Joint Assessment of Commodity Chemicals No. 35

Methacrylic Acid

CAS No. 79-41-4

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THE ECETOC SCHEME FOR THE JOINT ASSESSMENT OF COMMODITY CHEMICALS

This report has been produced as part of the ECETOC programme for preparing critical reviews of the toxicology and ecotoxicology of selected existing industrial chemicals.

In the programme, commodity chemicals, that is those produced in large tonnage by several companies and having widespread and multiple uses, are jointly reviewed by experts from a number of companies with knowledge of the chemical. It should be noted that in a JACC review only the chemical itself is considered; products in which it appears as an impurity are not normally taken into account.

ECETOC is not alone in producing such reviews. There are a number of organisations that have produced and are continuing to write reviews with the aim of ensuring that toxicological knowledge and other information are evaluated. Thus a Producer, Government Official or Consumer can be informed on the up-to-date position with regard to safety, information and standards. Within ECETOC we do not aim to duplicate the activities of others. When it is considered that a review is needed every effort is made to discover whether an adequate review exists already; if this is the case the review is checked, its conclusions summarised and the literature published subsequent to the review assessed. To assist ourselves and others working in this field we publish annually a summary of international activities incorporating work planned, in hand, or completed on the review of safety data for commodity chemicals. Interested readers should refer to our Technical Report No. 30 entitled "Existing Chemicals: Literature Reviews and Evaluations".

This document presents a critical assessment of the toxicology and ecotoxicology of Methacrylic Acid (CAS No. 79-41-4).

Methacrylic Acid CAS No. 79-41-4

CONTENTS

1. SUMMARY AND CONCLUSIONS

Methacrylic acid (MAA) is a clear, colourless, corrosive, flammable liquid with an acrid, repulsive odour. It is used as an intermediate in the chemical industry for the production of MAA esters and as a co-monomer in different kinds of polymers. In the EU, 34.8 kt of MAA were produced in 1993.

During production and use the release of MAA into the environment is generally very low. The majority of MAA entering the environment is expected to enter the hydrosphere. Only small amounts will distribute into the atmosphere. The atmospheric half life is estimated to be 6.12 hours. In the aquatic compartment no hydrolysis will occur, but MAA will readily biodegrade. It is not expected to absorb significantly to soil or sediment nor to bioaccumulate.

MAA has a low toxicity to bacteria, fish and crustacea, but is highly toxic to algae. Algae therefore appear to be the most sensitive aquatic species.

After inhalation exposure in experimental animals MAA is deposited initially in the mucous lining layer of the upper respiratory tract. MAA is a physiological substrate of the valine pathway and may be metabolised via citric acid cycle intermediates. MAA is formed in the first step of the metabolism of MAA esters as has been demonstrated for methyl methacrylate.

MAA has a low order of acute toxicity via the oral and inhalation route and is moderately toxic after dermal administration. The main signs of toxicity are irritation and/or corrosion at the site of contact.

MAA is irritating and/or corrosive to skin, eyes, respiratory tract and gastrointestinal tract. It is not a skin sensitiser in experimental animals.

Repeated exposure of rats and mice by the inhalation route, the most relevant route for human exposure, produced body and organ weight effects, and histologic alterations in the nasal turbinates. The body weight and organ weight effects are considered secondary to the irritation effect, which consists of irritative changes in the anterior and posterior regions of the nasal passages. A LOEL of 72 mg/m^3 (20 ppm) has been identified in a 90-day inhalation study with 2 strains of rats. Very slight irritation of the nasal mucosa was the only effect observed at this concentration. The NOEL in a mouse 90-day inhalation study was 72 mg/m^3 (20 ppm).

For the endpoints genotoxicity, carcinogenicity and reproductive toxicity only limited data are available on MAA itself, but information concerning potential hazards can be inferred from studies with methyl methacrylate which is rapidly metabolised to MAA and methanol in animals and humans. These studies

suggest that MAA is not expected to have a genotoxic or carcinogenic potential *in vivo* nor cause significant adverse effects to the developing embryo or foetus.

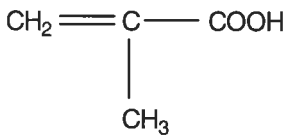
Despite the use of MAA for many years, no adverse systemic health effects have been reported. Local tissue irritation/corrosion at the site of contact will be the lead effect in humans. The sensitisation potential of MAA to humans seems to be low.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 IDENTITY

Name:	Methacrylic acid (MAA)
IUPAC name:	Methacrylic acid
Synonyms:	Acrylic acid, 2-methyl- a-Methacrylic acid a-Methylacrylic acid 2-Methylpropenoic acid Propionic acid, 2-methylene-
Danish:	Methacrylsyre 2-Methylpropensyre
Dutch:	Methacrylzuur
Finnish:	Metakryylihappo
French:	Acide méthacrylique (AMA) Acide 2-méthyl propenoique
German:	Methacrylsäure 2-Propensäure, 2-Methyl
Greek:	Μεθακρυλικό οξύ 2-Μεθυλοπροπενικό οξύ
Italian:	Acido metacrilico Acido 2-metil propenoico
Norwegian:	Metakrylsyre
Portuguese:	Ácido 2-metilpropenóico

	Ácido metacrílico
Spanish:	Ácido 2-metilpropenoico Ácido metacrílico
Swedish:	Metakrylsyra
CAS name:	2-Propenoic acid, 2-methyl-
CAS registry No:	79-41-4
EEC No:	607-088-00-5
EEC classification:	Concentration < 2% (w/w): not classified 2% ≤ concentration < 25% (w/w): irritant Concentration ≥ 25% (w/w): corrosive
EEC labelling:	2% ≤ concentration < 25% (w/w): symbol irritant (Xi), R36/38, nota D Concentration ≥ 25% (w/w): symbol corrosive (C), R34, nota D
EINECS No:	201-204-4
Formula:	$C_4H_6O_2$
Molecular mass:	86.09
Structural formula:	



2.2 PHYSICAL AND CHEMICAL PROPERTIES

At room temperature, MAA is a clear, colourless, corrosive, flammable liquid with an acrid, repulsive odour. It is moderately soluble in water and miscible with most organic solvents. Data on the physical and chemical properties of MAA are given in Table 1.

Table 1: Physical and Chemical Properties of MAA

Parameter, units	Value	Reference
Melting temperature, °C, approximately	14-16	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993
Boiling temperature, °C at 1,013 hPa	160-162	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993
Heat of polymerisation, kJ/kg	0.65	Riddick *et al*, 1986
Relative density D_4^{20} (density of water at 4°C is 1,000 kg/m^3)	1.015-1.02	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993
Viscosity, mPa·s at 20°C	1.3-1.45	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993
Refractive index, n_D 20°C	1.4314	Weast *et al*, 1989
Vapour pressure, hPa at 20°C	0.8-1.0	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993
Vapour density at 20°C (air=1)	2.97	Verschueren, 1983
Threshold odour concentration, ppm	0.032[a] 0.17[b]	Klimkina *et al*, 1973 Grudzinskii, 1988
Surface tension, mN/m at 23°C	19.8 27	Degussa, 1995a ICI Acrylics, 1993
Solubility in water, g/kg at 20°C at 25°C	98[c] 89	Degussa, 1994 Riddick *et al*, 1986
Solubility of water in MAA, g/kg at 20°C	28.5	Riddick *et al*, 1986
Miscible with most organic solvents	Yes	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993
Fat solubility, mg/100 g at 37°C	No data	
Dissociation constant, pKa	4.66	Nemec and Kirch, 1981
Partition coefficient, P_{ow} (octanol/water) at 20°C at 22°C	–0.28[d] 0.93[d] 0.93[e]	Degussa, 1992a Hansch and Leo, 1985 Sangster, 1989
Partition coefficient, log K_{oc} (organic carbon/water) at 20°C	0.23-1.72[e]	Hardies, 1990
Henrys Law constant, Pa·m^3/mol at 20°C at 25°C	0.07[f] 0.13[g] 0.039[h]	SRC in HSDB, 1993 SRC in HSDB, 1993 Khan *et al*, 1992
Flash point, °C, closed cup	65-73	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993
Explosion limits, % at 65-96°C and 1,000 hPa	1.6-8.7	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993
Auto-flammability, ignition temperature, °C	365-400	BASF, 1994; Degussa, 1994; Elf Atochem, 1994; ICI Acrylics, 1994; Rohm and Haas, 1994; Röhm, 1993

a Originally reported as 116 mg/l
b Originally reported as 0.6 mg/m^3
c pH = 1.2-2
d Calculated according to Hansch and Leo (1979)
e Measured, shake flask method
f Calculated, based on water solubility 98 g/l and vapour pressure of 0.8 hPa at 20°C
g Calculated, reported as 1.24x10^{-6} atm·m^3/mol, based on water solubility 8.9% (89 g/l) at 20°C (Riddick *et al*, 1986) and vapour pressure 0.975 mm Hg (1.3 hPa) at 25°C (Perry *et al*, 1984)
h Measured, originally reported as K_H = 2.58x10^3 mol/kg·atm

A typical commercial sample of glacial MAA has a specified purity of ≥ 99.5% (w/w) and contains water (≤ 0.2% w/w) and other impurities depending on the production process (Section 3.1), including hydroxyisobutyric acid (0.1% w/w), acetic acid (0.02% w/w), methyl methacrylate (0.02%) and traces of acetone, acetone cyanohydrin, MAA dimer, acrylic acid, propionic acid, 3-tetramethyl-2,6-dioxane-5-oxocyclopentane and isobutyric acid.

Technical grade MAA is 98% (w/w) pure and may contain water (≤ 0.3%), acetic acid (< 0.5% w/w), propionic acid (< 0.2% w/w), isobutyric acid (< 0.2% w/w) and acrylic acid (< 0.2% w/w).

MAA polymerises readily under the influence of heat, light or by catalysis (e.g. metals and radical forming substances such as peroxides), this being a strongly exothermic reaction. To prevent polymer formation, the monomer is stabilised by the addition of inhibitors such as hydroquinone (HQ) (≤ 100 ppm) and the monomethylether of hydroquinone (MeHQ, synonym *p*-methoxy phenol) (≤ 270 ppm).

Provision should be made to keep the MAA above the freezing point (Section 3.2).

2.3 CONVERSION FACTORS

Conversion factors for concentrations of MAA in air at 20°C and 1,013 hPa are:

- 1 ppm = 3.58 mg/m^3
- 1 mg/m^3 = 0.279 ppm

2.4 ANALYTICAL METHODS

2.4.1 Products

A host of chromatographic techniques have been used for assaying the purity of methacrylate monomers, monomer content in mixtures with other monomers, in solutions and (residual levels) in polymers. Other methods include polarography, colorimetry or spectrometry, the latter particularly for analysis of surgical cements and dental materials. These methods are equally valid for measurement of MAA (Nemec and Kirch, 1981, where further references can be found). Currently, the purity of the product (MAA monomer) is normally analysed by GC or HPLC (Bauer, 1993).

Mass spectrometry (MS) has been used to identify MAA and other acrylic monomers in resin-based dental materials (Gjøs and Urdal, 1983) and to characterise MAA-based paint and synthetic fibres after pyrolysis (Saferstein and Manura, 1977).

2.4.2 Environmental Media

Gibs *et al* (1987) evaluated the preparation of XAD-resin samplers for broad spectrum analysis of large-volume samples. The reviewed methods are suitable for determination of several compounds including MAA in polluted air, water and soil.

Ambient Air

Sollinger *et al* (1992) presented a method for the determination of organic acids such as MAA in ambient air using an ion-exchange resin; the detection limit is 2.0 ng MAA/l with additional preconcentration. The ion-exchange resin is used as an adsorbent for sampling and subsequently as a catalyst for the methylation of the adsorbed acids by methyl formate. The methyl esters are analysed by gas chromatography/mass spectrometry (GC/MS). The method can also be used to monitor workplace atmospheres.

Carboxylic acids, including MAA, in precipitation samples can be measured routinely by ion chromatography (IC) and detection by UV absorption (Elbert *et al*, 1989). The method combines sample preconcentration on a low-capacity anion exchange resin with separation by ion exclusion.

Czerczak and Rogaczewska (1980) analysed MAA in air by GC/FID (flame ionisation detector) after adsorption on charcoal with a detection limit of 2.5 mg/m^3 (0.7 ppm).

Workplace Air

MAA in workplace air can be determined by gas chromatography (GC) after absorption in water. The detection limit is 0.005 mg/m^3 (0.002 ppm) (Dmitriev and Komrakova, 1986a).

GC can be used for detecting MAA in air by direct sampling. This method makes it possible to detect MAA in a small volume (> 5 ml) of workplace air. Using a flame ionisation detector (FID), the detection limit was 4 mg/m^3 (1.1 ppm) (Podkorvyrina *et al*, 1981).

Workplace exposure concentrations of MAA may be determined by adsorption onto silica gel followed desorption of MAA in water, HPLC analysis and UV detection; the detection limit is 0.05 mg/sample (Röhm, 1994a).

MAA in workplace air can be determined by ion-exchange chromatography and UV detection in the eluate of silicagel Dräger tubes with a detection limit of 0.01 mg/m^3 (0.00279 ppm) (Degussa, 1995c).

Morris (1992) described a method to determine MAA in air inside animal exposure chambers by absorption into 1 mM NaOH-solution and subsequent HPLC analysis (detection limit not stated).

Water

MAA can be determined in water by HPLC analysis with UV-detection with a detection limit of 0.05 mg/l (Röhm, 1995). Another HPLC/UV method is used with a detection limit of 1 mg/l MAA in water (Degussa, 1995b).

MAA was determined in industrial waste water by capillary GC/MS analysis. A detection limit was not stated (Bursey and Pellizari, 1983)

2.4.3 Biological Media

Tissues

No method is available.

Blood

Bereznowski *et al* (1994) developed a method to determine MAA in rat blood serum by high pressure liquid chromatography (HPLC) with UV detection. The method was linear up to 5 mM with a detection limit of 0.5 mM.

Dmitriev and Komrakova (1986b) used GC/FID for the determination of MAA in blood with a detection limit of 0.5 mg/ml.

Liquid chromatography, liquid scintillation counting and NMR spectroscopy have been used to determine MAA and methacrylate blood levels *in vitro* (Corkill and Crout, 1982; Corkill *et al*, 1976).

Methyl methacrylate and MAA were determined simultaneously in blood using isotope dilution analysis (Crout *et al* (1979). Blood samples were spiked with a mixture of methyl methacrylate and MAA tritiated in the MAA moiety. Treatment of the halothane extract with ^{14}C-labelled N-phenyl-C-benzoylnitrone yielded isoxazolidine derivatives, which were separated by HPLC. The ratio tritium/^{14}C was determined in the HPLC eluate by liquid scintillation counting.

Urine

Dmitriev and Komrakova (1986b) used GC/FID for the determination of MAA in urine with a detection limit of 0.5 mg/ml.

MAA was determined in human urine after acidification, extraction with diethylether and derivatisation yielding trichloroethyl methacrylate ester which was determined by capillary GC/ECD (electron capture detector). The detection limit was 0.5 mmol/l and recovery was 99% (Rajaniemi *et al*, 1989).

3. PRODUCTION, STORAGE, TRANSPORT AND USE

3.1 PRODUCTION

The majority of MAA is produced commercially (i) via the acetone cyanohydrin route involving hydrolysis of methacrylamide sulphate or (ii) using ethylene as feed stock (C_2-route) producing MAA through an oxosynthesis by reaction of ethylene with synthesis gas, formaldehyde and oxygen (in this case MAA is an intermediate product which is for the most part esterified to make methyl methacrylate), the former route is more important (CEFIC, 1995). A third minor route is oxidation of isobutene or *tert*-butanol (C_4-route). MAA produced by other routes also serves as a key intermediate to methyl methacrylate. Another as yet not commercialised method of MAA production uses carbonylation of propene to isobutyric acid (Bauer, 1993).

In the EU, 34.8 kt of MAA were produced in 1993 (CEFIC, 1995).

3.2 STORAGE

To prevent polymer formation, the MAA monomer is stabilised by the addition of an inhibitor such as MeHQ (Section 2.2). The effectiveness of phenolic inhibitors depends on the presence of oxygen. To prevent polymer formation, the monomer must therefore be stored under air (not under inert gases), in the dark at a temperature below 30°C. During long term storage, stabiliser levels should be checked routinely.

MAA has a high melting temperature (14-16°C, Table 1) and the inhibitor may not distribute uniformly between phases if frozen MAA is partially thawed. Provision should be made to keep the MAA above the freezing point. If frozen, MAA should be melted at room temperature (25°C) and material should not be withdrawn until it is entirely thawed and well mixed (Nemec and Kirsch, 1981).

MAA is stored or shipped in containers lined with polyethylene, or made of glass, stainless steel or aluminium. MAA is corrosive to mild steel (Nemec and Kirsch, 1981). MAA is shipped in containers with a pressure relief valve to prevent the container from rupturing due to MAA polymerisation.

3.3 TRANSPORT

Stabilised MAA is transported by road, rail and sea in bulk tanks and drums. Quantities up to 1 kt are regularly transported by sea.

3.4 USE

MAA is used as internal and external intermediate in the chemical industry for the production of MAA esters and as co-monomer in different kinds of polymers. The main use of MAA is in the preparation of ethyl methacrylate and higher homologues by direct esterification. Methyl methacrylate production does not need input of MAA (see ECETOC, 1995). MAA is also used in the preparation of carboxylated polymers and as a minor constituent of emulsion polymers for adhesives, paints and textile applications.

The distribution of MAA consumption in the EU in 1993 is depicted in Table 2.

Table 2: Use Pattern in the EU in 1993 (CEFIC, 1995)

Type of use	%
Ester production	54
Dispersions (aqueous based polymers)	14
Polymers used as oil additives	8
Solid polymers, coatings, ionomers	11-13
Reactive resins/adhesives[a] (industrial applications)	2.0
Sales (comanufacturers, industrial users)	7
Export outside EU	2.0

a Monomer/polymer systems with 2-10% free MAA

4. ENVIRONMENTAL DISTRIBUTION AND TRANSFORMATION

4.1 EMISSIONS

4.1.1 Natural sources

Traces of MAA occur in the essential oil from Roman camomile (*Anthemis nobilis* L.) (Budavari *et al*, 1989).

4.1.2 Emissions During Production and Use

MAA is produced in closed systems and entry into the environmental compartments is dependent on the degree of exhaust treatment and acid recycling techniques.

Combined controlled discharges of MAA monomer into the atmosphere from MAA and methyl methacrylate production ranged from < 0.1 to 2 t/y at different production sites (CEFIC, 1995).

Controlled discharges of by-product acid from MAA and methyl methacrylate production and processing into the hydrosphere in accordance with national regulations ranged from not detectable to about 175 t/y (data of 1993) depending on the acid recovery process (CEFIC, 1995).

For the main uses of MAA (ester and polymer production) entry into environmental compartments was "negligible" (CEFIC, 1995).

MAA was detected at a concentration of 5.7 mg/l in 1 of 27 industrial waste-water sample extracts from the paint and ink industry. The concentration factor was unknown and the concentration in the original water sample could not be stated (Bursey and Pellizari, 1983).

Other Sources

MAA was detected in a liquid obtained by carbonisation of Karamatsu and Chishima-sasa (Japanese wood). The liquid is reported to be used as deodorant (Yasuhara and Sugiura, 1987).

Residual Levels in Polymers and Polymer Dispersions

The residual MAA monomer content of polymers manufactured from MAA and other monomers is usually very low, typically < 0.001% to 0.4%. The typical residual MAA content of emulsion polymers is < 0.01%, and of suspension polymers (bead polymers) < 0.2%. Reactive adhesives for industrial and

skilled trade use usually contain 2-10% (w/w) of MAA which results in estimated residual monomer concentrations of about 0.5% (w/w) included within the polymer matrix (i.e. in the solid set adhesive after application) (CEFIC, 1995).

Acrylic acid has been shown to form hydrogen bond dimers in the gas and liquid phase and in polymers. Similar effects have been observed for MAA. MAA may form hydrogen bond dimers in copolymers as well which results in a very low mobility of residual MAA monomer in MAA containing copolymers (Ansarian *et al*, 1981).

Residual MAA may be present in limb prostheses made of methacrylic polymers due to incomplete curing or polymerisation (Romaguera *et al*, 1989, 1990).

MAA monomer was among several volatile compounds produced upon experimental heating and UV irradiation of newly manufactured fibreglass of various composition. MAA was detected again following treatment of the same samples after 7 months. The amount of binders in the samples remained constant for at least 12 months after manufacture (Stankevich and Ovdienko, 1966). The MAA is thought to have migrated from the unpolymerised portion of the fibreglass present due to incomplete polymerisation.

MAA was present in vapours generated from heated fibreglass-reinforced plastic (Ilickin *et al*, 1976).

Residual MAA may be present in dental resins (Querens *et al*, 1981).

4.2 ENVIRONMENTAL DISTRIBUTION

The low value of Henry's Law constant (Table 1) suggests that MAA is essentially non volatile.

On the basis of its adsorption constant K_{oc} (Table 1), MAA is not expected to adsorb significantly to soil or sediment (Hardies, 1990).

The theoretical distribution of MAA has been estimated using the fugacity model of Mackay and Paterson (1981). The calculations indicate that the majority of MAA will enter the waterphase. Most of the remainder will be found in the air and negligible amounts in soils and sediments (Table 3).

Table 3: Estimated Distribution Between Environmental Compartments at 20°C (Röhm, 1994b)

Compartment	%
Air	2.41
Water	97.46
Soil	0.07
Sediment	0.06
Suspended matter aquatic	0.00
Biota	0.00

4.3 ENVIRONMENTAL FATE AND BIOTRANSFORMATION

4.3.1 Atmospheric Fate

In the atmosphere, MAA will react with the photochemically produced hydroxyl radicals (•OH). Based upon atmospheric concentrations of $5x10^5$ •OH/cm^3 and $7x10^{11}$ O_3/cm^3, the atmospheric half-life of MAA has been estimated to be 6.12 hours (Atkinson, 1987).

4.3.2 Aquatic Fate

If released into water, MAA will readily biodegrade (Section 4.3.4). Adsorption to sediments will not be significant.

An average half-life of 27.5 days has been estimated for evaporation of MAA from a model river of 1 m depth, flowing 1 m/s with a wind speed of 3 m/s (Howard, 1989).

Hydrolysis will not be an important process. MAA was found to be stable to hydrolysis at 25°C at pH 3, 7 and 11. The study was conducted in accordance with EPA and OECD guidelines (Kapostasy, 1990).

4.3.3 Terrestrial Fate

The adsorption and desorption of MAA were investigated, according to EPA and OECD guidelines, in 5 different types of soil, using six concentrations of ^{14}C MAA from 0.5 mg/ml to 8.9 mg/ml. The study included an adsorption cycle followed by 3 desorption cycles. For the five soils, the desorption K_{oc} values ranged from 1.7 to 52 with an average of 15 which indicates a very high mobility of MAA through the soils.

Once adsorbed, MAA was less readily desorbed from soil. Desorption constants ranged from 3.2 to 144 (Hardies, 1990).

4.3.4 Biodegradation

Aerobic

In a closed bottle test based on the consumption of oxygen (OECD, 1982a), a biodegradation of 86% was achieved within 28 days. The "pass" level of 60% being reached within 10 days of exceeding the 10% level, MAA can be considered as "readily biodegradable" (Douglas and Bell, 1992).

The BOD_5 value for MAA was found to be 0.89 g O_2/g MAA, the ThOD (theoretical oxygen demand) being 1.7 g O_2/g MAA (Lund, 1971).

A BOD_5 value of 0.255 g O_2/g glacial MAA was reported by Flaherty (1989) using acclimated, fresh dilution water with raw sewage from a local treatment plant as the seeding material. The COD under the same conditions was 1.61 g/g MAA.

MAA was found to be inherently biodegradable in a modified Zahn-Wellens test according to OECD (1982b) (BASF, 1988).

In a screening study using a domestic sewage inoculum, 68% of the theoretical CO_2 was produced within 19 days and 86% within 42 days. With adapted microorganisms, 87% of the theoretical CO_2 was produced in 22 days (Pahren and Bloodgood, 1961).

4.3.5 Bioaccumulation

From the *n*-octanol/water partition coefficient (P_{ow} = –0.28 to 0.93, Table 1) no bioaccumulation potential is expected. Using a regression equation (Lyman *et al*, 1990) a theoretical bioconcentration factor (BCF) ranging from 1 to 3 can be estimated.

4.3.6 Evaluation

Calculations for estimation of the distribution of MAA between the environmental compartments indicate that the majority of MAA released into the environment will remain in the water phase. Only small amounts will enter the atmosphere. MAA is readily biodegradable and is not expected to bioaccumulate. Atmospheric half-life was calculated to be 6.12 hours. Due to its low K_{oc} value MAA does not adsorb significantly to soil or sediment. In soil it is expected to rapidly biodegrade.

5. ENVIRONMENTAL LEVELS

5.1 ENVIRONMENTAL LEVELS

5.1.1 Air

No data are available.

5.1.2 Water

No data are available.

5.1.3 Soil

No data are available.

5.1.4 Biota

No data are available.

5.2 HUMAN EXPOSURE LEVELS AND HYGIENE STANDARDS

5.2.1 Non-occupational Exposure

No data are available.

5.2.2 Occupational Exposure

The process of the manufacture of MAA is highly contained in order to minimise exposure to other very toxic chemicals used in the manufacturing process (e.g. acetone cyanohydrin). Control measures are maintained to avoid workplace exposures to more hazardous chemicals such as cyanides (HCN) and these will be sufficient to protect from MAA exposure. The mean measured 8-h TWA exposure concentration was 0.5 ppm (range 0.3-0.7 ppm) (CEFIC, 1995).

Workplace exposure levels during emulsion, polymerisation, solid polymer production and production of other esters ranged from 0.005 and 2.5 ppm (CEFIC, 1995).

5.2.3 Hygiene Standards

On the basis of biodegradation and animal experiments and an acceptable daily intake of 0.05 mg MAA/kgbw was suggested by Klimkina *et al* (1973). A maximum permissible concentration of 1 mg MAA/l in Russian water bodies was also suggested.

In the EU, MAA occurs on the positive list of monomers used in the manufacture of plastics and coatings intended to come into contact with foodstuffs (CEC, 1990). The Scientific Committee for Food recommends a maximum group TDI (total daily intake) of 0.1 mg MAA/kgbw pending the results of an adequate oral study (CEC, 1994).

Workplace Air

Most industrialised countries have adopted occupational exposure limit values (Table 6).

Table 6: Occupational Exposure Limit Values

Country	TWA		STEL		Reference
	(ppm)	(mg/m^3)[a]	(ppm)	(mg/m^3)[a]	
Australia	20	70	-	-	RTECS, 1993
Belgium	20	70	-	-	ACGIH, 1995
Denmark	20	70	-	-	RTECS, 1993
France	20	70	-	-	INRS, 1993
Italy	20	70	-	-	ACGIH, 1995
Netherlands	20	70	-	-	Arbeidsinpectie, 1995
Norway	20	70	-	-	Arbeidstylsynet, 1995
UK	20	70	40[c]	140[c]	HSE, 1995
USA	20	70	60/100[d]	210/350[d]	ACGIH, 1995
	20	70	-	-	NIOSH, 1986 as quoted in RTECS, 1993

TWA Time-weighted average concentration (8-h working period)
STEL Short-term exposure limit (15 min, unless specified otherwise)
a Official values; some countries use different conversion factors and/or other ambient temperature
b Ceiling value
c 15 min
d 30 min/under no circumstances

6. EFFECT ON ORGANISMS IN THE ENVIRONMENT

6.1 MICROORGANISMS

The influence of MAA on the growth of Pseudomonas putida was investigated. The effect concentrations after 16.5 hours of exposure were found to be: EC_{10} = 100 mg/l, EC_{50} = 270 mg/l with neutralised MAA. The acidic solution appeared to be more toxic yielding EC_{10} and EC_{50} values of 12 mg/l and 32 mg/l respectively. According to the authors, this toxicity was due to the very low pH of the solution which ranged from 3.4 to 4.7 above 10 mg/l (Degussa, 1992b).

Another study reported an EC_{10} value of 28 mg/l MAA for P. putida growth inhibition in a test conducted in accordance with the Bringmann and Kühn method (Röhm, 1988).

6.2 AQUATIC ORGANISMS

LC_{50} concentrations for fish ranged from 85 to 224 mg MAA/l. The EC_{50} for *Daphnia magna* was > 100 mg/l, but below 180 mg/l (Table 7). A no-observed effect concentration (NOEL) of 53 mg/l was found in a 21-day reproduction study with *Daphnia magna* under flow-through conditions. The lowest observed effect concentration (LOEC) was 110 mg/l. Based on these data, the maximum acceptable toxicant concentration (MATC) was established to be between 53 and 110 mg/l. The 21-day EC_{50} estimated for this study was 70 mg/l (Putt, 1995).

Table 7: Effect Concentrations for Acute Tests on Fish and *Daphnia*

Organism	Biological endpoint	Time (h)	Concentration (mg/l)	Method	Reference
	Lethality				
Oncorhynchus mykiss	LC_0 LC_{50}	96	12 85	EPA 797, 1400 (1975)	Bowman, 1990
Brachydanio rerio	LC_0 LC_{50} LC_{100}	96	100 >100-180 180	OECD 203 (1984)	Degussa, 1990a
Leuciscus idus melanotus	LC_0 LC_{50} LC_{100}	48	200 224 250	DEV/DIN 38412 part 15 (1982)	Röhm, 1987
	Immobility				
Daphnia magna	EC_0 EC_{50} EC_{100}	24	56 >100-180 180	OECD 202 (1984)	Degussa, 1990b
Daphnia magna	EC_0 EC_{50}	48	130 >130	EPA 797, 1300 (1980)	Burgess, 1990

The 96-h static EC_{50} of MAA for the alga *Selenastrum capricornutum* was 0.59 mg/l. After 96 hours no MAA could be detected in the test solution. The author speculates that this might be due to MAA volatilisation or adsorption onto the glass walls and/or onto particulate matter including algal cells (Forbis, 1990). These 2 assumptions are unlikely because MAA is of low volatility and recovery after 96 hours was ≥ 97% in quality control samples. To be in full compliance with the current EU guideline (CEC, 1992), the pH should have been adjusted.

6.3 TERRESTRIAL ORGANISMS

An acute oral toxicity of > 111 mg/kgbw was reported for Redwinged Blackbirds after an 18 hour exposure. Due to the repellency of MAA to birds, there is no potential for acute avian poisoning (Schafer *et al*, 1983).

6.4 SUMMARY AND EVALUATION

MAA is of low acute toxicity to bacteria, fish and *Daphnia*. Algae appear to be the most sensitive aquatic species with a 96-h static EC_{50} value of 0.59 mg/l. However, due to its biodegradability and low accumulation potential MAA is expected to be readily eliminated from the aquatic environment.

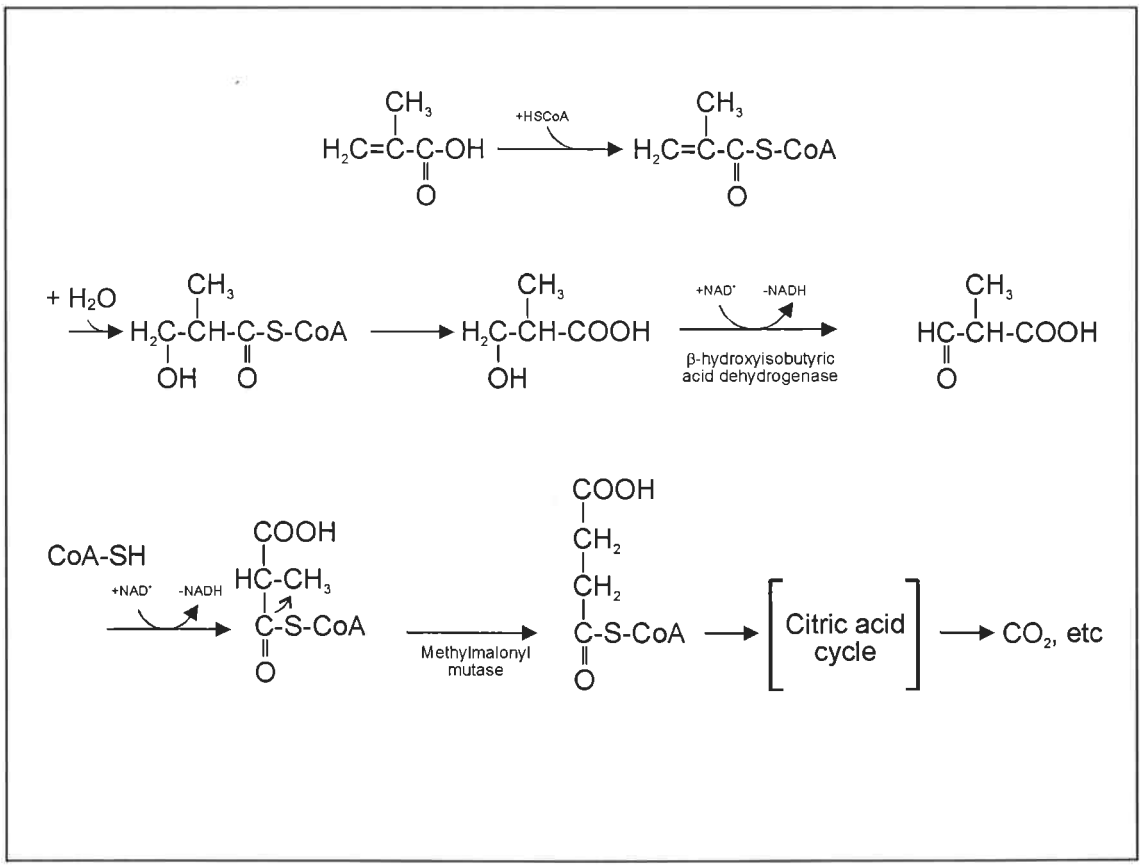
7. METABOLISM AND KINETICS

7.1 METABOLISM

MAA is a physiological metabolite of the valine pathway. After activation with acetyl-S-coenzyme-A (CoA) it is converted into methyl malonyl-CoA and succinyl-CoA which enter the citric acid cycle (Rawn, 1983).

There are no studies which specifically address the metabolism of exogenously applied MAA; the available information is derived from studies with its methyl ester (methyl methacrylate). The initial step in the major metabolism pathway of methyl methacrylate is the de-esterification to MAA and methanol. Hydrolysis of methyl methacrylate may already occur at the site of first contact, as could be demonstrated in the upper airways of rats exposed to methyl methacrylate by the inhalation route (Morris, 1992). Ester hydrolysis of methyl methacrylate is known to occur within minutes in human peripheral blood *in vivo* with a half-life of approximately 5 minutes (Crout *et al*, 1979). Studies of Bratt and Hathway (1977) and ICI (1977) in male Wistar rats dosed by gavage of radiolabelled methyl methacrylate in corn oil demonstrated that endogenously generated MAA will be metabolised utilising the pathway present in mammalian cells for the metabolism of valine, the ultimate metabolites being CO_2 and water (Figure 1).

Figure 1: Main Metabolic Pathway of MAA (after ICI, 1977; Bratt and Hathway, 1977)



It is anticipated that any absorbed MAA will also be metabolised via this pathway. For a detailed discussion of the evidence supporting this pathway see ECETOC (1995). However, the amount of exogenous MAA that will be absorbed and pass cell membranes cannot be estimated from experiments with methyl methacrylate. As MAA will be almost fully dissociated under physiological conditions it is expected that if amounts comparable to those used in the methyl methacrylate studies would be administered, less MAA would be available intracellularly and the metabolic fate of the substance would depend on the local concentrations and the reaction rates of the different steps of the metabolic pathway. The initial de-esterification of methyl methacrylate may have implications for an understanding of the toxicology of MAA. Thus where toxicological data on MAA is absent, information concerning potential hazards may be inferred from a consideration of the toxicology of methyl methacrylate.

7.2 UPTAKE IN THE UPPER RESPIRATORY TRACT

Deposition of MAA vapours in the surgically isolated upper respiratory tract (URT) of urethane anaesthetised male F344 rats was studied after inhalation of 70, 450, or 1,385 mg/l (21, 133, 410 ppm) using a unidirectional respiratory flow technique for 60 minutes. Control animals were exposed to humidified air only. Uptake of MAA was measured throughout the exposure. Deposition was determined by the difference in vapour concentration of MAA in the inspired and the URT exiting air. Responses of the nasal tissues were studied by determining nasal lavage albumin and protein concentration and nasal tissue non-protein sulphydryl (NPSH) levels. Increased levels of albumin and/or total protein can be indicative of mucous hypersecretion, cytotoxicity and transudation of blood proteins into the air space. Nasal non-protein sulphydryl levels can provide an index of direct reactivity of the compound with reduced sulphydryl groups (e.g. glutathione). Deposition rates (from 30 to 60 minutes of exposure) averaged 13, 87 and 255 mg/min in the low, medium and high dose group respectively representing a deposition of about 90% throughout the administered concentration range. MAA treatment at URT deposition rates as high as 255 mg/min was without significant effects on nasal lavage parameters and NPSH levels indicating no significant irritation or direct reactivity with nucleophiles. The authors conclude that MAA is likely to deposit initially in the mucous lining layer of the URT. However, the degree of penetration to underlying cells could not be derived from this experiment (Morris, 1992).

Similar results were reported by Morris and Frederick (1995). Uptake of MAA vapour in the URT of F344 rats was determined using an unidirectional flow technique at exposure concentrations of 450 mg/l (133 ppm). URT exiting air concentrations reached a plateau between 30 and 60 minutes of exposure. The deposition efficiency calculated from values obtained during this time period was 95% (mean of 4 animals) with an average absolute deposition rate of 86 mg/min. Nasal lavage parameters and NPSH levels were not affected by the MAA treatment (Morris and Frederick, 1995).

7.3 UPTAKE FROM THE GASTROINTESTINAL TRACT

Bereznowski *et al* (1994) reported the presence of MAA (quantity not determined) in Wistar rat blood serum 10 minutes after gavage administration of 2 ml of a 1-M solution of sodium methacrylate. After 60 minutes MAA could no longer be detected (detection limit 0.5 mmol/l). The validity of the study is questionable because MAA was not adequately identified (only by HPLC retention time).

7.4 SUMMARY

MAA is a physiological substrate for the valine pathway and may be metabolised via citric acid cycle intermediates. After inhalation exposure MAA is deposited initially in the mucous lining layer of the upper respiratory tract.

MAA is formed in the first step of the metabolism of MAA esters as has been demonstrated for methyl methacrylate. Thus where toxicological data is absent for MAA itself information concerning potential toxic effects may be inferred from a consideration of data obtained with methyl methacrylate.

8. EFFECTS ON EXPERIMENTAL ANIMALS AND *IN VITRO* TEST SYSTEMS

8.1 ACUTE TOXICITY

8.1.1 Oral

LD_{50} values following oral administration of MAA to mice, rats and rabbits are detailed in Table 8.

Table 8: Acute Oral Toxicity

Species	LD_{50} (mg/kgbw)	References
Mouse	1,250	Lobanova *et al*, 1979
Mouse	1,332	Klimkina, 1973
Mouse	1,600	Eastman Kodak, 1979
Rat	1,060	Klimkina, 1973
Rat	1,320[a]	Paulet, 1977
Rat	1,600	Lobanova *et al*, 1979
Rat	2,260	Eastman Kodak, 1979
Rat	2,220[b]	Rohm and Haas, 1957
Rabbit	1,200	Klimkina, 1973

a MAA was administered undiluted
b 2.18 ml/kg; severe gastric irritation

8.1.2 Dermal

LD_{50} values following dermal administration of MAA to rabbits and guinea pigs are detailed in Table 9.

Table 9: Acute Dermal Toxicity

Species	LD_{50} (g/kgbw)	References
Rabbit	0.5-1	Dow, 1977
Rabbit	< 2[a]	Rohm and Haas, 1973a
Guinea pig	1.0-5.1[b]	Eastman Kodak, 1979

a Mortality at 2 g/kgbw = 2/3 animals with intact skin and 3/3 animals with abraded skin; mortality at 3 g/kgbw = 6/6
b 1-5 ml/kgbw

8.1.3 Inhalation

LC_{50} values following exposure of rats to MAA vapour by inhalation to rats are detailed in Table 10.

Table 10: Acute Inhalation Toxicity

Species	Duration (h)	LC_{50} (ppm)	References
Rat	4	1,981[a]	Kelly, 1993
Rat	1	> 1,841[b]	Rohm and Haas, 1973a
Rat	1	< 56,916[c]	Rohm and Haas, 1973b

a Reported as 7.1 mg/l. Weight loss and respiratory irritation were recorded in the surviving animals

b Nominal concentration. Lethality was observed within 19 min, pulmonary oedema and haemorrhage, respiratory distress, and eye corrosion were recorded

c Nominal concentration. Lethality was observed within 19 min, no toxic effect

Exposure of rats by inhalation of air saturated with MAA (approximately 1,000 ppm) for 7 hours caused only eye irritation in rats (Dow Chemical, 1977 as quoted in ACGIH, 1980).

8.1.4 Intraperitoneal

Following intraperitoneal (i.p.) administration of MAA to mice, the LD_{50} was 0.564 mol/10^6 g (48.6 mg/kgbw) (Mir *et al*, 1973a; Lawrence, 1974). No data on toxic effects were reported.

8.1.5 Summary

Acute toxicity studies in experimental animals showed that MAA is of a low order of oral and inhalation toxicity, and that the toxicity by dermal application and by the i.p. route is moderate.

8.2 SKIN, RESPIRATORY TRACT AND EYE IRRITATION, SENSITISATION

8.2.1 Skin irritation

Application of 0.5 ml MAA for 4 hours, under an occlusive patch, to the clipped back of rabbits produced well defined erythema, eschar and oedema within 4 hours. Slight decrease in erythema occurred between 24 and 48 hours after removal of the patch (Rohm and Haas, 1973c).

Application of 0.5 ml MAA to intact and abraded skin of 6 rabbits for 2 hours resulted in severe erythema and oedema at 24 and 72 hours after application, on both intact and abraded skin (Röhm, 1977).

MAA was applied for 24 hours under an occlusive dressing to intact and abraded skin of 4 New Zealand White rabbits. Following removal of the dressing the resulting reactions were assessed immediately and again at 72 hours, using the Draize skin irritation scoring system. The primary irritation index was then calculated by combining the averages of the scores obtained for intact and abraded skin at 24 and 72 hours. Marked dermal injury was observed. Severe erythema, oedema and necrosis were seen in all animals at both time points. Maximum scores were recorded giving a Primary Irritation Score of 8.0 (Elf Atochem, 1980).

Gauze patches containing MAA (amount not indicated) were applied to shaved rabbit skin for 15 or 30 minutes or 24 hours respectively. After 15 and 30 minutes severe erythema, discoloration, slight to severe subcutaneous haemorrhage and slight lichenification was observed. After 24 hours one of 2 animals revealed moderate erythema while the other had severe discoloration, oedema and ulcerations. Uncovered application of MAA produced marked discoloration, slight subcutaneous haemorrhages, oedema and eschar formation 24 hours and 5 days after the initial application (Rohm and Haas, 1956).

Severe irritation effects have been reported in guinea pigs following dermal application of 1, 5, or 10 ml of MAA under occlusive patches for 24 hours. Daily application by "rub-on" the clipped backs of guinea pigs for 10 days produced necrosis (Eastman Kodak, 1979).

When a 4.8 % aqueous solution of MAA or its sodium salt was applied (3 x/wk) to the shaved backs of groups of 8 male ICR mice for 3 weeks, no skin irritation occurred. No pathological changes were seen in the skin of these mice. Application (3 x/wk) of MAA diluted in acetone (4.8%, 9.6% and 19.2%) showed concentration-related irritation, which was slight to moderate with the solution of 4.8 % and severe with the 9.6% and 19.2% solutions. Gross pathological changes seen in the skin of all animals treated with MAA in acetone included desiccation, thickening, eschar formation, reddening, firmness and "hairlessness". Corresponding histopathological changes were acanthosis, hyper- and parakeratosis, ulceration, epithelial necrosis and subacute dermatitis. Dermal fibrosis and keratin inclusions were seen in the skin of mice treated with 9.6% and 19.2 % solutions. Subacute subcutaneous inflammation and myositis in the underlying tissues was observed in the skin of the 19.2% dose animals (Rohm and Haas, 1986).

8.2.2 Eye Irritation

MAA (0.1 ml) was instilled into 1 eye of each of 2 New Zealand White rabbits. The lids were held together gently for 1 second and the eyes then rinsed with 20 ml of luke-warm water, 4 seconds after instillation. The eyes were examined using an ophthalmoscope at 10 seconds for evidence of ocular lesions. Corneal injury was assessed by application of 2% sodium fluorescein directly onto the cornea, flushing out the

excess, and examining the eye under UV light for fluorescent areas. Under the conditions employed, MAA caused marked ocular injury and severe corneal opacity (Elf Atochem, 1980).

Single instillation of 0.1 ml MAA into the eye of 6 albino rabbits resulted in severe corneal, iridial and conjunctival effects persisting until the 7th day (Rohm and Haas, 1973a).

Four Alderley Park specific-pathogen-free rats (2 males and 2 females) were exposed by inhalation (5 h) to 1,300 ppm MAA (4.5 mg/m^3, i.e. MAA satured air) for 5 days. Among other clinical signs eye irritation was recorded (Gage, 1970).

A 1-hour inhalation study in adult albino rats exposed to 204 mg MAA/l (56,916 ppm) produced a corrosive effect on the eyes (Rohm and Haas, 1973a).

Corneal opacity was seen in 1 out of 10 Crl:CDBR rats exposed to 5.9 mg MAA/l (1,646 ppm) in a 4-h inhalation LC_{50} study (Kelly, 1993). In the same study, corneal opacity (1 out of 10 animals) and ocular discharges were seen following exposure at 8.2 mg MAA/l (2,037 ppm).

8.2.3 Respiratory Tract Irritation

In a 4-months rodent study in rats and mice exposed by inhalation to 0.44, 8.9 and 221.3 mg MAA/m^3 (0.12, 2.5 and 61.7 ppm), reversible dose-dependent "dystrophic and destructive changes" (as stated in translation) were observed in the lungs (Lobanova *et al*, 1979). Little information is given in this study and the results are of questionable validity.

Sensory irritation potential of MAA was assessed using the method of Alarie (1981) by exposure of groups of 4 male Swiss Webster mice to atmospheres containing 4,900, 9,400, 18,000, 27,000 and 42,000 ppm MAA for 30 minutes. (Since the saturated vapour pressure of MAA represents approximately 1,000 ppm, the test atmospheres were a mixture of vapour and aerosol.) Breathing patterns of individual animals were recorded prior to, during and following exposure. During exposure to 4,900 ppm MAA sporadic changes indicative of mild sensory irritancy were observed and respiratory rate decreased by 8.1%. During exposure to the higher concentrations moderate to severe sensory irritation, evident as a concentration-related reduction in respiratory rate (reductions of 39.6, 44.8, 52. 57.6 and 62.8% for concentrations of 9,400, 18,000, 27,000, 27,000 and 42,000 ppm MAA respectively), was observed almost immediately after exposure commenced; this irritation persisted throughout the exposure period. Recovery to normal occurred rapidly following cessation of exposure. The RD_{50} (the concentration required to reduce the respiratory rate by 50%) calculated from these results was 22,000 ppm, indicating that MAA has a low potential for causing sensory irritation to the upper respiratory tract (Stadler, 1993).

Following exposure of 4 Alderley Park (Wistar derived) specific-pathogen-free rats (2 males and 2 females) by inhalation (5 h) to 1,300 ppm MAA (4.5 mg/m^3, i.e. MAA satured air) for 5 days, nasal and eye irritation were reported. An additional group of 4 male and 4 female rats of the same strain were exposed (6 h, 5d/wk) to 300 ppm MAA vapour for 4 weeks. No symptoms of irritancy were apparent (Gage, 1970). These results were not confirmed by the following more recent studies conducted according to current guidelines.

Results from a number of single and repeated exposure inhalation studies demonstrate that MAA is irritant to the respiratory tract. Exposure of groups of 5 male and 5 female Crl:CDBR rats to 4.3, 5.9, 7.3 and 8.2 mg MAA/l (1,200, 1,650, 2,040 and 2,290 ppm) for 4 hours (Kelly, 1993) produced clinical symptoms consistent with marked irritation to the respiratory tract (nasal discharge, gasping, irregular respiration, lung noise) and eyes (corneal opacities).

Three groups of Sprague-Dawley and F344/N rats and B6C3F$_1$ mice (20 male and 20 female animals/species/group) were exposed (6 h/d, 5 d/wk) to atmospheres containing 20, 100 and 300 ppm MAA for 90 days (CIIT, 1984). Clinical symptoms indicative of nasal tract irritancy (nasal encrustation and discharge) were observed. Histopathological changes, consistent with effects seen with exposure to mildly irritant materials, were observed in the nasal passages of the rats and mice after 4 and 90 days. These changes were reported as degeneration of the olfactory epithelium and inflammatory changes (rhinitis, ulceration, exudate) in the anterior regions. Effects were considered to be time and concentration related and mice were most susceptible at the highest concentration, followed by the F344/N and Sprague-Dawley rats respectively. As discussed in Section 8.3.3, evaluation of the individual animal data suggests that these effects were over-emphasised in the report, particularly with respect to those reported in the olfactory epithelium.

8.2.4 Gastrointestinal Tract Irritation

Severe gastric irritation was observed at autopsy in male albino rats after single oral gavage of 2.0 ml MAA/kgbw (2.0 g/kgbw) administered as an aqueous solution (Rohm and Haas, 1957).

8.2.5 Sensitisation

MAA did not sensitise any of 5 guinea pigs given an inducing dose by footpad injection and challenged 1 week later by a patch test on the back (Clayton and Clayton, 1982).

Parker and Turk (1983) injected (4 x 0.1 ml) the footpads of female Hartley guinea pigs with an emulsion of 2 mg/ml MAA in ethanol:saline (1:4) in Freund's complete adjuvant. In addition, 0.1 ml of the emulsion was injected into the nape of the neck. Each animal received 1 mg MAA. After 7 days and weekly thereafter for up to 12 weeks, 0.02 ml of a solution in acetone:olive oil (4:1) was dropped onto the shaved

flank of the animals. A different site was used for each application. The concentration of MAA used was not quoted, but either 5% or the maximum concentration which produced no non-specific irritation was employed. Using this protocol, MAA did not induce contact sensitisation.

Groups of 20 male Hartley guinea pigs were used to assess the potential for MAA to induce delayed contact hypersensitivity using the Buehler method (Moore, 1993). A sample (0.4 ml) of a 20% solution of MAA in deionised water was applied to the shaved left flank of the animals using an occlusive dressing for 6 hours. Since eschar formation was observed within 72 hours, a 15% solution was employed for subsequent applications (weekly for the 2 following weeks). The application site was wiped with deionised water after removal of the dressing and scored for irritation. The animals were allowed to rest for 14 days following the third induction and then challenged by application to the clipped right flank using the same procedure. Approximately 24, 48 and 72 hours after removal of the challenge application the site was examined for dermal irritation and/or signs of elicited sensitisation. Responses indicative of dermal irritation were seen in some animals at induction but there were no indications of sensitisation following challenge. Negative and positive control groups incorporated into the study gave the expected responses.

8.2.6 Evaluation

MAA causes adverse effects in experimental animals at the site of application. The undiluted liquid is corrosive to skin. Dependent on the concentration and frequency or time of exposure, skin irritation, ocular and corneal damage, nasal lesions and irritative effects in the gastrointestinal tract can occur. While methyl methacrylate gave the expected concentration-related decrease in respiratory rate, the sensory irritation potential of MAA appears (as evidenced by the high RD_{50}) relatively low. This apparent lack of correlation is consistent with sensory irritation results for methyl methacrylate (Stadler, 1993) and probably reflects also the physical characteristics of the test atmosphere (mixture of vapour and aerosol). This indicates that in the case of MAA the assessment of sensory irritation in the mouse is inappropriate to extrapolate potential irritancy in man.

The vapour produced histopathological changes consistent with exposure to an irritant in the anterior and posterior regions of nasal passages. The lowest concentration tested (20 ppm over 90 days) produced effects in rats and a no effect level has not been established for MAA. However, it is considered that this would be close to 20 ppm based on the limited changes and the small difference in incidence of effects seen in animals exposed to this concentration compared to controls (Section 8.3.3).

The result of the sensitisation studies with or without adjuvant showed that MAA is not a skin sensitiser.

8.3 SUBCHRONIC TOXICITY

8.3.1 Oral

Two studies are available. The validity of these studies is questionable due to insufficient information given in the publication.

In a 6-months study MAA in water was administered by gavage (dosing regime not specified) to 40 white rats at doses of 0, 0.05, 0.5, or 5 mg/kgbw. At the high dose the following effects were observed: hyporeflexia, changes in liver enzymes and electrolytes, erythropenia, decreased liver and adrenal weight, dystrophic changes in liver, kidney and adrenals. Some effects (without any further information) were recorded in the 0.5 mg/kgbw dose group. The NOAEL was reported to be 0.05 mg/kgbw (Klimkina *et al*, 1973).

In the same 6-months study, 20 rabbits received MAA in water by gavage (dosing regime not specified) at doses of 0, 0.05, 0.5 or 5 mg/kgbw. Loss of reflexes to positive stimulators, indication of a slight acidosis, erythopenia and a decrease in catalase activity, an increase in alkaline phosphatase, and a decrease in spleen and adrenals weight were recorded at 5 mg/kgbw. Some effects (without any further information) were recorded in the 0.5 mg/kgbw dose group. The NOAEL was reported to be 0.05 mg/kgbw (Klimkina *et al*, 1973).

8.3.2 Dermal

In a 3-week dermal irritation study groups of 8 male ICR mice received (3 x/wk) doses of 100 ml of 4.8% MAA in water or 4.8, 9.6 or 19.2% of MAA in acetone. No treatment related clinical signs or changes in body weights were observed in the treated group (for an evaluation of the dermal irritation potential, see Section 8.2.1) (Rohm and Haas, 1986).

Due to the corrosive nature of MAA additional dermal studies would not be recommended.

8.3.3 Inhalation

Gage (1970) found slight renal congestion in rats exposed (6 h/d) to atmospheres containing MAA at 300 ppm for 20 days.

In a 90-days study 3 groups of $B6C3F_1$ mice, F344 rats and Sprague-Dawley rats (20 males and 20 females/group) were exposed (6 h/d, 5 d/wk) to atmospheres containing 0, 20, 100 or 300 ppm of MAA. After 4 exposures 10 animals per sex/group were killed. No exposure-related death was recorded in the

study. Slight inflammatory changes (rhinitis, exudate) were already seen after 4 exposures in the sacrificed animals. After 90 days of exposure the most important effects were observed at 300 ppm. Significant decreases in body weight and liver weight were observed in male and female mice and male F344 rats. Increased incidence of lymphocytic hyperplasia in the mandibular lymph nodes was observed in rats. Development of cytomegaly of renal tubular epithelium was seen in male mice. Degeneration of olfactory epithelium was observed at histopathological examination in all species/strains. Minimal to mild degeneration was reported at five days and progressed to moderate degeneration at 90 days. At this concentration mice appeared to be the most susceptible followed by the F344 rats with Sprague-Dawley rats being the least susceptible. In rats, degeneration of the olfactory mucosa was reported to occur at all exposure levels (LOEL= 20 ppm) whereas in mice, olfactory changes were not observed at 20 ppm (NOEL) but were present at 100 and 300 ppm (CIIT, 1984). Evaluation by the Task Force of the individual animal data suggests that effects in the nasal passages were over-emphasised in the report and were confined predominantly to the anterior regions of the nasal passages. Undoubtably, inflammatory changes consistent with exposure to an irritant were seen in the anterior and mid-regions of the mouse at 100 and 300 ppm. While an increasing incidence and severity was seen also in both rat strains in the anterior region, a high background incidence of similar findings in control animals at termination complicates full interpretation of concentration-response relationships. Incidences of inflammatory changes in the controls were 12/20 in F344/N rats and 7/19 in Sprague-Dawley rats, while in the 20 ppm exposure groups the respective incidences were 16/20 and 11/20. Additionally, in the posterior region where the olfactory epithelium is situated, histological changes were absent from the majority of animals. Changes were evident in occasional individual animals only and showed no appreciable relationship to exposure concentration. The findings in the nasal passages should be interpreted as being consistent with exposure to any mildly irritant material.

8.3.4 Evaluation

The available studies by the oral and dermal route do not allow evaluation of the results due to insufficient information given in the reports.

Repeated exposure of rats and mice by the inhalation route, the relevant route for human exposure, produced body and organ weight effects, and histologic alterations in the nasal turbinates. Although an increased incidence of lymphocytic hyperplasia was seen in the mandibular lymph nodes of the high-dose rats of both strains, this is probably a consequence of the inflammatory response in the nasal turbinates. The occurrence of cytomegaly of the renal tubular epithelium, seen only in the high-dose male mice, was characterised as minimal to mild. In the absence of a dose-response and a similar response in the female mice or both strains of rats, this lesion is considered of little significance. The body weight and organ weight effects are considered secondary to the irritation effect.

Repeated exposure of rats and mice by the inhalation route, the relevant route for human exposure, produced irritative changes in the anterior and posterior regions of the nasal passages. A LOEL of 72 mg/m^3 (20 ppm) has been identified in a 90-day inhalation study with 2 strains of rats. Very slight irritation of the nasal mucosa was the only effect observed at this concentration. The NOEL in a mouse 90-day inhalation study was 72 mg/m^3 (20 ppm).

8.4 GENETIC TOXICITY

In vitro genetic toxicology assays are used routinely as the first screen for assessing the genotoxic activity of chemicals. These assays, however, provide information only on the intrinsic potential of these chemicals to cause damage to the DNA. To determine whether or not this potential is expressed in whole animals it is necessary to conduct *in vivo* genetic toxicology assays which take account of absorption, distribution, metabolism and excretion of the chemical and its metabolites. The results of *in vivo* assays therefore often overrule results obtained *in vitro*.

MAA itself has only been tested in the Ames test with *Salmonella typhimurium* TA 98, TA 100, TA 1535, TA 1537 with and without rat and hamster liver S9-mix in concentrations between 33 and 4,000 mg/plate. No significant increases in revertant colonies were observed (Haworth *et al*, 1983).

The methyl ester of MAA, methyl methacrylate, has been tested in a number of test systems *in vitro* as well as *in vivo*. Chromosomal aberrations were observed in a number of *in vitro* test systems suggesting a clastogenic potential *in vitro*. In *in vitro* studies for chromosome damage positive and negative results were obtained. The available data on the *in vitro* genotoxicity of methyl methacrylate are discussed in ECETOC (1995). For a better evaluation of the data available for methyl methacrylate the *in vivo* chromosome damage studies are discussed here in more detail.

ICI (1976a, 1979) has conducted a series of experiments to evaluate methyl methacrylate for its ability to induce chromosomal aberrations in the bone marrow of rats following single or multiple inhalation exposures. Groups of 2 to 5 male Alderley Park rats were exposed for a single 2-hour period to methyl methacrylate vapour concentrations of 0, 100, 1,000 or 9,000 ppm in 2 independent experiments. In a third experiment, groups of 4 to 7 male Alderley Park rats were exposed (5 h/d) to methyl methacrylate at concentrations of 0, 100, 1,000 or 9,000 ppm for 5 consecutive days. No rationale is provided for dose level selection. No measures of cytotoxicity in the target tissue are reported. Small increases In the percentage of cells with chromosomal aberrations were reported in animals exposed to methyl methacrylate at 1,000 or 9,000 ppm in all 3 studies (ICI, 1976a). However, the majority of the aberrations recorded were gap-type aberrations which are now considered to be of questionable biological significance. When the percentages of cells with chromosomal aberrations excluding those with only gap-type aberrations are considered, the observed increases were statistically not significant.

In a follow-up study (ICI, 1979) groups of 8 male Alderley Park rats were exposed for either a single 2-hour period or 5 h/d for 5 consecutive days to concentrations of 100, 400, 700 or 1,000 ppm methyl methacrylate. The maximum concentration tested caused significant reductions in mitotic activity in the bone marrow of the exposed animals following the single and multiple exposures thus justifying the top concentration selected. Small and non-dose related increases in the percentages of cells with chromosomal aberrations were again observed in the animals exposed to methyl methacrylate in either study. However, these increases were almost exclusively due to gap-type aberrations and when these were excluded from the data small increases were only observed at 400 ppm in the single exposure study and at 700 ppm in the multiple exposure study. Such small increases, observed only at the lowest concentrations tested, are not considered to be biologically significant.

The test procedure used for both studies (ICI 1976a, 1979) do not fulfil all requirements of the corresponding OECD guideline.

Hachiya et al (1981) reported data on mouse micronucleus tests. Methyl methacrylate was dosed orally at up to 4.52 g/kgbw in a single dose study and at 1.13 g/kgbw in a 4-dose study to groups of 6 mice. Sampling time in the single dose study was 24 hours and in the repeated dose study 5 days after the first administration. No significant increases in the incidence of micronucleated polychromatic erythrocytes were observed in either study.

Fedyukovich *et al* (1988) reported that methyl methacrylate is negative in a rat chromosomal aberration assay following a single i.p. administration at 0.5 LD_{50} whereas the same authors (Fedyukovich and Egorova, 1991) reported methyl methacrylate to be positive when tested up to the same dose level; these data are therefore contradictory. Very little information is given in the 1988 abstract but the 1991 paper shows increases in chromosomal aberrations following treatment with methyl methacrylate at 1.3 g/kgbw (0.5 LD50) in an acute study and following treatment (2 x/wk) with methyl methacrylate at 0.65 mg/kgbw (0.25 LD50) for periods of 2 and 4 weeks; no significant increases in chromosomal aberrations were observed following treatment twice a week for 6 and 8 weeks. In the absence of toxicity information there is no scientific rationale for such a pattern. In addition, no criteria for the analysis of chromosomal aberrations are provided; it is therefore not clear whether or not gap-type chromosomal aberrations, which are of questionable biological significance, have been included.

Ouyang et al (1989) reported a negative micronucleus test in rats, but no experimental details or data are available in the brief abstract.

Methyl methacrylate did not induce any dominant lethal mutations *in vivo* (ICI, 1976b).

8.4.1 Evaluation

From the available *in vivo* studies it can be concluded that there is no convincing evidence for an *in vivo* clastogenic activity of methyl methacrylate.

It can be expected that under the genotoxicity test conditions a major part of the methyl methacrylate was hydrolysed and present as intracellular MAA. The intracellular MAA concentrations resulting from methyl methacrylate hydrolysis are assumed to be higher than those obtained with MAA itself because the ester is likely to pass cell membranes more easily due to its high lipophilicity (Pow of methyl methacrylate = 1.38) and its non-ionic form at physiological pH. The pKa of 4.66 for MAA suggests that, if MAA is used as a test substrate, only a small amount (0.17%) of undissociated MAA would be available for diffusion through cell membranes. However, as the reaction rates of subsequent metabolic steps are unknown and only scanty measurements are available the resulting MAA concentrations are not known.

Based on this information, it is expected that MAA, like methyl methacrylate, will not be genotoxic *in vivo*.

8.5 CHRONIC TOXICITY AND CARCINOGENICITY

No studies are available. However, the methyl ester of MAA, methyl methacrylate, has been tested and has been shown to be non-carcinogenic. As outlined in Section 7.1, the studies on methyl methacrylate are applicable to MAA.

Methyl methacrylate has been tested in a 2-year drinking water study in Wistar rats at doses of 6, 60, or 2,000 mg/l, in several inhalation studies in F344/N rats (Rohm and Haas, 1979a; Lomax, 1992; Borzelleca et al, 1964) and Golden hamsters (Rohm and Haas, 1979b) at concentrations between 25 and 400 ppm, in male F344/N rats and female $B6C3F_1$ mice at concentrations of 500-1,000 ppm and in female F344/N rats at concentrations of 250-500 ppm (NTP, 1986). In the oral study no histopathological changes or neoplasms have been observed. The lead effect of methyl methacrylate in the inhalation studies in rodents is inflammatory degeneration of the nasal irritation; a NOEL of 25 ppm was derived. There are indications that the effects can be attributed to deposition of methyl methacrylate in the upper respiratory tract and its subsequent hydrolysis by carboxylesterase to MAA (Morris, 1992; Morris and Frederick, 1995) which is likely to cause the local irritation leading ultimately to the observed histopathological changes (for further details see ECETOC, 1995). Due to the yet unknown kinetic parameters quantitative conclusions for MAA from the chronic exposure data of methyl methacrylate cannot be drawn to establish a NOEL for MAA. However, from the data of the subchronic studies of MAA and methyl methacrylate it can be inferred that the chronic NOEL for MAA is in the same range.

8.6 REPRODUCTIVE TOXICITY

In an *in vitro* study, 10-day old rat embryo cultures were exposed to MAA (neutralised with NaOH) at concentrations ranging from 1.2 to 2.1 mM (103 to 181 mg/l) for 24 to 26 hours. At these concentrations MAA produced concentration dependent decreases in growth parameters such as crown-rump length, number of somites and embryo protein content. MAA also induced abnormal neurulation and, less frequently, hypoplasia of the prosencephalon, oedema, malpositioned heart, abnormal flexion and dilated otic vesicles. The authors also reported an increase in MAA-induced cell death (Rogers et al, 1986). Although this study produced lesions which in an in vivo test could be interpreted as foetotoxic/teratogenic effects, its *in vitro* nature means that its significance for human risk assessment is uncertain.

However, methyl methacrylate has been tested in a teratogenicity study and been shown to be not teratogenic, embryo- or foetotoxic (Solomon *et al*, 1993). This study is considered relevant for MAA because of the short half-life of methyl methacrylate in blood (Section 7.1) and because it can be assumed that MAA and methanol are predominantly reaching the placental barrier although the rates of delivery to the foetus are not known. The study with methyl methacrylate was conducted in Crl:CDBR rats exposed (6 h/d) by the inhalation route to concentrations of 99, 304, 1,178, 2,028 ppm from day 6 to 15 of gestation (for further details see ECETOC, 1995).

In the 90-day inhalation study in rats and mice (Section 8.3.3) no gross- or histopathological changes were observed in the oviducts, ovaries, uteri and mammary glands of females and the testes, epididymes, seminal vesicles, mammary glands and prostates of males of the high exposure (300 ppm) group (CIIT, 1984). These results provide no indication of toxic effects on the reproductive system.

8.7 OTHER STUDIES

Spontaneous contraction of isolated guinea pig ileum was inhibited by MAA at concentration levels between 0.01 and 0.04% in the perfusion medium. MAA antagonised the stimulant actions of acetylcholine and barium chloride, thus affecting the neuromuscular as well as the muscular stimulation (Mir *et al*, 1973b).

At concentrations between 0.001% and 0.1% MAA reduced cardiac rate, force of contraction and cardiac flow of the isolated and perfused rabbit heart (Mir et al, 1973a).

Dogs receiving i.v. doses of 9.5-47.6 ml MAA/kgbw showed an initial dose-related decrease in blood pressure followed by a slight increase of blood pressure above the initial level before dosing. A decrease in heart rate and an increase in respiratory rate were also observed (Mir *et al*, 1974).

The binding of dissolved DNA to the membrane of *E. coli* cells in the presence of MAA at concentrations of 50 and 500 mmol and rat liver S9 mix and/or lysozyme was studied by Kubinski *et al* (1981). DNA cell membrane adducts were detected by gel electrophoresis in the presence of S9 and presence and absence of lysozyme.

Fourteen male rats and 15 mice (sex and strain not specified) were exposed (8 h/d) for 3 months to vapours developed by heating a glas fibre polyester resin to 50°C. The temperature in the animal exposure chamber was 24-27°C. The vapours contained average concentrations of 0.73 mg/m^3 of acetone (0.41 ppm), 6.38 mg/m^3 MAA (1.78 ppm) and 0.15 mg/m^3 of unspecified aldehydes. Slight, readily reversible, changes were observed in the mitotic index of the cornea and elevated haemoglobin levels were reported in the treated animals. No hispathological changes were observed in internal organs (Ilickin, 1976). The validity of this study with respect to MAA exposure is questionable due to the mixed exposure.

9. EFFECTS ON HUMANS

9.1 ACUTE AND SUBCHRONIC TOXICITY

No data are available.

9.2 IRRITATION AND SENSITISATION

9.2.1 Eye and Respiratory Tract Irritation

Irritation of the eyes and the upper airways was reported in 21 volunteers (aged between 22 and 30 years) exposed to MAA vapours at concentrations of 0.4-3 mg/m^3 (1.4-10.7 ppm) (Grudzinskii, 1988). The exposure concentrations could not be validated.

9.2.2 Skin Irritation and Sensitisation

MAA did not elicite an allergic skin response in patients known to be sensitised to hydroxypropyl acrylate (Lovell *et al*, 1985), or to various methacrylic esters (Fisher, 1980; Condé-Salazar *et al*, 1988).

None of 3 patients with allergic contact dermatitis to methacrylate-based anaerobic sealants showed an allergic skin response when challenged with MAA (1% in petrolatum) (Dempsey, 1982).

One case of a positive patch test result with MAA (0.1% in petrolatum) and different acrylates and methacrylates was reported by Romaguera *et al* (1985) in a patient with a dermatitis against a prosthesis manufactured from methyl methacrylate. The origin and purity of the MAA used for the patch test, however, was not reported.

Patch testing of 45 patients with shoe contact dermatitis gave only one positive result when tested with MAA (purity, concentration, stabiliser content, vehicle not indicated). However the authors did not differentiate between allergic and irritant dermatitis (Grimalt and Romaguera, 1975).

Humans (37 individuals) coming in contact with preparations of MAA esters showed contact eczema on their fingers and/or hands (Jansen, 1974). The results of this study can not be evaluated, because it is not clear from the publication which preparations were used.

9.2.3 Evaluation

Despite the use of MAA for many years, no adverse systemic health effects have been reported. Local tissue irritation/corrosion at the site of contact is expected to be the lead effect in humans. The sensitisation potential of MAA to humans appears to be low.

9.3 HAZARD ASSESSMENT

For the endpoints mutagenicity, carcinogenicity and toxicity to reproduction only limited data are available on MAA itself. However, information concerning potential hazards can be inferred from studies with methyl methacrylate which is rapidly metabolised to MAA in animals and humans. Studies with methyl methacrylate focused on these endpoints suggest that MAA is unlikely to have a mutagenic or carcinogenic potential *in vivo* and is not expected to cause significant adverse effects to the reproductive organs or to the developing embryo or fetus.

The main population likely to be exposed to MAA are workers involved in production and in particular in industrial manufacture of polymers and manufacture and use of reactive adhesive preparations, whereas consumer exposure and indirect exposure via the environment are considered negligible.

The lead effect of MAA identified in acute and subchronic animal studies is the local irritation at the site of contact.

The major route of occupational exposure is the inhalation route, despite of the low vapour pressure of MAA. For this route of exposure, only very slight irritation of the nasal epithelium was seen at the LOEL of 20 ppm in a 90-day inhalation study in rats (CIIT, 1984). At the next highest concentration of 100 ppm, only slight irritation of the nasal epithelium was seen. Therefore, it can be assumed that 20 ppm is very close to a NOEL in rats. In a similar study in mice, 20 ppm was the NOEL. Additional work in rats has shown that concentrations of 20, 100, and 300 ppm produced only minimal to slight irritation lesions in the nasal epithelium at 5 days. Only the lesions seen at 300 ppm showed progression from minimal to slight, and from slight to moderate after 90 days. These results indicate that the slight irritation effects observed at 20 and 100 ppm do not progress and no increase in severity would be expected at longer exposure durations.

It is generally accepted that the rat is more sensitive to nasal irritants than man due to physiological and anatomical differences. The rat is an obligate nose breather with significantly more complex nasal passages than man. The relative surface area per unit volume in the nose of the rat is 8 times that of man (DeSesso, 1993). Therefore, as a model for inhalation hazard of irritant chemicals, the rat provides

an additional safety factor when evaluating the risk to man. It is concluded that a LOEL or NOEL of 20 ppm, observed in the 90-day studies, can be used as the basis for a risk evaluation in man.

10. FIRST AID AND SAFE HANDLING ADVICE

10.1 FIRST AID AND MEDICAL TREATMENT

There is no specific treatment or antidote for over-exposure to MAA. Supportive medical treatment as indicated by the patient's condition is recommended.

10.1.1 Skin and Eye Injuries

Clothing grossly contaminated with MAA should be removed and either discarded or laundered before reuse. Affected areas of skin must be washed with copious quantities of water. The skin must be rinsed for at least 10 min. If the eyes are splashed, they should be irrigated immediately with eye-wash solution or clean water, holding the eyelids apart for at least 10 minutes. A physician should then be consulted.

10.1.2 Inhalation

The patient must be taken into fresh air, kept warm and at rest if he experiences difficulty in breathing after inhaling MAA fumes. If the patient stops breathing, artificial respiration should be administered until qualified medical personnel are able to take over. Medical aid should be summoned immediately.

10.1.3 Ingestion

If MAA has been swallowed, do not induce vomiting. Never give anything by mouth to an unconscious person. A physician should be consulted immediately.

10.2 SAFE HANDLING

10.2.1 Safety at Work

The main risk of injury stems from MAA's irritating action on the skin and mucous membranes. Contact with the skin and eyes should therefore be avoided as should inhalation of high concentrations of MAA vapour. MAA should be used only in well ventilated areas. As MAA vapour is denser than air, pits and confined spaces should be avoided.

Suitable respiratory equipment must be worn on occasions when exposure to MAA vapour above the recommended exposure limit is likely.

The following protective clothing must be worn when handling MAA: eye-face protection and rubber gloves (preferably nitrile) which should be changed regularly to avoid permeation. Rubber boots should also be worn when handling large quantities.

10.2.2 Storage Safety

MAA is stable in the presence of a polymerisation inhibitor. It is susceptible to polymerisation initiated by prolonged heating or a catalyst. Therefore, the following precautions must always be observed when storing MAA.

- MAA must be stored under air (not under inert gases as the stabiliser, hydroquinone monomethylether, is only effective in the presence of oxygen), in the dark at a temperature below 30°C. During long-term storage, stabiliser levels should be checked routinely.
- Heat and direct sunlight must be excluded, as these promote polymerisation.
- Provision should be made to keep the MAA above the freezing point. If frozen, MAA should be melted at room temperature (25°C) and material should not be withdrawn until it is entirely thawed and well mixed (to redistribute the stabiliser).
- MAA should be shipped in containers with a pressure relief valve to prevent the rupture of the container due to MAA polymerisation.
- Care should be taken to prevent contamination, as contaminants can render the stabiliser ineffective or can react with MAA and promote polymerisation.

10.2.3 Fire Safety and Extinguishants

MAA is classified as a highly flammable liquid. It can form an explosive mixture in air; adequate ventilation should be provided and smoking prohibited. Precautions should be maintained to eliminate all sources of ignition of MAA when in contact with air. MAA may polymerise on heating. Sealed containers may rupture if hot. Heat, UV-light, peroxide, azo-compounds, alkalis and oxidising agents may cause rapid polymerisation resulting in explosion. Fires can be extinguished with water, alcohol-resistant foam, dry powder or CO_2.

If fire does break out, neighbouring tanks and pipelines must be kept cool with plenty of water, otherwise the heat generated by the fire will cause their contents to polymerise.

10.2.4 Protection against Fire and Explosion

To avoid ignition, the following precautions are recommended.

- All plant and equipment should be explosion-proof as laid down in national standards

- All containers must be earthed
- All sources of ignition must be excluded
- No smoking is allowed
- No welding should be done until all tanks and pipelines have been drained and thoroughly flushed with water or hot caustic soda.

10.3 MANAGEMENT OF SPILLAGE AND WASTE

In all cases of spillage naked flames should be extinguished. Smoking and sparks must be avoided. Small spills of a few litres can be soaked up with suitable absorbent materials such as sand or earth. MAA should not be absorbed onto sawdust or other combustible materials. Larger spills must be prevented from spreading by the use of earth or sand and the material should be pumped into containers.

Surfaces contaminated with MAA should be washed well, first with alcohol and then with soap and water. All wastes should be sealed in vapour-tight plastic bags for eventual disposal.

MAA should not be allowed to drain into domestic sewers as serious explosion hazards could result. Local authorities should be informed immediately if spilt liquid MAA has entered surface water drains.

Waste quantities of MAA can be incinerated in accordance with local, state or national regulations. Empty storage drums must be decontaminated before recycling.

When aqueous waste containing MAA is discharged to adapted biological waste-water treatment plants it is expected to be mineralised. No disturbance of the bacterial activity of sewage treatment plants is expected if MAA is properly diluted.

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