: Rabbits
Strain: Unknown
Route of administration: Inhalation
Duration of test: 14 days
Doses: 0.5, 2, 5, 10 ppm (2.91, 11.6, 29.1, 58.2 mg/m^3, calculated daily dose: 0.26, 1.04, 2.62, 5.24 mg/kg/day)
Sex: Unknown
Exposure period: 13 days
Frequency of treatment: 6 hours/day, daily
Control group and treatment: Concurrent vehicle
Post exposure observation period: 1 day
Statistical analysis: Unknown
Test condition: 4 weeks recovery study was conducted.

Results
NOAEL: 2.91 mg/m^3 (0.26 mg/kg/day)
LOAEL: 11.6 mg/m^3 (1.04 mg/kg/day)
Toxic effects: 11.6 mg/m^3:
Degeneration of the nasal olfactory epithelium
29.1 mg/m^3:
Olfactory epithelial degeneration, and the hyperplasia, erosions, ulcers and inflammation of the nasal epithelium

58.2 mg/m^3:
Olfactory epithelial degeneration, and the hyperplasia, erosions, ulcers and inflammation of the nasal epithelium

Remarks: After 4-week recovery period, there was complete reversibility of these changes except for olfactory epithelial degeneration observed at 29.1 and 58.2 mg/m^3, which showed only partial reversibility. At 11.6 mg/m^3, nasal tissue was indistinguishable from that of control at one month post-exposure.

Conclusions Repeated dose toxicity in rabbits by inhalation is degeneration, hyperplasia, etc., in nasal tissues and NOAEL is 0.5 ppm (equivalent to 0.26 mg/kg/day).

Data Quality Valid with restriction because of unknown on purity, method, sex, strain and GLP, and unpublished

Reference Cieszlak, F. *et al.*, Unpublished report of The Dow Chemical Company (Short-term inhalation in rabbits with recovery period) (1996)

Other October 1, 1999

(h)
Species/strain: Rabbits
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Route of Administration: Inhalation
Exposure period: 26 weeks
Frequency of treatment: 6 hours/day, 6 days/week
Post exposure observation period:
Dose: 15.3, 206 mg/m^3 (calculated daily dose: 1.18, 15.9 mg/kg/day)
Control group: Yes **[ ]**; No **[ ]**; No data **[X]**;
Concurrent no treatment **[ ]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL:
LOAEL: 15.3 mg/m^3 (1.18 mg/kg/day)
Results: A wide range of chronic toxic effects, such as lesion in central nervous system, cardiovascular system, liver and kidney, and other degenerative changes in brain and coverings, were observed. Moreover, there were changes of cardiac EKG (not diagnostic of specified effects) and erythrocyte count. At 206 mg/m^3, all the changes were more pronounced and the pathological lesions only got worsened after the exposure of glycidyl methacrylate was ceased. On the other hands, the changes at 15.3 mg/m^3 were sparse and slight, and almost all vanished one month after the exposure was ended.

Because of the higher vapor pressure and lower purity, the author suggested that the test material used in this study contained components other than glycidyl methacrylate, which may have contributed to the toxicity observed.

Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**

Test substance: Purity: 92 %
Reference: Ouyang Guoshun *et al*.: 1990

*5.5 GENETIC TOXICITY IN VITRO

A. BACTERIAL TEST

(a)

Test Substance Glycidyl methacrylate
Produced by Aldrich Chemical Co., Purity: 98 %

Method

Method: Other
Test type: Reverse mutation assay
System of testing: Bacterial
GLP: No
Year: 1986
Species/Strain: *Salmonella typhimurium* TA97, TA98, TA100, TA1535
Metabolic activation S9 from hamster liver, induced with aroclor 1254-induced, or rat liver induced with aroclor 1254
Concentration: 0, 10, 33, 100, 333, 1000 µg/plate
Statistical methods: Not reported
Test conditions: Number of replicates: once at least
Plates/test: 3
Positive controls: With metabolic activation: 2-aminoanthracene (all strains)
Without metabolic activation: sodium azide (TA 100, TA 1535), 9-aminoacridine (TA 97), 4-nitro-o-phenylenediamine (TA 98)

Results

Cytotoxic concentration: Unknown
Genotoxic effects:

	+	?	-
With metabolic activation:	**[X]**	**[ ]**	**[ ]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**

Remarks: Glycidyl methacrylate showed positive result in TA97, TA100, TA1535 with and without metabolic activation but not in TA98.

Conclusions Bacterial gene mutation is positive with and without metabolic activation.

Data Quality Valid with restriction because of no GLP and no specified Test Guideline

Reference Dorothy, A.C. et al., *Mutat.Res.*, 172, 105-138 (1986)

Other September 20, 1999

(b)

Test Substance Glycidyl methacrylate
Produced by Alcodac Inc., Purity: Unknown

Method

Method: Health, Safety and Government Compliance test method, 79-10
Test type: Reverse mutation assay
System of testing: Bacterial
GLP: No
Year: 1981
Species/Strain: *Salmonella typhimurium* TA98, TA100, TA1535, TA1537
Metabolic activation S9 from Aroclor 1254-induced rat liver
Concentration: With metabolic activation: 32, 100, 320, 1,000 μg/plate
Without metabolic activation: 100, 320, 1,000, 2,000 μg/plate
Statistical methods: Not reported
Test conditions: Number of replicates: 1
Plates/test: Not reported
Procedure: Pre-incubation
Solvent: Dimethylsulfoxide
Negative control: Dimethylsulfoxide
Positive controls:
With metabolic activation: 2-aminofluorene, 2-aminoanthracene, dimethylbenz(a)anthracene
Without metabolic activation: 2-nitrofluorene, sodium azide, quinacrene mustard

Results

Cytotoxic concentration: Unknown
Genotoxic effects:

	+	?	-
With metabolic activation:	**[X]**	**[ ]**	**[ ]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**

Remarks: Glycidyl methacrylate induced a significant, reproducible, dose-dependent increase in the number of revertant colonies per plate for tester strain TA 100 and TA 1535 with and without metabolic activation.

Conclusions Bacterial gene mutation is positive with and without metabolic activation.

Data Quality Valid with restriction because of unknown purity, no GLP and no official publication

Reference The Goodyear Tire & Rubber Company, Laboratory Report No. 81-4-5 (1981)

Other September 20, 1999

(c)
Type: Gene mutation test
System of testing: *Salmonella typhimurium* TA95, TA100
Concentration: 112, 224, 448, 896 μg/plate
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
S9; Unknown
Results: Glycidyl methacrylate induced no increase in colonies of TA95 with and without metabolic activation. There was a marked increase in

the number of colonies of TA100 with and without metabolic activation.

Cytotoxicity conc: With metabolic activation:
Without metabolic activation:

Precipitation conc:

Genotoxic effects:

	+	?	-
With metabolic activation:	**[X]**	**[ ]**	**[ ]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**

Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: 92 %
Remarks: Positive control: MMS, 2-aminofluorene, 2-amine anthracene
Reference: OuYang *et al.*: 1988

(d)
Type: Gene mutation study
System of testing: *Klebsiella pneumoniae*
Concentration: 0.05, 0.1, 0.2, 0.5, 1.0 mmol/L
Metabolic activation: With **[ ]**; Without **[X]**; With and Without **[ ]**; No data **[ ]**
Results:
Cytotoxicity conc: With metabolic activation:
Without metabolic activation:

Precipitation conc:

Genotoxic effects:

	+	?	-
With metabolic activation:	**[ ]**	**[ ]**	**[ ]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**

Method: Other
GLP: Yes **[ ]** No **[**X**]** ? **[ ]**
Test substance: purity: 92 %
Remarks:
Reference: Voogd *et al.*: 1981

(e)
Type: SOS-Chromotest
System of testing: *Escherichia coli* PQ 37
Concentration: 0.1, 0.3, 1.0 mmol/L
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**
Results:
Cytotoxicity conc: With metabolic activation:
Without metabolic activation:

Precipitation conc:

Genotoxic effects:

	+	?	-
With metabolic activation:	**[X]**	**[ ]**	**[ ]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**

Method: Other
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: purity: 97 %
Remarks:
Reference: von der Hude *et al.*: 1990

(f)

Type:	Analysis of the phenotype and the restriction enzyme mapping level of mutations
System of testing:	*Escherichia coli* HB 101
Concentration:	0.1, 0.3, 1.0 mmol/l
Metabolic activation:	With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
Results:	The transformation efficiency of glycidyl methacrylate-bound pBR322 was much lower than that of pBR322 alone. Glycidyl methacrylate-bound pBR322 induced phenotype changes in competent cells (i.e., tetracycline-resistance inactivation or ampicillin-resistance inactivation). There were two mutants of pBR322, ApRTCS and ApSTcR, in the transformants and a deductive mutant ApsTcs in the nontransformants. All of the selected mutants were stable and heritable. When restriction enzyme maps were used to analyze the mutant ApRTcS, four of seven maps were changed, some sites were shifted to other resistant gene regions, for example, sites of Bg/I, EcoRI, HindIII, HincII, etc., and there was a new recognition site for HincII (252). No DNA fragment insertion or deletion was observed on any maps.
Cytotoxicity conc:	With metabolic activation: Without metabolic activation:
Precipitation conc:	
Genotoxic effects:	+ ? - **[X] [ ] [ ]**
Method:	Other
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	purity: unknown
Remarks:	Plasmid pBR322 was used for *in vitro* binding, mutant screening, and restriction enzyme mapping. The binding between glycidyl methacrylate and DNA *in vitro* has been verified by means of a spectrophotometric method. These results suggest that when glycidyl methacrylate is covalently linked to the plasmid DNA, it gives rise to a premutagenic lesion of DNA that is converted in vivo into a point mutation.
Reference:	Xie *et al*.: 1990a

B. NON-BACTERIAL IN VITRO TEST

(a)

Test Substance	Glycidyl methacrylate Produced by Japan Oil Ltd., Lot No. 50905Y, Purity: 99.93 %

Method

Method:	Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD TG 473
Test type:	Chromosomal aberration test
System of testing:	Non bacterial
GLP:	Yes
Year:	1997
Species/Strain:	CHL/IU cell
Metabolic activation	S9 from rat liver, induced with phenobarbital and 5,6-benzoflavone

Concentration: -S9 (continuous treatment): 0.0031, 0.0063, 0.013, 0.025, 0.050 mg/ml
-S9 (short-term treatment): 0.0055, 0.011, 0.022, 0.044, 0.088 mg/ml
+S9 (short-term treatment): 0.022, 0.044, 0.088, 0.18, 0.35 mg/ml

Statistical methods:

Test conditions: For continuous treatment, cells were treated for 24 or 48 hours without S9. For short-term treatment, cells were treated for 6 hours with and without S9 and cultivated with fresh media for 18 hours.
Plates/test: 2
Solvent: Dimethylsulfoxide
Positive controls: Mitomycin C for continuous treatment
Cyclophosphamide for short-term treatment

Results

Cytotoxic concentration: With metabolic activation: not observed
Without metabolic activation:
0.044 mg/ml (short-term treatment)
0.0063 and 0.025 mg/ml (24 hr-continuous treatment)
0.013 and 0.025 mg/ml (48 ht-continuous treatment)

Genotoxic effects:	clastogenicity			polyploidy		
	+	?	-	+	?	-
With metabolic activation:	**[X]**	**[ ]**	**[ ]**	**[ ]**	**[X]**	**[ ]**
Without metabolic activation:	**[X]**	**[ ]**	**[ ]**	**[X]**	**[ ]**	**[ ]**

Remarks: Structural chromosomal aberrations (including gap) and polyploidy were induced. However, a trend test showed no dose-dependency for the induction of polyploidy with the 24 hours continuous treatment and the short-term treatment with the metabolic activation system.

Conclusions Structural chromosome aberration of CHL/IU cells is positive with and without metabolic activation.

Data Quality Valid without restriction

Reference Ministry of Health and Welfare: Japan, *Toxicity Testing Reports of Environmental Chemicals* 5, 359-385 (1997)

Other September 20, 1999

(b)

Type: Chinese hamster ovary cell/hypoxanthine-guanine-phosphoribosyl transferase (CHO/HGPRT) forward gene mutation assay

System of testing: Chinese hamster ovary cells

Concentration: With metabolic activation: 25 - 600 μg/ml
Without metabolic activation: 5 - 80 μg/ml

Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[X]**; No data **[ ]**

S9: Rat liver, induced with Aroclor 1254

Results: With metabolic activation, reproducible increases in the mutation frequencies were observed at several doses. Statistical analysis indicated significant trend both in the initial and confirmatory assays. However, none of the pair-wise comparisons of treated vs negative control group was significant. On the other hand, without metabolic activation, non-treatment related and non-reproducible increases in the

	mutation frequencies were observed in treated cultured cells. Statistical analysis indicated a significant linear dose-related trend in the initial but not confirmatory assay.
Cytotoxicity conc:	
	With metabolic activation: 500 µg/ml and more
	Without metabolic activation: 50 µg/ml and more
Precipitation conc:	
Genotoxic effects:	+ ? -
	With metabolic activation: **[X] [ ] [ ]**
	Without metabolic activation: **[ ] [ ] [X]**
Method:	Other
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Test substance:	purity: 99.5 % ± 0.04 %
Remarks:	Two separate assays were conducted (initial and confirmatory assay).
Negative control:	Dimethyl sulfoxide (DMSO, solvent)
Positive control:	
	With metabolic activation: 20-methylcholanthrene
	Without metabolic activation: Ethyl methanesulfonate
Reference:	Linscombe and Engle: 1995

(c)

Type:	Sister-chromatid exchanges
System of testing:	Chinese hamster V79 cells
Concentration:	0, 0.02, 0.039, 0.078, 0.16, 0.31 mM
Metabolic activation:	With **[ ]**; Without **[X]**; With and Without **[ ]**; No data **[ ]**
Results:	
Cytotoxicity conc:	
Precipitation conc:	
Genotoxic effects:	+ ? -
	Without metabolic activation: **[X] [ ] [ ]**
Method:	Other
GLP:	Yes **[ ]** No **[**X**]** ? **[ ]**
Test substance:	purity: 97 %
Remarks:	
Reference:	von der Hude *et al*.: 1991

(d)

Type:	Unscheduled DNA assay
System of testing:	Lymphocytes of human
Concentration:	no data
Metabolic activation:	With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
Results:	Glycidyl methacrylate induced of unscheduled DNA synthesis.
Cytotoxicity conc:	With metabolic activation:
	Without metabolic activation:
Precipitation conc:	
Genotoxic effects:	+ ? -
	[X] [ ] [ ]
Method:	Other
GLP:	Yes **[ ]** No **[ ]** ? **[X]**
Test substance:	purity: unknown
Remarks:	

Reference: Xie *et al*.: 1990b

(e)
Type: Unscheduled DNA assay
System of testing: Lymphocytes of rat
Concentration: no data
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
Results: Glycidyl methacrylate induced of unscheduled DNA synthesis.
Cytotoxicity conc: With metabolic activation:
Without metabolic activation:
Precipitation conc:
Genotoxic effects: + ? -
[X] [ ] [ ]
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: purity: unknown
Remarks:
Reference: Xie *et al*.: 1990b

(f)
Type: DNA replication
System of testing: Lymphocytes of human
Concentration: no data
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
Results: Glycidyl methacrylate induced non-reverse type inhibition of the DNA replication.
Cytotoxicity conc: With metabolic activation:
Without metabolic activation:
Precipitation conc:
Genotoxic effects: + ? -
[X] [ ] [ ]
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: purity: unknown
Remarks:
Reference: Xie *et al*.: 1989

(g)
Type: DNA replication
System of testing: Lymphocytes of rat
Concentration: no data
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
Results: Glycidyl methacrylate induced non-reverse type inhibition of the DNA replication.
Cytotoxicity conc: With metabolic activation:
Without metabolic activation:
Precipitation conc:
Genotoxic effects: + ? -
[X] [ ] [ ]
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**

Test substance: purity: unknown
Remarks:
Reference: Xie *et al.*: 1989

(h)
Type: Transformation assay
System of testing: Golden Syrian hamster embryo cells (diploid)
Concentration: 0.9 - 14.2 mg/L
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
S9:
Results: Transformation was induced. Cells in a transformed focus exhibited 3-dimensional growth and crossing-over the periphery of the focus. These cells had an increased nucleus to cytoplasm ratio and were more basophilic usually. In addition, there were also further evidences for the cell transformation, including the agglutinability following exposure to concanavalin A and colony formation on the soft agar medium.
Cytotoxicity conc:
Precipitation conc:
Genotoxic effects: + ? -
[X] [ ] [ ]
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Yang *et al.*: 1996

(i)
Type: Transformation assay
System of testing: Syrian hamster embryonic cells
Concentration: no data
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
S9:
Results: Transformation was induced.
Cytotoxicity conc:
Precipitation conc:
Genotoxic effects: + ? -
[X] [ ] [ ]
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Xie *et al.*: 1992

(j)
Type: DNA binding study
System of testing: no data
Concentration: no data
Metabolic activation: With **[ ]**; Without **[ ]**; With and Without **[ ]**; No data **[X]**
S9:
Results: The maximums of calf thymus DNA and GMA were shifted toward

longer wavelengths (a change of more than 15 nm) and the absorbance decreased after incubation at room temperature for 15 min or more. The result indicates that binding of DNA and GMA had occurred. The binding force is strong, not affected by the addition of concentrated sodium chloride solution, and only slightly decreased by the addition of 8 M urea solution.

Cytotoxicity conc:
Precipitation conc:
Genotoxic effects: + ? -
[X] [ ] [ ]
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks: The absorption spectrum shift method was used.
The bond between DNA and GMA might be covalent.
Reference: Xie *et al.*: 1990b

* 5.6 GENETIC TOXICITY IN VIVO

(a)

Test Substance Glycidyl methacrylate
Produced by Japan Oil Ltd., Lot No. 50905Y, Purity: 99.93 %

Method

Method: Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD TG 474
Test type: Micronucleus test
GLP: Yes
Year: 1997
Species: Mice
Strain: Crj: BDF1
Sex: Male/Female
Route of administration: Oral (a single dose by gavage)
Doses: Male: 188, 375 and 750 mg/kg
Female: 250, 500 and 1,000 mg/kg
Exposure period: 48 hours
Statistical methods: Fisher's exact test with a Bonferroni correction for multiple comparisons
Test conditions: Age at study initiation was 9 weeks old. Number of animals per sex per dose was 5. Three samples were collected from each animal at 48 hour after administration.
Solvent: Olive oil
Negative control: vehicle
Positive controls: Cyclophosphamide (50 mg/kg)

Results

Genotoxic effects: + ? -
[X] [ ] [ ]
Remarks: The frequency of micronucleated polychromatic erythrocytes was significantly increased in both sexes at the highest doses (750 mg/kg for male and 1,000 mg/kg for female), compared to control. In

addition, it showed a significant tendency to increase with dose-dependency. Inhibition of bone marrow cell proliferation was observed at the highest doses in both sexes under the test conditions.

Conclusions Micronucleus test in mice by oral administration is positive but only at the highest doses.

Data Quality Valid without restriction

Reference Ministry of Health and Welfare: Japan, *Toxicity Testing Reports of Environmental Chemicals* 5, 359-385 (1997)

Other October 1, 1999

(b)

Type: Micronucleus test
Species/strain: Mice
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Intraperitoneal (twice 24 hours apart)
Exposure period:
Doses: 25, 50, 100 mg/kg b.w.
Results: There was an increase in the number of cells with micronuclei, but this change was very slight and inversed dose-response.
Effect on mitotic index or P/N ratio:
Genotoxic effects: + ? -
[ ] [X] [ ]
Method: Other
GLP: Yes **[ ]** No **[X]** ? **[ ]**
Test substance: Purity: 92 %
Remarks: The animals were sacrificed at 6 hours after treatment.
Negative control: Distilled water
Positive control: Methyl pterine
Reference: Ou-Yang *et al.*: 1988

(c)

Test Substance Glycidyl methacrylate
The Dow Chemical Company Lot # IL 13016601, Purity: 99.5 $\pm$ 0.04%

Method

Method: 40 CFR 798.5395 (The Dow Chemical Company)
Test type: Micronucleus test
GLP: Yes
Year: 1995
Species: Mice
Strain: CD-1 (ICR) BR
Sex: Male/Female
Route of administration: A single intraperitoneal injection
Doses: 75, 150 and 300 mg/kg
Exposure period: 24, 48 and 72 hours

Statistical methods: Dunnett's t-tests, one-sided for micronucleated polychromatic erythrocytes and tow-sided for percent polychromatic erythrocytes

Test conditions: Age at study initiation was 9 weeks old. Number of animals per sex per dose was 5. Bone marrow samples were obtained from both femurs.
Solvent: Corn oil
Negative control: Vehicle
Positive controls: Cyclophosphamide (120 mg/kg)

Results

Genotoxic effects: + ? -
[ ] [ ] [X]

Remarks: Mice in positive control group was treated orally with 120 mg/kg cyclophosphamide and sacrificed at 24 hours after treatment. One male at 300 mg/kg died and one female at 300 mg/kg was moribund at the sacrifice time. The diagnosis in both cases was foreign material peritonitis.

Conclusions Micronucleus test in mice by intraperitoneal administration is negative up to the highest dose, 300 mg/kg.

Data Quality Valid without restriction

Reference Lick, S. *et al.*, Unpublished report of The Dow Chemical Company (mouse micronucleus) Study ID: K-031916-011 (1995)

Other October 6, 1999

(d)
Type: Micronucleus test
Species/strain: Mice
Sex: Female **[ ]**; Male **[ ]**; Male/Female **[ ]**; No data **[X]**
Route of Administration: Intraperitoneal
Exposure period: Unknown
Doses: 42.2, 133, 422, 464 mg/kg b.w.
Results: There was no increase in the number of cells containing micronuclei.
Genotoxic effects: + ? -
[ ] [ ] [X]
Method: Other
GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: INBIFO Report: 1979

(e)
Type: Assay of unscheduled DNA synthesis
Species/strain: Mice
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Unknown
Exposure period: Unknown
Doses: Unknown

Results: Unscheduled DNA synthesis (UDS) was increased in the germ cells, but this change was very slight and not dose-related.

Effect on mitotic index or P/N ratio:

Genotoxic effects: + ? -
[ ] [X] [ ]

Method: Other

GLP: Yes **[ ]** No **[ ]** ? **[X]**

Test substance: Purity: Unknown

Remarks:

Reference: Xie *et al.*: 1990b

(f)

Type: Gene mutation assay

Species/strain: Transgenic Big Blue® Fischer 344 rats

Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**

Route of Administration: Inhalation

Exposure period: Unknown (6 hours/day, 5 days/week)

Doses: 1, 10, 25 ppm (5.82, 58.2, 145.5 mg/m^3, calculated daily dose: 0.71, 7.08, 17.70 mg/kg/day)

Results: There were no statistically significant increases in the frequencies of *lacI* mutants in either the olfactory or respiratory epithelium of rats exposed to glycidyl methacrylate at 145.5 mg/m^3, compared to the negative control group.

Effect on mitotic index or P/N ratio:

Genotoxic effects: + ? -
[ ] [ ] [X]

Method: Other

GLP: Yes **[ ]** No **[ ]** ? **[X]**

Test substance: Purity: Unknown

Remarks: The induction of gene mutations at the *lacI* locus by glycidyl methacrylate was evaluated using transgenic Big Blue® Fischer 344 rats (15 rats/group).
After the last exposure, 3 rats/group were immediately sacrificed and gross pathological and histopathological examinations in the nasal epithelium were conducted. The remaining 12 rats/group were maintained under standard laboratory conditions for 4 weeks for the fixation and expression of induced DNA lesions into mutations. After this expression time, the rats were sacrificed, and various tissues were collected and stored. Individual genomic DNA samples were extracted from the olfactory epithelium of 5 rats/group. For respiratory epithelium, tissue samples from 3 individual animals within each group were pooled (4 pooled samples/group from 12 rats) for DNA extraction. Mutations in the target gene (*lacI*) were analyzed by recovering the shuttle vector from the genomic DNA, packaging into bacteriophage lambda (λ) and plating on indicator bacteria.

Histopathological lesions observed in the nasal epithelium of glycidyl methacrylate exposed rats justified the highest exposure concentration employed in the study.

Reference: No reference in Draft Workplace Environmental Exposure Level Guide (1999)

5.7 CARCINOGENICITY

There was no available data.

*5.8 TOXICITY TO REPRODUCTION

(a)

Test Substance Glycidyl methacrylate
Produced by Japan Oil Ltd, Lot No. 50905Y, Purity: 99.93 %, Kept at cold and closed dark place until use

Method

Method: OECD TG 422
Test type: Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test
GLP: Yes
Year: 1997
Species: Rats
Strain: Cij; CD (SD)
Route of administration: Oral (by gavage)
Doses: 10, 30, 100 mg/kg/day (in corn oil)
Sex: Male/Female
Control group and treatment: Concurrent vehicle
Frequency of treatment: Daily
Duration of test: 40-47 days
Premating exposure period for males: 14 days
Premating exposure period for females: 14 days
Statistical analysis: Multi-comparison analysis for continuous data and Chai square test for quantal data
Test condition: Age at study initiation was 10 weeks old (males: 382-414 g, females: 245-282 g). Number of parents per sex per dose was 12. Male/female per cage was 1/1, length of cohabitation was 10 days at the longest, and proof of pregnancy was judged by sperm detection in vagina. Functional observation, sperm examination, measurement of anogenital distance and so on except estrous cycle length and pattern were not performed because the test was conducted by the TG adopted in 1990. As additional histological examination, observation of seminiferous epithelium cells in seminiferous tubule was conducted at 100 mg/kg because of low fertility observed.

Results

NOAEL: 30 mg/kg for parents and 100 mg/kg for F1 offsprings
Toxic effects: Parental toxicity:
<u>At 100 mg/kg</u>

The fertility index (number of delivered animals/ number of mated animals) dropped to 16.7 %, compared to 81.8 %, 100 % and 91.7 % at 0, 10 and 30 mg/kg, respectively. There were no effects on the estrous cycle, copulation index, or gestation length. No significant changes in the numbers of corpora lutea, implants, pups born and live pups as well as the implantation and delivery indices were observed. There were no significant differences in the gestation index, live birth index or viability index on day 4.

Histopathological analysis of the gonads showed no significant effect. No change in the number of gonocyte per Sertoli cell was observed in epithelium of seminiferous tubules (stage VIII) of all survival males at 100 mg/kg.

Toxicity to offspring:
No abnormalities were noted in the body weights of live pups or on necropsy of pups of any treated group.

Remarks: Decrease of fertility index at 100 mg/kg was reproducible. There was a tendency for decrease in the number of corpora lutea, implants, pups born and live pups born, implantation index and delivery index at 100 mg/kg. However, these changes were not statistically significant.

Conclusions Reproductive toxicity in rats by oral administration is a decrease of fertility index and NOAEL is 30 mg/kg/day.

Data Quality Valid without restriction

Reference Ministry of Health and Welfare: Japan, *Toxicity Testing Reports of Environmental Chemicals* 5, 359-385 (1997)

Other September 17, 1999

(b)
Type: Fertility **[ ]**; One-generation study **[ ]**; Two-generation study **[ ]**; Other **[X]** Sperm abnormality test
Species/strain: Mice
Sex: Female **[ ]**; Male **[X]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Intraperitoneal
Exposure period: 5 days
Frequency of treatment: Daily
Doses: 0, 5, 25, 100 mg/kg/day
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**; Corn oil
Concurrent no treatment **[ ]**; Concurrent vehicle **[X]**; Historical **[ ]**
NOAEL 5 mg/kg/day
Results: At 100 mg/kg mice had decreased caudal epididymal weights, slightly lower testicular weights, decreased sperm counts and increased abnormal sperm. Mice given 25 mg/kg/day showed decreased sperm counts and increased abnormal sperm. The NOAEL for spermatotoxicity was 5 mg/kg/day
Method: Other

GLP: Yes **[ ]** No **[ ]** ? **[X]**
Test substance: Purity: Unknown
Remarks:
Reference: Vedula *et al.*: 1994

*5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY

(a)
Test Substance Glycidyl methacrylate
Purity: 92 %

Method
Method: Other
GLP: Unknown
Year: 1988
Species Rats
Strain: Wistar
Route of administration: Oral (by gavage)
Doses: 5.38, 10.76, 21.52, 108.0 mg/kg/day
Sex: Female
Exposure period: Day 5 to day 15 of gestation
Frequency of treatment: Daily
Control group and treatment: There was negative control, but no more data.
Duration of test: 15 days
Statistical methods: Unknown
Test conditions: 93 pregnant rats (200 - 280 g) were divided into six groups with 14 to 18 animals in each group. The animals were sacrificed on the 19th day of pregnancy.
Positive control: Phonetic (DIKUSHUANG in Chinese report) at 1.0 mg/kg.

Results
NOAEL Maternal Toxicity: 21.52 mg/kg/day
NOAEL teratogenicity: 108.0 mg/kg/day
Toxic effect: Maternal general toxicity
At 108.0 mg/kg:
Significant decrease in body weight gain
Pregnancy/litter data:
At 108.0 mg/kg:
A statistically significant increase in the fetal resorption rate (12.7 %, compared to 5.18 % of control group)
Foetal data:
No external, skeletal or organ abnormalities
No significant difference in body weight from the control
Remarks: The percentage of pups stillborn was somewhat higher than control at all dose levels (0 % for control, and 1.35 %, 7.58 %, 1.26 % and 6.03 % for treated group at 5.38, 10.76, 21.52 and 108.0 mg/kg/day, respectively). However, this change was not dose-dependent and statistically significant change was only at 10.76 mg/kg. This was not considered to be dose-related change.

Conclusions Developmental toxicity in rats by oral administration is not observed at the highest dose, 108 mg/kg/day which induces maternal toxicity.

Data Quality Valid with restriction because method and GLP are unknown

Reference Ou-Yang, G.S. *et al.*, *J.Hyg.Res.*, 17 (3), 1-5 (1988)

Other October 4, 1999

(b)

Test Substance Glycidyl methacrylate
Received from the Epoxy Products Department of Texas Operations, The Dow Chemical Company, Freeport, Texas, Lot #IL 13016601, Purity: 99.5 % ± 0.04 % and 99.67 % at the first and second purity check, respectively

Method

Method: Other
GLP: Yes
Year: 1995
Species Rabbits
Strain: New Zealand White
Route of administration: Inhalation (vapour)
Doses: 5, 10, 50 ppm (29.1, 58.2, 291 mg/m^3, calculated daily dose: 2.62, 5.24, 26.2 mg/kg/day)
Sex: Female
Exposure period: From day 7 through 19 of gestation
Frequency of treatment: 6 hours/day, daily
Control group and treatment: Concurrent vehicle
Duration of test: 14 days
Statistical methods: Statistical significance by Dunnett's test or Wilcoxon Rank-Sum test with a Bonferroni correction for multiple comparisons
Fischer exact probability test for pregnancy rates
Test conditions: Adult females, approximately 5.0 to 6.0 months of age, were naturally mated with bucks of the same strain. The observed day of breeding was considered day 0 of gestation. Number of animals per dose was 7. On day 20 of gestation, all animals were euthanized and necropsied.

Results

NOAEL Maternal Toxicity: Not determined
NOAEL teratogenicity: 58.2 mg/m^3 (5.24 mg/kg/day)
Toxic effect: Maternal general toxicity:

<u>At 29.1 mg/m^3</u>
Histopathologic alterations of the nasal respiratory and olfactory epithelium (hyperplasia, necrosis, etc.) in all animals
<u>At 58.2 mg/m^3</u>
Reddened eyes, swollen eyes and mucus discharge from eyes, and wet muzzle and sneezing after exposure

Histopathologic alterations of the nasal respiratory and olfactory epithelium (hyperplasia, necrosis, etc.) in all animals
At 291 mg/m^3
Decrease in feed consumption and fecal out put during the exposure period in all animals

Labored breathing, reddened eyes and nares, swollen eyelids, squinting, decreased activity, nasal congestion, lacrimation, dorsal extension of the head, wet muzzle, excessive sneezing after exposure and colored nasal discharge

Histopathologic alterations of the nasal respiratory and olfactory epithelium (hyperplasia, degeneration, etc.) in all animals

Pregnancy/litter data:
No adverse effect on any reproductive parameters at 29.1 and 58.2 mg/m^3

Foetal data:
No adverse effect on any embryo/fetal parameters at 29.1 and 58.2 mg/m^3

Remarks: Due to the respiratory distress during exposure and clinical signs of respiratory difficulties post-exposure, rabbits at 291 mg/m^3 were removed from study after the third exposure, euthanized and necropsied. Therefore, evaluation of reproductive and embryonal/fetal parameters was precluded.

Conclusions Developmental toxicity in rabbits by oral administration is not observed at the highest dose, 10 ppm (equivalent to 5.24 mg/kg/day) which induces maternal toxicity.

Data Quality Valid with restriction because of unspecified Test Guideline

Reference Vedula, U., Unpublished report of The Dow Chemical Company (inhalation teratology test) (1995)

Other October 6, 1999

(c)
Species/strain: New Zealand White rabbits
Sex: Female **[X]**; Male **[ ]**; Male/Female **[ ]**; No data **[ ]**
Route of Administration: Inhalation
Duration of the test: 13 days
Exposure period: Day 7 to day 19 of gestation
Frequency of treatment: 7 hours/day, daily
Doses: 0.5, 2, 10 ppm (2.91, 11.6, 58.2 mg/m^3, calculated daily dose: 0.31, 1.22, 6.11 mg/kg/day)
Control group: Yes **[X]**; No **[ ]**; No data **[ ]**;
Concurrent no treatment **[X]**; Concurrent vehicle **[ ]**; Historical **[ ]**
NOAEL Maternal Toxicity: 2.91 mg/m^3 (0.31 mg/kg/day)
NOAEL teratogenicity: 58.2 mg/m^3 (6.11 mg/kg/day)
Results: Maternal general toxicity:

The principal indication of maternal toxicity was inflammation of the nasal olfactory and respiratory epithelium at the 11.6 and 58.2 mg/m^3.

Pregnancy/litter data:

Foetal data: There was no teratogenic effect.

Method: Other

GLP: Yes **[ ]** **No [ ]** ? **[X]**

Test substance: Purity: Unknown

Remarks:

Reference: Vedula *et al.*: 1996

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

Type: Neurotoxicity

Results: 13-week inhalation neurotoxicity study was performed in Fischer 344 rats. At week 4, there was a low incidence of nasal discharge and enlarged nostrils at 3.9 and 12 mg/m^3. There were no treatment-related effects in any of the other measures. There was no evidence of neurotoxic effects at any exposure level.

Remarks: Fischer 344 rats were exposed by inhalation to glycidyl methacrylate at approximately 0.5, 2 or 15 ppm (2.9, 12, 87 mg/m^3), 6 hours/day, 5 days/ week for 13 weeks (calculated daily dose: 0.35, 1.46, 10.59 mg/kg/day). The animals were weighted and clinically examined weekly. A functional observation battery (FOB) and motor activity (MA) were conducted preexposure and at the end of each month of exposure. In addition, the postexposure neurotoxicity evaluation focused on evoked potential testing of the visual (FEP), auditory (ABR), somatosensory system (SEP), and caudal nerves (CNAP), and a comprehensive neuropathological examination.

References: Mattsson *et al.*: 1996

B. Toxicodynamics, toxicokinetics

Type: Toxicokinetics

Results: Toxicokinetics of glycidyl methacrylate was investigated in rabbits. After an intravenous injection at 200 mg/kg, the concentration-time curve of this chemical could exactly fit the two-compartment open model, and over 95 % of the parent compound had disappeared from the blood within 10 minutes. Following a subcutaneous injection at 800 mg/kg, the toxicokinetics appeared to fit a first-order absorption one-compartment open model. This chemical was metabolized by a first-order process in incubation with whole blood, plasma, erythrocyte suspension, and homogenates of brain, heart, liver, lung, spleen, kidney, small intestine, and muscle. The highest rate of elimination had been found in blood and liver homogenate. The subcutaneous co-administration of tri-o-cresyl-phosphate (an carboxylesterase inhibitor) with this chemical resulted in about a ten-fold increase in the maximum blood concentrations of this chemical, compared to those of animals dosed with this chemical alone. *In*

vitro, elimination rate could be also decreased by tri-o-cresyl phosphate.

Remarks:

References: Shi Tao *et al.*: 1988

Type: Toxicokinetics

Results:

Remarks: The metabolism of glycidyl methacrylate in mammals will likely proceed by at least two different and competing enzyme systems, epoxide hydratase and non-specific carboxylesterases. Species differences in the activity of these enzymes suggest that the carboxylesterase route of metabolism may predominate in the nasal tissue of rabbits (yielding glycidol and methacrylic acid) whereas the epoxide hydratase route would likely predominate in rats and humans (producing glycerol methacrylate, then glycerol and methacrylic acid by carboxylesterase).

References: Bogdanffy *et al.*: 1987, Dahl *et al.*: 1987, Glatt *et al.*: 1984, Mattes and Mattes: 1992, Pacifici *et al.*: 1981

* 5.11 EXPERIENCE WITH HUMAN EXPOSURE

A. Sensitization

(a)

Type: Patch test

Results: Sensitizing **[X]**; Not sensitizing **[ ]**; Ambiguous **[ ]**

Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**

Method: Other

GLP: Yes **[ ]** No **[ ]** ? **[X]**

Test substance: purity: unknown

Remarks: Three cases of allergic contact hypersensitivity to glycidyl methacrylate used in adhesive sealant manufacturing were reported. Both closed and open patch testing with 1% glycidyl methacrylate solution in petrolatum was positive in all 3 cases. Symptoms included erythema, edema, and vesiculation and a strong 2+ reaction as scored according to the International Contact Dermatitis Research Group classification

Reference: Dempsey: 1982

(b)

Type: Patch test

Results: Sensitizing **[X]**; Not sensitizing **[ ]**; Ambiguous **[ ]**

Classification: Sensitizing **[ ]**; Not sensitizing **[ ]**

Method: Other

GLP: Yes **[ ]** No **[X]** ? **[ ]**

Test substance: purity: unknown

Remarks: Patch test was conducted for a 31-year-old non-atopic woman, who had worked as a chemist and mixed emulsions used to impregnate paper and textile materials to make them oil and water resistant. In this work, she had been in contact with acrylate derivatives (glycidyl methacrylate, ethoxyethyl acrylate etc.). In relation to this work, she

had a history of recurrent acute vesiculopapular hand dermatitis with severe itching and burning mainly on the fingertips, palmar and dorsal aspects of the fingers, and both palms. As a result of patch test, she reacted only to nickel, glycidyl methacrylate (0.01 and 0.05 % acet.) and ethoxyethyl acrylate among the European standard series and (meth) acrylate series. This reaction to nickel was relevant to her jewely intolerance.

Reference: Matura *et al.*: 1995

6. REFERENCES

BIBRA working group, *Toxicity profile*, 4 p (1988)

Bogdanffy, M.S. *et al., Toxcol.Appl.Pharmacol.*, 88, 183-194 (1987)

Cieszlak, F. *et al.*, Unpublished report of The Dow Chemical Company (Short-term inhalation in rabbits with recovery period) (1996)

Canter, D.A. *et al*., *Mutat.Res*., 172, 105-138 (1986)

Dahl, A.R. *et al., Tox.Letters*, 36, 129-136 (1987)

Dempsey, K., *J.Am.Acad.Dermatol.*, 7(6), 779-784 (1982)

Dorothy, A.C. et al., *Mutat.Res.*, 172, 105-138 (1986)

Draft Workplace Environmental Exposure Level Guide, Glycidyl Methacrylate (1999)

DuPont Haskell Laboratory, OTS Document 84003A ID 878220440, 12/82

EPA/OTS; Doc #88-920010076, NTIS/OTS0555558 (1992)

Glatt, H.R. *et al., Biochemical Basis of Chemical Carcinogenesis*, pp 107-121, Edited by Greim, H. *et al.*, Raven Press, New York (1984)

Hadidian, Z. *et al., J.Natl.Cancer Inst.*, 41: 985-1036 (1968)

Haag H.B., Report "Acute Inhalation Toxicity Studies on Vapors of GMA Monomer" 2/3/53. National Technical Information Service (Springfield, VA 22161), Formerly U.S. Clearing house for Scientific & Technical Information, OTS0530684.

INBIFO Report, No. Ao384/1623. Sponsored by Rohm GmbH (micronucleus test) (1979)

Landry, T. *et al.*, Unpublished report of The Dow Chemical Company (2-wk inhalation in rats) (1991)
Landry, T. *et al.*, Unpublished report of The Dow Chemical Company (13-wk inhalation in rats) (1996)

Lick, S. *et al.*, Unpublished report of The Dow Chemical Company (mouse micronucleus) (1995)

Linscombe, V. and Engle, K., Unpublished report of The Dow Chemical Company (CHO/HPGRT assay) (1995)

Lockwood, D., Unpublished report of The Dow Chemical Company (DOT skin test) (1991)

Mattes, P.M. and Mattes, W.B., *Toxcol.Appl.Pharmacol*., 114, 71-76 (1992)

Mattsson, J. *et al.*, Unpublished report of The Dow Chemical Company (13-wk inhalation neurotoxicity in rats) (1996)

Matura, M. *et al.*, *Contact Dermatitis*, 33, 123 (1995)

Ministry of Health and Welfare: Japan, *Toxicity Testing Reports of Environmental Chemicals* 5, 359-385 (1997)

National Technical Information Service (Springfield, VA 22161), Formerly U.S. Clearing house for Scientific & Technical Information, OTS0530684.

Nitschke, K. *et al.*, Unpublished report of The Dow Chemical Company (acute inhalation) (1990)

Olson, K., Unpublished report of The Dow Chemical Company (1960)

Ou-Yang, G.S. *et al., J.Hyg.Res.*, 17 (3), 1-5 (1988)

Ouyang Guoshun, *et al*., *Gongye Weisheng Yu Zhiyebing*, 16 (1), 1-6 (1990)

Pacifici, G.M. *et al., Xenobiotica*, 11, 73-79 (1981)

Petrov I.G., *Mater, Povolzh Konf Fiziol Uchastiem Biokhim, Farmakol Morfol*, 6(2), 49-50 (1973)

Shi Tao *et al*., *Zhongguo Yaolixue Yu Dulixue Zazhi*, 2(3), 226-31 (1988)

Smyth, H.F.Jr. *et al., Am.Ind.Hyg.Assoc.J.*, 30(5), 470-476 (1969)

The Dow Chemical Company, unpublished report (dermal sensitization) (1992)

The Goodyear Tire & Rubber Company, Laboratory Report No. 81-4-5 (1981)

Vedula, U. *et al.*, Report of The Dow Chemical Company (1994).

Vedula, U., Unpublished report of The Dow Chemical Company (inhalation teratology test) (1995)

Vedula, U. *et al.*, Unpublished report of The Dow Chemical Company (inhalation teratology test) (1996)

von der Hude, W. *et al*., *Mutat.Res*., 231(2), 205-218 (1990)

von der Hude, W. *et al*., *Mutat.Res*., 249 (1), 55-70 (1991)

Voogd, C.E. *et al*., *Mutat.Res*., 89 (4), 269-282 (1981)

Xie D.Y. *et al., Environ.Mol.Mutagen.*, 14(Suppl.15), 222-223 (1989)

Xie D.Y. *et al. Biomed.Environ.Sci.*, 3(2), 146-155 (1990a)

Xie D.Y. *et al., Biomed.Environ.Sci.*, 3(3), 281-289 (1990b)

Xie, D.Y. *et al., Weisheng Dulixue Zazhi*, 6(2), 91-93 (1992)

Yang, J. *et al., Weisheng Yanjiu*, 25(5), 261-264 (1996)

Zdravko, B.I. *et al., Gigiena i Sanitariya*, 0(2), 67-69 (1985)

Appendix 1

Glycidyl methacrylate

scenario 1

	emission rate	conc.	amount	percent	transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	reaction	advection
air	1,000	1.9.E-06	1.9.E+04	77.0	7.9E+02	1.9.E+02
water	0	1.9.E-04	3.8.E+03	15.2	1.6E+01	3.8.E+00
soil	0	1.2.E-03	1.9.E+03	7.7	2.4E+00	
sediment		1.4.E-04	1.4.E+01	0.1	5.9E-03	2.9.E-04
		total amount	2.5.E+04			

scenario 2

	emission rate	conc.	amount	percent	transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	reaction	advection
air	0	8.3.E-08	8.3.E+02	0.4	3.4.E+01	8.3.E+00
water	1000	9.4.E-03	1.9.E+05	99.1	7.7.E+02	1.9.E+02
soil	0	5.2.E-05	8.3.E+01	0.0	1.1.E-01	
sediment		7.2.E-03	7.2.E+02	0.4	2.9.E-01	1.4.E-02
		total amount	1.9.E+05			

scenario 3

	emission rate	conc.	amount	percent	transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	reaction	advection
air	0	2.2.E-07	2.2.E+03	0.4	8.9.E+01	2.2.E+01
water	0	2.5.E-03	5.0.E+04	9.0	2.0.E+02	5.0.E+01
soil	1000	3.2.E-01	5.0.E+05	90.6	6.4.E+02	
sediment		1.9.E-03	1.9.E+02	0.0	7.7.E-02	3.8.E-03
		total amount	5.6.E+05			

scenario 4

	emission rate	conc.	amount	percent	transformation rate [kg/h]	
	[kg/h]	[g/m^3]	[kg]	[%]	reaction	advection
air	600	1.2.E-06	1.2.E+04	9.4	4.9.E+02	1.2.E+02
water	300	3.2.E-03	6.4.E+04	50.0	2.6.E+02	6.4.E+01
soil	100	3.2.E-02	5.2.E+04	40.4	6.5.E+01	
sediment		2.4.E-03	2.4.E+02	0.2	9.9.E-02	4.9.E-03
		total amount	1.3.E+05			

Physico-chemical parameter

molecular weight	142.15	Measured	Temp. [℃]	25

melting point ［℃］		- 10	Measured
vapor pressure [Pa]		4.20E+02	Measured
water solubility [g/m^3]		50000	Measured
log Kow		0.96	Measured
half life [h]	in air	17	Estimated
	in water	170	Estimated
	in soil	550	Estimated
	in sediment	1700	Estimated

Environmental parameter

		volume	depth	area	organic	lipid content	density	residence
		[m^3]	[m]	[m^2]	carbon [－]	[－]	[kg/m^3]	time [h]
bulk air	air	1.0E+13					1.2	100
	particles	2.0E+03						
	total	1.0E+13	1000	1E+10				
bulk water	water	2.0E+10					1000	1000
	particles	1.0E+06			0.04		1500	
	fish	2.0E+05				0.05	1000	
	total	2.0E+10	10	2E+09				
bulk soil	air	3.2E+08					1.2	
	water	4.8E+08					1000	
	solid	8.0E+08			0.04		2400	
	total	1.6E+09	0.2	8E+09				
bulk sediment	water	8.0E+07					1000	
	solid	2.0E+07			0.06		2400	50000
	total	1.0E+08	0.05	2E+09				

Intermedia Transport Parameters ［m/h］

air side air-water MTC	5	soil air boundary layer MTC	5
water side air water MTC	0.05	sediment-water MTC	1E-04
rain rate	1E-04	sediment deposition	5E-07
aerosol deposition	6E-10	sediment resuspension	2E-07
soil air phase diffusion MTC	0.02	soil water runoff	5E-05
soil water phase diffusion MTC	1E-05	soil solid runoff	1E-08

EXTRACT FROM IRPTC LEGAL FILES

file: 17.01 LEGAL rn : 1142403
systematic name:2-Propenoic acid, 2-methyl-, oxiranylmethyl ester
common name :glycidylmethacrylate
reported name :glycidylmethacrylate
cas no :106-91-2
area : RUS type : REG

subject	specification	descriptor
AIR	OCC	MAC CLASS

CLV: 3.0MG/M3 (VAPOUR) HAZ. CLASS: III
entry date: MAY 1990 effective date: NOV1989

amendment: PDKAD*, PREDELNO DOPUSTIMYE KONTSENTRATSII VREDNYKH VESHCHESTV V VOZDUKHERABOCHEI ZONY (MAXIMUM ALLOWABLE CONCENTRATIONS OF HARMFUL SUBSTANCES IN OCCUPATIONAL AIR), 5149-89 , , , 1989

****

file: 17.01 LEGAL rn : 1143331
systematic name:2-Propenoic acid, 2-methyl-, oxiranylmethyl ester
common name :glycidylmethacrylate
reported name :glycidylmethacrylate
cas no :106-91-2
area : RUS type : REG

subject	specification	descriptor
AQ	SURF	MAC CLASS

0.09MG/L HAZARD CLASS: III
entry date: JUL 1990 effective date: 1JAN1989

amendment: SPNPV*, SANITARNYE PRAVILA I NORMY OKHRANY POVERKHNOSTNYKH VOD OT ZAGRIAZNENIA (HEALTH REGULATION AND STANDARDS OF SURFACE WATER PROTECTION FROM CONTAMINATION), 4630-88 , , , 1988

****

file: 17.01 LEGAL rn : 1301121
systematic name:2-Propenoic acid, 2-methyl-, oxiranylmethyl ester
common name :glycidylmethacrylate
reported name :2-Propenoic acid,2-methyl-,oxiranylmethyl ester
cas no :106-91-2
area : USA type : REG

subject	specification	descriptor
MANUF	REQ	PRMT
USE	OCC	PRMT
SAFTY	OCC	MXL

; Summary - THE FOLLOWING CHEMICAL IS INCLUDED ON A LIST OF CHEMICALS

AND MIXTURES FOR WHICH REPORTING IS CURRENTLY REQUIRED UNDER THE TOXIC SUBSTANCES CONTROL ACT SECTION 2607A. THIS TOXIC SUBSTANCE IS SUBJECT TO PRELIMINARY ASSESSMENT INFORMATION RULES ON PRODUCT ION QUANTITIES, USES, EXPOSURES, AND ADVERSE EFFECTS. MANUFACTURERS INCLUDING IMPORTERS MUST SUBMIT A REPORT FOR THIS LISTED CHEMICAL MANUFACTURED AT EACH SITE.
entry date: OCT 1991 effective date: 1982

title: PRELIMINARY ASSESSMENT INFORMATION RULES
original : FEREAC, FEDERAL REGISTER, 47 , , 26998 , 1982
amendment: CFRUS*, CODE OF FEDERAL REGULATIONS, 40 , 712 , 30 , 1990

****

file: 17.01 LEGAL rn : 1408578
systematic name:2-Propenoic acid, 2-methyl-, oxiranylmethyl ester
common name :glycidylmethacrylate
reported name :METHACRYLIC ACID, 2,3-EPOXYPROPYL ESTER
cas no :106-91-2
area : EEC type : REG

subject	specification	descriptor
FOOD		RQR
GOODS		MXL
GOODS		PRMT

THE SUBSTANCE IS INCLUDED IN THE LIST OF MONOMERS AND OTHER STARTING SUBSTANCES, WHICH MAY CONTINUE TO BE USED FOR THE MANUFACTURE OF PLASTICS AND ARTICLES INTENDED TO COME INTO CONTACT WITH FOODSTUFFS UNTIL 1 JANUARY 1997 PENDING A DECISION ON THEIR INCLUSION IN THE LIST OF AUTHORIZED SUBSTANCES. THE USE OF THE SUBSTANCE IS SUBJECT TO THE RESTRICTIONS SPECIFIED THEREIN. PLASTIC MATERIALS AND ARTICLES SHALL NOT TRANSFER THEIR CONSTITUENTS TO FOODSTUFFS IN QUANTITIES EXCEEDING 10MG/DM2 OF SURFACE AREA OF MATERIAL OR ARTICLE OR 60 MG/KG OF FOODSTUFFS IN THE SPECIFIED CASES. VERIFICATION OF COMPLIANCE WITH THE MIGRATION LIMITS SHALL BE CARRIED OUT IN ACCORDANCE WITH DIRECTIVES 82/711/EEC AND 85/572/EEC.
entry date: SEP 1995 effective date: 01JAN1991

title: COMMISSION DIRECTIVE OF 23 FEBRUARY 1990 RELATING TO PLASTICS MATERIALS AND ARTICLES INTENDED TO COME INTO CONTACT WITH FOODSTUFFS (90/128/EEC)
original : OJEC**, OFFICIAL JOURNAL OF THE EUROPEAN COMMUNITIES, L75 , , 19 , 1990
amendment: OJEC**, OFFICIAL JOURNAL OF THE EUROPEAN COMMUNITIES, L90 , , 26 , 1993