European Chemicals Bureau

Institute for Health and Consumer Protection

European Chemicals Bureau

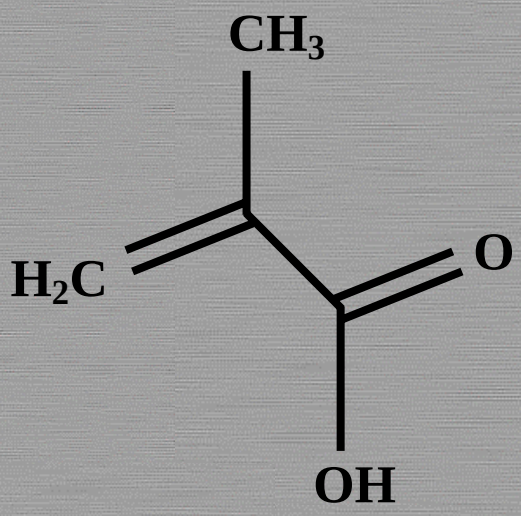
Existing Substances

European Union Risk Assessment Report

CAS No: 79-41-4

EINECS No: 201-204-4

methacrylic acid



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European Union Risk Assessment Report

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RISK ASSESSMENT

Cataloguing data can be found at the end of this publication

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METHACRYLIC ACID

CAS No: 79-41-4

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RISK ASSESSMENT

Final Report, 2002

Germany

The risk assessment of methacrylic acid (MAA) has been prepared by Germany on behalf of the European Union.

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Date of Last Literature Search:	**1995**
Review of report by MS Technical Experts finalised:	**1999**
Final report:	**2002**

(The last full literature survey was carried out in 1995 - targeted searches (for example on grouting) were carried out subsequently, and information found through scanning certain sources has also been included).

Foreword

We are pleased to present this Risk Assessment Report which is the result of in-depth work carried out by experts in one Member State, working in co-operation with their counterparts in the other Member States, the Commission Services, Industry and public interest groups.

The Risk Assessment was carried out in accordance with Council Regulation (EEC) 793/93[1] on the evaluation and control of the risks of "existing" substances. "Existing" substances are chemical substances in use within the European Community before September 1981 and listed in the European Inventory of Existing Commercial Chemical Substances. Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of these substances if they are produced or imported into the Community in volumes above 10 tonnes per year.

There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each substance on a priority list, a Member State volunteers to act as "Rapporteur", undertaking the in-depth Risk Assessment and recommending a strategy to limit the risks of exposure to the substance, if necessary.

The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[2], which is supported by a technical guidance document[3]. Normally, the "Rapporteur" and individual companies producing, importing and/or using the chemicals work closely together to develop a draft Risk Assessment Report, which is then presented at a Meeting of Member State technical experts for endorsement. The Risk Assessment Report is then peer-reviewed by the Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) which gives its opinion to the European Commission on the quality of the risk assessment.

If a Risk Assessment Report concludes that measures to reduce the risks of exposure to the substances are needed, beyond any measures which may already be in place, the next step in the process is for the "Rapporteur" to develop a proposal for a strategy to limit those risks.

The Risk Assessment Report is also presented to the Organisation for Economic Co-operation and Development as a contribution to the Chapter 19, Agenda 21 goals for evaluating chemicals, agreed at the United Nations Conference on Environment and Development, held in Rio de Janeiro in 1992.

This Risk Assessment improves our knowledge about the risks to human health and the environment from exposure to chemicals. We hope you will agree that the results of this in-depth study and intensive co-operation will make a worthwhile contribution to the Community objective of reducing the overall risks from exposure to chemicals.

Barry Mc Sweeney
Director-General
DG Joint Research Centre

Catherine Day
Director-General
DG Environment

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[1] O.J. No L 084, 05/04/199 p.0001 – 0075

[2] O.J. No L 161, 29/06/1994 p. 0003 – 0011

[3] Technical Guidance Document, Part I – V, ISBN 92-827-801 [1234]

0 OVERALL RESULTS OF THE RISK ASSESSMENT

CAS no:	79-41-4
EINECS no:	201-204-4
IUPAC name:	2-propenoic acid, 2-methyl
Synonyms:	methacrylic acid (MAA)

Environment

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

This conclusion applies to all environmental spheres regarded for the production and processing of methacrylic acid and the use of polymeric products made from methacrylic acid.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

This conclusion is reached because of concerns for effects on the aquatic ecosystem as a consequence of exposure arising from the use of acrylate based grouting agents.

During the use of a grouting agent containing hydroxyethylmethacrylate high concentrations of methacrylic acid are released via the drainage water. Due to the high mobility of methacrylic acid in soils, a potential for leaching to groundwater has to be expected. The exposure assessment for surface water was based on measured concentration at a tunnel construction site. A quantitative extrapolation to other construction sites seems not possible, but similar conditions might be anticipated. Data improvement is not the proposed option, because an environmentally safe handling of the grouting agent has to be achieved independent of the local circumstances. Therefore, risk reduction measures at Community level are recommended.

Human health

Human health (toxicity)

Workers

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

This conclusion is reached because of

- concerns for respiratory tract irritation as a consequence of short term inhalation exposure arising from the production, further processing as a chemical intermediate in the chemical industry, the manufacture of adhesives in the industrial area and the industrial and skilled trade use of adhesives,

- concerns for local respiratory effects as a consequence of repeated inhalation exposure arising from manufacture and use of adhesives.

Consumers

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Humans exposed via the environment

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Combined exposure

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Human health (risks from physico-chemical properties)

MAA has no explosive or oxidising properties due to structural reasons and is not highly flammable. Therefore with regard to the physico-chemical properties and with regard to the occupational exposure and consumer exposure, MAA is not expected to cause specific concern relevant to human health.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

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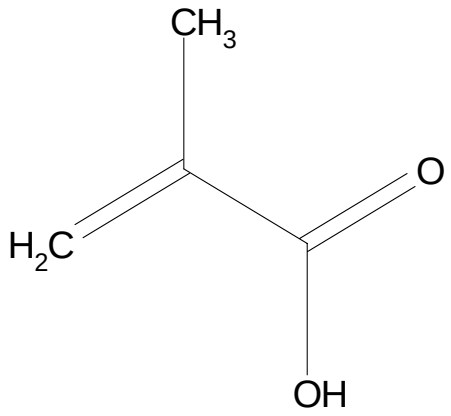
Euses Calculations can be viewed as part of the report at the website of the European Bureau:
http://ecb.jrc.it

TABLES

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS-No.: 79-41-4
EINECS-No.: 201-204-4
IUPAC name: 2-propenoic acid, 2-methyl
Synonyms: methacrylic acid (MAA)
Molecular weight: 86.09 g/mol
Molecular formula: $C_4H_6O_2$
Structural formula:



1.2 PURITY/IMPURITIES, ADDITIVES

Purity: > 99% w/w (Degussa, 1994a)
Impurity: ≤ 0.3% w/w distilled water (Degussa, 1994a)
≤ 1.5% w/w various ester adducts (ECETOC, 1995a; Ullmann, 1990)
α-hydroxyisobutyrate (traces)
Additives: ≤ 270 ppm hydrochinone and hydrochinone methyl ether or 4-methoxyphenol (stabilisers) (ECETOC, 1995a; Ullmann, 1990)

Table 1.1 Physico-chemical properties

Physical state	liquid at 20°C	
Melting point	14 - 16°C	Ullmann (1990); Kirk-Othmer (1981)
Boiling point	159 - 163°C at 1,013 hPa	Kirk-Othmer (1981); Merck Index (1983)
Relative density	1.015 at 20°C	Ullmann (1990); Merck Index (1983)
Vapour pressure	0.9 hPa at 20°C	Ullmann (1990); Perry (1984)
Surface tension	65.9 mN/m [1)]	Degussa (1995a)
Water solubility	89 g/l at 25°C	Riddick (1984)
Dissociation constant	pKa = 4.66	Kirk-Othmer (1981)
Partition coefficient	log Pow 0.93 at 22°C [2)] log Pow 0.99 [3)]	Sangster (1989); Meylan Howard (1995)
Flash point	77°C (open cup)	Ullmann (1990)
Flammability	365°C [4)]	BASF (1988)
Explosive properties	not explosive [5)]	Chemsafe (1994)
Oxidizing properties	no oxidizing properties [5)]	Chemsafe (1994)
Henry's law constant	0.087 ± 0.003 Pa · m^3 · mol^{-1}	

1) Experimental value (ring method)
2) Experimental value (shaking method); this value is used in the following risk assessment calculations.
3) Calculated value
4) Inition temperature according DIN 51794
5) No test conducted because of structural reasons

1.3 CLASSIFICATION

Classification according to Annex I of directive 67/548/EEC[4]:

Classification:	Xn; R21/22	Harmful in contact with skin and if swallowed
	C; R35 Note D	Corrosive; Causes severe burns
Labelling:	C R: 21/22-35	S: (1/2-)26-36/37/39-45

Concentration limits: $C \geq 25\%$; C; R21/22-35
$10\% \leq C < 25\%$; C; R35
$5\% \leq C < 10\%$; C; R34
$1\% \leq C < 5\%$; Xi; R36/37/38

According to the data presented below and to the criteria of the Directive 92/21/EEC, methacrylic acid has not to be classified as dangerous to the environment.

[4] The classification of the substance is established by Commission Directive 2001/59/EC of 6 August 2001 adapting to the technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 225, 21.8.2001, p.1).

2 GENERAL INFORMATION ON EXPOSURE

Data from 6 producers/importers are included in the IUCLID database. The maximum production volumes per site are from 5,000 up to 50,000 t/a. The maximum cumulative production volume from the indicated ranges amounts to 120,000 t/a. Up to 5,000 t/a are imported to the EU.

Figures on the actual production volume or production capacity are only provided by four producers. Taking into account these actual figures and the upper value of the ranges given by the other producers in IUCLID, a total production volume of 40,000 tons is calculated. Taking the import volume into consideration, 45,000 t/a are assumed to be available in the European market.

According to CEFIC (1995), the actual cumulative production volume was 34,800 tons in 1993.

For the generic local exposure assessment the maximum production volume of 50,000 t/a per site from IUCLID is used although the actual production volumes are significantly lower. This seems justified because the actual volumes may change within the indicated ranges given in IUCLID and it has been reported recently that methacrylate chemistry is an increasing market at least in Germany (Nachr.Chem.Tech.Lab., 1998). However, as with respect to the actual situation more specific data are available for the largest production site the generic scenario has not been carried through to risk characterisation.

The specific information from the production sites is taken into account for all other exposure scenarios and the calculations are based on a total volume of 40,000 t/a for production and 45,000 t/a for processing.

2.1 USES

According to CEFIC (1995), MAA is used as an internal and external intermediate in the chemical industry for the production of methacrylic acid 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. In addition, MAA is used in the preparation of carboxylated polymers and emulsion polymers for paints, adhesives and textile applications (ECETOC, 1996).

According to the 1996 ECETOC report (ECETOC, 1996) input of MAA is not needed for the production of the methyl ester (methyl methacrylate, MMA) although in the 1995 report (ECETOC, 1995) it is mentioned that MAA produced by other routes than described below (see production methods) serves as a key intermediate to MMA. However, it is understood that referring to the total production volume of MMA (470,000 t in 1996) only small amounts are produced via the free acid and that the applied MAA amount is covered in this assessment report.

The quantitative breakdown of the use pattern was estimated by CEFIC (1995) as follows:

Table 2.1 Use pattern

Type of use	appr. % in this application
Ester production	54
Dispersions (aqueous based polymers)	14
Polymers used as oil additives	8
Solid polymers, coatings, ionomers	13
Reactive resins/adhesives with 2 to 10% free MAA	2 (1% industrial, 1% skilled trade)
Sales (co-manufacturers, industrial users)	7
Export outside the EU	2

However, from specific information provided recently by the main producers it is most obvious that the figure for sales to co-manufacturers is greatly underestimated. From the available data it has to be concluded that ca. 2/3 of the total production quantity is sold to customers and not processed at the production sites. For the exposure assessment it is assumed that the percentages given for the different types of use are applicable for the amount processed externally (2/3) as it is for the amount of on-site processing (1/3).

A summary of the content of MAA in different products is presented in the Danish Product Register from January 1995 (no production in Denmark). The most frequent product types are paint, lacquers and varnishes, construction materials, binding agents and printing inks.

Table 2.2 Content of MAA in different products

Content of MAA in the product	number of products	quantity [t/a]
0 - 1%	284	8
1 - 10%	28	4
10 - 80%	7	
80 - 100%	1	
not determined	13	

In the Norwegian Product Register from 1994, 10 products containing a total quantity of 111 tons MAA are registered. The most frequent product types are anti-corrosion paint (40 t/a) and ship primers (40 t/a).

In the following table an overview is given on the main, industrial and use category combinations:

Table 2.3 Overview on the main, industrial and use category combinations

Main category (MC)	Industrial category (IC)	Use category (UC)
Isolated intermediate (1b)	chemical industry (3)	intermediate (33)
Isolated intermediate (1c)	chemical industry (3)	intermediate (33)
Inclusion into a matrix (2)	polymers industry (11)	intermediate (33)
Non dispersive use (3)	pulp, paper and board industry (12)	intermediate (33)
Non dispersive use (3)	paints, lacquers and varnishes industry (14)	intermediate (33)
Non dispersive use (3)	engineering industry (16)	adhesives (2)

From the information available it is not possible to give a quantitative breakdown of the amounts assignable to these categories. About 50 to 60% of the MAA produced is converted into different types of esters (IC 3) but most of these esters are used for the production of polymers, as it is the case for the free acid. Therefore, for the most part of MAA produced, IC 11 is applicable.

2.2 PRODUCTION METHODS

The majority of MAA is produced commercially via the acetone cyanohydrin route involving hydrolysis of methacrylamide sulphate. In another less important production process ethylene is used as feedstock producing MAA through an oxosynthesis by reaction of ethylene with formaldehyde and oxygen.

For MAA production a closed automated production process is used. The process is highly contained in order to minimise exposure to other very toxic chemicals used in the manufacturing process e.g. acetone cyanohydrin. Possible emission sources could occur during sampling, weighing, cleaning, reprocessing, disposal and maintenance operations (CEFIC, 1995). Due to the aqueous workup from the production process emissions via wastewater are expected to be relevant.

The esterification process is performed in a closed system, the conversion of MAA to its alkyl and hydroxy esters is very high, unreacted acid is recycled. Hydroxy methacrylates contain generally less than 0.1% MAA (CEFIC, 1995).

The production of polymers, emulsions or suspensions containing MAA as comonomer is performed in closed semiautomated systems. Unreacted MAA remains in the solid polymer, in the emulsions or in the water phase, which is treated in the wastewater treatment plant or is incinerated (CEFIC, 1995).

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Environmental releases

Releases of MAA into the environment are to be expected during production and processing with wastewater and, to a lesser extent, exhaust gases. Regarding the formulation step relevant releases may occur during the formulation of polymer dispersions.

Further releases are expected through residual monomeric MAA contents in the final products. According to the producers, methacrylates as final products contain generally less than 0.005% MAA. The residual monomer content of polymers manufactured from MAA and other monomers is expected to be between 0.001 and 0.4%.

From the use of grouting agents containing hydroxyethylmethacrylate releases of MAA to the hydrosphere occur via drainage water.

Direct releases to agricultural or natural soil are not expected.

3.1.2 Environmental fate

3.1.2.1 Degradation

Photooxidation

In the atmosphere, MAA will react with the photochemically produced hydroxyl radicals. The atmospheric half-life of MAA has been estimated to be 20 hours based upon atmospheric concentrations of $5 \cdot 10^5$ OH/cm^3 and 24 hours based upon atmospheric concentrations of $7 \cdot 10^{11}$ O_3/cm^3 (Atkinson, 1987). From these half-lifes an overall rate constant of 1.49 d^{-1} for photodegradation in the atmosphere is calculated.

Hydrolysis

Methacrylic acid is stable to hydrolysis at pH 3, 7 and 11 (T=25°C) over 28 days (MPA, 1990c). Hydrolysis will not be an important fate process.

Biodegradation

From the result of a Closed-Bottle-Test (OECD GL 301 D: 86% degradation after 28 days; 10-day window criterion was fulfilled), methacrylic acid can be considered as readily biodegradable in the aquatic compartment (MPA, 1992). Furthermore, results from non-standard tests are available which show high degradation rates of ca. 86% after 42 days (Pahren, 1961). 96% degradation after 2 days was observed in a Zahn-Wellens-Test.

Results from biodegradation simulation tests in WWTPs, in surface water and soil are not available. The respective degradation rates are estimated according to the procedure described in

Chapter 3, Subchapter 2.3.6 of the Technical Guidance Document (TGD). In Appendix A1, the calculations are presented.

Table 3.1 Estimated biodegradation rates

Compartment/medium	Biodegradation rate
Activated sludge (WWTP)	k_{WWTP} = 1 h^{-1}
Surface water	k_{sw} = 0.047 d^{-1}
Sediment	k_{sed} = 0.0023 d^{-1}
Soil	k_{soil} = 0.023 d^{-1}

3.1.2.2 Distribution

The Henry's law constant of H = 0.087 Pa·m^3/mol at 20°C suggests that MAA is only moderate volatile from water. Taking additionally into account the dissociation constant of MAA it can be concluded that evaporation from surface water to the atmosphere is not an important fate process.

The adsorption and desorption behaviour of MAA was investigated, according to EPA guidelines, in 5 different types of soil. The adsorption coefficient (K_p) ranged from 0.076 to 0.24 l/kg which indicates a high mobility of MAA through the soils. Once adsorbed, MAA was less readily desorbed from soil. Desorption coefficient ranged from 0.069 to 2.04 l/kg (MPA, 1990). Since no correlation between adsorption coefficient (K_p) and the organic carbon contents was observed, the method proposed in the TGD to estimate the partition coefficients in the different compartments using default organic carbon contents in the different compartments is not applicable. Therefore, a uniform K_p value was chosen to be used for all compartments (soil, sediment, suspended matter and sludge). Depending on the data basis on which the mean value is calculated (from all the measured adsorption and desorption coefficients or from the given ranges), the resulting values are 0.4 l/kg and 0.6 l/kg, respectively. For the risk assessment purpose an average K_p value of 0.5 l/kg was chosen.

Using the fugacity model of Mackay (level III, EQC-model), the theoretical distribution of MAA at equilibrium can be estimated:

Table 3.2 Estimation of the theoretical distribution of MAA at equilibrium

Compartment	Air	Water	Soil
%	2.9	97	0.1

Based on the physico-chemical properties of MAA, the hydrosphere is the preferred target compartment and the percentage for the water phase may even be underestimated considering the dissociation constant of the substance.

Elimination in WWTPs

Based on the above-cited physico-chemical properties (log H = -1; logPow = 0.93), as well as the biodegradation rate of 1 h^{-1} in WWTP, the elimination through biodegradation and distribution can be estimated with the model SIMPLETREAT 3.0 (1997):

Table 3.3 Estimation of the elimination through biodegradation and distribution

% evaporation to air	0
% release to water	12.6
% adsorption to sludge	0.1
% biodegradation	87.3
% removal from water	87.4

3.1.2.3 Accumulation

There are no experimental results on bioaccumulation available. The measured logPow of 0.93 does not indicate a high potential for bioaccumulation though.

According to the relation developed by Veith et al. (1979) and proposed in the TGD, a **BCF of 1.2 $l \cdot kg^{-1}_{wet\ fish}$** can be estimated for fish.

Although it has to be kept in mind that calculations on the basis of the logPow are in general not applicable for a dissociating substance like MAA, the overall result that bioaccumulation is of low concern for MAA is justified.

The average Kp value of 0.5 l/kg derived from experimental data indicates a low potential for geoaccumulation. Methacrylic acid released to soil may leach with seepage to the groundwater.

3.1.3 Aquatic compartment (incl. sediment)

Specific information from the production sites is taken into account for the exposure assessment. For those sites where no actual production volumes had been provided, the maximum values from the ranges given in IUCLID are used.

From these figures a cumulative production volume of 40,000 t/a is calculated and considering the import volume a total amount of 45,000 t/a for processing is assumed to be available in the European market.

3.1.3.1 Estimation of $Clocal_{water}$ / generic approach: production and processing

In the TGD a generic (i.e. non site-specific) exposure scenario (Emission Scenario Document, ESD) for the release into surface water of intermediates during production and processing is proposed.

As described in Section 2 for this generic local exposure estimation the maximum production volume of 50,000 t/a per site from the range given in IUCLID is used although the actual production volumes are significantly lower. However, as for the actual situation more specific

data are available for the largest production site (see below) the generic scenario has not been carried through to risk characterisation.

Using the default emission factors of 0.3% for production and 0.7% for processing, 300 days of emission per year, an elimination rate of 87.4% in WWTP according to SIMPLETREAT and a default river flow of 60 m^3/sec a $Clocal_{water}$ of app. 40 µg/l can be estimated. The calculations are presented in Appendix A2.

3.1.3.2 Estimation of $Clocal_{water}$ / site-specific approach: production and processing

Using the available specific data for the production sites, more precise PEC estimations can be performed. The site-specific production, processing and import volumes are confidential.

Unless further details are provided it is assumed that processing takes place at the same sites as production and the default emission factor from the TGD of 1% for production and processing is used.

If specific release data are available for a production site, in most cases the releases are attributable to production only because ca. 2/3 of the total production volume is sold for external processing. The further processing may either be ester production or polymerization.

If the site-specific flow rate of the receiving river is not known the default value of 60 m^3/sec from the Emission Scenario Document of the TGD is used.

The data basis used and the resulting calculated local concentrations are summarised in **Table 3.4**.

Table 3.4 Site-specific local releases from production and processing

Site	River flow	Release to WWTP	Release to hydrosphere	Specific data	$Clocal_{water}$ [µg/l]
A	specific	5.86 t/a	0.74 t/a	actual release estimated by the producer, but data basis for the assumptions made is not clear	0.03
		1%	6.3 t/a	default release	0.23
B	default	1%	6.3 t/a	default release, specific data on wastewater flow of WWTP	4.03
C	default	0.7%	4.4 t/a	default release for processing, no production at this site	2.84
D	specific	75 t/a	9.4 t/a	release estimation by the producer, specific data on wastewater flow of WWTP	0.49
E	specific		32 t/a *	release estimation based on measured effluent concentrations, no WWTP	220 (fresh water) * 81 (marine) *
F1	specific	0.5 t/a	0.06 t/a	release estimation by the producer, specific data on wastewater flow of WWTP	0.47
F2	specific	0.1 t/a	0.01 t/a	release estimation by the producer, specific data on wastewater flow of WWTP	0.0007

* The release amount is calculated on the basis of effluent monitoring performed during 1998. Weekly composite samples (n=55) were analysed with a detection limit of 1 mg/l. Concentrations in the positive samples (n=22) ranged between 2 mg/l and 119 mg/l with an average of 22 mg/l and a 90%ile of 44 mg/l. For the calculation of the annual release a concentration of 1 mg/l is assumed in the negative samples. The calculation of $Clocal_{water}$ is based on the average release concentration of 22 mg/l, which was exceeded during 5 weeks in 1998 and is considered to be the realistic worst case for the present situation at this site.

The outlet discharges into a man-made channel where a dilution of 1:2 with other discharge effluents can be assumed. This channel is essentially a dead water course and is not considered as an environmental protection target. It joins the estuary of a river after approximately 1.25 km. Two different estuary models are available to calculate the site-specific dilution in the receiving estuary, i.e. a Tideway 2DV model and a 3D model. The latter is not width-averaged and cannot take factors such as sediment oxygen demand or chemical processes into account, but is considered powerful enough for the estimation of the site-specific dilution.

From the Tideway 2DV model a worst-case dilution factor of 135 can be derived for the estuary. The 3D model provides dilution factors of <50 for about the first 3 km downstream from the mouth of the channel, 50-100 for a distance up to approximately 7-10 km downstream, 100-500 up to ca. 15 km and >500 further down.

For the river (fresh water) a dilution factor of 50 is chosen and the dilution factor of 135 from the 2DV model is used to derive a PEC representing the worst-case situation for marine waters.

3.1.3.3 Estimation of $Clocal_{water}$ / generic approach: processing by non producers/importers

MAA is also used as an external intermediate, i.e. considerable quantities are sold within the EU to non-producers/importers for processing at sites different from those considered above. The number of external sites and amounts of MAA handled there for polymerization or esterification are not known.

According to the use pattern presented in Section 2 (**Table 2.1**) it is assumed that 54% of the amount available to co-manufacturers is used for ester production (external polymerization is considered in Section 3.1.3.4 below).

For a worst-case scenario the following assumptions are made:

- 27,000 t/a are sold to co-manufacturers (ca. 2/3 of the production volume),
- 14,600 t/a hereof are used for ester production (54% according to use pattern),
- 4,800 t/a are handled at the main external site (1/3 of the total amount).

Using the same default values as described in Section 3.1.3.1 with no release for production, a **$Clocal_{water}$ of 2.7 µg/l** is estimated (for the calculation see Appendix A3).

3.1.3.4 Estimation of $Clocal_{water}$ / generic approach: use

Besides the ester production the manufacturing of polymers is the main application area for MAA. The ester production is already covered in the processing step above.

For the estimation of the releases from the manufacturing of polymers specific information about the MAA contents in the polymeric products provided by one company can be used (Röhm, 1995):

MAA is the minor monomeric component in the polymeric products. To obtain the polymeric portion of the different products, only about 0.5 to 1% of MAA is normally applied. In **Table 3.5**, for the three main types of products the data used to estimate the residual monomeric MAA amounts are presented:

Table 3.5 Polymeric products made from MAA

Type of product	Polymer dispersions	Solid polymers, coatings, ionomers	Polymer solutions
Amounts of MAA applied (see Table 2.1, use pattern)	6,300 t/a (14%)	5,900 t/a (13%)	3,600 t/a (8%)
Portion of polymeric material in the product	50%	100%	50%
Portion of MAA in the polymeric material	1%	0.7%	0.5%
⇒ Tonnage of product obtained	1,260,000 t/a	850,000 t/a	1,440,000 t/a
Average residual monomeric MAA-content in the product	5 ppm	35 ppm	80 ppm
⇒ Residual monomeric MAA	6 t/a	30 t/a	115 t/a

For the estimation of the local concentrations in surface water the following exposure scenarios and respective amounts of MAA and polymeric products are considered relevant:

Table 3.6 Exposure scenarios and respective amounts of MAA and polymeric products

Application area	Percentage of total MAA tonnage	Amount of monomeric MAA applied	Tonnage of polymeric products	Scenario (emission table, TGD)
Dry polymerization	13% + 8%	9,500 t/a	2,290,000 t/a	A/B-Table A3.10, B3.9
Wet polymerization	14%	6,300 t/a	1,260,000 t/a	A/B-Table A3.10, B3.9
Formulation of paints	14%	6,300 t/a	1,260,000 t/a	ESD IC-14 and A/B-Table A2.1, B2.3
Paper recycling	ca. 1/3 of 13%	2,000 t/a	280,000 t/a	ESD IC-12

From dry polymerization no relevant releases with wastewater into the aquatic compartment have to be assumed (emission factor = 0 according to the TGD, Table A3.10).

For wet polymerization a default calculation according to the TGD implies the following assumptions:

- Tonnage of product: ca. 1,260,000 t per year
- ⇒ fraction of main source: 0.05 (TGD, Table B3.9), emission episode: 300 d/a
- Tonnage of MAA: 6,300 t/a
- ⇒ local tonnage of MAA at the biggest site = ca. 315 t/a
- Emission factor: 0.01 (TGD, Table A3.10), standard WWTP: 2,000 m^3/d
- Elimination in WWTP: 87.4%, dilution in surface water 1:10.

The respective calculation is presented in Appendix A4, a **$Clocal_{water}$ of 66 µg/l** is estimated.

Due to actual data provided by industry it is possible to supplement the generic scenario by specific information on this downstream use. The volumes of MAA applied for wet polymerization were provided for 28 European sites covering a total annual amount of 8,120 t MAA.

Table 3.7 Volumes of MAA applied for wet polymerization

Number of plants	14	10	2	2
Annual use of MAA	< 100 t/a	100-500 t/a	500-1,000 t/a	> 1,000 t/a

For four sites covering a total amount of app. 775 t/a zero release to the hydrosphere had been confirmed as a wastewater reutilization/recycling-system is employed.

For all remaining sites where more than 100 t MAA are known to be annually handled a calculation of the $Clocal_{water}$ is performed:

Table 3.8 Calculation of the $Clocal_{water}$

Site	$Clocal_{water}$
G	147 µg/l
H	95 µg/l
I	74 µg/l
K	53 µg/l
L	42 µg/l
M	36 µg/l
N	21 µg/l
O	0.7 µg/l
P	0.4 µg/l
Q	0.3 µg/l
R	0.1 µg/l
S	0.1 µg/l

The above-compiled results of C_{local} calculations are based on site-specific volumes, site-specific information on wastewater treatment and dilution, as far as available, and default release factors. The underlying site-specific data are confidential.

For the formulation of paints it is assumed that the total amount of aqueous based polymers produced from MAA in the EU (1,260,000 t/a) are used for this application.

There is an emission scenario document for paints, laquers and varnishes (ESD IC-14) proposed in the TGD, but for the use of this ESD the type of paint under consideration has to be identified and the type and application area of the MAA-containing paints are not known.

However, for non-volatile water-soluble components in the ESD the localised emissions from the formulation step are in the range of 1-2% and this is in good accordance with the emission factor of 0.02 (2%) proposed in the TGD, Table A2.1 for fomulation which is used for the calculation.

Altogether for paint formulation the following assumptions are made:

- Tonnage of product: ca. 1,260,000 t per year
- ⇒ fraction of main source 0.4 (TGD, Table B2.3), emission episode: 300 d/a
- Residual monomeric MAA content: 5 ppm (6 t/a, 2.4 t/a at the biggest site)
- Emission factor 0.02 (TGD, Table A2.1), standard WWTP: 2,000 m^3/d
- Elimination in WWTP: 87.4%, dilution in surface water 1:10.

The respective calculation is presented in Appendix A5, a **$Clocal_{water}$ of 1 µg/l** is estimated.

The private use of paints seems not to be a relevant path of exposure because only small amounts of residual monomeric MAA (at maximum 6 t/a) are handled annually for this kind of wide dispersive use. Therefore a quantitative local exposure assessment is not performed.

As MAA-based polymers are used for coatings of paper, the residual MAA monomer may be released during the paper recycling process. Neither the amount of MAA used for paper coating products, nor the amount of paper coating products containing MAA is known.

According to the use pattern presented in Section 2 and the information available on the polymeric products, in a first approach it is assumed on a worst-case basis, that app. 1/3 of the total amount of polymeric product of this scope (1/3 of 850,000 t/a = 280,000 t/a) is relevant for paper coating products.

To estimate the emissions during the paper recycling process an emission scenario document for the pulp, paper and board industry (ESD IC-12) is proposed in the TGD.

According to this, the following assumptions are made for the calculation:

- Residual monomeric MAA content: 35 ppm (9.8 t/a)
- Recycling rate: 50%, de-inking rate: 90%, fraction not adsorbed 20%
- Emission episode: 250 d/a
- Number of sites: 35 (i.e. 10% of all European paper recycling facilities)
- Standard WWTP: 2,000 m^3/d, elimination in WWTP: 87.4%, dilution in surface water 1:10.

The respective calculation is presented in Appendix A6, a **$Clocal_{water}$ of 0.6 µg/l** is estimated.

3.1.3.5 Monitoring data

No monitoring data in the aquatic environment are available.

MAA measurements had been performed in the drainage water from a tunnel construction site in Norway. During the application of a grouting agent containing hydroxyethylmethacrylate high concentrations of MAA were found in the drainage water of the tunnel.

During application of the product (a total amount of 57 t, about 10 t per injection) MAA concentrations up to 4 mg/l were detected in the drainage water. After injection was terminated, the concentrations decreased rapidly (within one week) to a level around 50 µg/l. After the last two injections concentrations remain higher, between 100-200 µg/l.

The drainage water was collected in a treatment plant and the effluent concentrations were analysed. In general, MAA concentrations did not exceed 20 µg/l, but when the influent concentrations were above 1,000 µg/l MAA elimination was not significant and during the

injection periods (about 2 weeks per injection) effluent concentrations between 1,000 and 4,000 µg/l were measured.

These values represent a site-specific situation and extrapolation to other tunnel constructing sites may not be adequate due to varying draining conditions. However, the alkaline milieu (pH values between 9 and 12), which is responsible for the formation of MAA from the hydroxyethylesters is most likely at all construction sites where cement is used.

From the measured effluent concentrations the $Clocal_{water}$ in the receiving surface water can be calculated. The effluent is transported via the river Alna into the *Oslofjord*. As the Alna is partially covered by casing, it may not represent the ecosystem to be protected. The concentrations in the *Oslofjord* can be estimated using a default dilution factor of 10 for dilution in the Alna and an additional factor of 10 for dilution in the *Oslofjord*.

According to the available reports on the tunnel construction site (Aquateam, 1999) the calculation can also be performed on the basis of specific information on dilution. The annual average flow of the Alna of 75,000 l/min is devided by a factor of 3 to estimate a low flow of 25,000 l/min according to the TGD. The average flow of drainage water during the construction period (nearly one year) was 2,550 l/min. Dilution factors for the Alna in the *Oslofjord* are available for different distances from the mouth of the Alna.

Regarding a realistic worst-case situation the measured effluent concentration of 4 mg/l is used for the calculations of the $Clocal_{water}$:

Table 3.9 Calculation of the $Clocal_{water}$

Distance	100 m	200 m	300 m	400 m	500 m	default
Dilution factor	2	6	9	13	18	10
$Clocal_{water}$	204 µg/l	68 µg/l	45 µg/l	31 µg/l	23 µg/l	40 µg/l

3.1.3.6 Sediment

As neither monitoring data on concentrations of MAA in sediment nor experimental results with benthic organisms are available and there is no evidence for relevant adsorption of MAA onto sediment, there is no need for performing a quantitative risk assessment for this compartment. In addition, as MAA dissociates in water and no correlation had been found between adsorption and organic carbon content for this substance the standard estimation method proposed in the TGD seems not applicable.

3.1.4 Atmosphere

As there is no emission scenario document available to estimate the releases into the atmosphere of intermediates during production and processing the emission tables of the TGD can be used.

For the generic exposure assessment the maximum production and processing volume per site of 50,000 t/a as given in the IUCLID data base is used. It is assumed that dedicated equipment is used and production proceeds in closed systems (TGD, main category 1b for production, Table A1.2 and main category 1c for processing, Table A3.3).

As the vapour pressure at 20°C is in the range of 10 to 100 Pa, a release fraction of 0.00001 during production and 0.00001 during processing is proposed.

This results in a release amount of 1 t/a and additional releases to air from the WWTP are not expected (see SIMPLETREAT estimation).

Assuming 300 d of emission per year, a concentration in air in the vicinity of that site of 0.9 µg/m^3 is calculated. **$Clocal_{air}$ = 0.9 µg/m^3**

The total deposition rate during emission episode amounts to **DEPtotal = 1.3 µg · m^{-2} · d^{-1}.**

The total annual deposition rate amounts to **$DEPtotal_{ann}$ = 1.1 µg · m^{-2} · d^{-1}**.

The respective calculations are presented in Appendix A7.

The above-presented generic scenario represents a worst-case scenario for production sites and may not reflect the actual situation in Europe, but nevertheless seems justified because the actual volumes may change within the indicated ranges given in IUCLID and it has been reported recently that methacrylate chemistry is an increasing market.

In comparison to the generic approach, from one production site a total release of MAA and its methyl ester of app. 2 t/a is reported, but MAA will contribute to a minor extent to the total release amount. From several other production sites even lower releases are reported. However, more precise site-specific local exposure estimations will only become necessary if from the generic scenario a risk to the environment is deduced.

For the regional exposure assessment (see Section 3.1.7) the actual European production and processing volumes are used.

Local exposure of the atmosphere from wet polymerization by downstream users has to be considered as well. The appropriate emission factor proposed in Table A3.10 of the TGD is 0.001 for wet and dry polymerization processes.

For a plant annually processing 1,000 t MAA (realistic worst case based on specific data, see Section 3.1.3.4) emissions of 1 t/a are estimated. This is exactly the same amount as estimated from the generic scenario for production presented above. Therefore, an additional exposure calculation is unnecessary and the results from above are considered qualified for risk assessment purpose.

Local exposure of the atmosphere from the manufacturing, formulation and use of polymers is expected to be significantly below the generic emissions calculated above and therefore quantification seems not necessary.

3.1.5 Terrestrial compartment

The release of MAA to soil is expected to occur through atmospheric deposition after local release to the atmosphere at the production and processing sites. The input through sludge application on agricultural soil is considered negligible, as MAA does not partition to a significant extent to sewage sludge in the WWTP (see SIMPLETREAT estimation).

With the worst-case deposition rate calculated above of **$DEPtotal_{ann}$ = 1.1 µg · m^{-2} · d^{-1}** the maximum equilibrium soil concentration in the vicinity of production/processing plants can be

calculated according to the procedure proposed in the TGD. The calculations are presented in Appendix A8, the resulting concentrations in natural soil and agricultural soil are equal.

bulk soil concentration: **$Clocal_{soil}$ = 0.12 µg/kg ww = $Clocal_{agr.soil}$**

porewater concentration: **$Clocal_{soil\text{-}porew}$ = 0.2 µg/l = $Clocal_{agr.soil\text{-}porew}$**

3.1.6 Secondary poisoning

MAA does not present indications of bioaccumulation potential. Therefore, a quantitative risk assessment for secondary poisoning is not required.

3.1.7 Regional concentrations

For the estimation of the regional background concentrations, all releases, from diffuse as well as point sources have to be taken into account. According to the TGD it is normally assumed that 10% of the total release volume is emitted into the defined EU standard regional model. However, from the specific data available for MAA production and processing it is more realistic to assume that 1/3 of the total amounts are attributable to a region and 2/3 to the remaining continent. For external processing and use the default distribution of 10% into the region and 90% into the continent is applicable.

Point releases to the aquatic compartment

In Sections 3.1.3.2 to 3.1.3.4 releases to the aquatic compartment from point sources are estimated. In **Table 3.10**, all release amounts are compiled:

Table 3.10 Compilation of all release amounts

Site / scenario	Emissions to water with WWTP-effluent	Direct emissions to water
A	0.7 t/a	--
B	6.3 t/a	--
C	4.4 t/a	--
D	9.4 t/a	--
E	--	32 t/a
F	0.1 t/a	--
External processing	12.9 t/a	--
Wet polymerization	8.9 t/a	--
Paint formulation	<0.01 t/a	--
Paper recycling	<0.01 t/a	--

For external processing (ester production) the releases are calculated on the basis of the total amount of 14,600 t/a applied, the default release factor of 0.7% and an elimination of 87.4% in the treatment plants.

For external wet polymerization the releases are calculated on the basis of the total amount of 7,825 t/a applied minus 775 t/a for which zero release to hydrosphere was confirmed. The default release factor of 0.01 and an elimination of 87.4% in the treatment plants were assumed.

A total amount of 75 t/a is estimated to be released to the aquatic compartment through point sources. For the distribution to regional and continental model see below.

Point releases to air

The default release fractions to air for production (0.00001) and processing (0.00001) are used. For a maximum production volume of 40,000 t/a and a processing volume of 35,000 t/a the releases into the atmosphere amount to 0.75 t/a.

A processing volume of 35,000 t/a is used because app. 10,000 t/a out of the total amount processed in Europe (45,000 t/a) are covered by the polymerization scenario below.

From the polymerization step a releases fraction to the atmosphere of 0.001 is estimated according to Table A3.10 of the TGD. Assuming a total amount of 15,800 t/a MAA used for polymer production (14% + 13% + 8%) and further assuming that 1/3 of it is polymerized on site at the production plants (those emissions are already included in the processing step above), about 10,000 t/a are polymerized elsewhere and a total release of 10 t/a is estimated.

Releases to air from the further processing and formulation of polymers are expected to be low. Diffuse releases from the use of the polymeric products are taken into account below.

Point releases to soil

No direct point releases to soil were identified.

Diffuse releases

Diffuse releases are to be expected from residual monomeric MAA in the polymeric products. An estimation of the amounts of MAA in the polymeric products could be made with the information from the product registers (see Section 2). However, it is not evident whether the recorded contents of MAA in the products are uniformly attributed to the monomeric or to the polymeric substance.

A more reliable estimation of the diffuse releases can be performed on the basis of specific information about the polymeric products provided by one company (Röhm, 1995) and presented in **Table 3.5**, Section 3.1.3.4.

From the known average residual monomeric MAA content in the three main types of products the maximum tonnage MAA released to the environment can be estimated.

Table 3.11 Residual monomeric MAA content in the three main types of products

Type of product	Polymer dispersions	Solid polymers	Polymer solutions
Residual monomeric MAA	6 t/a	30 t/a	115 t/a

About 150 t/a of monomeric MAA are calculated to be contained in the polymeric products available in the European market.

During use and disposal of the products the residual monomer can be washed out or evaporate. It is assumed that 80% of the monomer (120 t/a) is released during use and disposal and that 20% remains in products which are incinerated.

As the aquatic compartment is the target compartment of MAA, it is assumed that 75% of the releases (90 t/a) occur into the hydrosphere and 25% (30 t/a) into the atmosphere.

With a connection rate of 70% to WWTPs, 27 t/a are calculated to be released directly and 63 t/a into WWTPs of which 8 t/a (12.6%) are released with the effluent to surface water.

As it was mentioned at the beginning of this section for production and on site processing 1/3 of the point-source releases are assumed to occur into a region. This is done on the basis of specific data on plant sizes available.

From external processing, formulation and use according to the TGD only 10% of the point-source releases are allocated to the region. From the diffuse releases likewise 10% are considered for the region.

In **Table 3.12**, the releases used for the calculation of the regional PEC are summed up:

Table 3.12 Releases used for the calculation of the regional PEC

Compartment	Total releases [t/a]	Regional [t/a]	Continental [t/a]
Air (production sites)	0.8	0.3	0.5
Air (external processing)	10	1	9
Air (diffuse releases)	30	3	27
Total	41	4	37
Soil	-	-	-
Water (direct)	32 + 27 = 59	0 * + 3 = 3	32 * + 24 = 56
WWTP (production sites)	167	55.7	111.3
(external processing)	175	17.5	157.5
(diffuse releases)	63	6.3	56.7
Total	405	80	325
Water (WWTP effluent) (production sites)	21	7	14
(external processing)	22	2	20
(diffuse releases)	8	0.8	7.2
Total	51	10	41

* Site E is emitting into an estuary of a river. The releases are not assumed to occur into the region to avoid an unrealistic worst case. However, site E is located in a highly industralised region and the releases are considered for the continent. This is done to be consistent with the TGD approach for fresh water, where the continental contribution of releases into one river to the regional background concentration of another river is not dependant on the geographic connections between the rivers.

In addition, it seems not appropriate to link the decision of whether or not to consider releases for the continent to a fixed distance between the point of discharge and the mouth of the river.

In Appendix A9, the input and output figures of a Simple Box 2.0 calculation adapted to the TGD and EUSES 1.00 are presented. (The results of this calculation are consistent with EUSES). The resulting regional concentrations are:

$$\mathbf{PECregional_{aquatic}} = \mathbf{0.14\ \mu g/l}$$

$$\mathbf{PECregional_{air}} = \mathbf{0.1\ ng/m^3}$$

$$\mathbf{PECregional_{agr\ soil}} = \mathbf{3\ ng/kg\ ww}$$

$$\mathbf{PECregional_{agr\ soil\ porewater}} = \mathbf{5\ ng/l}$$

3.2 EFFECTS ASSESSMENT: HAZARD IDENTIFICATION AND DOSE CONCENTRATION) - RESPONSE (EFFECT) ASSESSMENT

3.2.1 Aquatic compartment

Available effect data

Only few toxicity tests with aquatic organisms are available. Recently, effects of methacrylic acid on algae have been investigated in more detail. The relevant results for the effects assessment of methacrylic acid are listed below.

Table 3.13 Toxicity data for aquatic organisms

Species	Endpoint	Effect Conc.	Reference
Oncorhynchus mykiss	96-h LC_{50}	85 mg/l	MPA (1990a)
Brachydanio rerio	96-h LC_{50}	>100 <180 mg/l	Degussa (1990a)
Leuciscus idus	48-h LC_{50}	224 mg/l	Röhm (1987)
Daphnia magna	48-h EC_{50} 24-h EC_{50}	>130 mg/l >100 <180 mg/l	MPA (1990b) Degussa (1990b)
Daphnia magna	21-d NOEC (parent mortality, reproduction rate)	53 mg/l	MPA (1995)
Selenastrum capricornutum	96-h EC_{50} 96-h NOEC	0.59 mg/l 0.38 mg/l	MPA (1990e)
Selenastrum capricornutum	72-h E_rC_{50} 72-h E_bC_{50} 72-h NOEC	45 mg/l 20 mg/l 8.2 mg/l	Zeneca (1999)

The acute toxicity of methacrylic acid (MAA) to *Oncorhynchus mykiss* was investigated in a flow-through system according to a US EPA guideline (MPA, 1990a). After 96 hours a LC_{50} of 85 mg/l was derived, based on measured concentrations.

Mortality occurred at the highest test concentration of 97 mg/l only, first after 48 hours. At lower concentrations sublethal/behaviorial responses as surfacing, quiescence, fish on bottom of test vessel, labored respiration, loss of equilibrium and excitability were noted among all fish starting at 23 mg/l, observable after 24 hours already.

The pH decreased slightly with an increase in MAA concentration from 7.8 in the control up to 5.3 in the highest test concentration. Therefore it cannot be excluded that mortality was influenced by the low pH value.

In a semi-static OECD guideline test with *Brachydanio rerio* the concentration-effect relationship was not suitable for an exact calculation of a LC_{50} (Degussa, 1990a). The value is located between 100 and 180 mg/l MAA (nominal concentrations) after 96 hours. Up to 100 mg/l no mortality and no abnormal conditions of the fish could be observed visually. 180 mg/l caused 100% mortality after 4 hours already. But at this concentration the pH was $\leq$ 5.1 and therefore it is possible that this might be due to a pH effect.

For *Leuciscus idus melanotus* a LC_{50} of 224 mg/l was calculated after 48 hours (Röhm, 1987). At a nominal concentration of 250 mg/l MAA all of the fish were dead, at 200 mg/l no mortality occurred. A German standard method was used where the pH was adjusted at 7.7.

For *Daphnia magna* acute toxicity was investigated in a flow-through test with US EPA standard conditions (MPA, 1990b). No EC_{50} for immobilisation was reached after 48 hours at the highest measured concentration of 130 mg/l and no abnormal effects could be observed. The pH-values were measured between 7.9 and 7.0 at the end of the test, decreasing with increasing MAA concentration.

According to another test after 24 hours an EC_{50} value for *Daphnia magna* can be estimated between 100 and 180 mg/l MAA (nominal concentration, Degussa, 1990b). At 180 mg/l all daphnids were immobile, but this might be due to a pH effect as a pH in the range of 4.8 - 5.0 was measured. At 100 mg/l only 10% immobilisation was observed and the mobile daphnids moved somewhat irregularly and slowly (pH = 6.0 - 7.5). The pH of the control was 7.8.

A long-term study was conducted with *Daphnia magna* in a flow-through system (OECD 202, MPA, 1995). After 21 days no influence on parent mortality and reproduction rate could be observed at a measured concentration of 53 mg/l MMA. At 110 mg/l all daphnids were dead at the end of the test period. During the test the pH-values ranged from 6.6 to 7.6 at 53 mg/l and from 5.6 to 7.0 at 110 mg/l so that the toxicity effects can be ascribed to MMA.

Conflicting test results are available on MAA algae toxicity with *Selenastrum capricornutum*:

In a study conducted according to US EPA/ASTM protocols, an EC_{50} of 0.59 mg/l and a NOEC of 0.38 mg/l were derived for reduction of biomass after 96 hours test duration. The 72-hour values were 0.62 and 0.38 mg/l, respectively. These are nominal concentrations and at the end of the test MAA concentrations were below the detection limit of 0.1 mg/l (MPA, 1990e, further referred to as ABC study). It has to be noted, that reported pH values are remarkably low in all treatments. However, at low test concentrations it is not likely that the results are related to pH effects. Significant inhibition of cell multiplication by 90% is observed at 0.75 mg/l and pH 5.9, whereas at 0.38 mg/l and pH 6.0 no effects at all are reported after 96 hours. (For comparison, 3.0 mg/l MAA led to a pH of 4.5).

A more recent investigation (ZENECA, 1999a-d) revealed about 25-fold higher effect concentrations. The ZENECA study was done according OECD testing guideline 201 (with slightly modified medium to resemble ABC study) and it comprised various experimental conditions, namely open and closed vessels, Ca^{++} augmentation, and several approaches of pH adjustment. These experimental variations had been applied with the aim of clarifying possible reasons for high MAA toxicity reported in the ABC study.

A number of particulars have been addressed regarding the conflicting results of the various ZENECA test runs compared to the ABC study (cf. also **Table 3.14**).

- Considering the physico-chemical properties of MAA (complete dissociation at test pH, low volatility even of undissociated form), reported differences of MAA loss in open and closed vessels do not enable a satisfying explanation for possible reasons of MAA disappearance; lowest recovery rates are reported at low test concentrations.

- Water hardness (Ca^{++}) provides no sufficient explanation for different algal sensitivities to MAA, comparing both tests under discussion (NOEC 0.38 mg/l versus about 9 mg/l, the latter only slightly increased with Ca^{++} augmentation).

- pH effects are not identified as relevant cause for reported effects at test concentrations not exceeding 10 mg/l (data for treatment 9.8 mg/l, non-pH adjusted: pH 6.5 (day 0) up to pH 7.6 (day 3), 100% of control growth rate).

- An additional range finding test has been conducted to specifically address the question if pH values only slightly above 6 might be an important reason for increased MAA toxicity due to lower dissociation rates of MAA. At test start, pH was adjusted to ca. 6.3 in all treatments. Light intensity and cell inoculum density had been reduced to avoid quick pH increase (ZENECA, 1999d). The lowest test concentration of 5 mg/l caused no effects and the EC values provisionally calculated from the raw data via probit transformation differed only slightly from the other ZENECA test variations so that no explanation for much lower EC values of the ABC study was provided.

In conclusion, some unknown experimental particulars of the ABC study are regarded as a cause for considerably increased MAA toxicity. Since these experimental particulars could neither be identified nor be reproduced, the ABC study results are not used for PNEC derivation on a weight of evidence basis.

A number of EC values are reported for the various test runs of the ZENECA study and compiled in **Table 3.14**. Among these data, the $E_{growthrate}C_{10}$ (8.2 mg/l) from the closed vessel test run is considered as most relevant.

Table 3.14 Experimental details and results of algae toxicity tests with *Selenastrum capricornutum*

	Open vessels non-pH adjusted *	Open vessels pH 6.3 adjusted (range finding **)	Open vessels not pH adjusted	Open vessels neutral pH-adjusted	Closed vessels	Closed vessels (preliminary run)	Closed vessels, Ca^{++} augmented (preliminary run)
Reference	ABC (1990)	ZENECA (1999d)	ZENECA (1999b)	ZENECA (1999b)	ZENECA (1999c)	ZENECA (1999a)	ZENECA (1999a)
pH start (respective MAA concentration)	4.1 (6.0 mg/l) up to 7.5 (control)	6.27 (5.0 mg/l) up to 6.32 (50 mg/l)	3.99 (100 mg/l) up to 7.29 (control)	6.84 (18 mg/l) up to 7.42 (230 mg/l)	6.39 (105 mg/l) up to 8.21 (2 mg/l)	no data	no data
pH end (respective MAA concentration)	4.0 (6.0 mg/l) up to 7.2 (control)	7.29 (control) up to 7.81 (50 mg/l)	3.95 (100 mg/l) up to 9.39 (1.6 mg/l)	7.48 (230 mg/l) up to 9.04 (control)	6.11 (105 mg/l) up to 9.69 (control)	no data	no data
nominal test concentrations [mg/l]	0.38 - 0.75 - 1.5 - 3.0 - 6.0	5.0 - 25.0 - 50.0	0.86 - 1.9 - 4.1 - 9.1 - 20 - 45 - 100	9.1 - 20 - 45 - 100 - 220	0.86 - 1.9 - 4.1 - 9.1 - 20 - 45 - 100	0.86 - 1.9 - 4.1 - 9.1 - 20 - 45 - 100	
MAA loss i.e. % loss in measured conc. over test duration (at nominal MAA conc. given in brackets)	100 (all concentrations)	no data	0 (100 mg/l) up to 67 (4.1 mg/l)	0 (100, 220 mg/l) up to 67 (9.1 mg/l)	-11 (increase) (1.9 mg/l) up to 17 (4.1 mg/l)	-2 (increase) (4.1 mg/l) up to 100 (20 mg/l)	0 (100 mg/l) up to 100 (20 mg/l)
Effect data							
EC values based on	nominal test concentrations	nominal test concentrations	nominal test concentrations	nominal test concentrations	mean measured concentrations (i.e. mean of all measurements at beginning and end of test run)	nominal test concentrations	nominal test concentrations
E_rC_{50} [mg/l]	0.6	33	14	160	45	54	not included in preliminary test protocol – according to raw data, the corresponding EC values are higher than without Ca-augmentation, but ranging in the same order of magnitude
NOE_rC [mg/l]	0.38	13.6	9.8	18	8.2	9.1	
E_bC_{50} [mg/l]	not included in test protocol	15.4	10	41	20	not included in preliminary test protocol	
NOE_bC [mg/l]	0.38	6.2	9.8	-	8.2		

* Remark: NOEC 0.38 mg/l (pH 6.1 [0h] pH 6.0 [96h]), LOEC 0.75 mg/l (> 90% inhibition at pH 5.9 [0 and 96h])

** EC_{50} and EC_{10} provisionally calculated via probit transformation

Determination of $PNEC_{aqua}$

Results from acute tests with species from 3 trophic levels are available. In addition, for daphnia a prolonged toxicity test is available. The lowest test result considered relevant for PNEC derivation was recorded with algae (*Selenastrum capricornutum*: $E_{growthrate}C_{10}$ = 8.2 mg/l).

For the determination of the PNEC this EC_{10} is regarded as a long-term NOEC test result, according to the TGD. An assessment factor of 50 is proposed for a data basis like the one available for MAA.

Therefore: **$PNEC_{aqua}$ = 8.2 mg/l / 50 = 164 µg/l**

Determination of $PNEC_{microorganisms}$

A cell multiplication inhibition test (German standard guideline) was performed with *Pseudomonas putida* (Degussa, 1992). In a neutralized medium an EC_{50} value of 270 mg/l and an EC_{10} of 100 mg/l (nominal) were measured after 16.5 hours. The pH was 7.1 in the control, 6.5 at 320 mg/l MAA and 6.0 at 1,000 mg/l.

From another test using acidic solutions with pH values of 3.4 to 4.7 ten times lower effect values are reported.

According to the procedure described in the TGD for assessing the toxicity of a substance to microorganisms, an assessment factor in the range of 1 to 100 is applied for tests on microorganisms with different sensitivity and different endpoints.

To determine the $PNEC_{microorganisms}$, an assessment factor of 1 is applied to the NOEC value of 100 mg/l with *Pseudomonas putida* according to the TGD.

Therefore: **$PNEC_{microorganisms}$ = 100 mg/l / 1 = 100 mg/l**.

Sediment

As neither monitoring data on concentrations of MAA in sediment nor experimental results with benthic organisms are available, and as there is no evidence for relevant adsorption of MAA onto sediment, there is no need for performing a quantitative risk assessment for this compartment.

3.2.2 Atmosphere

It is not possible to derive a PNEC for the atmospheric compartment due to the lack of experimental data.

3.2.3 Terrestrial compartment

Data on effects to terrestrial organisms are not available. In an indicative risk assessment for the soil compartment, the aquatic PNEC will be used and compared to the concentration in soil pore water:

$PNEC_{soil}$ = 164 µg/l (soil pore water)

3.2.4 Secondary poisoning

MAA does not present an indication of a bioaccumulation potential. An effect assessment for secondary poisoning is not required.

3.3 RISK CHARACTERISATION

3.3.1 Aquatic compartment

Wastewater treatment plants

Because of the significant differences in responsibilities, functional control measures and data quality the possible risk to microorganisms is evaluated separately for municipal and industrial wastewater treatment plants.

The following effluent concentrations were calculated for the standard treatment plants of 2,000 m^3/d which might be considered as municipal plants. For the downstream use of wet polymerization besides the default scenario the specific site G was chosen to represent the worst case:

$PEC_{microorganisms}$	=	**0.66 mg/l**	(external wet polymerization, default)
$PEC_{microorganisms}$	=	**4 mg/l**	(external wet polymerization, site G)
$PEC_{microorganisms}$	=	**10 µg/l**	(formulation of paints)
$PEC_{microorganisms}$	=	**6 µg/l**	(paper recycling)

The assessment for industrial treatment plants is carried out with the worst-case effluent concentration calculated on the basis of default releases and specific data on the size of the treatment plant:

$PEC_{microorganisms}$	=	**1 mg/l**	(industrial plant)

With a **$PNEC_{microorganisms}$** of **100 mg/l**, for all considered scenarios the PEC/PNEC ratio is below one and therefore a risk to microorganisms in WWTPs is not expected (**conclusion (ii)**).

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Surface waters

In **Table 3.15**, the comparison between PEC and PNEC (164 µg/l) for all relevant exposure scenarios is presented:

Table 3.15 Comparison between PEC and PNEC for all relevant exposure scenarios

Scenario	C_{local} + $PEC_{regional}$ = PEC_{local} [µg/l]	PEC/PNEC
Production and processing site:		
A	0.2 + 0.1 = 0.3	<0.01
B	4.0 + 0.1 = 4.1	0.03
C	2.8 + 0.1 = 2.9	0.02
D	0.5 + 0.1 = 0.6	<0.01
E	220 (fresh water)	1.3
	81 (marine waters)	0.5
F	0.5 + 0.1 = 0.6	<0.01
External processing (esterification)	2.7 + 0.1 = 2.8	0.02
External wet polymerization:		
default	66 + 0.1 = 66	0.4
G	147 + 0.1 = 147	0.9
H	95 + 0.1 = 95	0.6
I	74 + 0.1 = 74	0.6
K	53 + 0.1 = 53	0.3
L	42 + 0.1 = 42	0.3
M	36 + 0.1 = 36	0.2
N	21 + 0.1 = 21	0.1
O	0.7 + 0.1 = 0.8	<0.01
P	0.4 + 0.1 = 0.5	<0.01
Q	0.3 + 0.1 = 0.4	<0.01
R	0.1 + 0.1 = 0.2	<0.01
S	0.1 + 0.1 = 0.2	<0.01
Paint formulation	1.0 + 0.1 = 1.1	<0.01
Paper recycling	0.6+ 0.1 = 0.7	<0.01
Use of grouting agent (default)	40	0.2
100 m from the mouth of the river	204	1.2

For one production site a PEC/PNEC-ratio slightly above one is calculated. The PEC was derived on the basis of measured effluent concentrations and estimated site-specific dilution factors. The company indicated that further emission reducing measures are under way and effluent measurements are continued. From the available monitoring results for 1999 (January to October) it can be seen that effluent concentrations leading to PECs higher than the PNEC were only measured during two weeks in 1999. Therefore, it can be assumed that the identified risk is adequately handled and the indicated improvements of the emission situation at this site are further monitored (**conclusion (ii)**).

During the use of a grouting agent containing hydroxyethylmethacrylate high concentrations of MAA are released via the drainage water. A PEC/PNEC-ratio above one is calculated and a risk for the local aquatic environment has to be deduced. The exposure assessment was based on measured concentration at a tunnel construction site. A quantitative extrapolation to other construction sites seems not possible, but similar conditions might be anticipated. Data improvement is not the proposed option, because an environmentally safe handling of the grouting agent has to be achieved independent of the local circumstances. Therefore, risk reduction measures at Community level are recommended (**conclusion(iii)**).

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Sediment

As neither monitoring data on concentrations of MAA in sediment nor experimental results with benthic organisms are available, and as there is no evidence for relevant adsorption of MAA onto sediment, there is no need for performing a quantitative risk assessment for this compartment. From the current manufacturing and use of MAA no risk for the sediment compartment is expected (**conclusion (ii)**).

3.3.2 Atmosphere

Due to the fast atmospheric photooxidation and the low resulting concentrations in air, adverse effects on organisms and abiotic effects upon the atmosphere, like global warming and ozone depletion are not expected from methacrylic acid (**conclusion (ii)**).

3.3.3 Terrestrial compartment

A generic exposure scenario representing a worst-case situation in the vicinity of a production and processing site was used for the calculation of the concentration in the soil porewater due to atmospheric deposition.

The $Clocal_{soil\text{-}porew}$ was 0.2 µg/l in the vicinity of such a plant and on a regional scale a concentration of 5 ng/l was estimated.

An indicative risk assessment can be performed on the basis of the aquatic PNEC resulting in a $PNEC_{soil}$ of 164 µg/l (soil pore water) and a PEC/PNEC ratio of << 0.01.

As PEC/PNEC < 1, a risk for the soil compartment is not deduced for the present data configuration. There is therefore no need for further testing and/or gathering of exposure information (**conclusion (ii)**).

3.3.4 Secondary poisoning

MAA does not present indications of a bioaccumulation potential. A risk characterisation for secondary poisoning is not required (**conclusion (ii)**).

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 General discussion

Methacrylic acid is primarily used as a chemical intermediate which is further processed to methacrylic esters, homo- and copolymers. Moreover the substance is a component of reactive adhesive preparations, which are used in skilled trade applications where they are a potential source of exposure (CEFIC, 1995).

The occupational exposure limit for methacrylic acid is 70 mg/m^3 (20 ml/m^3) in Denmark, Belgium, France, Norway**,** Sweden, the UK, the USA (NIOSH/OSHA; ACGIH) and Australia (ILO, 1994). In Sweden the short-term exposure limit is 100 mg/m^3 (30 ml/m^3) and in the UK 140 mg/m^3 (40 ml/m^3).

For workers the inhalation and dermal exposure route is the most likely.

Methacrylic acid is used in different consumer products, e.g. in adhesives (Swedish product register), as hardener in 2-component adhesives or it is present as residual monomer from methacrylic acid containing copolymers, e.g. as binder for paints and varnishes, leather or textil additive, oil additive, and thermoplastics (IUCLID Dataset; CHEMIS, 1998).

For consumers inhalation route is most likely for exposure. Dermal exposure with small amounts of methacrylic acid deriving from contact with textiles containing residual methacrylic acid monomer is an additional route for potential consumer exposure.

4.1.1.2 Occupational exposure

Methacrylic acid is primarily used as a chemical intermediate which is further processed to methacrylic esters, homo- and copolymers. Moreover the substance is used in reactive adhesive preparations (one (anaerobic)- and two-package polymerization adhesives).

The special methacrylate adhesives, the anaerobics, have found use for threadlocking and bearing retention and are widely used as such in machinery construction, automotive engines and similar applications (Kirk-Othmer, 1991); the two-package polymerization adhesives are used for bonding metals, plastics and silicate-containing materials.

Low levels of exposure are to be expected for the manifold uses of homo- and copolymerisates on the basis of MAA e.g. as binders in paints and varnishes, leather or textile additives as well as oil additives. Since the products contain only traces of residual monomeric MAA (< 0.07%) scenarios regarding the use of these products are regarded to be of minor relevance and are not included in the occupational exposure assessment.

For tunnelling and sewer processes the use of methacrylate ester compounds as grouting agents is known. Investigations of the UK indicate that there would have been large amounts of liquid and possibly mist generated during tunnelling. During application of the product MAA

concentrations up to 4 mg/l were detected in the drainage water. This value represent a site-specific situation and extrapolation to other tunnel constructing sites may not be adequate due to varying draining conditions. However, the alkaline milieu (pH values between 9 and 12), which is responsible for the formation of MAA from the hydroxyethylesters is most likely to occur at construction sites where cement is used. Based on the information, MAA is assumed to be formed after contact with highly alkaline draining water. The half-life value of decomposition of the main methacrylate compound amounts to app. 30 h (pH = 9). Taking into account the available information, exposures by inhalation to mist and vapour are regarded to be of minor relevance. Dermal exposure is expected to occur after the injection process if workers are in contact with the alkaline drainage water. Based on the above-given concentration of MAA, dermal exposure is regarded to be of minor relevance, too.

4.1.1.2.1 Occupational exposure during production and further processing in the chemical industry

Production and further processing as a chemical intermediate

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 with respect to workplace exposures to more hazardous chemicals such as cyanides as these will be sufficient to protect from MAA exposure (CEFIC, 1995).

Operations in production and further processing with the possibility of exposure include sampling, filling operations, reprocessing, and maintenance operations. High standards of control are practised in areas where the containment may be breached, e.g. during maintenance and the taking of process samples. Exposure by inhalation in other areas is minimised by purpose-designed tanker filling stations and the use of local exhaust extraction ventilation around drum filling stations (CEFIC, 1995).

Low numbers of persons are involved in the highly automated production process. Predominantly male workers are occupied in MAA production. Only one female was reported to be exposed intermittently. From 4 European companies a total number of 144 people was reported to be involved in the production of MAA, 28 continuously (> 50% of the working hours), 93 intermittently (< 50% of the working hours), and 23 occasionally (once or twice a year) (CEFIC, 1995).

About 250 male persons were reported to be involved in the industrial use of MAA in 4 European companies.

Typical specifications of residual monomer content of MAA in polymers manufactured from MAA and other monomers are below 0.001% to 0.2%, in some cases below 0.4% (CEFIC, 1995). According to the information of two producers polymer products (e.g. lacquers) contain as a rule less than 0.01% (100 ppm) residual methacrylic acid monomer (Röhm, 1995a) and in aqueous emulsion and solution acrylic paints supplied for the automotive industry residual levels of MAA have been determined as being 0.007% and 0.07% (ICI, 1995).

Workplace measurements

The analytical method used was HPLC with UV detection after absorption of the substance to water or NaOH. The limit of detection is 0.05 µg/sample (Röhm, 1999).

In European companies exposure concentrations from 0.9 - 7.35 mg/m^3 (0.2 - 2.0 ml/m^3, n=10) were determined (CEFIC, 1998). As a reasonable worst case of this measurement collective 5.6 mg/m^3 (1.6 ml/m^3) is estimated (Röhm, 1999).

During filling and sampling operations exposure concentrations between 0.24 and 3.6 mg/m^3 (0.07 and 1 ml/m^3) (duration of sampling: 38 min to 135 min, 4 measurements) were determined using personal sampling and a worst-case strategy for an exposure assessment (CEFIC, 1995). The exposure measurements for the sampling operations were taken over 120 min. The measurement result is an average exposure over the measurement time of 120 min, therefore the corresponding exposure peak level has to be higher.

Two short-term measurements in the monomer production (production, packaging) show concentrations of 23 mg/m^3 (6.4 ml/m^3) and 8.6 mg/m^3 (2.4 ml/m^3) (Röhm, 1999).

In emulsion polymer production (dispersions) workplace exposure concentrations of 0.04 mg/m^3 (0.01 ml/m^3) (8-hr TWA) have been determined using personal active sampling methods and a random strategy (CEFIC, 1995).

In solid copolymer production workplace concentrations have been estimated from measurements of another monomer used in the same polymerization process to range between 0.02 and 0.04 mg/m^3 (0.005 and 0.01 ml/m^3) (CEFIC, 1995).

In the production of high-resistance foam boards three workplace exposure concentrations were below 1.8 µg/m^3 (0.0005 ml/m^3) (CEFIC, 1998).

In hydroxyester production workplace exposure concentrations were reported in 1995 to be below 3.58 mg/m^3 (1 ml/m^3) (8-hr TWA) (CEFIC, 1995) and in 1998 to be below 0.04 mg/m^3 (0.01 ml/m^3) (8-hr TWA) (CEFIC, 1998).

In a pilot plant one short-term measurement (duration of sampling: 13 min) during hand pumping amounted to a concentration of app. 21 mg/m^3 (6 ml/m^3) (CEFIC, 1995). In the meantime the producer confirmed that this method is not in use anymore (Degussa, 1999).

Manufacture of adhesives

MAA is used as an additive for the production of one- and two packages (anaerobic and radiation-hardened) polymerization adhesives. In the manufacturing of these special-purpose adhesives for high-quality bonding of metal methacrylic acid is added (concentration: 2 - 12%) (BgVV, 1996). Adhesives are manufactured either quasi-continuously or batchwise in both closed and partially open systems (lidded mixer). For the production of solvent-based adhesives it is known, that only high volume preparations are produced quasi-continuously. Therefore batchwise production is to be assumed within the chemical industry, whereby applied partially open systems operate in conjunction with local ventilation systems. In the case of methacrylate based anaerobic curing adhesives enclosed vessels are used to formulate the intermediate high viscosity oligomers and the adhesive products (NIOSH, 1987).

Within the chemical industry exposure by inhalation is possible during sampling and analysis, filling and drumming, as well as during cleaning, maintenance and repair work. Because there is no detailed information, exposure is assumed for two hours daily (manufacturing of formulations).

Workplace measurements

Neither workplace measurements nor information on the duration and frequency of the exposure or on the collective of the exposed group are available.

Dermal exposure

On account of the corrosive effect of MAA (labelling as corrosive was agreed at 5% MAA and above, see classification, Chapter 1) and of the highly accepted use of suitable protective equipment it can be assumed that, as a rule, daily repeated immediate skin contact is avoided to a large extent by using suitable personal protective equipment (PPE, here gloves and eye protection). During activities like drumming, filling, cleaning and maintenance potential exposure is assumed only by single contacts. The corresponding exposure level is assessed by the EASE-model (see Section 4.1.1.2.4).

Daily repeated dermal exposure is assessed as low.

4.1.1.2.2 Occupational exposure in fields of manufacturing and use in the further processing industry, outside the chemical industry

Manufacture of adhesives

Further processing of MAA to special-purpose adhesives may not be limited to the large-scale chemical industry but instead occurs in the industrial area, too, as well as in small and medium-sized chemical companies. Batchwise production is also assumed (see Section 4.1.1.2.1).

In these areas it cannot be excluded, that the substance or the corresponding preparations are handled also in open systems during certain tasks, e.g. metering and filling activities, and that suitable technical measures (LEV, local exhaust ventilation) are not used (Voullaire and Kliemt, 1995).

Exposure by inhalation is possible during sampling and analysis, filling and drumming, as well as during cleaning, maintenance and repair work. Because there is no detailed information, exposure is assumed for two hours daily (manufacturing of formulations) and the exposure assessment is performed applying the EASE model (see Section 4.1.1.2.4).

The use of personal protective equipment (PPE, here gloves and eye protection) is assumed during certain tasks (e.g. filling, drumming) considering the corrosive effect of the pure MAA as educt and the produced preparations (labelling at ≥ 5% MAA, see classification, Chapter 1). Furthermore at a site at which corrosive educts and products are handled it is assumed, that the workers will protect themselves even if they handle preparations with irritant effects.

The daily dermal exposure for these scenarios is assessed to be low. During activities like filling, transfer, cleaning, maintenance and repair work, potential exposure is assumed only by single contacts.

Workplace measurements

Neither workplace measurements nor information on the duration and frequency of the exposure or on the collective of the exposed group are available.

Use of adhesives

In the field of engineering, device and tool construction industries, one- and two packages adhesives are used to bond metals or metal and glas either anaerobically or radiation-hardened during assembly. Automatic or semi-automatic bonding machines are employed within continuous production processes (production lines). Only low amounts of these preparations are used in their application process (CEFIC, 1995). After the bonding step, which generally involves small areas, the workpiece bonded with radiation-hardened adhesives is hardened by UV light within closed systems. Afterwards the components which are still warm, are in some cases stored in open systems, so that residual gases could evaporate into the workplace atmosphere. Beside of this two-package polymerization adhesives which contain methacrylic acid monomer (up to 12%) in the reactive adhesive component are also in use e.g. in the automotive industry.

Inhalation and dermal exposure is possible during charging and bonding work (semi-automated machines), during cleaning, maintenance and repair work. Additionally only exposure by inhalation is possible during work in the vicinity of openly-stored components which are still warm. It is to be assumed that not every workplace is equipped with suitable ventilation equipment (Kliemt, 1995). Since there is no detailed information and exposure within continuous production processes cannot be excluded, exposure is assumed over the shift length and daily.

Workplace measurements

Neither workplace measurements nor information on the duration and frequency of the exposure or on the collective of the exposed group are available.

Dermal exposure

On account of the corrosive effect of adhesives (labelling at ≥ 5% MAA, see classification, Chapter 1) it can be assumed, as a rule, that daily repeated immediate skin contact is avoided to a large extent by using suitable personal protective equipment (PPE, here gloves and eye protection). In this case daily dermal exposure is assessed to be low. During activities like filling, cleaning and maintenance potential exposure is assumed only by single contacts. The corresponding exposure level is assessed applying the EASE-model (see Section 4.1.1.2.4).

In the case of handling adhesives which are not labelled as corrosive, frequent immediate skin contact has to be taken into consideration. Generally workers avoid immediate skin contact with adhesives that can be removed only with difficulties (Kliemt, 1995). The adhesives under consideration could be removed more easily, because they harden only slowly, and thus have the opportunity to penetrate the skin. These adhesives are removed later with the aid of skin cleaning agents which are also employed after contact with paints. The corresponding exposure level is assessed applying the EASE-model (see Section 4.1.1.2.4).

Neither workplace measurements nor information on the duration and frequency of exposure or on the collective of the exposed group are available.

4.1.1.2.3 Occupational exposure in the skilled trade sector

Use of adhesives

When metal workpieces or glas-metal bondings have to be repaired, it is to be assumed that special-purpose adhesives including adhesives which may contain methacrylic acid are used.

Workers may be subjected to inhalation and dermal exposure when handling these adhesives openly. It is to be assumed that exhaust ventilation systems are absent, and that suitable personal protective equipment is not worn, if non-corrosive labelled adhesives are handled. For further description of dermal exposure during the handling of corrosive or non corrosive labelled adhesives see Section 4.1.1.2.2, paragraph "use of adhesives".

It is to be assumed, that the adhesives are not handled daily and that the duration is much shorter than the shift length.

Workplace measurements

Neither workplace measurements nor information on the duration and frequency of exposure or on the collective of the exposed group are available.

4.1.1.2.4 Estimation of exposure according to the EASE-model

Inhalation exposure

The following exposure data (8-h TWA) are estimated by applying the EASE-model for conditions appropriate to the different uses:

- Inhalation exposure during production and further processing as an intermediate and during the production of reactive adhesives in the large-scale chemical industry as well as manufacturing and use of reactive adhesives in industrial areas (with LEV):

Input parameters:	T = 20°C;	
	closed system	significant breaching
	non dispersive use	
	LEV (local exhaust ventilation)	
Estimated exposure level:	2 - 11 mg/m^3 (0.5 - 3 ml/m^3)	

- Inhalation exposure during manufacturing and use of the reactive adhesives in industrial areas (without LEV):

Input parameters:	T = 20°C;
	non dispersive use
	direct handling
	dilution ventilation present
Estimated exposure level:	36 - 180 mg/m^3 (10 - 50 ml/m^3)

Dermal exposure

Dermal potential exposure during drumming filling, cleaning and maintenance within the chemical industry and industrial areas because of single contacts with the pure substance and adhesives requiring labelling as corrosive (MAA content ≥ 5%):

Input parameters: T = 20°C;
non dispersive use
direct handling
incidental
Estimated exposure level: 0 - 0.1 mg/cm^2/day

Use of adhesives: Considering the content of MAA of 12% the exposure level is estimated to
0 - 0.01 mg/cm²/day

Dermal exposure via immediate skin contact when using adhesives containing < 5% methacrylic acid (not labelled as corrosive):

Input parameters: T = 20°C;
wide dispersive use
direct handling
intermittent
Estimated exposure level: 0.1 - 1 mg/cm^2/day

Use of adhesives: Considering the content of MAA is app. ≤ 5%, the exposure level is estimated to
0.005 - 0.05 mg/cm^2/day

4.1.1.2.5 Integrated Assessment

General

Methacrylic acid is primarily used as a chemical intermediate which is further processed to methacrylic esters, homo- and copolymers. Moreover the substance is used in reactive adhesive preparations (one (anaerobic)- and two-package polymerization adhesives).

The special methacrylate adhesives, the anaerobics, have found use for threadlocking and bearing retention and are widely used as such in machinery construction, automotive engines and similar applications (Kirk-Othmer, 1991); the two-package polymerization adhesives are used for bonding metals, plastics and silicate-containing materials.

Production and further processing in the chemical large-scale industry

Production and further processing as a chemical intermediate

The measurement value of 5.6 mg/m^3 (1.6 ml/m^3) is estimated as a reasonable worst case (Section 4.1.1.2.1). This value should be used for the assessment of the risks of daily exposure via inhalation. Between the measured data and those estimated by the EASE-model (2 - 11 mg/m^3, 0.5 - 3 ml/m^3) (see Section 4.1.1.2.4) there is a good agreement. For the assessment of the short-term exposure two concentrations related to the monomer production and packaging

were submitted. The highest concentration of about 23 mg/m^3 (6.4 ml/m^3) is used for risk assessment purposes.

In the EU more than 390 workers (data of 4 European companies) are employed in manufacturing and further processing of methacrylic acid; a total number of 144 people was reported to be involved in the production of MAA, 28 continuously, 93 intermittently and 23 occasionally (data of 4 European companies). For the manufacturing of adhesives no data of the collective of the exposed group are available.

Manufacture of special-purpose adhesives

Within the chemical industry exposure via inhalation is possible during sampling and analysis, filling and drumming, as well as during cleaning, maintenance and repair work. Because there is no detailed information, exposure is assumed for two hours daily (manufacturing of formulations).

Workplace measurements are not available, consequently inhalation and dermal exposures are estimated in application of the EASE model. In the case of workplaces provided with suitable local exhaust ventilation systems, the exposure level by inhalation is calculated to 2 – 11 mg/m^3 (0.5 - 3 ml/m^3) (see Section 4.1.1.2.4). Taking into consideration a daily duration of exposure of 2 hours, exposures of 0.5 - 2.75 mg/m^3 (0.1 - 0.75 ml/m^3, with LEV) result.

Dermal exposure

On account of the corrosivity of pure methacrylic acid and adhesives (labelling at ≥ 5% MAA, see classification, Chapter 1) immediate skin contact is only assumed by single contacts, because, in general, suitable personal protective equipment (PPE, here gloves and eye protection) are worn to avoid the contact to a large extent. The estimation of a potential exposure by single contacts according to the EASE-model is about 0 - 0.1 mg/cm^2/day; on account of an exposed skin area of about 420 cm^2 an exposure level of 0 - 42 mg/p/day would result. Taken into consideration that the use of gloves has a high acceptance within the chemical industry, daily dermal exposure is assessed to be low, even if non-corrosive adhesives are handled.

<u>Manufacture and use of adhesives in the further processing industry and in the skilled trade, outside the large-scale chemical industry</u>

Manufacture of special-purpose adhesives

Further processing of methacrylic acid to one- and two-packages polymerization adhesives may not be limited to the large-scale chemical industry but occurs in the industrial area, too, as well as in small and medium-sized chemical companies. In these areas it cannot be excluded, that the substance or the corresponding preparations are handled also in open systems during certain tasks, e.g. metering and filling activities, and that suitable technical measures (LEV, local exhaust ventilation) and personal protective equipment (PPE, here gloves) are not used (Voullaire and Kliemt, 1995), when non-corrosive preparations are handled.

Workplace measurements are not available. Consequently inhalation and dermal exposures are estimated in application of the EASE model. In the case of workplaces provided with suitable local exhaust ventilation systems, the inhalation exposure is calculated as 2 - 11 mg/m^3 (0.5 – 3 ml/m^3) (see Section 4.1.1.2.4). If it is assumed that no exhaust ventilation system is present, the level of inhalation exposure amounts to 36 - 180 mg/m^3 (10 - 50 ml/m^3). Taking into consideration a

daily duration of exposure of 2 hours, exposures of 0.5 - 2.75 mg/m^3 (0.1 - 0.75 ml/m^3, with LEV) or 9 - 45 mg/m^3 (2.5 - 12.5 ml/m^3, without LEV) result.

The use of personal protective equipment (PPE, here gloves and eye protection) is assumed during certain tasks (e.g. filling, drumming) considering the corrosive effect of the pure methacrylic acid as educt and the produced preparations (labelling at > 5%, see classification, Chapter 1). Furthermore if corrosive educts and products are handled at the same site it is assumed, that the workers will protect themselves even if they handle preparations with irritant effects. The daily dermal exposure for these scenarios is assessed to be low. During activities like filling, transfer, cleaning, maintenance and repair work, potential exposure is assumed only by single contacts. Considering the exposure level of 0 - 0.1 mg/cm^2/day assessed using the EASE model and an exposed area of 420 cm^2, the exposure amounts to 0 - 42 mg/person/day.

Use of special-purpose adhesives in the further processing industry

It is to be assumed that, in the further processing industry, the adhesives (containing 2 - 12% MAA) are sometimes handled in open systems during certain activities such as dosage, filling and bonding. Further if radiation-hardened adhesives are used, methacrylic acid can partially evaporate after the (UV) hardening process if the warm workpiece is stored openly. Estimation in application of the EASE model (measuring results are not available) produces a potential exposure of 2 - 11 mg/m^3 (0.5 - 3 ml/m^3) for workplaces with local exhaust ventilation (LEV) and of 36 - 180 mg/m^3 (10 - 50 ml/m^3) for workplaces without LEV. For workplaces without local exhaust ventilation, the lower value of the estimated concentration range appears to be more realistic in view of the method of use (bonding of small areas with low amounts of adhesives). Because of the lack of occupational exposure data an estimated exposure level of 2 - 11 mg/m^3 (0.5 - 3 ml/m^3) for workplaces with LEV and of 36 mg/m^3 (10 ml/m^3) for workplaces without LEV should be used for the assessment of the risks of daily inhalation exposure.

In the case of handling corrosive adhesives, potential dermal exposure is assumed only by single contacts. The exposure level estimated using the EASE model amounts to 0 - 0.01 mg/cm²/day. Generally, small areas of the body are affected. Assuming that an area of 210 cm^2 (fingers) is exposed, a level of 0 - 2.1 mg/p/day is obtained. Taking into account the corrosive effect of adhesives, daily repeated skin contact is avoided to a large extent by using suitable personal protective equipment, so that daily dermal exposure is assessed to be low.

If non-corrosive preparations are handled (< 5% MAA), e.g. drumming of adhesives, it cannot be excluded that the workers do not wear gloves. In this case dermal exposure is assessed applying the EASE-model to 0.005 - 0.05 mg/cm^2/day. Considering an exposed area of 210 cm^2, dermal exposure amounts to 1 - 10.5 mg/p/day.

Use of methacrylic acid-containing adhesives in the skilled trade sector

Workers will be subjected to inhalation and dermal exposure during open handling of two-package polymerization adhesives (e.g. during repair bonding work) which contain methacrylic acid monomer (up to 12%). It is to be assumed that exhaust ventilation systems are absent, and that suitable personal protective equipment is not worn, if not labelled as corrosive adhesives are handled.

If it is taken into account that the overall duration of open handling of these adhesives is assumed to be much shorter than the shift duration, the inhalation exposure level is assumed to be lower (< 36 mg/m^3) than in the comparable industrial sector (further processing industry).

The dermal exposure levels may be in the same order of magnitude or even lower than assessed for the use of corrosive and non-corrosive adhesives in the industrial sector (corrosive adhesives: low, potential exposure only by single contacts: 0 - 2.1 mg/p/day, non-corrosive: 1 - 10.5 mg/p/day). It is to be assumed that these activities are not done daily. Since neither workplace measurements nor information on the duration and frequency of exposure are available, no further statements can be made.

Table 4.1 shows the exposure data which are relevant for occupational risk assessment.

Table 4.1 Summary of exposure data relevant for occupational risk assessment

Area of production and use	Form ofexposure	Activity	Duration and frequency	Inhalation exposure		Dermal exposure			
				Exposure level shift average [mg/m³]	Method	Exposure level [mg/cm²/day]	Exposed area [cm²]	Shift average [mg/p/day]	Method
Chemical industry									
Production and further processing as a chemical intermediate	vapour (liquid)	filling, sampling, cleaning, maintenance, repair	shift length / daily	5.6	expert judgement	low	---	low	expert judgement
			single contacts	---	---	0 - 0.1	420 (palms of two hands)	0 - 42	EASE
		activity unknown, i.e. packaging	short term / not daily	23 (short term)	workplace measurement	---	---	---	---
Manufacture of adhesives (up to 12% MAA)	vapour (liquid)	weighing, filling, mixing, drumming	assumed 2h / daily	0.5 - 2.75	EASE with LEV	low	---	low	expert judgement
			single contacts	---	---	0 - 0.1	420 (palms of two hands)	0 - 42	EASE
Industrial area: production of preparations									
Manufacture of adhesives (up to 12% MAA)	vapour (liquid)	weighing, filling, mixing, drumming	assumed 2 h / daily	0.5 - 2.75 9 - 45	EASE with LEV without LEV	low	---	low	expert judgment
			single contacts	---	---	0 - 0.1	420 (palms of two hands)	0 - 42	EASE

Table 4.1 continued overleaf

Table 4.1 continued Summary of exposure data relevant for occupational risk assessment

Area of production and use	Form of exposure	Activity	Duration and frequency	Inhalation exposure		Dermal exposure			
				Exposure level shift average [mg/m³]	Method	Exposure level [mg/cm²/day]	Exposed area [cm²]	Shift average [mg/p/day]	Method
Industrial area: use									
Use of adhesives (up to 12% MAA)	vapour (liquid)	handling gluing							
a) ≥ 5% methacrylic acid (proposed labelling as corrosive)			assumed shift length, daily	2 - 11 36	EASE with LEV without LEV	low		low	expert judgment
			single contacts	---	---	0 - 0.01	210 (fingers)	0 -2.1	EASE
b) < 5% methacrylic acid (not labelled as corrosive)			contact level intermittent / assumed shift length, daily	2 - 11 36	EASE with LEV without LEV	0.005 - 0.05	210 (fingers)	1 - 10.5	EASE
Skilled trade									
Use of adhesives (up to 12% MAA)	vapour (liquid)	handling, gluing							
a) ≥ 5% methacrylic acid (proposed labelling as corrosive)			assumed shorter than shift length, not daily	< 36	expert judgment	low	---	low	expert judgment
			single contacts	---	---	0 - 0.01	210 (fingers)	0 - 2.1	EASE
b) < 5% methacrylic acid (not labelled as corrosive)			contact level intermittent / assumed shorter than shift length, not daily	< 36	expert judgment	0.005 - 0.05	210 (fingers)	1 - 10.5	EASE

4.1.1.3 Consumer exposure

Inhalation exposure

The EPA computer model SCIES was used to estimate the inhalation exposure of consumers to methacrylic acid from the use of dispersion paints, lacquers and 2-component adhesives. The content of methacrylic acid is assumed as total monomer content, but residual monomer contents in paints are much lower, they vary widely depending on the type of polymer. Therefore, the calculations are finally related to the product-specific monomer contents.

The standard values of the model have been used as room ventilation, inhalatory volume, etc. As a rule, an adult of 60 kg body weight will be considered as a standard consumer.

Dispersion paints

The producer declares that up to 2.5% methacrylic acid is used in the monomer mixture in dispersions; after polymerization the product contains less than 0.2% methacrylic acid monomer.

Using the SCIES standard scenario for dispersion paints (frequency of use 6 events/year; mass of product 13.6 kg; room size 40 m^3; duration of use 4.9 h; house air exchange rate 0.2; room air exchanges/h; user inhalation rate 1.3 m^3/h) the resulting methacrylic acid (monomer) exposure of the consumer by the inhalatory route was calculated to be in the lower microgram/kg bw and day range (0.0012 mg/kg bw/d, yearly average). This calculation is based on a weight fraction of 0.0000075 as due to producer information. During application of the dispersion paint the inhalatory exposure of the consumer per event was calculated to reach peak concentrations up to 0.7 mg/m³.

Paints on solvent basis

The producer declares that up to 2.5% methacrylic acid is used in the monomer mixture; after polymerization the product contains less than 0.7% methacrylic acid monomer.

Using the SCIES standard scenario for oil based (solvent based) paints (frequency of use 6 events/year; mass of product 6.71 kg; room size 40 m^3; duration of use 3.2 h; house air exchange rate 0.2; room air exchanges/h; user inhalation rate 1.3 m^3/h) the resulting methacrylic acid exposure of the consumer by the inhalatory route was calculated to be in the lower microgram/kg bw and day range (0.0017 mg/kg bw/d, yearly average). This calculation is based on a weight fraction of 0.000026 as given by the producer information. During the application of paint the inhalatory exposure of the consumer per event was calculated to reach peak concentrations up to 1.6 mg/m³.

2-component-adhesives

For the calculation of consumer exposure by inhalation to methacrylic acid using the EPA model SCIES the following conditions were applied: appropriate use and reasonable worst case.

Assuming the appropriate use (frequency of use 4 events/year; mass of product 1.0 gram; room size 40 m³; duration of use 1 h; house air exchange rate 0.2; room air exchanges/h; user inhalation rate 1.3 m³/h) and that MAA is 2.5% of total monomers the maximal concentration during use of the MAA monomer would be theoretically 0.0125 mg/m³. Taken into consideration that most of the monomer will polymerize soon after use, the residual monomer available for inhalation is much lower. Taking the residual monomer content of 0.2% as mentioned under paints the concentration that can lead to acute exposure is 0.000025 mg/m³ (=0.025 µg/m³).

Acute exposure by inhalation can therefore be neglected. According to the unfrequent use chronic exposure will not occur.

Thus, concentration leading to acute exposure from inhalation to MAA by use of two-component adhesives is in the middle pg-range.

Dermal exposure

Paints

Estimation of dermal exposure using dispersion paints (worst case) is based on the following assumptions:

Table 4.2 Estimation of dermal exposure using dispersion paints

Amount of paint used	13,600	g
Overspray	0.1	%
Amount of paint in contact with skin	13.6	g
Residual monomer in paints	0.02	%
Amount of MAA in paints	2.5	%
Amount of MAA in contact with skin (incl. splashes)	0.070	mg

A rough calculation of amounts that can come into contact with skin and thus lead to dermal exposure is based on an overspray of 0.1%, which means that 13.6 g may contact the skin. Assuming a thickness of layer of 0.01 cm, the maximum area of contact will amount to 1,400 cm² which is rather similar to the area of both forearms. Taking this amount of paint, the exposure to MAA will result in an amount of 0.070 mg. Direct dermal exposure due to uncontrolled splash of paint to skin in relation to bodyweight is then ~1 µg/kg per event. It should be mentioned, however, that after polymerization, the exact amount that is possibly absorbed is not known and may be much lower.

Dermal exposure by contact of air with skin can be calculated taking the estimated air concentration of 0.7 mg/m³ and a hypothetical volume of 194 cm³ (= 19,400 cm²[body surface]·0.01 cm [thickness of layer on skin]) contacting skin resulting in a value of ~0.13 µg (= 0.7·0.194) of MAA, which is negligible.

Textiles

Polymers manufactured with methacrylic acid as co-monomer are also used as textile additive in textile industry (no quantitative data are available). Thus, using the textiles consumers may be exposed to very small amounts of residual-monomers.

Oral exposure

Plastic products

In the EC, methacrylic acid is listed in the monomer positive list for monomers used for plastics and coatings coming into contact with foodstuffs without any restriction concerning the migration limits (EC, 1990). The scientific committee for food recommended a group total daily

intake of 0.1 mg/kg (temporary TDI) for all methacrylates (including methacrylic acid) based on a 2-year oral study in rats and several other studies with methyl methacrylate (EC, 1994b).

Conclusion

Polymers manufactured with methacrylic acid as co-monomer are used in consumer products for private use. The sum of all types of exposure is expected to be in the lower microgram/kg bw and day range when the products are used as intended (1-10 µg/kg bw/d range).

4.1.1.4 Humans exposed via the environment

According to Appendix VII of Chapter 2 of the TGD the indirect exposure to humans via the environment, i.e. through food, drinking water and air is estimated. As a worst-case scenario, the maximum intake due to exposure in the vicinity of a point source (generic model) is calculated. This is compared to an average intake due to exposure via the regional background concentration. In Appendix A10, the detailed calculations are presented.

Table 4.3 Used input parameters

	Local scenario	Regional scenario
Concentration in agricultural soil: Concentration in grassland soil:	0.22 µg/kg ww	2.7 ng/kg ww
Concentration in surface water:	33 µg/l *	0.14 µg/l
Concentration in the atmosphere:	0.76 µg/ m³	0.1 ng/ m³
Concentration in groundwater:	0.2 µg/l	0.005 µg/l

* The annual average local aquatic concentration of 33 µg/l calculated for a generic production and processing site is chosen as a realistic worst case, because the emission to atmosphere and soil was estimated on the basis of the same scenario.

The higher result i.e. 250 µg/l for one production site and 36 - 400 µg/l for wet polymerization were not used to avoid unreasonable combination of worst-case emissions.

Although the concentrations in surface water mentioned above are up to 12 times higher than the chosen one, the overall scenario is still regarded as a worst case.

The resulting total daily dose is:

$$\mathbf{DOSE_{tot} = 1.5\ \mu g \cdot kg\ bw^{-1} \cdot d^{-1}\ (local\ scenario)}$$

$$\mathbf{DOSE_{tot} = 4\ ng \cdot kg\ bw^{-1} \cdot d^{-1}\ (regional\ scenario)}$$

The calculated total doses comprise the following routes (**Table 4.4**):

Table 4.4 Routes of indirect exposure via the environment

Route	% of total dose	
	local	regional
Drinking water	61	91
Fish	4	6
Stem	24	1
Root	< 0.1	0.6
Meat	< 0.1	<0.1
Milk	< 0.1	<0.1
Air	11	0.5

The main route of indirect exposure is the intake via drinking water for the local and the regional scenario.

4.1.1.5 Combined exposure

A person who is exposed indirectly to MAA through the environment may also be exposed through different applications via inhalation as well as via the dermal route. However, in such cases the sum of all types of exposure will be expected to amount to 1-10 µg/kg bw/d (lower microgram range).

4.1.2 Effects assessment: Hazard identification and Dose (concentration) - response (effect) assessment

4.1.2.1 Toxicokinetics, metabolism and distribution

Specific studies on toxicokinetics of the existing chemical methacrylic acid including metabolism and potential reactivity with tissue components of mammals are not available. Therefore, all statements on these topics are of speculative character, even under consideration of existing publications on acrylic acid, esters of acrylic acid and esters of methacrylic acid.

Methacrylic acid is a low molecular weight molecule, with a relatively high-water solubility (89 g/l) and a low octanol/water partition coefficient (log Pow = 0.93). Vapour pressure of 0.8 - 0.9 hPa (20°C) indicates some volatility. The acidity is characterised by pKa = 4.66. The substance (stabilised with 200 ppm hydroquinone monomethyl ether, the lowest stabilisator content commercially available) is stable for one week in 10 to 25% aqueous solutions or 0.1 M hydrochloric acid at room temperature. Therefore, it can be concluded that methacrylic acid does not polymerize spontaneously in aqueous media (Degussa AG, 1995).

Deposition of methacrylic acid vapours in the surgically isolated upper respiratory tract (URT) of anaesthetised rats was studied after inhalation of 450 µg/l (133 ppm) using a unidirectional respiratory flow technique (cyclic flow studies were not possible due to vapour absorption on the cyclic flow pump) for 60 min (Morris and Frederick, 1995). Deposition of methacrylic acid was measured throughout exposure determining the difference in vapour concentration of methacrylic acid in the inspired and the URT expiring air. Deposition rates (from 30 to 60 min of exposure) of about 95% were observed under 200 ml/min unidirectional flow conditions. However, the degree of penetration to underlying cells could not be derived from this experiment.

These results indicate that after inhalation in rats most of the methacrylic acid does not reach the lung. This result is in accordance with the results of 90-day inhalation studies in which the predominant effect was nasal irritation, a local effect at the site of the contact.

After a single oral administration of the sodium salt of methacrylic acid to Wistar rats (540 mg/kg bw) methacrylic acid was detected in the blood serum by means of HPCL. The maximum concentration was found after 10 min, whereas after 60 min no more methacrylic acid was detectable (Bereznowski et al., 1994).

There are no studies which specifically address the metabolism of exogenously applied methacrylic acid. However it is generally accepted that methacrylic acid-coenzyme-A is a naturally occurring intermediate of the valine pathway. Methacrylic acid-CoA is rapidly converted into (S)-3-hydroxyisobutyryl-CoA by the enzyme enoyl-CoA-hydratase. This pathway joins the citrate cycle, carbon dioxide, and water being the final products (Rawn, 1983; Shimomura et al., 1994; Boehringer, 1992).

Structurally related compound

After a single oral administration of methyl methacrylate to male Wistar rats (800 mg/kg bw) methacrylic acid was already detectable after 5 min (Bereznowski, 1995). Between 10 and 15 min after administration of the ester the maximal level of methacrylic acid in the serum was observed (quantitative determination by means HPLC separation and UV detection). After that period the methacrylic acid concentration declined steadily, reaching a level below the level of

detection after 1 hr. It is concluded that methyl methacrylate is rapidly hydrolyzed by serum nonspecific carboxylesterases.

The methyl ester of methacrylic acid can be used as model substance in toxicological studies to deliver methacrylic acid itself in target organs. Results obtained from the ester can be regarded as worst-case assumptions as the ester is likely to be absorbed more readily and to a much higher extent than the acid due to its higher lipophilicity (log P_{ow} = 1.38), the non-ionic character and the minor reactivity at the site of application.

The toxicokinetic data of methyl methacrylate have been described in detail in the EU risk assessment report of methyl methacrylate. However, microdosimetric relationships for the acid versus the ester may differ and thereby complicate such comparisons. During ester exposure, the acid is produced intracellularly via carboxylesterase. In contrast, inspired acid vapour initially deposits extracellularly on the mucus lining layer and must diffuse through this layer prior to interacting with the epithelium.

Frederick et al. (1998) constructed a hybrid computational dynamics (CFD) and physiologically-based pharmacokinetics inhalation model to estimate the regional tissue dose of acrylic acid in the rat and human nasal cavity, respectively. The rat model uses two olfactory compartments to incorporate both the olfactory epithelium in the projection extending along the dorsal meatus and the ethmoid olfactory region, based on a compartmental rat nasal model of Bush et al. (1998). The human model uses one olfactory compartement (Subramaniam et al., 1998). In their model the liquid phase was modified to include the effect of buffering capacity of the acid.

Frederick (1998) reported also on interspecies comparisons with a hybrid computational fluid dynamics and physiologically-based pharmacokinetic model for methacrylic acid. To modify the acrylic acid model for methacrylic acid, the specific partition coefficients for methacrylic acid were measured for a variety of tissues. In addition, the model incorporated the molecular weight and pKa of methacrylic acid. All other model parameters were assumed not to differ from the structurally similar acrylic acid.

Simulated exposure of the human nasal cavity at a unidirectional flow rate of 18.9 l/min resulted in a predicted whole nose extraction of 78% of the inhaled concentration (10-80 ppm methyl methacrylate). Under the same exposure conditions (unidirectional flow or cyclic flow), the model predicted 2-3 fold lower olfactory tissue concentrations of acrylic acid in the human nasal cavity relative to the rat nasal cavity (Frederick, 1998).

For the interpretation of the findings, various aspects have not been taken into account in an appropriate way. First, the parameters set for the rat model is “validated” for measured deposition results at only one exposure concentration of methacrylic acid (about 130 ppm). Model simulations of vapour concentrations were carried out for 0 to 75 ppm. The tissue dose concentration curves were non-linear for rat and mouse. Second, no parameters for a mouse model are available. Third, no experimental data for cyclic flow simulations are available. Fourth, sensitivity data for parameters are not given. Fifth, clearance mechanism such as mucociliary function and metabolism are not incorporated in the model. However, the company argues that both processes are slower than uptake so that they could not influence the actual concentration in the tissue to a relevant degree.

As a major drawback it has to be mentioned that the model predictions for the human situation were not supported by measurements for uptake from inhalation. Furthermore, the well-known intraspecies differences which are even found in textbooks and which should translate into confidence limits around any predictions are not taken into consideration. Thus, the point

estimate for the predicted concentration has to be taken with caution as it suggests a precision which is not appropriate for the real *in vivo* situation.

Furthermore, whilst the model is addressing interspecies differences in toxicokinetics it is not considering interspecies differences in toxicodynamics. Without further data it is supposed that the concentration-response relationship is the same across the species. This assumption adds to the uncertainties with respect to the quantitative estimates for a safe level of exposure emerging from the model.

In conclusion, whilst the model gives some interesting aspects for possible mechanisms of the local kinetics of MAA it does not take appropriately the variability into account. A discussion of the dynamic part of the model is lacking. Interspecies differences (rat vs. man) of the concentration-effect relationship have not been addressed. Intraspecies (between human subjects) variability should also have been taken into consideration in deriving an estimate of a range of safe exposure levels.

Summary of toxicokinetics, metabolism and distribution

Methacrylic acid is rapidly absorbed in rats after oral and inhalation administration. A high-dose orally administered methyl methacrylate was rapidly hydrolysed by esterases and the methacrylic acid concentration in the blood serum reached a very low level after one hour. In an inhalation study deposition efficiency of 95% was measured in the surgically isolated upper respiratory tract of anaesthetized rats. However, the degree of penetration to underlying cells could not be derived from this experiment. There are no studies which specifically address the metabolism of exogenously applied methacrylic acid.

4.1.2.2 Acute toxicity

Studies in animals

The majority of the reported data on the acute toxicity of methacrylic acid are of limited validity and important test details are lacking. Respective figures are given in IUCLID.

Oral

Acute oral toxicity is moderate as judged by several reported oral LD_{50} values for several animal species; for rats oral LD_{50} values between 1,320 mg/kg body weight (Elf Atochem, 1977, undiluted methacrylic acid, unpublished report) and 2,260 mg/kg (Eastman Kodak Company, 1979, 10% solution of methacrylic acid in corn oil, unpublished report) respectively 2,224 mg/kg (Rohm and Haas, 1957, 25% aqueous solution, unpublished report) have been found. The differences are most probably caused by differences in concentrations and vehicles applied. The majority of oral LD_{50} values calculated for rats, rabbits and mice are <2,000 mg/kg.

Undiluted methacrylic acid (purity 99%) caused a LD_{50} of 1,320 mg/kg body weight for rats: After application of 900 mg/kg no deaths occurred, after application of 1,000 mg/kg 2/10, after 1,250 mg/kg 4/10, after 1,500 mg/kg 6/8 and after 1,750 mg/kg 8/8 rats died within 24 hours (Elf Atochem, 1977, unpublished report).

A 10% substance solution in corn oil administered to groups of 4 male rats at 200, 400, 800, 1,600 and 3,200 mg/kg body weight resulted in a LD_{50} of 2,260 mg/kg: the animals were observed for 14 days. Weakness and rough haircoat are the only clinical signs reported; no

necropsies were conducted. A similar test was conducted with mice: A LD_{50} of 1,600 mg/kg resulted when the 10% corn oil solution was administered to groups of 4 male mice at 200, 400, 800, 1,600, 3,200 mg/kg body weight. Animals were observed for 14 days; necropsies were not conducted. Clinical signs were the same as with rats: weakness and rough haircoat (Eastman Kodak Company, 1979, unpublished reports).

With a 25% aqueous solution of methacrylic acid a LD_{50} of 2,210 ml/kg (2,224 mg/kg) resulted for male rats: the solution was administered to 10 male albino rats/dose group (doses: 6.5, 8.0, 10.0, 12.0 ml/kg). One out of ten rats died after application of 6.5 ml/kg, 4/10 died after 8.0 ml/kg, 7/10 after 10.0 ml/kg and 9/10 after 12.0 ml/kg. Most deaths occurred during the first 24 hours, but a few ranged over the succeeding five-day period. Marked weakness was the only clinical sign reported. Necropsy revealed severe gastric irritation (Rohm and Haas, 1957, unpublished report).

Dermal

Only scarcely documented tests on acute toxicity by the dermal route are available: in a range finding study on skin absorption with rabbits a dermal LD_{50} between 500 mg/kg and 1,000 mg/kg was detected for methacrylic acid (no data on purity). Dose groups of 2 rabbits each were tested with 0.5 g/kg, 1 g/kg and 2 g/kg as 50% aqueous solution. Results: No mortality after application of 500 mg/kg, both rabbits died after application of 1,000 mg/kg. Clinical signs: Slight weight loss and severely burned skin after application of 500 mg/kg; 1,000 mg/kg and 2,000 mg/kg killed all animals overnight respectively within 2 hours (Dow Chemical Company, 1956, unpublished report).

Inhalation

Acute toxicity by the inhalation route is reported to be low for rats. In a study according to OECD guideline 403 an inhalation LC_{50} of 7.1 mg/l/4h was detected for methacrylic acid (purity 98.5%): five female and 5 male rats/dose group were exposed to aerosol/vapour (aerodynamic mass median diameter: 10, 6.5, 5.5, 7.2 µm). Clinical signs reported were weight loss; necropsy revealed respiratory tract irritation after an observation period of 13-14 days (DuPont de Nemours and Company, 1993, unpublished report).

In an acute inhalation toxicity study with rats using 3 different vapour concentrations, inhalation of 1,000 ppm vapour for 1 hour resulted in lung discoloration but no deaths: Acute inhalation toxicity studies were conducted on glacial methacrylic acid, wherein 6 albino rats/exposure group were exposed to maximum attainable vapour concentrations of 100, 250 and 1,000 ppm for 1 hour in a 325 l inhalation chamber. After exposure, all rats were observed for the following 14 days. After exposure to 100 and to 250 ppm there were no deaths or untoward behavioural reactions; necropsy examinations revealed no gross pathologic alterations. During exposure to 1,000 ppm the rats exhibited a bloody nasal discharge. This reaction subsided within 3 hours after termination of the exposure. Necropsy examinations revealed slight to mild diffuse or focal discoloration of lungs in 5/6 rats (no more data on clinical signs or necropsy) (Rohm and Haas, 1973, unpublished report).

Sensory irritation as reported from a study of respiratory function (RD_{50}, concentration that will produce a 50% depression in respiratory rate) reflects only a slight sensory irritating potential. In a test with mice a RD_{50} value of 22,000 ppm/30 minutes was detected (method according to ASTM) for methacrylic acid (purity 98.5%). Respiratory function parameters were monitored during preexposure (10 min), exposure and postexposure (10 min) periods using 4 mice/dose

group (exposure concentrations 4,900, 9,400, 18,000, 27,000, 42,000 ppm). Mild sensory irritation was observed at 4,900 ppm during the first minutes of exposure. A dose-dependent decrease in respiratory frequency was observed (DuPont de Nemours and Company, 1993b, unpublished report).

Studies in humans

Not available.

Summary of acute toxicity

Human data on acute toxicity of MAA are not available. The main clinical sign in animal tests on acute toxicity of methacrylic acid is severe irritancy at the site of contact. Methacrylic acid is a chemical substance exhibiting potent chemical reactivity at the site of application. Oral LD_{50} values of 1,320-2,260 mg/kg for rats and a dermal LD_{50} value between 500 and 1,000 mg/kg for rabbits were detected. According to Annex I of Directive 67/548/EEC, methacrylic acid is classified as "R21/22 (Harmful in contact with skin and if swallowed)", see Chapter 1.

4.1.2.3 Irritation/Corrosivity

Studies in animals

Methacrylic acid is a corrosive substance and contact will cause severe burns on skin (US American TLV, 1980; Elf Atochem, 1980, unpublished report) and eyes (Rohm and Haas, 1957, unpublished report).

In a study with rabbits, skin irritation indicative of corrosivity (i.e. concave eschar) was observed after 4 hours, after 1 hour and after 3 minutes of exposure. In a Draize skin test with rabbits according to OECD Guideline 404 / EEC Directive 92/69/EEC B.4 0.5 ml of undiluted methacrylic acid (purity 99.38%) was applied topically to the shaved intact skin of one male rabbit. The application site was semi-occluded for 4 hours. After the 4-hour exposure, the application site was wiped with paper towels saturated with tap water and blotted dry with paper towels. Skin irritation was evaluated according to Draize criteria at approximately 1, 24, 48, 72 hours and at 7 and 14 days after patch removal. No mortality or clinical signs of systemic toxicity were observed during the study. Severe erythema and skin effects indicative of corrosivity (i.e. concave eschar) were observed. Since corrosive findings were evident at 4 hours, additional rabbits were tested to determine US Department of Transportation (DOT) Packing Group classification. The undiluted test substance (0.5 ml) was applied topically to the shaved intact skin of 1 male rabbit on 2 separate sites for 1 hour (left side) and 3 minutes (right side). The 1-hour application site was semi-occluded with fabric cuff and the 3-minute site was uncuffed during the exposure period. After each exposure period, the application sites were wiped with paper towels saturated with tap water and blotted dry with paper towels. Severe erythema and skin effects indicative of corrosivity (i.e. concave eschar and erosion/ulceration) were observed on the 1-hour and 3-minutes sites: Observations after 1-hour exposure demonstrated severe erythema (grade 4) and edema (grade 3) after 1 hour and after 24 hours, after 24 hours all layers of dermis were destroyed, subcutaneous muscle layer was visible and reddened. Observations after the 3-minute exposure revealed severe erythema (grade 4) and edema (grade 3) after 1 hour, concave eschar was detected at the 48-hour observation, animal was euthanised after day 7 observation when conclusive evidence of irreversible damage to the dermis was noted (Rohm and Haas, 1997, unpublished report).

Severe corneal, iridial and conjunctival irritation persisting through the 7-day observation period, resulted in a Draize eye test comparable to OECD guideline 405 with methacrylic acid (no data on purity): single instillations of 0.1 ml of methacrylic acid into right eyes of 6 albino rabbits resulted in corneal opacity grade 4, iridial irritation grade 2, conjunctival redness grade 3 and conjunctival edema grade 3 after 24 hours for all animals. These lesions persisted unchanged until day 4. The test was terminated after 7 days (scores given for that observation time: corneal opacity grade 4, iridial irritation, conjunctival irritation grade 3-4); chemical burns, epithelial sloughing and hypopyon were noted (Rohm and Haas, 1973, unpublished report).

If methacrylic acid contacts the eyes, a grave emergency exists. Even dilute aqueous solutions of MA can produce serious eye injury. Direct contact with eyes or skin with liquid methacrylic acid can result in blindness and skin corrosion, respectively (Documentation of Threshold Limit Values for substances in workroom air; 1980).

For local irritation effects observed after repeated inhalation exposure see Section 4.1.2.5.

Studies in humans

Not available.

Summary of irritation/corrosivity

Methacrylic acid causes adverse effects at the site of application, depending on the concentration and frequency or time of exposure. The undiluted acid causes skin and eye corrosion and respiratory tract lesions. According to Annex I of Directive 67/548/EEC, methacrylate acid is classified “C, Corrosive” and labelled as “R35, Causes severe burns”, see Chapter 1.

4.1.2.4 Sensitisation

Studies in animals

Methacrylic acid has not shown sensitising properties in a modified Buehler test with guinea pigs (DuPont de Nemours and Company, 1993, unpublished data). After the first induction application of a 20% aqueous solution of MAA, 16/20 guinea pigs exhibited eschar by 72 hours. Therefore, the concentration was reduced to 15% and applied to a second-test site for the second and third induction application. No other than slightly patchy redness was exhibited at 48 hours by 2/20 test animals, no redness was observed after the challenge application of a 10% aqueous MAA solution; 2/10 vehicle control animals exhibited similar symptoms.

A Polak adjuvant-test with guinea pigs (Parker and Turk, 1983) demonstrated a similar situation: at day 0, 15 animals of either sex were each injected, via the footpad (4 injections), 0.1 ml of an emulsion containing 2 mg/ml of the chemical, in ethanol: saline (1:4), in FCA. In addition, 0.1 ml of emulsion was injected into the nape of the neck. The guinea pigs received a total of 1 mg of chemical. On day 7, open skin testing was performed by dropping 0,02 ml of a solution of the chemical in acetone: olive oil (4:1) onto the shaved flank, with 1% or 5% of methacrylic acid. Skin tests were repeated weekly at different sites on the flank for up to 12 weeks. During the 3 months of the experiment, no contact sensitivity skin reaction was induced.

There is no information available on the potential for methacrylic acid to produce respiratory sensitisation in animals.

Studies in humans

A group of six patients presenting allergic contact dermatitis to anaerobic acrylic sealants was patch-tested with various acrylates and methacrylates. The test with methacrylic acid was negative in all cases (Condé-Salazar et al., 1988).

Summary of sensitisation

Methacrylic acid is not a sensitising substance as demonstrated by human experience and by animal tests.

4.1.2.5 Repeated dose toxicity

Studies in animals

In a valid 90-day inhalation study (CIIT, 1984) Sprague-Dawley rats, Fischer-344 rats and B6C3F1-mice were exposed (whole body exposure) to 20, 100, and 300 ppm (equivalent to 0.0714, 0.357, and 1.071 mg/l) of methacrylic acid (purity > 99%) on 6 hours/day and 5 days/week. Each dose and control group consisted of 10 males and 10 females. Additionally, 10 animals per sex/group were exposed for 4 days and killed on day 5.

The study was performed according to the Annex VB.29, 67/548/EEC with some minor restrictions (the list of serum chemistry parameters was limited, i.e. there were no parameters of protein metabolism. Adrenals were not weighed).

No exposure-related death was recorded. After 90 days of exposure high-dose animals had reduced body weight gains (-10%) and food consumption (-9%) (male F-344 rats) or reduced body weight gains (both sexes of B6C3F1-mice -11% in males, (-12% in females). Reduced leukocyte counts and an increased activity of alkaline phosphatase were observed in female high-dose mice. An increased level of BUN was seen in high-dose males of F-344 rats.

In both rat strains reduced absolute liver weights were found in high-dose males, as well as in both sexes of high-dose B6C3F1-mice. The liver/body weight ratio was comparable to that of the controls, only after adjustment to the brain weight a significant decrease of relative liver weight was obvious. In mice, the liver/body weight ratio was lower in high-dose mice of both sexes (significant only in males), the liver/brain weight ratio was significantly higher in high-dose males and significantly lower in high-dose female mice.

Microscopically, all treatment groups of both rat strains and mice of the high-dose group showed a rhinitis of the anterior regions of the turbinates (level A, **Tables 4.5, 4.6 and 4.7**). The incidences in rats showed no clear dose relationship. The high-dose rats had a more severe inflammation than the other groups. A low-grade rhinitis almost without additional lesions was also evident in some of the control rats (not seen in mice). At high-dose level the incidence of rhinitis was increased compared to control rats; in some of the treated rats rhinitis was accompanied by ulceration, epithelial hyperplasia and vesiculation, goblet cell hyperplasia, and exudation of the respiratory epithelium. Ulceration of the anterior part of the nose was also observed in some high-dose male and female mice. A degeneration of olfactory epithelium of the mid part of the nasal cavity was observed in mice at mid- and high-dose level, but not in the rat nose. The lesion consisted of intracellular accumulation of an orange-pink material in the cytoplasm of ciliated cells (eosinophilic globules) which appeared to be the sustencular cells lining the middle portions of the septum and dorso-medioal aspects of the dorsal scroll of the

nasal turbinates in histological sections at level B and C. In severe cases this material filled the cell, displaced the nucleus or in most severely affected areas epithelial cells dropped out.

In all treated Sprague-Dawley groups increased lymphocytic infiltrations in the larynx were found in both sexes, in males a higher incidence of focal aggregates of lymphocytes in the lung periphery was seen (both findings showed no clear dose relation).

Outside the upper respiratory tract, lymphocytic hyperplasia of mandibular lymph nodes were more frequent in high-dose animals of both rat strains compared to controls. The kidneys of male high-dose mice showed cytomegaly of tubular epithelium. Other findings showed no relationship to treatment.

After interim sacrifice on day 5 satellite animals of each strain showed acute inflammation and, in mice, necrosis of the anterior respiratory epithelium of the turbinates similar to the findings reported after 90 days. Food consumption (-16% in males, - 14% in females), body weight gain (-30% in males, -38% in females) and lower final mean body weights (-5% in males and -6% in females, non significant) were reduced in high-dose F344 rats. At this time, high-dose mice also presented lower final mean body weights (-8% in males, -7% in females) and high-dose males of the SD strain showed a reduction of food consumption of 13%.

Due to the toxicity on the nasal epithelia in rats of all dose tested and in mice of the mid and high doses, the LOAEC was 20 ppm in rats (0.0714 mg/l) and NOAEC was 20 ppm in mice (0.0714 mg/l) for local effects on the respiratory tract. No sign of systemic toxicity was observed in rats of both strains. The reduced final body weights corresponded to lower food consumption, which possibly was caused by the irritative properties of the test substance on the nasal epithelia. Conclusively, the high dose of 300 ppm (1.071 mg/l) represented the NOAEC for systemic effects in rats. In mice, lower body weight gains at the high dose (300 ppm) were not associated to a reduction of food consumption, so that 100 ppm (0.357 mg/l) was the NOAEC for systemic effects. The decrease of absolute liver weights was not considered to represent a clear adverse effect because of the lack of corresponding findings (clinical pathology and histopathology). For explanation, reduction of the absolute weights may be related to lower final body weight as liver/body weight ratio was normal in rats and not conclusive in mice. Similarly, the higher incidence of lymphocytic hyperplasia in the mandibular lymph nodes of male rats was not considered to be a clear adverse effect. More likely this effect can be interpreted to be related to the inflammatory changes of the upper and lower respiratory tract and to the assumption that minimum traces of MAA were swallowed.

There are no further valid studies on methacrylic acid.

Table 4.5 Methacrylic acid induced nasal lesions in F-344 rats

	Males				Females			
Conc. (ppm)	0	20	100	300	0	20	100	300
Nasal turbinate, Level A (No. examined)	10	9	10	9	10	10	10	10
Acute rhinitis	5 (1.2) *	6 (1.33)	4 (1.25)	9 (2.1)	5 (1.2)	9 (1.44)	1 (2)	7 (1.5)
Epithelial vesicles				2			1	7
Lymphocytic infiltrate						1	1	
Exudate	1	1		4				4
Epithelial hyperplasia		2		1		4		1
Goblet cell hyperplasia		2			3	3		
Acute inflammation								1
Level B (No. examined)	10	10	10	10				
Acute rhinitis			1 (2)					
Level C (No. examined)	10	10	10	10	10	10	10	10
Acute rhinitis						1 (1)		
Exudate								1
Lymphocytic infiltrate						1		

* Number of animals affected; in parentheses: mean severity (grading 1-5), only reported here for rhinitis

Table 4.6 Methacrylic acid induced nasal lesions in Sprague-Dawley rats

	Males				Females			
Conc. (ppm)	0	20	100	300	0	20	100	300
Nasal turbinate, Level A (No. examined)	10	10	10	10	10	10	10	10
Acute rhinitis	5 (1) *	6 (1.5)	10 (1.3)	8 (1)	2 (1)	4 (2)	2 (1.5)	7 (1.14)
Exudate		2	7	4		2	2	4
Acute inflammation		1						
Goblet cell hyperplasia		3						
Epithelial vesicles			2	2				
Epithelial hyperplasia		3	5	3		1	1	3
Level B (No. examined)	10	10	10	10	10	10	10	10
Acute rhinitis			1 (1)*					
Exudate								1
Level C (No. examined)	10	10	10	10	10	10	10	10
Acute rhinitis		1 (1)*						
Exudate		1				1		1
Level D (No. examined)	10	10	10	10	10	10	10	10
Exudate			1					

* Number of animals affected; in parentheses: mean severity (grading 1-5), only reported here for rhinitis

Table 4.7 Methacrylic acid induced nasal lesions in B6C3F1 mice

	Males				Females			
Conc. (ppm)	0	20	100	300	0	20	100	300
Nasal turbinate, Level A (No. examined)	10	10	10	10	10	10	10	10
Acute rhinitis				4 (1) *				3 (1)
Ulceration				3 (1)				2 (1)
Level B (No. examined)	10	10	10	10	10	10	10	10
Acute rhinitis								1 (1)
Eosinophilic globules, degeneration of olfactory epithelium			1 (1) *	1 (2)			1 (1)	9 (1.4)
Level C (No. examined)	10	9	10	10	10	10	10	10
Eosinophilic globules, degeneration of olfactory epithelium			1 (2) *	8 (1.75)			3 (1)	9 (2)

* Number of animals affected; in parentheses: mean severity (grading 1-5).

Further information on toxic effects after repeated exposure

Further studies with inhalation or dermal administration are not valid. Because of incompleteness or deficiency of the testing method and documentation of the results, most of the studies were published as abstract only. They were evaluated as additional information.

From these investigations additional substance-related effects on central nervous system (neurofunctional disorder), hemopoietic system, liver, kidneys, skin and biochemical changes were assumed (Gage et al., 1970; Labonov et al., 1979; Rumyantsev et al., 1981; Rohm and Haas, 1986). Reliability and relevance of these assumed effects were uncertain. Despite the defaults the cited studies were reported hereafter.

Insufficient information was given in the study of Labonov et al. (1979), in which chronic inhalation (no data on duration and recovery time) of animals (no data on species used) induced decreased renal lactate dehydrogenase LDH1/LDH5 ratio indicative for the ratio of aerobic/anaerobic glycolysis (no data on the doses affected). At all doses administered (0.44, 8.9 and 221.3 mg/m³) effects were seen on the nervous system, pituitary-adrenal axis, red and white blood cells, lung, liver and kidney function and/or body weight gain. There were no further data on the study design and no exact descriptions or quantitative data of the findings observed.

Similar effects were reported by Rumyantsev et al. (1981) on rats exposed by inhalation of methacrylic acid. No data on exposure route, doses, number of animals per sex, used strain, and no details on the methods used and the results were available (translated publication in Chemical Abstracts). Lactate dehydrogenase activity in serum decreased and in the liver and kidney activities fluctuated within the physiological range. LD1 (LD isoenzyme 1) and LD2 of the kidneys responsible for aerobic glycolysis decreased, whereas LD4 and LD5 showed a relative increase (catalyze anaerobic glycolysis). Authors concluded that in the kidney aerobic glycolysis decreased but anaerobic glycolysis was identified. A similar pattern was also seen in the liver. These aerobic and anaerobic glycolysis changes finally led to tissue hypoxia.

Gage et al. (1970) reported that two male and two female rats exposed to saturated methacrylic acid (1,300 ppm, 4.5 mg/l) 5 hours on 5 days showed nose and eye irritation and weight loss. Blood and urine tests were normal, autopsy revealed no changes on organs. Exposure to 300 ppm of four male and four female rats for 20 days and 6 hours daily revealed no toxic signs and no changes in autopsy. A slight congestion of the kidney was an uncertain finding. No further details on the observed findings were described. The number of animals and the number of organs examined in histopathology were limited and were not exactly reported for the test substance.

Skin irritative effects of methacrylic acid are reported in Section 4.1.2.3. In the study of Rohm and Haas (1986) eight male mice treated dermally with 0.56 M methacrylic acid in water showed no skin irritation in the shaved back region after 3 weeks of treatment (three times a week) comparable to the control animals treated with water only. Doses of 0.56 M of methacrylic acid in acetone induced slight to moderate skin irritation. At higher doses (1.12 M and 2.24 M of methacrylic acid in acetone) skin lesions were more severe. Any body weight changes were attributable to the methacrylic acid treatment. No other parameters of systemic toxicity were examined, therefore the study is not suitable to give accurate information on systemic toxicity after dermal application.

There are no valid studies on subacute, subchronic, and chronic toxicity with oral or dermal administration.

Studies in humans

In an abstract, Stulova et al. (1962) reported effects on workers after chronic inhalation exposure of methacrylic acid vapours cited as follows: in the production area of methacrylic acid concentration of methacrylic acid was 0.006-1.2, mostly 0.08 - 0.02 mg/l. 109 workers who were in contact with methacrylic acid and 63 workers having no contact with methacrylic acid were examined 3 times at intervals of 6 months. For the majority of workers who were in contact with methacrylic acid, a tendency towards thrombopenia was noted. For a part of the workers, tachycardia, hypotonia, changes of the temporal shoulder coefficient, asymmetry of oscillatory index, excessive reaction to nitroglycerin, hypothermia, weakened reaction to heating, and ultraviolet exposure, pathologic changed reflexes of Ashner and location, acrocyanosis, tremor of extended fingers of the hands, and pathologic and dermographic reactions. Irritations of the mucous membranes of the upper breathing passages and eyes were not disclosed.

No further data on the methods and results were reported in this abstract, coexposure to other chemicals was not excluded.

Other information

Methacrylic acid-containing solutions produced a pharmacodynamic suppression on rate and force of contraction and coronary flow rate of the isolated perfused rabbit heart (Mir et al., 1973).

No (lowest) observed adverse effect level (NOAEL/LOAEL)

From the 90-day inhalation study (6 h/d, 5 d/wk) in rats and mice (CIIT, 1984), NOAEC/LOAEC for local effects on the respiratory tract:

NOAEC: 20 ppm (equivalent to 0.0714 mg/l), mouse
LOAEC: 20 ppm (equivalent to 0.0714 mg/l), rat

NOAEC for systemic effects:

NOAEC: 100 ppm (equivalent to 0.357 mg/l), mouse
NOAEC: 300 ppm (equivalent to 1.071 mg/l), rat

4.1.2.6 Mutagenicity

For methacrylic acid only data of a bacterial mutation test are available. The bacterial mutation test was negative in concentrations up to 4,000 µg/plate with and without S-9 mix (Salmonella strains TA 1535, TA 1537, TA 98, TA 100). Doses from 4,000 µg/plate upwards induced toxic effects. The test was conducted as preincubation modification with rat and hamster liver S-9 mix. The purity of the tested substance is not given (Haworth et al., 1983).

No further experimental data on methacrylic acid are available.

Data on structurally related substances

Methyl methacrylate was negative in bacterial gene mutation tests. From mammalian cell culture assays it may be concluded that methyl methacrylate is a high-toxicity clastogen (i.e. induction of chromosomal aberrations is bound to highly toxic doses). The effect is not dependent on presence of S-9 mix. These findings are in line with results from mouse lymphoma assays where

positive findings seem to be due to the induction of small colonies. Marginal increases in SCE frequencies are of low significance.

In vivo an oral mouse bone marrow micronucleus test was negative for doses up to 4,520 mg/kg. No clear conclusion could be drawn from bone marrow chromosomal aberration assays with rats. A dominant lethal assay with male mice led to a negative result.

In vitro MMA has the potential for induction of mutagenic effects, esp. clastogenicity; however, this potential seems to be limited to high doses with strong toxic effects. Furthermore, the negative *in vivo* micronucleus test - and to some extent the negative dominant lethal assay - indicates that this potential is probably not expressed *in vivo*.

Summary of mutagenicity

Methacrylic acid is negative in a bacterial gene mutation test. Further testing on methacrylic acid is lacking. However, taking into consideration the data on the structurally related substance methyl methacrylate - which indicate that this substance does not express a genotoxic potential *in vivo* - there is no need for further testing.

4.1.2.7 Carcinogenicity

No cancer studies on methacrylic acid are available. Focal hyperplasia of the respiratory epithelium or lymphatic hyperplasia of mandibular lymph nodes as seen in the CIIT study (1984) were not interpreted as a preneoplastic lesion; this lesions were considered to represent reactive or inflammatory processes to the irritant effect of the test substance.

Structurally related compound

Data from methyl methacrylate, the methyl ester of methacrylic acid, can be taken into consideration since formation of methacrylic acid can be anticipated due to a relatively rapid ester cleavage by carboxylesterases**.**

Experimental studies in animals

- Inhalation

Groups of 50 male F344/N rats were exposed to MMA (purity >99%; containing 0.04 mg/l equivalent to 10 ppm monomethylethyl ether of hydroquinone as an inhibitor of polymerization) by inhalation at 0, 2.1, 4.2 mg/l (equivalent to 500 or 1,000 ppm), female F344/N rats at 0, 1.0 or 2.1 mg/l (equivalent to 250 or 500 ppm) and male and female B6C3F1 mice at 2.1 or 4.2 mg/l (equivalent to 500 or 1,000 ppm), 6/d, 5 d/wk for 102 weeks (NTP, 1986; Chan et al., 1988). Animals were killed at 111-112 weeks (rats) or 113-114 weeks (mice) of age. Survival rates in the control, low and high dose at the end of the experiment were 26, 29, 28 males and 30, 27 and 29 females (rats) and 44, 42 and 47 males and 27, 26 and 33 females (mice). During most of the second year of the study, the mean body weights of treated male mice and high-dose female mice were 10-18% lower than those of the controls.

The marginal increase in the incidence of mononuclear-cell leucaemia observed in female rats (control 11/50; low dose 13/50; high dose 20/50) fell within the range of values seen in historical controls. Both in mice and rats no treatment-related tumors were observed.

No treatment-related increases in tumor incidence occurred in golden hamsters exposed to 0, 25, 100 or 400 ppm (0, 102.5, 410 or 1,640 mg/m³) MMA 6 h/d, 5 d/wk for 78 weeks. At the high dose, body weight decreased and mortality increased (Rohm and Haas, 1979c, cited from Chan et al., 1994).

- Oral

An early 2-year chronic study in dogs and rats treated orally with MMA revealed no adverse effect other than a lower body weight gain in high-dose dogs and elevated kidney weights in high-dose female rats (Borzelleca et al., 1964). In this study two male and two female dogs received gelatine capsules with 10, 100 and 1,000 ppm MMA dissolved in corn oil. The high dose was reduced to 500 ppm on day 2, 0 ppm on day 3-13 and 300 ppm on day 14 due to vomiting and then increased to 1,200 ppm at week 5 and to 1,400 ppm at week 7 to 1,500 ppm at week 9. 25 male and 25 female rats were administered with 6, 60 and 2,000 ppm MMA in the drinking water, the low and medium doses increased to 7 and 70 ppm after five months.

These studies in dogs and rats revealed no increase of neoplastic lesions. However the reliability of these studies is limited due to their non-conformance to current carcinogenicity test guidelines (e.g. histopathologic examination was performed on a limited number of organs).

Cancer epidemiology

A retrospective mortality study has been conducted among workers exposed to the vapour phase of MMA, low percentages of ethyl acrylate (EA) and volatile by-products of the MMA and EA polymerization process in acrylic sheet manufacture in two US plants. Detailed analyses of colorectal cancer mortality were performed for each of the three cohorts (Cohort I: 3,934 white males employed between 1933 and 1945; Cohort II: 6,548 white males hired between 1946 and 1986; Cohort III: 3,381 white males hired between 1943 and 1982). Exposure was estimated on the basis of a job-specific semi-quantitative rating scale. Mortality from colon cancer was significantly increased in cohort I and non-significantly increased in cohort III. The risk for colon cancer was highest in the most exposed workers, who worked extensively in the early 1940s. No regular increase according to years elapsed since first exposure or intensity of exposure was observed for colon cancer. The rate for rectal cancer was increased in cohort I (Walker et al., 1991; IARC, 1994). Some evidence of increased death rate from respiratory cancer or non-malignant respiratory disease was reported for cohort III (Rohm and Haas, 1987).

Another retrospective mortality study (Collins et al., 1989) included a cohort of 2,671 male workers employed between 1951 (1957 respectively) and 1974 in two acrylic fibre production plants. Exposed to MMA were only 1,561 men of the cohort at mean concentrations below or equal to 1 ppm. A small excess of respiratory cancer was reported. There was no significant increase in the number of cancer deaths.

In the cohort study of Tomenson et al. (1994), colorectal cancer rate was as expected (17 observed deaths versus 16.9 expected) and respiratory cancer mortality rate was lower than expected (SMR=93). Mortality due to stomach cancer was increased by approximately one third.

The epidemiologic data on humans do not provide consistent evidence on the carcinogenic effect in humans. The studies did not allow a strong association of increased tumor rates in a distinct organ or several organs to MMA as the responsible agent.

Summary of carcinogenicity

There are no data on carcinogenicity from methacrylic acid itself; from methyl methacrylate data, there is no concern on carcinogenic properties of methacrylic acid.

4.1.2.8 Toxicity for reproduction

Fertility impairment

No studies on methacrylic acid are available.

In a 90-day inhalation study with up to 300 ppm methacrylic acid (CIIT, 1984; described in Section 4.1.2.5) no changes in the reproductive organs of male and female rats and mice were detected histopathologically.

Structurally related compound

On the methyl ester of methacrylic acid a dominant lethal study has been conducted with exposure of groups of 20 male CD-1 mice via inhalation to methyl methacrylate atmospheres of 100, 1,000, or 9,000 ppm for 6 h/day for a period of 5 days. These concentrations, which were based on preliminary toxicity studies, resulted in the death of 1/20, 1/20, and 6/20 males in the 100, 1,000, and 9,000 ppm groups respectively. Each surviving male was mated with two virgin females each week for a period of 8 weeks. For this study design any adverse effects on fertility and preimplantation development had not been detected (ICI, 1976a). However, the exposure period of 5 days is too short, in view of the length of spermatogenesis cycle in mice (35 days).

Definite assessment of possible fertility impairment of methyl methacrylate will be provided from a 2-generation inhalation study planned in the USA for the near future.

Developmental toxicity

No data on methacrylic acid are available.

Structurally related compound

The methyl ester of methacrylic acid, however, had been tested in a series of developmental toxicity studies in mice and rats.

In a developmental toxicity study according to OECD 414 conducted in compliance with GLP standards (Rohm and Haas, 1991) methyl methacrylate (99.9% active ingredient) was administered by inhalation exposure to 5 groups (27 rats/group) of presumed pregnant rats (Crl: CDBR) at concentrations of 0 (control), 99, 304, 1,178, and 2,028 ppm (0, 412, 1,285, 4,900, 8,436 mg/m³) for 6 hrs/day on days 6-15 of gestation (G). All doses were administered by a whole-body inhalation exposure under dynamic conditions. Clinical signs were recorded daily on days 0-20 G. The dams were weighed on days 0, 6, 8, 10, 13, 16, and 20 G. Feed consumption was recorded during gestation. On day 20 G, the dams were euthanised and the thoracic and abdominal cavities were examined for gross changes. Each uterus was weighed and corpora lutea, implantation sites and resorptions were counted. The number of fetuses per litter were counted and their location within the uterus recorded. All fetuses were weighed, sexed, examined for external alterations and one-half of the fetuses from each litter were examined for

visceral alterations (Staples technique). All fetuses were then macerated, stained, and examined for skeletal alterations.

No treatment-related deaths were noted at any concentrations tested. The only clinical sign noted was a minimal increase in the incidence of scant feces at 2,028 ppm. At all exposure levels tested losses in maternal body weight or decreases in maternal body weight gain and decreases in maternal feed consumption were noted. Loss in maternal body weight during the first two days of exposure followed by an overall reduced increase in maternal body weight gain during the treatment period was detected for the 1,178 and 2,028 ppm groups. Slight effects were observed for the 99 and 304 ppm treatment group as indicated by a transiently (during the first two days of exposure) reduced maternal body weight gain. According to the authors, a maternal no observed effect level (NOEL) could therefore not be demonstrated. No embryo or fetal toxicity was evident and no increase in the incidence of malformations or variations was noted at exposure levels up to and including 2,028 ppm. Therefore toxicity to the conceptus was not evident even at exposure levels that resulted in overt maternal toxicity.

In two independent experiments in rats 0, 100, and 1,000 ppm methyl methacrylate was given via inhalation from day 6 to day 15 of pregnancy. The maternal NOAEL was reported to be 1,000 ppm. The fetuses did not show any morphological abnormality or malformation. The authors reported that in the high-dose group an increase in numbers of early resorptions in both experiments and late resorption in only one experiment was observed and derived an embryonal NOAEL of 100 ppm for methyl methacrylate from their results (ICI, 1977). This study, however, suffers from methodological difficulties (insufficient randomisation of test animals, insufficient test protocol, poor documentation of results), so that the authors' interpretation of the results cannot be followed.

Further data are available from a study with inhalation exposure to doses slightly less than acute lethal doses (Nicholas et al., 1979). Groups of 22 to 27 pregnant Sprague-Dawley rats were exposed to 110 mg/l [26,800 ppm] methyl methacrylate vapour (head only), for 17 and 54 min per day (about 25 and 75% of the time to death of 50% of animals after a single exposure of 72.2 min), respectively, from days 6 to 15 of gestation. The fetuses were examined for gross and skeletal malformations only. Both doses were toxic to the dams, as shown by maternal death, loss of body weight during the first few days of treatment and decreased food intake throughout. The highest dose caused a small but significant increase in early fetal deaths and both doses reduced fetal body weight and crow-rump length. The highest dose induced increased incidences of hematomas and retarded ossification.

Methyl methacrylate was further administered as a liquid by intraperitoneal injection within the investigation of a series of methacrylate esters to groups of 5 female Sprague-Dawley rats at doses of 0, 0.133, 0.266, and 0.443 ml/kg bw (1/10, 1/5, and 1/3 of the acute LD_{50} value of 1.33 ml/kg bw) on day 5, 10, and 15 of gestation (Singh et al., 1972). Maternal toxicity of the dams was not examined in this study. The following parameters of adverse effects were investigated: embryonic-fetal toxicity, as evidenced by resorptions and stillbirths; gross (external) malformations of fetuses; skeletal malformations and fetal weight. No treatment-related effects in comparison to sham treated controls (distilled water or normal saline) had been revealed at termination on gestation day 20 with respect to resorptions, numbers of live or dead fetuses or mean fetal body weight. A dose-related increase of gross abnormalities (haemangiomas) was found in the fetuses, but there were no skeletal malformations.

In a further study groups of 12 mated female Dutch rabbits were treated by intraperitoneal injections with doses of 0.004, 0.04, and 0.4 ml/kg bw/day from day 6 to 18 of pregnancy

(ICI, 1976b). Animals were weighed at intervals during the experiment and were observed daily for any change in clinical condition. On day 29, the animals were killed and their uteri examined for live fetuses and early and late resorptions. The fetuses were removed, weighed, sexed and examined for viability and abnormalities. Nine animals, distributed evenly between the groups died or were killed prematurely during the study. In addition, there was a high incidence of peritonitis probably due to the irritant properties of methyl methacrylate and an increase in respiration rate in the top-dose level group. Fetal weight was significantly reduced at the 0.4 ml/kg bw/day level and an increase in the numbers of early resorptions were observed at the top dose only. There were no increases in soft tissue or skeletal abnormalities.

Studies in humans

No data on methacrylic acid are available.

Structurally related compound

From a study evaluating a cohort of women having been occupationally exposed to methyl methacrylate from 1976 during 1985, increased incidences in spontaneous abortion and clinical findings in their newborns were reported (Fedetova, 1997). The study was solely based on the retrospective evaluation of older hospital records. The evaluation of a total of 502 pregnancies resulted in the finding of a statistically significant increase in the rate of early abortions (up to 12 weeks of pregnancy) for those which had been assigned to workplace concentrations of > 20 mg/m^3 when compared to those involved in workplace concentrations of < 10 mg/m^3 or to a not further described non-exposed control group. The evaluation of a total of 319 deliveries also resulted in the finding of a higher rate of late abortions and of complications during pregnancy for those who had been assigned to the higher workplace concentrations. As to the evaluation of the data sheets of newborns, those whose mothers had been assigned to workplace concentrations of < 10 mg/m^3 were reported to display higher incidences of asphyxia, congenital malformations (not further specified) and still births in comparison to background data. Besides overall insufficient documentation, the main limitation of that study is, that it does not provide any details of the workplace and exposure conditions related to the investigated patients. Due to the very poor definition of the exposure situation for the evaluated cohort, the significance of the study and the meaning of the reported data remain unclear. Considering the lack of details and the unclear exposure situation, it is not possible to link these effects primarily to MMA. Due to the uncertain validity of this study, data from this investigation are not further considered for the risk assessment. Sexual disorders (not further specified) in male and female workers occupationally exposed to both methyl methacrylate and vinyl chloride have been reported from two Russian studies (Makarov, 1984; Makarov et al., 1984). Due to the uncertain validity of these studies (abstracts) data from these two investigations were not further considered for the risk assessment.

Summary of toxicity for reproduction

There are no data on reproductive toxicity of methacrylic acid. However, data from studies concerning the methyl ester of methacrylic acid can be taken into consideration as an alternative, since due to unspecific carboxylesterases a relatively rapid ester cleavage can be anticipated (as outlined in Section 4.1.2.1). On the basis of these findings, there is no concern in relation to reproductive toxicity.

4.1.3 Risk characterisation

4.1.3.1 General aspects

Specific studies on toxicokinetics of the existing chemical methacrylic acid including metabolism and potential reactivity with tissue components of mammals are not available. The methyl ester of methacrylic acid, however, is useful as a model substance in certain toxicology studies to deliver methacrylic acid itself in target organs. Results obtained from the methyl ester can be regarded as worst-case assumptions as the ester is likely to be absorbed more readily and to a much higher extent than the acid due to its higher lipophilicity, the non-ionic character and the minor reactivity at the site of application.

Following inhalatory exposure, experiments studying the deposition of methacrylic acid in the upper respiratory tract of rats indicate that most of the methacrylic acid does not reach the lung; the predominant effect was nasal irritation, a local effect at the site of the contact.

Despite of its physico-chemical properties, the systemic availability of methacrylic acid is estimated to be low. This is based on the presumption that particularily in a first step a partial cytolysis is occurring due to high corrosive potential of methacrylic acid. This is observed in the upper cell layers of the respiratory tract. There are in a sufficient amount low molecular physiological reaction partners as well as enzymatic activities both released from cytosol which are suited to form e.g. coenzym A-thioesters of methacrylic acid. This pathway finally joints the citrate cycle with carbon dioxide and water being the final products.

Following oral application of sodium methacrylate as well as of the methylester of methacrylic acid the acid occurs in the blood, however, it is removed very efficiently. The low systemic availability of methacrylic acid is in line with its low systemic toxicity. Data on dermal absorption are lacking.

The main effect of methacrylic acid identified in acute and subchronic animal studies is irritation/corrosivity at the site of contact. In repeated dose inhalation studies the relevant toxic effect was irritation of the nasal mucosa. Rhinitis was observed in rats $\geq$20 ppm (71.4 mg/m³) and mice at 300 ppm (1,071 mg/m³) when animals were exposed for 90 days. Additionally, in mice, degenerative lesions of the olfactory epithelium occurred at doses from 100 ppm 357 mg/m³). A NOAEL for the local effects of 20 ppm (resp. 71.4 mg/m³) was derived from a study in mice. MAA reduced body growth in mice at 300 ppm. The NOAEC for systemic toxic effects was identified to be 100 ppm in mice and 300 ppm in rats. Toxic effects after dermal or oral application routes are unknown. Due to the very low systemic availability of methacrylic acid, and the assessed exposure scenario for the consumer, there is no cause for concern on systemic toxic effects.

Methacrylic acid is negative in a bacterial gene mutation test. Further testing on methacrylic acid is lacking. However, taking into consideration the data on the structurally related substance methyl methacrylate - which indicate that this substance does not express a genotoxic potential *in vivo* - there is no need for further testing.

No relevant data are available concerning possible effects of methacrylic acid in humans.

No specific human population at risk could be identified within the general population.

4.1.3.2 Workers

In the following table a summary of the effects which are relevant for occupational risk assessment is given.

Table 4.8 Summary of effects relevant for occupational risk assessment

	Inhalation	Dermal
Acute toxicity	LC50 (rat) of 7,100 mg/m³	LD50 of 500-1,000 mg/kg bw, corrosive, rabbit
Irritation/Corrosivity	Respiratory tract irritant	Corrosive
Sensitisation	No data, not suspected to be a respiratory tract sensitiser	No skin sensitiser
Repeated dose toxicity (local)	NAEC about 20 ppm (72 mg/m³) (direct and adjusted)	Corrosive
Repeated dose toxicity (systemic)	NAEC: 100 ppm (357 mg/m³) (direct and adjusted)	NAEL14,000 mg/person/d (based on inhalation data, adjusted)
Mutagenicity	Not considered to be genotoxic (based on bacterial gene mutation test and SAR)	
Carcinogenicity	No carcinogenicity study, not suspected to be carcinogenic	
Fertility impairment Developmental toxicity	Based on screening data and on methyl methacrylate data: not considered to be a reproductive toxicant	

For the purpose of the risk assessment it is assumed that inhalation of vapour and skin exposure are the main routes of exposure. Oral exposure is not considered to be a significant route of exposure under normal working practices.

4.1.3.2.1 Acute toxicity

Inhalation

A rat LC_{50} of 7,100 mg/m^3 for a 4-hour aerosol exposure is reported. Concerning respiratory tract irritation following inhalation exposure, see "Irritation/Corrosivity/Inhalation" and "Repeated dose toxicity/Inhalation (local effects)". This rat LC_{50} of 7,100 mg/m^3 is much higher than the highest estimated value for inhalation exposure of 45 mg/m^3 (EASE, without LEV) during the manufacture of adhesives in the industrial area (scenario 3).

Therefore acute inhalation risks (lethality) are not considered of concern (**conclusion (ii)**).

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Dermal

A screening test with rabbits revealed a dermal LD_{50} of 500 to 1,000 mg/kg bw. The dose applied was corrosive to the skin. Acute dermal toxicity data with non-irritating dosages are not available.

The highest estimated dermal exposure is 42 mg/p/d (0.6 mg/kg/d) in the chemical industry and the industrial area. The risks of lethality due to skin contact are not considered of concern (**conclusion (ii)**).

4.1.3.2.2 Irritation/Corrosivity

Dermal/Eyes

Undiluted methacrylic acid is corrosive to the rabbit skin even following a 3-minute exposure period. In a Draize eye test undiluted methacrylic acid caused severe damage to the eyes (e.g. high grade corneal opacity). Section 4.1.2.3 does not contain specific data on the corrosive or irritating properties of dilutions of methacrylic acid.

The study from Rohm and Haas (1986) provides information on dermal local toxicity following repeated exposure (study of limited validity). Mice treated dermally with 5% (0.56 M) methacrylic acid in water (9 applications in three weeks) showed no skin irritation. The same concentration in acetone induced slight to moderate skin irritation. At higher concentrations (10% and 20%) skin lesions were more severe.

For risk characterisation purposes (according to the general rules of the preparations directive) a concentration of 5% methacrylic acid is considered to be corrosive, while preparations between 1% and 5% methacrylic acid are considered to be irritating to skin and eyes. Specific concentration limits cannot be deduced from the studies included in the report. The Rohm and Haas study, which is of limited validity, provides no evidence, that there is significant chronic dermal irritation below the general concentration limit of 1% for acute irritation of methacrylic acid.

Handling of corrosive methacrylic acid preparations

The following exposure scenarios refer to the handling of material considered to be corrosive:

Table 4.9 Exposure scenarios relating to the handling of corrosive material

Chemical industry	(1)	Production/Processing
	(2)	Manufacture of adhesives
Industrial area	(3)	Manufacture of adhesives
	(4a)	Use of adhesives (> 5%)
Skilled trade	(5a)	Use of adhesives (> 5%)

In these exposure scenarios daily repeated immediate contact is avoided to a large extent by using suitable PPE. Potential exposure is only assumed by single contacts.

Eye, skin, corrosive material: **Conclusion (ii)**.

Handling of irritating methacrylic acid preparations

Exposure scenarios relating to the handling of material considered to be irritating to skin and eyes (preparations between 2-5% methacrylic acid):

Table 4.10 Exposure scenarios relating to the handling of irritating material

Industrial area	(4b)	Use of adhesives (< 5%)
Skilled trade	(5b)	Use of adhesives (< 5%)

For these scenarios splashes to the eye and to small skin areas as well as hand-to-eye contact are considered to represent incidents which do not only occur accidentally but may occur in most exposure situations. **Conclusion (ii)** is reached on the grounds that control measures exist which can minimise exposure and risk of irritation, thereby reducing concern. However, these controls must be implemented and complied with to reduce the risk of damage to eyes and skin.

Skin, eye, irritating preparations: **Conclusion (ii)**.

Inhalation

A threshold for acute respiratory irritation is not described. With reference to the section on repeated dose toxicity, it is anticipated, that the respiratory tract irritation threshold for single (8 h) exposure does not significantly differ from that for repeated (8 h) exposure. This consideration implies that the chronic irritation threshold of slightly below 20 ppm (72 mg/m³) (see "Repeated dose toxicity") may be used for the assessment of single (8 h) exposure as well. Experimental data concerning different exposure duration per day are not available. As a pragmatic, but cautious approach, it is assumed that the irritation threshold of about 20 ppm is also appropriate to assess short-term (<8 h) exposure.

In addition to the critical scenarios due to chronic inhalation exposure (see **Table 4.11**) data on short-term exposure in the chemical industry (MOS: 3.1) and the (intermittent) use of adhesives in the skilled trade sector (MOS: > 2) are evaluated as being of (weak) concern.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

4.1.3.2.3 Sensitisation

Dermal

Methacrylic acid is not considered to be a skin sensitiser (based on animal tests and human experience). Dermal exposure of workers is therefore not anticipated to result in skin sensitisation (**conclusion (ii)**).

Inhalation

Respiratory sensitisation has not been reported in humans. For the time being, and taking into account the results on skin sensitisation, methacrylic acid is not suspected to be a respiratory sensitiser (**conclusion (ii)**).

4.1.3.2.4 Repeated dose toxicity

Inhalation (local effects)

Vapours of methacrylic acid are irritant to the upper respiratory tract. The assessment of local irritation potency particularly relies on the findings of the 90-day rat and mice inhalation studies.

In mice the predominant adverse effect was degeneration of the olfactory epithelium at 100 ppm and above. No adverse effects occurred at the low-dose level of 20 ppm. For both of the tested rat strains the predominant adverse effect was inflammation and epithelial hyperplasia in the

anterior part of the nasal cavity. There was no clear-cut dose-effect relationship in rats somewhat restricting the reliability of the rat LOAEL of 20 ppm (lowest dose tested). Taking into account the degree of adverse effects of the mid and high-dose levels (100 ppm and 300 ppm) mice proved to be slightly more sensitive than rats. Thus occupational risk assessment may be based on the assumption of a NAEC for both species slightly below 20 ppm (72 mg/m^3).

For chronic risk assessment it may be assumed that the nasal irritation threshold for methacrylic acid which was established in the 90-day inhalation study will not substantially change with longer duration of exposure. This assumption is made for several reasons. After interim sacrifice on day 5 experimental animals showed local effects similar to the findings reported after methacrylic acid treatment for 90 days (see hazard assessment). For methacrylic acid itself there are no further studies on repeated dose toxicity which allow an estimate of the necessity of a duration adjustment from the 90-day to a 2-year period of exposure. However, there is supporting evidence from the structurally related substances acrylic acid and methyl methacrylate (see corresponding EU risk assessment reports) that the dose response for damage of olfactory epithelium will not substantially change with the duration of exposure. Furthermore, results of a chronic inhalation study with methyl acrylate indicate that most changes in the rat nasal mucosa developed during the first 12 months of exposure and increased only moderately with ongoing exposure up to 24 months (Reininghaus et al., 1991).

The main problem in methacrylic acid risk assessment is species extrapolation from rodents to humans. Rodents show a nasal anatomy and respiratory physiology different from man. For instance, architecture of nasal passages is more complex in rodents than in humans. These species differences will influence toxicokinetics of substances in the upper respiratory tract.

A CFD/PBPK model was constructed for interspecies (rat, mouse, humans) extrapolation of methacrylic acid tissue dose in the olfactory region of the nasal cavity. The model simulations indicate that under similar exposure conditions human olfactory epithelium is exposed to a 2- to 3- fold lower dose compared to rat olfactory epithelium. However, this model is not considered valid enough to account quantitatively for potential interspecies variation (see Section 4.1.2.1). Thus, for the time being, it is proposed to rely occupational risk assessment for methacrylic acid on the experimental results in the most sensitive species.

In conclusion, occupational risk assessment is based on an anticipated human NAEC of about 20 ppm (72 mg/m^3). This extrapolated human NAEC does not differ from the experimental data because duration adjustment is not considered necessary and because PBPK modelling is not considered valid enough to definitely conclude a lower sensitivity of humans.

For the different exposure scenarios MOS values from 2 to 144 (lowest and highest value) are calculated (see **Table 4.11**). Principally, for adjusted MOS values below 1 (the exposure level exceeds the adjusted NOAEC) chronic respiratory irritation is anticipated to occur. For methacrylic acid, there are no scenarios with adjusted MOS values lower than 1. However, because of remaining uncertainties concerning the human dose response relationship (no clear-cut experimental NOAEC, no chronic toxicity data, limited validity of the PBPK model) exposure scenarios including a MOS range of up to about 2 to 3 are considered of concern (see **Table 4.11**) (**conclusion (iii)**).

Inhalation (systemic effects)

In the 90-day inhalation studies (with nasal cavity toxicity as primary effect) the highest dose of 300 ppm represented the systemic NOAEC for rats. In mice, lower body weight gains at the highest dose level of 300 ppm were not associated with a reduction of food consumption, so that

the level of 100 ppm is considered to be the NOAEC. Minimal changes of liver weights at the level of 300 ppm are not considered toxicologically relevant. Because it cannot be excluded that lower body weight gains at 300 ppm partly are secondary to severe local effects, duration adjustment is not recommended. Thus, the systemic NOAEC is considered to be about 5-times greater than the local NOAEC.

This relationship between local and systemic effects of methacrylic acid implies that the lowest systemic MOS value is 10. Further bearing in mind that the key effect of methacrylic acid is a local one, there is no exposure scenario with concern for workers regarding systemic health risks due to chronic inhalation exposure (**conclusion (ii)**) (the scenario-specific systemic MOS values may be calculated easily by multiplication of the local MOS values with the factor of 5).

Dermal (local)

The available data on irritation/corrosivity of methacrylic acid following acute or repeated dermal exposure are described and evaluated in the section on "irritation/corrosivity". These data suggest that there might be no concern for chronic dermal irritation following exposure to concentrations/dilutions of methacrylic acid that are not considered irritating by acute dermal exposure (**conclusion (ii)**).

Dermal (systemic)

For chronic dermal contact to methacrylic acid preparations which are not labelled as corrosive the potential for systemic adverse effects needs to be discussed.

There are no valid repeated dose studies with oral or dermal administration. For preliminary considerations the results of the 90-day inhalation studies may be used to assess possible systemic toxicity. In these studies (with nasal cavity toxicity as primary effect) lower body weight gains in mice were observed at the high-dose level of 300 ppm; the corresponding NOAEC was 100 ppm (357 mg/m^3). Using that NOAEC for human risk assessment and assuming a breathing volume of 10 m^3 per shift, an inhalatory intake of 3,570 mg/person/day may be calculated as dosage without systemic effects.

The actual dermal threshold for systemic effects may be substantially higher than that dosage of 3,570 mg/person/day because dermal penetration rates generally are assumed to be lower than those by inhalation. For methacrylic acid absorption by inhalation is assumed to be 100%. Substance-specific data on dermal absorption are not available. With reference to acrylic acid, a dermal absorption of 25% may be used for preliminary dermal risk assessment of methacrylic acid. Thus, for the calculation of an adjusted MOS a dermal NOAEL (human, chronic) of about 14,000 (3,570 · 4) mg/person/day is assumed.

The lowest direct MOS value of 340 (that corresponds to an adjusted value of 1,360) is calculated for scenario 4b (see **Table 4.11**). Based on this risk characterisation, systemic health risks by chronic dermal exposure are not considered of concern (**conclusion (ii)**).

Table 4.11 Repeated dose toxicity (inhalation/local and dermal contact/systemic): MOS values and conclusions

Area of production and use	Inhalation (local)			Dermal contact (systemic effects)		
	Shift average value [mg/m³]	MOS [1]	Conclusion	Shift average value [mg/p/d]	MOS [2]	Conclusion
Chemical Industry						
(1) Production and further processing as a chemical intermediate (filling, sampling, cleaning, maintenance, repair)	5.6 [3]	13	ii	low [4]	high	ii
(2) Manufacture of adhesives - 2 -12% methacrylic acid (weighing, filling, mixing, drumming)	0.5 - 2.75 [5]	26-144	ii	low [4]	high	ii
Industrial area: production of preparations						
(3) Manufacture of adhesives - 2-12% methacrylic acid (weighing, filling, mixing, drumming)	0.5 - 2.75 [5] 9 - 45 [6]	26 - 144 2 -8	ii **iii**	low [4]	high	ii
Industrial area: use						
(4) Use of adhesives - (4a) ≥ 5% methacrylic acid (handling, gluing)	2 – 11 [5] 36 [6]	6.5 - 36 2	ii **iii**	low [4]	high	ii
- (4b) < 5% methacrylic acid (handling, gluing)	2 - 11 [5] 36 [6]	6.5 - 36 2	ii **iii**	1 - 10.5 [7]	> 340 – 3,570	ii

[1] MOS (adjusted) = MOS (direct), NAEC (local): 72 mg/m³
[2] NAEL used for calculations: > 3,570 mg/p/d
[3] workplace measurement
[4] expert judgement
[5] EASE (inhalation, with LEV)
[6] EASE (inhalation, without LEV)
[7] EASE (dermal, without PPE)

Combined exposure (systemic effects)

Systemic health effects due to combined exposure (inhalation and dermal contact) are to be assessed in addition to route-specific risk estimates.

The MOS values for combined exposure are calculated by the formula:

$$\frac{1}{MOS_{comb.}} = \frac{1}{MOS_{inh.}} + \frac{1}{MOS_{derm.}}.$$

Scenario 4b (use of adhesives with less than 5% methacrylic acid, industrial area) is the only scenario with relevant concomitant chronic exposure via inhalation and dermal contact. The other scenarios are scenarios for which chronic dermal exposure is not assumed (e.g. because of the corrosive property of the material).

Table 4.12 Combined exposure (repeated dose toxicity, systemic)

Exposure scenario	MOS $_{inhalation}$ *	MOS $_{dermal}$ *	MOS $_{combined}$
(4b) Use of adhesives (< 5% methacrylic acid)	32 (with LEV) 10 (without LEV)	340	29 10

* lowest MOS values of ranges are used; MOS $_{inhalation}$ calculated as the fivefold MOS (inhalation, local) from Table 4.11.

The route-specific MOS values for systemic effects are not considered of concern (see "Repeated dose toxicity, inhalation and dermal"). The MOS for combined exposure does not differ significantly from the MOS for inhalation exposure.

Because the lowest MOS value for combined exposure is 10 and specific systemic toxicity was not detected, these values are not considered of concern. Systemic risks by combined exposure are not expected (**conclusion (ii)**).

4.1.3.2.5 Mutagenicity

Methacrylic acid is negative in a bacterial gene mutation test. Further mutagenicity testing on methacrylic acid is lacking. Taking into consideration the data on the structurally related compound methyl methacrylate, which is not considered to be genotoxic *in vivo*, there is no need for further testing. For the risk assessment, methacrylic acid is regarded as non-genotoxic (**conclusion (ii)**).

4.1.3.2.6 Carcinogenicity

There are no data on carcinogenicity for methacrylic acid itself. Based on mutagenicity data available and based on methyl methacrylate carcinogenicity data there is no indication of a carcinogenic potential of methacrylic acid itself. Corresponding risks at the workplaces are not anticipated to occur (**conclusion (ii)**).

4.1.3.2.7 Reproductive toxicity

Fertility impairment

For methacrylic acid, studies on the impairment of male or female reproductive functions are not available. In a 90-day inhalation study with concentrations up to 300 ppm no histopathological changes in the reproductive organs of male and female rats and mice were detected. From screening data on methyl methacrylate no indications of fertility impairment have been obtained. Based on these screening data, methacrylic acid is not considered to be a reproductive toxicant (fertility impairment).

For general systemic effects, a NOAEC of 100 ppm and a LOAEC of 300 ppm was established. Corresponding risk evaluation does not result in concern (see "Repeated dose toxicity, systemic"). With reference to the available screening data, there is no indication of fertility impairment at exposure levels with slight general systemic effects. Consequently, **conclusion (ii)** is reached for all exposure scenarios.

Developmental toxicity

No data on methacrylic acid are available. In developmental toxicity studies with methyl methacrylate developmental toxicity could not be revealed. Between 100 and 300 ppm a transiently (during the first two days of exposure) reduced maternal body weight gain was reported. The NOAEC for developmental toxicity (for methyl methacrylate) was determined to be 2,028 ppm (highest dose tested). This NOAEC is about 20 times greater than the NOAEC of 100 ppm for general systemic toxicity of methacrylic acid. For the highest exposure level reported in **Table 4.11** (12.6 ppm) a MOS value of greater than 161 (2,028/12.6) is calculated. In analogy to the decision for fertility impairment, **conclusion (ii)** is reached for all exposure scenarios concerning developmental toxicity.

4.1.3.2.8 Summary of risk characterisation for workers

The conclusions of the occupational risk assessment are summarised in **Table 4.13**.

Table 4.13 Conclusions of the occupational risk assessment of methacrylic acid

	Acute toxicity (inhalation, dermal)	Irritation/ Corrosivity (dermal)	Irritation/ Corrosivity (inhalation)	Sensitisation (inhalation, dermal)	Repeated dose toxicity (local, inhalation)	Repeated dose toxicity (local, dermal)	Repeated dose toxicity (systemic/ inhalation, respiratory, dermal)	Repeated dose toxicity (combined exposure, systemic)	Mutagenicity *	Carcino-genicity	Reproductive toxicity
Chemical industry											
(1) Production and further processing as a chemical intermediate	ii	ii	**iii**	ii	ii	ii	ii	ii	ii	ii	ii
(2) Manufacture of adhesives	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
Industrial area											
(3) Manufacture of adhesives											
with LEV	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
without LEV	ii	ii	**iii**	ii	**iii**	ii	ii	ii	ii	ii	ii
(4a,b) Use of adhesives											
with LEV	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
without LEV	ii	ii	**iii**	ii	**iii**	ii	ii	ii	ii	ii	ii
Skilled trade											
(5a,b) Use of adhesives	ii	ii	**iii**	ii	ii	ii	ii	ii	ii	ii	ii

Blank fields: **Conclusion (ii)** is applied
Conclusion (iii): There is a need for limiting the risks; risk reduction measures which are being applied shall be taken into account

4.1.3.3 Consumers

4.1.3.3.1 Acute toxicity

Following the exposure assessment, consumers are not expected to be exposed to methacrylic acid in the range of values which are derived from acute oral, dermal, and inhalation toxicity figures based on animal LD_{50} (oral: 1,230-2,200 mg/kg bw; dermal: 500-1,000 mg/kg bw) or LC_{50} (7.1 mg/l/4 h (aerosol exposure)) values.

Information on acute toxicity by the dermal route is available (screening test with two rabbits per dose group documenting a dermal LD_{50} value of 500 – 1,000 mg/kg bw), demonstrating a relevant acute dermal toxic risk by contact with MAA. But following the exposure assessment, to consumers, the substance is of no concern in relation to acute toxicity (**conclusion (ii)**).

4.1.3.3.2 Irritation/Corrosivity

Irritation and corrosivity are the main effects at the site of contact (skin, eye, oral, and inhalation studies). Skin and eyes can be severely affected in contact with the substance due to the corrosive properties.

No reliable information concerning possible effects of methacrylic acid in humans is available.

Following the exposure assessment, consumers are expected to be exposed only to concentrations, which are far below the effective concentrations (**conclusion (ii)**).

4.1.3.3.3 Sensitisation

There is no evidence for skin sensitising properties of methacrylic acid either as a result of animal tests or experience with humans (**conclusion (ii)**).

4.1.3.3.4 Repeated dose toxicity

Following the exposure assessment there is no chronic exposure to MAA.

During the application of dispersion paints consumers may be exposed to an average concentration of about 0.5 mg/m³ with a possible peak concentration of 0.7 mg/m^3. The inhalation exposure resulting from residual monomeric MAA does not reflect a realistic chronic exposure scenario. Nevertheless, this scenario represents a “worst case”, therefore, a risk characterisation is performed.

In 90-day inhalation studies in rats and mice the predominant target organ was the respiratory tract. MAA caused irritancy at the site of contact (nasal cavity). All treatment groups of both rat strains and mice of the high-dose group showed a rhinitis of the anterior regions of the turbinates. A low-grade rhinitis almost without additional lesions was also evident in some of the control rats, however it was not seen in mice. A degeneration of olfactory epithelium of the mid part of the nasal cavity was observed in mice at mid- and high-dose level, but not in the rat nose. No specific systemic toxic effects were detected.

A NOAEC for local effects of 20 ppm (resp. 71.4 mg/m^3) was derived from a study in mice (LOAEC in rats: 20 ppm).

For the decision on the appropriateness of MOS, the following aspects regarding the critical effect as well as exposure have been considered and taken into account:

- Overall confidence in the database

The data taken into account for performing the risk characterisation have been evaluated with regard to their reliability, relevance and completeness according to Section 3.2 of the TGD. The data were published in peer-reviewed journals or submitted to the Competent Authority in private reports being adequately detailed and in accordance with internationally recognised guidelines and to GLP.

The findings of all studies are not contradictory so that the judgement can be based on the database.

There are no reasons to assume limited confidence.

- Uncertainty arising from the variability in the experimental data

The NOAEC for local effects of 71.4 mg/m^3 (20 ppm) was derived from a 90-day inhalation study in mice which was well performed and the results were in conformity with the findings of the other study in rats giving a LOAEC of 71,4 mg/m³. The rat study suffers from the finding of a low-grade rhinitis almost without additional lesions which was also evident in some of the control rats (not seen in mice).

There are no reasons to assume a special extent of uncertainty which has to be taken into account.

- Intra- and interspecies variation

It is possible that humans may be less sensitive than rodents to lesions of the nasal epithelium, however, the currently available data are inadequate to account quantitatively for potential interspecies variation in sensitivity. Using the PBPK modelling for a calculation of such interspecies variability seems to be not sufficiently supported by the limited data available on humans. Therefore, a lower MOS seems not to be justified at present.

- Nature and severity of the effect

No exposure related deaths were recorded.

The main effects considered as “critical effects” are irritancy and/or corrosivity at the site of contact (irreversible, serious health effect).

There are no reasons to assume that the effects shown in the animal experiments are limited to the species tested, thus being not of relevance for humans. Because of the seriousness of the effect there is concern, which has to be expressed in the magnitude of the MOS.

- Dose-response-relationship

The incidences in rats showed no clear dose-response-relationship. In mice, a dose-response-relationship is not demonstrated (lack of higher exposure data).

No data are available for judging on the steepness of the dose-response-relationship.

There is no reason to assume concern which has to be expressed in an increased MOS taking into account the exposure level.

- Differences in exposure (route, duration, frequency and pattern)

Following the exposure assessment, the consumer may be exposed to MAA via inhalation, whereas oral and dermal exposure can be neglected. The described human exposure scenarios (dispersion paints and 2-component adhesives) do not represent real chronic scenarios. The NOAEC used for the discussion of the MOS regarding these applications is derived from a 90-day inhalation study in mice. Because MAA acts primarily at the nasal cavity, systemic effects have not been considered. Moreover, the NOAEC for systemic effects was considered to be 100 ppm (357 mg/m^3) in the same study.

There are no reasons to assume that special concern can be derived neither from this procedure nor from the available toxicokinetic information.

- Human population to which the quantitative and/or qualitative information on exposure applies

Following the inhalation exposure there is no reason to assume a special risk for elderly, children or other people suffering from special diseases.

- Other factors

There are no other factors known requiring a peculiar margin of safety.

<u>MOS for inhalation exposure scenario</u>

During application of dispersion paints for 4.9 hours (6 times per year) the consumer may be exposed to an average concentration of 0.5 mg/m³ with a possible peak value of 0.7 mg/m³. This exposure does not reflect a real chronic exposure scenario. Therefore, the margin of safety between the

estimated exposure level of 0.5 mg/m³

and the

NOAEC for local irritation effects of 71.4 mg/m³

is judged to be sufficient because a worst-case exposure scenario was taken into consideration.

During application of paint on solvent basis (average concentration 1.0 mg/m³ with a possible peak value of 1.6 mg/m³), the margin of safety between the

estimated exposure level of 1 mg/m³

and the

NOAEC for local irritation effects of 71.4 mg/m³

is judged to be sufficient because a worst-case exposure scenario was taken into consideration.

Considering the possible peak value exposure see Section "Acute toxicity".

Following the exposure assessment there is no chronic exposure to two-component adhesive (**conclusion (ii)**).

MOS for dermal exposure scenario

The dermal exposure was estimated to be lower than 1 µg/kg per event.

In repeated dose toxicity studies in mice (90-day inhalation) the NOAEC for systemic effects was 100 ppm (0.357 mg/l). The derived concentration in air is converted as follows to the inhaled amount of the substance using the respiratory minute volume 1.3 l/min/kg and a exposure duration of 360 min/day:

0.357 mg/l · 1.3 l/min/kg · 360 min/day = 167 mg/kg bw/d

Comparison dermal exposure / NOAEL

$$\frac{\text{Dermal exposure}}{\text{NOAEL}} = \frac{< 0.001 \text{ mg/kg bw/d}}{167 \text{ mg/kg bw/d}}$$

The margin of safety expressed by the magnitude between the estimated exposure and the NOAEC is very low (**conclusion (ii)**).

MOS for oral exposure scenario

The oral uptake is considered as negligible (**conclusion (ii)**).

4.1.3.3.5 Mutagenicity

A bacterial mutation test using methacrylic acid was negative. Further testing on methacrylic acid is lacking. However, taking into consideration the data on the structurally related substance methyl methacrylate - which indicate that this substance does not express a genotoxic potential *in vivo* - there is no need for further testing (**conclusion (ii)**).

4.1.3.3.6 Carcinogenicity

Following the exposure assessment there is no evidence for relevant exposure to methacrylic acid. There is no evidence from experimental data on mutagenicity and on carcinogenicity from tests with methyl ester of methacrylic acid. The substance is of no concern in relation to carcinogenicity (**conclusion (ii)**).

4.1.3.3.7 Reproductive toxicity

Following the exposure assessment, there is no evidence for relevant exposure to methacrylic acid. There are no experimental data on reproductive toxicity of methacrylic acid available.

A N(L)OAEL/exposure ratio cannot be derived.

The available data from studies with methyl methacrylate did not give evidence for adverse effects on reproductive organs. Also in developmental toxicity studies with methyl methacrylate a specific teratogenic, embryo- or fetotoxic potential could not be revealed (**conclusion (ii)**).

4.1.3.4 Humans exposed via the environment

Indirect exposure to methacrylic acid via the environment occurs mainly by drinking water. Following the local scenario data (at a point source) an intake of a total daily dose of 0.15 µg/kg bw/d is calculated (as a worst case). For the regional scenario, the respective figure is smaller (4 ng/kg bw/d). In repeated dose toxicity studies in mice (90-day inhalation) the NOAEC for systemic effects was 100 ppm (0.357 mg/l).

The derived concentration in air is converted as follows to the inhaled amount of the substance using the respiratory minute volume 1.3 l/min/kg and exposure duration of 360 min/day:

0.357 mg/l · 1.3 l/min/kg · 360 min/day = 167 mg/kg bw/d

Comparison indirect exposure - Local scenario/NOAEL

$$\frac{\text{Indirect exposure}}{\text{NOAEL}} = \frac{0.00015 \text{ mg/kg bw/d}}{167 \text{ mg/kg bw/d}}$$

The margin of safety expressed by the magnitude between the calculated exposure and the NOAEL is very low for the local scenario. Thus, the substance is of no concern in relation to indirect exposure via the environment (**conclusion (ii)**).

Comparison indirect exposure - Regional scenario/NOAEL

$$\frac{\text{Indirect exposure}}{\text{NOAEL}} = \frac{0.000004 \text{ mg/kg bw/d}}{167 \text{ mg/kg bw/d}}$$

The margin of safety expressed by the magnitude between the calculated exposure (regional scenario) and the NOAEL is very low for the regional scenario. Thus, the substance is of no concern in relation to indirect exposure via the environment (**conclusion (ii)**).

4.1.3.5 Combined exposure

Taking into account the sum of all types of exposure the combined exposure was estimated to amount to 1-10 µg/kg bw/d (lower microgram range).

Comparison combined exposure / NOAEL

$$\frac{\text{Combined exposure}}{\text{NOAEL}} = \frac{< 0.01 \text{ mg/kg bw/d}}{167 \text{ mg/kg bw/d}}$$

The margin of safety expressed by the magnitude between the estimated exposure and the NOAEL is very low. Thus, the substance is considered of no concern in relation to combined exposure (**conclusion (ii)**).

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

MAA has no explosive or oxidising properties due to structural reasons and is not highly flammable. Therefore with regard to the physico-chemical properties and with regard to the occupational exposure (described in Section 4.1.1.2) and consumer exposure (described in Section 4.1.1.3) MAA is not expected to cause specific concern relevant to human health. There is no need for further information and/or testing with regard to physico-chemical properties (**conclusion (ii)**).

4.2.1 Risk characterisation

4.2.1.1 Workers

MAA polymerizes at increased temperatures, and in the case of contact with radical donors (e.g. peroxides and azo compounds). Uncontrolled exothermic polymerization in closed systems might lead to explosion caused by increasing pressure. To prevent polymerization MAA is stabilized with approx. 200 ppm hydroquinone monomethylether. Care has to be taken, because solidification of MAA can result in a depletion of the polymerization inhibitor in the solidified areas (Degussa, 1988). Risk reduction measures beyond those which are being applied already are not considered necessary (**conclusion (ii)**).

5 RESULTS

5.1 ENVIRONMENT

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

This conclusion applies to all environmental spheres regarded for the production and processing of methacrylic acid and the use of polymeric products made from methacrylic acid.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

This conclusion is reached because of concerns for effects on the aquatic ecosystem as a consequence of exposure arising from the use of acrylate based grouting agents.

During the use of a grouting agent containing hydroxyethylmethacrylate high concentrations of methacrylic acid are released via the drainage water. Due to the high mobility of methacrylic acid in soils, a potential for leaching to groundwater has to be expected. The exposure assessment for surface water was based on measured concentration at a tunnel construction site. A quantitative extrapolation to other construction sites seems not possible, but similar conditions might be anticipated. Data improvement is not the proposed option, because an environmentally safe handling of the grouting agent has to be achieved independent of the local circumstances. Therefore, risk reduction measures at Community level are recommended.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

This conclusion is reached because of

- concerns for respiratory tract irritation as a consequence of short term inhalation exposure arising from the production, further processing as a chemical intermediate in the chemical industry, the manufacture of adhesives in the industrial area and the industrial and skilled trade use of adhesives,

- concerns for local respiratory effects as a consequence of repeated inhalation exposure arising from manufacture and use of adhesives.

Consumers

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Humans exposed via the environment

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Combined exposure

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

5.2.2 Human health (risks from physico-chemical properties)

MAA has no explosive or oxidising properties due to structural reasons and is not highly flammable. Therefore with regard to the physico-chemical properties and with regard to the occupational exposure and consumer exposure, MAA is not expected to cause specific concern relevant to human health.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

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ABBREVIATIONS

ADI	Acceptable Daily Intake
AF	Assessment Factor
ASTM	American Society for Testing and Materials
ATP	Adaptation to Technical Progress
AUC	Area Under The Curve
B	Bioaccumulation
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
BCF	Bioconcentration Factor
BMC	Benchmark Concentration
BMD	Benchmark Dose
BMF	Biomagnification Factor
bw	body weight / *Bw*, *bw*
C	Corrosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
CA	Chromosome Aberration
CA	Competent Authority
CAS	Chemical Abstract Services
CEC	Commission of the European Communities
CEN	European Standards Organisation / European Committee for Normalisation
CEPE	European Committee for Paints and Inks
CMR	Carcinogenic, Mutagenic and toxic to Reproduction
CNS	Central Nervous System
COD	Chemical Oxygen Demand
CSTEE	Scientific Committee for Toxicity, Ecotoxicity and the Environment (DG SANCO)
CT_{50}	Clearance Time, elimination or depuration expressed as half-life
d.wt	dry weight / dw
dfi	daily food intake
DG	Directorate General
DIN	Deutsche Industrie Norm (German norm)
DNA	DeoxyriboNucleic Acid
DOC	Dissolved Organic Carbon
DT50	Degradation half-life or period required for 50 percent dissipation / degradation
DT90	Period required for 50 percent dissipation / degradation
E	Explosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)

EASE	Estimation and Assessment of Substance Exposure Physico-chemical properties [Model]
EbC50	Effect Concentration measured as 50% reduction in biomass growth in algae tests
EC	European Communities
EC10	Effect Concentration measured as 10% effect
EC50	median Effect Concentration
ECB	European Chemicals Bureau
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECVAM	European Centre for the Validation of Alternative Methods
EDC	Endocrine Disrupting Chemical
EEC	European Economic Communities
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EN	European Norm
EPA	Environmental Protection Agency (USA)
ErC50	Effect Concentration measured as 50% reduction in growth rate in algae tests
ESD	Emission Scenario Document
EU	European Union
EUSES	European Union System for the Evaluation of Substances [software tool in support of the Technical Guidance Document on risk assessment]
F(+)	(Highly) flammable (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
FAO	Food and Agriculture Organisation of the United Nations
FELS	Fish Early Life Stage
foc	Organic carbon factor (compartment depending)
GLP	Good Laboratory Practice
HEDSET	EC/OECD Harmonised Electronic Data Set (for data collection of existing substances)
HELCOM	Helsinki Commission -Baltic Marine Environment Protection Commission
HPLC	High Pressure Liquid Chromatography
HPVC	High Production Volume Chemical (> 1000 t/a)
IARC	International Agency for Research on Cancer
IC	Industrial Category
IC50	median Immobilisation Concentration or median Inhibitory Concentration
ILO	International Labour Organisation
IPCS	International Programme on Chemical Safety
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database (existing substances)
IUPAC	International Union for Pure and Applied Chemistry
JEFCA	Joint FAO/WHO Expert Committee on Food Additives

JMPR	Joint FAO/WHO Meeting on Pesticide Residues
Koc	organic carbon normalised distribution coefficient
Kow	octanol/water partition coefficient
Kp	solids-water partition coefficient
L(E)C50	median Lethal (Effect) Concentration
LAEL	Lowest Adverse Effect Level
LC50	median Lethal Concentration
LD50	median Lethal Dose
LEV	Local Exhaust Ventilation
LLNA	Local Lymph Node Assay
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
LOED	Lowest Observed Effect Dose
LOEL	Lowest Observed Effect Level
MAC	Maximum Allowable Concentration
MATC	Maximum Acceptable Toxic Concentration
MC	Main Category
MITI	Ministry of International Trade and Industry, Japan
MOE	Margin of Exposure
MOS	Margin of Safety
MW	Molecular Weight
N	Dangerous for the environment (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC
NAEL	No Adverse Effect Level
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
NOEC	No Observed Effect Concentration
NTP	National Toxicology Program (USA)
O	Oxidizing (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational Exposure Limit
OJ	Official Journal
OSPAR	Oslo and Paris Convention for the protection of the marine environment of the Northeast Atlantic
P	Persistent
PBT	Persistent, Bioaccumulative and Toxic
PBPK	Physiologically Based PharmacoKinetic modelling

PBTK	Physiologically Based ToxicoKinetic modelling
PEC	Predicted Environmental Concentration
pH	logarithm (to the base 10) (of the hydrogen ion concentration $\{H^+\}$
pKa	logarithm (to the base 10) of the acid dissociation constant
pKb	logarithm (to the base 10) of the base dissociation constant
PNEC	Predicted No Effect Concentration
POP	Persistent Organic Pollutant
PPE	Personal Protective Equipment
QSAR	(Quantitative) Structure-Activity Relationship
R phrases	Risk phrases according to Annex III of Directive 67/548/EEC
RAR	Risk Assessment Report
RC	Risk Characterisation
RfC	Reference Concentration
RfD	Reference Dose
RNA	RiboNucleic Acid
RPE	Respiratory Protective Equipment
RWC	Reasonable Worst Case
S phrases	Safety phrases according to Annex III of Directive 67/548/EEC
SAR	Structure-Activity Relationships
SBR	Standardised birth ratio
SCE	Sister Chromatic Exchange
SDS	Safety Data Sheet
SETAC	Society of Environmental Toxicology And Chemistry
SNIF	Summary Notification Interchange Format (new substances)
SSD	Species Sensitivity Distribution
STP	Sewage Treatment Plant
T(+)	(Very) Toxic (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
TDI	Tolerable Daily Intake
TG	Test Guideline
TGD	Technical Guidance Document
TNsG	Technical Notes for Guidance (for Biocides)
TNO	The Netherlands Organisation for Applied Scientific Research
UC	Use Category
UDS	Unscheduled DNA Synthesis
UN	United Nations
UNEP	United Nations Environment Programme

US EPA	Environmental Protection Agency, USA
UV	Ultraviolet Region of Spectrum
UVCB	Unknown or Variable composition, Complex reaction products of Biological material
vB	very Bioaccumulative
VOC	Volatile Organic Compound
vP	very Persistent
vPvB	very Persistent and very Bioaccumulative
v/v	volume per volume ratio
w/w	weight per weight ratio
WHO	World Health Organization
WWTP	Waste Water Treatment Plant
Xn	Harmful (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
Xi	Irritant (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)

Appendix A1 Distribution and fate

Substance: Methacrylic Acid CAS-Nr.: 79-41-4

melting point:	MP = 288 K
vapour pressure:	VP = 90 Pa
water solubility:	SOL = 89,000 $mg \cdot l^{-1}$
part. coefficient octanol/water:	$LOGP_{OW}$ = 0.93
moleculare weight:	MOLW = 0.086 $kg \cdot mol^{-1}$
gas constant:	R = 8.3143 $J \cdot mol \cdot K^{-1}$
Temperature:	T = 293 K
conc. of suspended matter in the river:	$SUSP_{water}$ = 15 $mg \cdot l^{-1}$
density of the solid phase:	RHO_{solid} = 2,500 $kg \cdot m^{-3}$
volume fraction water in susp. matter:	$Fwater_{susp}$ = 0.9
volume fraction solids in susp.matter:	$Fsolid_{susp}$ = 0.1
volume fraction of water in sediment:	$Fwater_{sed}$ = 0.8
volume fraction of solids in sediment:	$Fsolid_{sed}$ = 0.2
volume fraction of air in soil:	$Fair_{soil}$ = 0.2
volume fraction of water in soil:	$Fwater_{soil}$ = 0.2
volume fraction of solids in soil:	$Fsolid_{soil}$ = 0.6
aerobic fraction of the sediment comp.:	$Faer_{sed}$ = 0.1
product of CONjunge and $SURF_{air}$:	product = 10^{-4} Pa

Distribution air/water: Henry-constant

$$HENRY = \frac{VP \bullet MOLW}{SOL} \qquad HENRY = 0.087\ Pa \cdot m^3 \cdot mol^{-1}$$

$$\log\left(\frac{HENRY}{Pa \bullet m^3 \bullet mol^{-1}}\right) = -1.061$$

$$K_{air\text{-}water} = \frac{HENRY}{R \bullet T} \qquad K_{air\text{-}water} = 3.57 \cdot 10^{-5}$$

Solid/water-partition coefficient Kp_{comp} and total compartment/water-partition coefficient $K_{comp\ water}$

Suspended matter

$Kp_{susp} = 0.5\ l \cdot kg^{-1}$

$K_{susp\_water} = Fwater_{susp} + .Fsolid_{susp} \cdot Kp_{susp} \cdot RHO_{solid}$ $K_{susp\_water} = 1.025$

factor for the calculation of $Clocal_{water}$:

factor = $1 + Kpsusp \cdot SUSP_{water}$ factor = 1

Sediment

$Kp_{sed} = 0.5\ l \cdot kg^{-1}$

$K_{sed\_water} = Fwater_{sed} + Fsolid_{sed} \cdot Kp_{sed} \cdot RHO_{solid}$ $K_{sed\_water} = 1.05$

Soil

$Kpsoil = 0.5\ l \cdot kg^{-1}$

$Ksoil\_water = Fair_{soil} \cdot K_{air\_water} + Fwater_{soil} + Fsolid_{soil} \cdot Kp_{soil} \cdot RHO_{solid}$

$K_{soil\_water} = 0.95$

Sludge

$Kps_{ludge} = 0.5\ l \cdot kg^{-1}$

Elimination in STPs

Rate constant in STP: $k = 1\ h^{-1}$ elimination P = f (k, logpow, logH) = 87.3%

fraction directed to surface water $Fstp_{water}$ = 12.6%

Biodegradation in different compartments

Surface water

$Kbio_{water} = 4.7 \cdot 10^{-2}\ d^{-1}$ (TGD, Table 5)

Soil

$DT50bio_{soil} = 30$ d (TGD, Table 6)

$$kbio_{soil} = \frac{\ln(2)}{DT_{50}bio_{soil}} \qquad kbio_{soil} = 0.023\ d^{-1}$$

Sediment

$$kbio_{sed.} = \frac{\ln(2)}{DT_{50}bio_{soil}} \cdot Faer_{sed} \qquad kbio_{sed} = 2.31 \cdot 10^{-3}\ d^{-1}$$

Degradation in surface waters

$khydr_{water.} = 1 \cdot 10^{-10}\ d^{-1}$

$kphoto_{water.} = 1 \cdot 10^{-10}\ d^{-1}$

$kdeg_{water} = khydr_{water} + kphoto_{water} + kbio_{water}$

$kdeg_{water} = 0.047\ d^{-1}$

Atmosphere

Calculation of CONjunge · SURFaer for the OPS-model

$$VPL = \frac{VP}{\exp\left[6.79\left(1 - \frac{MP}{285K}\right)\right]}$$

VP = if (MP > 285 K use VLP, otherwise VP)

VP = 96.668 Pa

$$Fass_{aer} = \frac{product}{VP + product}$$

$Fass_{aer} = 1.034 \cdot 10^{-6}$

Degradation in the atmosphere

$kdeg_{air}$=1,49 d^{-1} (see AOP-calculation -AOPwin vers. 1.65)

Appendix A2 Calculation of C_{local} for aquatic compartment during production and processing of chemicals at one site

status: TGD, ESD, IC-3

Site: generic model
Chemical: Methacrylic acid CAS-Nr.: 79-41-4

d = 86,400 s a = 365 d µg = 10^{-9} kg

Production volume: (highest by level)	$T_1 = 50{,}000\ t \cdot a^{-1}$
Processing volume:	$T_2 = 50{,}000\ t \cdot a^{-1}$
Emission factor for production:	$f_1 = 0.3\%$
Emission factor for processing:	$f_2 = 0.7\%$
Duration of emission for production (TGD, Table B1.1):	$Temission_1 = 300\ d \cdot a^{-1}$
Duration of emission for processing (TGD, Table B3.2):	$Temission_2 = 300\ d \cdot a^{-1}$
Fraction of emission directed to water: (SimpleTreat, k: 1h^{-1}; logH: -1; $logK_{ow}$: 0.93)	$Fstp_{water} = 12.6\%$
River flow rate (TGD, IC 3):	$V = 60\ m^3 \cdot s^{-1}$
Factor ($1 + K_p \cdot SUSPwater$):	FACTOR = 1

Emission per day:

$$Elocal_{water} = \frac{T_1 \bullet f_1}{Temission_1} + \frac{T_2 \bullet f_2}{Temission_2} \qquad Elocal_{water} = 1.67 \cdot 10^3\ kg \cdot d^{-1}$$

Concentration in surface water:

$$Clocal_{water} = \frac{Elocal_{water} \bullet Fstp_{water}}{V \cdot FACTOR} \qquad Clocal_{water} = 40.51\ \mu g \cdot l^{-1}$$

Annual average local concentration in surface water:

$$Clocal_{water\_ann} = Clocal_{water} \bullet \frac{Temission_1}{365 \cdot d \cdot a^{-1}} \qquad Clocal_{water\_ann} = 33.295\ \mu g \cdot l^{-1}$$

Release to hydrosphere:

$RELEASE_{sw} = (T1 \cdot f1 + T2 \cdot f2) \cdot Fstp_{water}$ $RELEASE_{sw} = 63\ t \cdot a^{-1}$

Remarks: Generic exposure scenario with the highest production and processing volume and default data input.

Appendix A3 Calculation of Clocal for aquatic compartment during processing of chemical

status: TGD, ESD, IC-3

Site: generic scenario for external esterification
Chemical: Methacrylic acid CAS-Nr.: 79-41-4

d = 86,400 s a = 365 d µg = 10^{-9} kg

Tonnage:	$T = 4{,}800\ t \cdot a^{-1}$
Emission factor:	F = 0.7%
Fraction of emission directed to water: (SimpleTreat; k:1 h^{-1}; logPow:0.93; logH:-1)	$Fstp_{water} = 12.6\%$
River flow rate:	$FLOW = 60\ m^3 \cdot s^{-1}$
Duration for emission (assumption):	$Temission = 300\ d \cdot a^{-1}$
Plant capacity per day:	$PK = \frac{T}{Temission}$ $PK = 16\ t \cdot d^{-1}$
Factor (1+Kp · SUSPwater):	FACTOR = 1

Emission per day:

$Elocal_{water} = PK \cdot f$ $Elocal_{water} = 112\ kg \cdot d^{-1}$

Concentration in surface water:

$Clocal_{water.} = \frac{Elocal_{water} \cdot Fstp_{water}}{FLOW \cdot FACTOR}$ $Clocal_{water} = 2.72\ \mu g \cdot l^{-1}$

Release to wwtp:

$RELEASE_{wwtp} = Elocal_{water} \cdot Temission$

$RELEASE_{wwtp} = 33.6\ t \cdot a^{-1}$

Release to hydrosphere:

$RELEASE_{sw} = RELEASE_{wwtp} \cdot Fstp_{water}$

$RELEASE_{sw} = 4.23\ t \cdot a^{-1}$

Annual average local concentration in surface water:

$Clocal_{water\_ann.} = Clocal_{water} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$ $Clocal_{water\_ann} = 2.24\ \mu g \cdot l^{-1}$

Appendix A4 Default Exposure Estimation of $Clocal_{water}$

status: TGD, Tables A and B

Chemical: MAA

Stage of life cycle: processing (polymerisation), wet
IC/UC/MC: 11/33/III
d = 86,400 s a = 365 d µg = 10^{-9} kg

Total annual tonnage of chemical:	TONNAGE = 6,300 $t \cdot a^{-1}$
Release factor (A-Table: A3.10):	$F_{emission}$ = 0.01
Fraction of main source (B-Table: B3.9):	Fmainsource = 0.05
Wastewater flow of wwtp:	$EFFLUENT_{stp}$ = 2,000 $m^3 \cdot d^{-1}$
Duration of emission (B-Table: B3.9):	Temission = 300 $d \cdot a^{-1}$
Fraction of emission directed to water: (SimpleTreat; k: 1 h^{-1}; logPow: 0.93; logH: -1)	$Fstp_{water}$ = 12.6%
Dilution factor (TGD):	DILUTION = 10
Factor (1+Kp · SUSPwater):	FACTOR = 1

Emission per day:

$$Elocal_{water} = \frac{TONNAGE \cdot Fmainsource \cdot f_{emission}}{Temission}$$

$Elocal_{water}$ = 10.5 $kg \cdot d^{-1}$

Influent concentration:

$$Clocal_{inf} = \frac{Elocal_{water}}{EFFLUENT_{stp}}$$

$Clocal_{inf} = 5.25 \cdot 10^3$ $\mu g \cdot l^{-1}$

Effluent concentration:

$Clocal_{eff} = Clocal_{inf} \cdot Fstp_{water}$

$Clocal_{eff}$ = 661.5 $\mu g \cdot l^{-1}$

Concentration in surface water:

$$Local_{water} = \frac{Clocaleff}{FACTOR \cdot DILUTION}$$

$Clocal_{water}$ = 66.15 $\mu g \cdot l^{-1}$

Appendix A5 Default calculation of PEC_{local} for the hydrosphere

status: TGD for Existing Substances / USES

MAA

d = 86,400 s μg = 10^{-9} kg

Formulation of paints

Tables: A2.1, B2.3

tonnage: $T = 6 \cdot t$ (residual monomer)

release factor (A2.1): $r = 0.02$

fraction of main source (B2.3): $f = 0.4$

wastewater flow of the WWTP: $Q = 2{,}000\ m^3 \cdot d^{-1}$

number of days for releases: $D = 300 \cdot d$

$$C_{inf} = \frac{T \cdot r \cdot f}{Q \cdot d} \qquad C_{inf} = 0.08\ mg \cdot l^{-1}$$

Elimination in WWTP related to SIMPLETREAT

P = 87.4% P = f (biodegradation, log Pow, log H)

$C_{eff} = C_{inf} \cdot (1\text{-}P)$ $C_{eff} = 0.01\ mg \cdot l^{-1}$

Calculation of Clocal_water

partition coefficient for susp.matter: $K_{p\_susp} = 2\ kg^{-1} \cdot l$

concentration of suspended matter: $c_{susp} = 15\ mg \cdot l^{-1}$

dilution factor for receiving surface $D = 10$

$$Clocal_{water} = \frac{C_{eff}}{\left(1 + K_{p\_susp} \cdot c_{susp}\right) \cdot D} \qquad Clocal_{water} = 1.008\ \mu g \cdot l^{-1}$$

Appendix A6 Exposure during paper recycling

status: mod. UCD-Scenario

MAA

a = 365 d µg = 0.001 mg

total annual consumption of the substance	$Ws = 9{,}800\ kg \cdot a^{-1}$
rate of recycling	RR = 50%
de-inking rate	DR = 90%
not absorbed quantity	NA = 20%
number of working days	$N = 250\ d \cdot a^{-1}$
volume of wastewater	$V = 2{,}000\ m^3 \cdot d^{-1}$
number of plants	A = 35

influent concentration

$$c_{inf\,l} = \frac{Ws \cdot RR \cdot DR \cdot NA}{N \cdot V \cdot A}$$

$c_{infl} = 0.05\ mg \cdot l^{-1}$

elimination in WWTP; $k=1 \cdot h^{-1}$ (logH=-1; logPow=0.93) P=87.4%

effluent concentration

$c_{eff}=c_{infl} \cdot (1-P)$

$c_{eff}=0.006\ mg \cdot l^{-1}$

dilution factor D=10

Clocal_water: $Clocal_{water} = c_{eff} \cdot D^{-1}$

$Clocal_{water} = 0.635\ \mu g \cdot l^{-1}$

Appendix A7 Atmosphere (OPS-model)

Calculation of $Clocal_{air}$ and $PEClocal_{air}$

Substance: Methacrylic acid CAS-Nr.: 79-41-4

stage of life cycle: production and processing

d = 86,400 s a = 365 d mg = 10^{-6} kg

Production and processing volume:	TONNAGE = 50,000 $t.a^{-1}$
release factors (A-table:1.2 MC:Ib and A3.3 MC:Ic):	$f_{emission}$ = 0.00002
fraction of main source:	Fmainsource = 1
days of use per year (B-table):	Temission = 300 $d \cdot a^{-1}$
release during life cycle to air:	$RELEASE = TONNAGE \cdot f_{emission}$
	$RELEASE = 1 \cdot t \cdot a^{-1}$
local emission during episode to air:	$Elocal_{air} = \frac{Fmainsource \cdot RELEASE}{Temission}$
	$Elocal_{air} = 3.333\ kg \cdot d^{-1}$
concentration in air at source strength of 1kg/d	$Cstd_{air} = 2.78\ 10^{-4}\ mg \cdot m^{-3} \cdot kg^{-1} \cdot d$
fraction of the emission to air from STP	$fstp_{air}$ = 0%
local emission rate to water during emission episode	$Elocal_{water} = 1{,}670\ kg \cdot d^{-1}$
local emission to air from STP during emission episode	$Estp_{air} = Fstp_{air} \cdot Elocal_{water}$
	$Estp_{air} = 0\ kg \cdot d^{-1}$
local concentation in air during emission episode	$Clocal_{air} = \max(Elocal_{air}, Estp_{air}) \cdot Cstd_{air}$
	$Clocal_{air} = 9.267 \cdot 10^{-4}\ mg \cdot m^{-3}$
annual average concentration in air, 100 m from point source	$Clocal_{air\_ann} = Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$
	$Clocal_{air\_ann} = 7.616 \cdot 10^{-4}\ mg \cdot m^{-3}$
regional concentration in air	$PECregional_{air} = 1.2 \cdot 10^{-8}\ mg \cdot m^{-3}$
annual average predicted environmental concentration in air	$PEClocal_{air\_ann} = Clocal_{air\_ann} + PECregional_{air}$
	$PEClocal_{air\_ann} = 7.617 \cdot 10^{-4}\ mg \cdot m^{-3}$

Calculation of the deposition rate

standard deposition flux of aerosol-bound compounds at a source strength of 1kg/d

$$DEPstd_{aer} := 1 \cdot 10^{-2} \cdot mg \cdot m^{-2} \cdot d^{-1} \cdot kg^{-1} \cdot d$$

fraction of the chemical bound to aerosol (see: Distribution and Fate)

$$Fass_{aer} := 1.034\,10^{-6}$$

deposition flux of gaseous compounds as a function of Henry`s Law coefficient,at a source strength of 1kg/d

logH<-2	5*10 $^{-4}$ mg*m^{-2}*d^{-1}
-2<logH<2	4*10^{-4} mg*m^{-2}*d^{-1}
logH>2	3*10^{-4} mg*m^{-2}*d^{-1}

$$DEPstd_{gas} := 4 \cdot 10^{-4} \cdot mg \cdot m^{-2} \cdot d^{-1} \cdot kg^{-1} \cdot d$$

total deposition flux during emission episode

$$DEPtotal := \left(Elocal_{air} + Estp_{air}\right) \cdot \left[Fass_{aer} \cdot DEPstd_{aer} + \left(1 - Fass_{aer}\right) \cdot DEPstd_{gas}\right]$$

$$DEPtotal = 1.333 \cdot 10^{-3} \cdot mg \cdot m^{-2} \cdot d^{-1}$$

annual average total depostion flux

$$DEPtotal_{ann} := DEPtotal \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$$

$$DEPtotal_{ann} = 1.096 \cdot 10^{-3} \cdot mg \cdot m^{-2} \cdot d^{-1}$$

Appendix A8 Exposure of soil

Substance: Methacrylic acid CAS-Nr.: 79-41-4

stage of life cycle: production and processing

d = 86,400 s a = 365 d ppm = $mg \cdot kg^{-1}$ i = 1..3

annual average total deposition flux: $DEPtotal_{ann} = 1.096 \cdot 10^{-3}\ mg \cdot m^{-2} \cdot d^{-1}$

soil-water partitioning coefficient: $K_{soil\_water} = 0.95$

concentration in dry sewage sludge: $C_{sludge} = 0\ mg \cdot kg^{-1}$

air-water partitioning coefficient: $K_{air\_water} = 3.57 \cdot 10^{-5}$

rate constant for for removal from top soil: $Kbio_{soil} = 0.023 \cdot d^{-1}$

PECregional: $PECregional_{natural\_soil} = 0\ mg \cdot kg^{-1}$

Defaults:

mixing depth of soil: $DEPTH_{soil,i}$ =

0.2 m
0.2 m
0.1 m

bulk density of soil: $RHO_{soil} = 1{,}700\ kg \cdot m^{-3}$

average time for exposure: T_i =

30 d
180 d
180 d

partial mass transfer coefficient at air-side of the air-soil interface: $Kasl_{air} = 120\ m \cdot d^{-1}$

partial mass transfer coefficient at soilair-side of the air-soil interface: $Kasl_{soilair} = 0.48\ m \cdot d^{-1}$

partial mass transfer coefficient at soilwater-side of the air-soil interface: $Kasl_{soilwater} = 4.8.10^{-5}\ m \cdot d^{-1}$

fraction of rainwater that infiltrates into soil: $Finf_{soil} = 0.25$

rate of wet precipitation: $RAINrate = 1.92 \cdot 10^{-3}\ m \cdot d^{-1}$

dry sludge application rate:

$$APPLsludge_i :=$$

$0.5 \cdot kg \cdot m^{-2} \cdot a^{-1}$
$0.5 \cdot kg \cdot m^{-2} \cdot a^{-1}$
$0.1 \cdot kg \cdot m^{-2} \cdot a^{-1}$

Calculation:

aerial deposition flux per kg of soil:

$$D_{air_i} := \frac{DEPtotal_{ann}}{DEPTHsoil_i \cdot RHO_{soil}}$$

rate constant for valatilisation from soil:

$$k_{volat_i} := \left[\left(\frac{1}{kasl_{air} \cdot K_{air\_water}} + \frac{1}{kasl_{soilair} \cdot K_{air\_water} + kasl_{soilwater}} \right) \cdot K_{soil\_water} \cdot DEPTHsoil_i \right]^{-1}$$

rate constant for leaching from soil layer:

$$k_{leach_i} := \frac{Finf_{soil} \cdot RAINrate}{K_{soil\_water} \cdot DEPTHsoil_i}$$

removal from top soil:

$$k_i := k_{volat_i} + k_{leach_i} + kbio_{soil}$$

concentration in soil

concentration in soil due to 10 years of continuous deposition:

$$Cdep_{soil\_10_i} := \frac{D_{air_i}}{k_i} \cdot \left(1 - \exp\left(-365 \cdot d \cdot 10 \cdot k_i\right)\right)$$

concentration just after the first year of sludge application:

$$Csludge_{soil\_1_i} := \frac{C_{sludge} \cdot APPLsludge_i \cdot a}{DEPTHsoil_i \cdot RHO_{soil}}$$

initial concentration in soil after 10 applications of sludge:

$$Csludge_{soil\_10_i} := Csludge_{soil\_1_i} \cdot \left[1 + \left[\sum_{n=1}^{9} \left(\exp\left(-365 \cdot d \cdot k_i\right)^n \right) \right] \right]$$

dry sludge application rate:

$$APPLsludge_i :=$$

$0.5 \cdot kg \cdot m^{-2} \cdot a^{-1}$
$0.5 \cdot kg \cdot m^{-2} \cdot a^{-1}$
$0.1 \cdot kg \cdot m^{-2} \cdot a^{-1}$

Calculation:

aerial deposition flux per kg of soil:

$$D_{air_i} := \frac{DEPtotal_{ann}}{DEPTHsoil_i \cdot RHO_{soil}}$$

rate constant for valatilisation from soil:

$$k_{volat_i} := \left[\left(\frac{1}{kasl_{air} \cdot K_{air\_water}} + \frac{1}{kasl_{soilair} \cdot K_{air\_water} + kasl_{soilwater}} \right) \cdot K_{soil\_water} \cdot DEPTHsoil_i \right]^{-1}$$

rate constant for leaching from soil layer:

$$k_{leach_i} := \frac{Finf_{soil} \cdot RAINrate}{K_{soil\_water} \cdot DEPTHsoil_i}$$

removal from top soil:

$$k_i := k_{volat_i} + k_{leach_i} + kbio_{soil}$$

concentration in soil

concentration in soil due to 10 years of continuous deposition:

$$Cdep_{soil\_10_i} := \frac{D_{air_i}}{k_i} \cdot \left(1 - \exp\left(-365 \cdot d \cdot 10 \cdot k_i\right)\right)$$

concentration just after the first year of sludge application:

$$Csludge_{soil\_1_i} := \frac{C_{sludge} \cdot APPLsludge_i \cdot a}{DEPTHsoil_i \cdot RHO_{soil}}$$

initial concentration in soil after 10 applications of sludge:

$$Csludge_{soil\_10_i} := Csludge_{soil\_1_i} \cdot \left[1 + \left[\sum_{n=1}^{9} \left(\exp\left(-365 \cdot d \cdot k_i\right)^n \right) \right] \right]$$

sum of the concentrations due to both processes:

$$C_{soil\_10_i} := Cdep_{soil\_10_i} + Csludge_{soil\_10_i}$$

average concentration in soil over T days:

$$Clocal_{soil_i} := \frac{D_{air_i}}{k_i} + \frac{1}{k_i \cdot T_i} \cdot \left(C_{soil\_10_i} - \frac{D_{air_i}}{k_i} \right) \cdot \left(1 - \exp\left(-k_i \cdot T_i \right) \right)$$

$$PEClocal_{soil_i} := Clocal_{soil_i} + PECregional_{natural\_soil}$$

	$\frac{Clocal_{soil_i}}{ppm}$
$Clocal_{soil}$ =	$1.246\,10^{-4}$
$Clocal_{agr.soil}$ =	$1.246\,10^{-4}$
$Clocal_{grassland}$ =	$2.244\,10^{-4}$

	$\frac{PEClocal_{soil_i}}{ppm}$
$PEClocal_{soil}$ =	$1.246\,10^{-4}$
$PEClocal_{agr.soil}$ =	$1.246\,10^{-4}$
$PEClocal_{grassland}$ =	$2.244\,10^{-4}$

Indicating persistency of the substance in soil

initial concentration after 10 years:

$\frac{C_{soil\_10_i}}{ppm}$
$1.246\,10^{-4}$
$1.246\,10^{-4}$
$2.244\,10^{-4}$

initial concentration in steady-state situation:

$$Facc_i := e^{-365 \cdot d \cdot k_i}$$

$$C_{soil\_ss_i} := \frac{D_{air_i}}{k_i} + Csludge_{soil\_1_i} \cdot \frac{1}{1 - Facc_i}$$

$\frac{C_{soil\_ss_i}}{ppm}$
$1.246\,10^{-4}$
$1.246\,10^{-4}$
$2.244\,10^{-4}$

fraction of steady-state in soil achieved:

$$Fst\_st_i := \frac{C_{soil\_10_i}}{C_{soil\_ss_i}}$$

Fst_st_i
1
1
1

concentration in pore water

$$Clocal_{soil\_porew_i} := \frac{Clocal_{soil_i} \cdot RHO_{soil}}{K_{soil\_water}}$$

		$\frac{Clocal_{soil\_porew_i}}{mg \cdot l^{-1}}$
$Clocal_{soil\_porew}$	=	$2.23 \cdot 10^{-4}$
$Clocal_{agr.soil\_porew}$	=	$2.23 \cdot 10^{-4}$
$Clocal_{grassland\_porew}$	=	$4.016 \cdot 10^{-4}$

$$PEClocal_{soil\_porew_i} := \frac{PEClocal_{soil_i} \cdot RHO_{soil}}{K_{soil\_water}}$$

		$\frac{PEClocal_{soil\_porew_i}}{mg \cdot l^{-1}}$
$PEClocal_{soil\_porew}$	=	$2.23 \cdot 10^{-4}$
$PEClocal_{agr.soil\_porew}$	=	$2.23 \cdot 10^{-4}$
$PEClocal_{grassland\_porew}$	=	$4.016 \cdot 10^{-4}$

concentration in ground water

$PEClocal_{grw} = PEClocal_{agr\_soil\_porew}$

Appendix A9 SimpleBox2.0a - Calculation of regional and continental PECs

Adaptation to TGD (1996) / EUSES

INPUT - MAA			
Parameter names acc. SimpleBox20	Unit	Input	Parameter names according Euses
Physicochemical properties			
COMPOUND NAME	[-]	MAA	Substance
MOL WEIGHT	[g.mol^{-1}]	86.09	Molecular weight
MELTING POINT	[° C]	16	Melting Point
VAPOR PRESSURE(25)	[Pa]	90	Vapour pressure at 25°C
log Kow	[log10]	0.93	Octanol-water partition coefficient
SOLUBILITY(25)	[mg.l^{-1}]	89,000	Water solubility
Distribution - Partition coefficients			
- Solids water partitioning (derived from K_{oc})			
Kp(soil)	[l.kg$_d^{-1}$]	0.5	Solids-water partitioning in soil
Kp(sed)	[l.kg$_d^{-1}$]	0.5	Solids-water partitioning in sediment
Kp(susp)	[l.kg$_d^{-1}$]	0.5	Solids-water partitioning in sudpended matter
- Biota-water			
BCF(fish)	[l.kg$_w^{-1}$]	1.2	Biocentration factor for aquatic biota
Degradation and Transfromation rates			
- Characterisation and STP			
PASSreadytest	[y / n]	y	Characterization of biodegradability
- Environmental Total Degradation			
kdeg(air)	[d^{-1}]	1.49	Rate constant for degradation in air
kdeg(water)	[d^{-1}]	$4.70 \cdot 10^{-2}$	Rate constant for degradation in bulk surface water
kdeg(soil)	[d^{-1}]	$2.30 \cdot 10^{-2}$	Rate constant for degradation in bulk soil
kdeg(sed)	[d^{-1}]	$2.30 \cdot 10^{-3}$	Rate constant for degradation in bulk sediment
Sewage treatment (e.g. calculated by SimpleTreat)			
- Continental			
FR(volatstp) [C]	[-]	0.00	Fraction of emission directed to air (STPcont)
FR(effstp) [C]	[-]	$1.26 \cdot 10^{-1}$	Fraction of emission directed to water (STPcont)
FR(sludgestp) [C]	[-]	$1.00 \cdot 10^{-3}$	Fraction of emission directed to sludge (STPcont)
- Regional			
FR(volatstp) [R]	[-]	0.00	Fraction of emission directed to air (STPreg)
FR(effstp) [R]	[-]	$1.26 \cdot 10^{-1}$	Fraction of emission directed to water (STPreg)
FR(sludgestp) [R]	[-]	$1.00 \cdot 10^{-3}$	Fraction of emission directed to sludge (STPreg)

Release estimation

- Continental

Edirect(air) [C]	[t.y^{-1}]	37	Total continental emission to air
STPload [C]	[t.y-1]	325	Total continental emission to wastewater
Edirect(water1) [C]	[t.y-1]	56	Total continental emission to surface water
Edirect(soil3) [C]	[t.y-1]	0	Total continental emission to industrial soil
Edirect(soil2) [C]	[t.y-1]	0	Total continental emission to agricultural soil

- Regional

Edirect(air) [R]	[t.y-1]	4	Total regiontal emission to air
STPload [R]	[t.y-1]	80	Total regiontal emission to wastewater
Edirect(water1) [R]	[t.y-1]	3	Total regiontal emission to surface water
Edirect(soil3) [R]	[t.y-1]	0	Total regiontal emission to industrial soil
Edirect(soil2) [R]	[t.y-1]	0	Total regiontal emission to agricultural soil

OUTPUT - MAA

Parameter names acc. SimpleBox20	Unit	Output	Parameter names according Euses
Physicochemical properties			
COMPOUND NAME	[-]	MAA	Substance
Output			
- Continental			
PECsurfacewater (total)	[mg.l^{-1}]	1.54 10^{-5}	Continental PEC in surface water (total)
PECsurfacewater (dissolved)	[mg.l^{-1}]	1.54 10^{-5}	Continental PEC in surface water (dissolved)
PECair	[mg.m^{-3}]	1.90 10^{-8}	Continental PEC in air (total)
PECagr.soil	[mg.kg$_{wwt}^{-1}$]	2.03 10^{-7}	Continental PEC in agricultural soil (total)
PECporewater agr.soil	[mg.l^{-1}]	3.63 10^{-7}	Continental PEC in pore water of agricultural soils
PECnat.soil	[mg.kg$_{wwt}^{-1}$]	2.70 10^{-7}	Continental PEC in natural soil (total)
PECind.soil	[mg.kg$_{wwt}^{-1}$]	2.70 10^{-7}	Continental PEC in industrial soil (total)
PECsediment	[mg.kg$_{wwt}^{-1}$]	1.16 10^{-5}	Continental PEC in sediment (total)
- Regional			
PECsurfacewater (total)	[mg.l^{-1}]	1.40 10^{-4}	Regional PEC in surface water (total)
PECsurfacewater (dissolved)	[mg.l^{-1}]	1.40 10^{-4}	Regional PEC in surface water (dissolved)
PECair	[mg.m^{-3}]	1.06 10^{-7}	Regional PEC in air (total)
PECagr.soil	[mg.kg$_{wwt}^{-1}$]	2.70 10^{-6}	Regional PEC in agricultural soil (total)
PECporewater agr.soil	[mg.l^{-1}]	4.83 10^{-6}	Regional PEC in pore water of agricultural soils
PECnat.soil	[mg.kg$_{wwt}^{-1}$]	1.52 10^{-6}	Regional PEC in natural soil (total)
PECind.soil	[mg.kg$_{wwt}^{-1}$]	1.52 10^{-6}	Regional PEC in industrial soil (total)
PECsediment	[mg.kg$_{wwt}^{-1}$]	1.07 10^{-4}	Regional PEC in sediment (total)

Appendix A10 Calculations of indirect exposures via the environment

Name Methylacrylic Acid CAS - No.:79-41-4

Input

chemical properties

octanol-water partitioning coefficient [-]	$\log K_{OW} := 0.93$ $K_{OW} := 10^{\log K_{OW}}$
Henry - partitioning coefficient [Pa*m^3*mol^{-1}]	$HENRY := 0.087 \cdot Pa \cdot m^3 \cdot mol^{-1}$
air-water partitioning coefficient [-]	$K_{air\_water} := 3.57 \cdot 10^{-5}$
fraction of the chemical associated with aerosol particles [-]	$F_{ass\_aer} := 1.034\,10^{-6}$
half-life for biodegration in surface water [d]	$DT_{50\_bio\_water} := 15 \cdot d$

environmental concentrations

annual average local PEC in surface water (dissolved) [mg$_{chem}$ * l$_{water}^{-1}$]	$PEClocal_{water\_ann} := 0.033 \cdot mg \cdot l^{-1}$
annual average local PEC in air (total) [mg$_{chem}$ * m$_{air}^{-3}$]	$PEClocal_{air\_ann} := 0.000762 mg \cdot m^{-3}$
local PEC in grassland (total), averaged over 180 days [mg$_{chem}$ * kg$_{soil}^{-1}$]	$PEClocal_{grassland} := 0.00022 mg \cdot kg^{-1}$
local PEC in porewater of agriculture soil [mg$_{chem}$ * l$_{porewater}^{-1}$]	$PEClocal_{agr\_soil\_porew} := 0.0002 mg \cdot l^{-1}$
local PEC in porewater of grassland [mg$_{chem}$ * l$_{porewater}^{-1}$]	$PEClocal_{grassland\_porew} := 0.0002 mg \cdot l^{-1}$
local PEC in groundwater under agriculture soil [mg$_{chem}$ * l$_{water}^{-1}$]	$PEClocal_{grw} := 0.0002 mg \cdot l^{-1}$
regional PEC in surface water (dissolved) [mg$_{chem}$ * l$_{water}^{-1}$]	$PECregional_{water} := 0.00014 mg \cdot l^{-1}$
regional PEC in air (total) [mg$_{chem}$ * m$_{air}^{-3}$]	$PECregional_{air} := 0.0000001 mg \cdot m^{-3}$
regional PEC in agriculture soil (total) [mg$_{chem}$*kg$_{soil}^{-1}$	$PECregional_{agr\_soil} := 0.0000027 mg \cdot kg^{-1}$
regional PEC in porewater of agriculture soils [mg$_{chem}$*l$_{water}^{-1}$	$PECregional_{agr\_soil\_porew} := 0.000005 mg \cdot l^{-1}$

Results of calculation

$DOSE_{tot_{local}} = 0.001553 \cdot \frac{mg}{kg_{bw} \cdot d}$

$DOSE_{tot_{regional}} = 4.386738 \cdot 10^{-6} \cdot \frac{mg}{kg_{bw} \cdot d}$

$RDOSE_{drw_{local}} = 60.715134 \cdot \%$

$RDOSE_{drw_{regional}} = 91.183934 \cdot \%$

$RDOSE_{air_{local}} = 10.514757 \cdot \%$

$RDOSE_{air_{regional}} = 0.488485 \cdot \%$

$RDOSE_{stem_{local}} = 24.382133 \cdot \%$

$RDOSE_{stem_{regional}} = 1.208737 \cdot \%$

$RDOSE_{root_{local}} = 0.073322 \cdot \%$

$RDOSE_{root_{regional}} = 0.648906 \cdot \%$

$RDOSE_{meat_{local}} = 7.480484 \cdot 10^{-4} \cdot \%$

$RDOSE_{meat_{regional}} = 6.168442 \cdot 10^{-4} \cdot \%$

$RDOSE_{milk_{local}} = 0.013942 \cdot \%$

$RDOSE_{milk_{regional}} = 0.011497 \cdot \%$

$RDOSE_{fish_{local}} = 4.299964 \cdot \%$

$RDOSE_{fish_{regional}} = 6.457823 \cdot \%$

European Commission

EUR 19837 EN **European Union Risk Assessment Report**
Methacrylic acid, Volume 25

Editors: B.G. Hansen, S.J. Munn, F. Berthault, C. Musset, M. Luotamo, J. de Bruijn, S. Pakalin, S. Vegro, G. Pellegrini, R. Allanou, S. Scheer.

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The report provides the comprehensive risk assessment of the substance methacrylic acid. It has been prepared by Germany in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to man and the environment, laid down in Commission Regulation (EC) No. 1488/94.

The evaluation considers the emissions and the resulting exposure to the environment and the human populations in all life cycle steps. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic, terrestrial and atmospheric compartment has been determined. For human health the scenarios for occupational exposure, consumer exposure and humans exposed via the environment have been examined and the possible risks have been identified.

The human health risk assessment for methacrylic acid concludes that there is at present concern for workers. For consumers and humans exposed via the environment the risk assessment concludes that there is no risk. The environmental risk assessment for methacrylic acid concludes that there is at present concern for aquatic ecosystem, while no concerns were identified for the atmosphere, terrestrial ecosystem or for microorganisms in the sewage treatment plant from sources of methacrylic acid covered by Regulation 793/93.

The conclusions of this report will lead to risk reduction measures to be proposed by the Commission's Committee on risk reduction strategies set up in support of Council Regulation (EEC) 793/93.

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European Commission – Joint Research Centre
Institute for Health and Consumer Protection
European Chemicals Bureau (ECB)

European Union Risk Assessment Report

methacrylic acid

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