European Chemicals Bureau

Institute for Health and Consumer Protection

European Chemicals Bureau

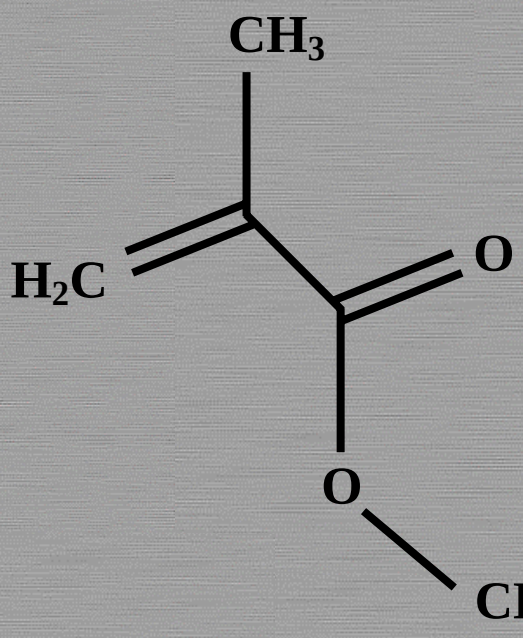
Existing Substances

European Union Risk Assessment Report

CAS No: 80-62-6

EINECS No: 201-297-1

methyl methacrylate



1st Priority List

Volume: 22

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

EUR 19832 EN

CAS: 80-62-6
EC: 201-297-1

PL-1
22

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RISK ASSESSMENT

Cataloguing data can be found at the end of this publication

Luxembourg: Office for Official Publications of the European Communities, 2002
ISBN 92-894-1253-4

Printed in Italy

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RISK ASSESSMENT

Final Report, 2002

Germany

The Rapporteur for the risk assessment of methyl methacrylate (MMA) is the Federal Institute for Occupational Safety and Health.

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

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.

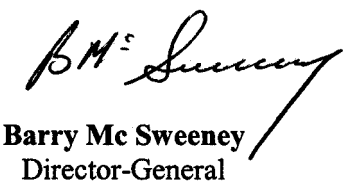
There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each 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.



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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: 80-62-6
EINECS no: 201-297-1
IUPAC name: 2-Methyl-2-propenoic acid, methyl ester

Environment

A potential risk to the local aquatic environment is identified from wet polymerisation processes by downstream users of monomeric MMA (default calculations for generic site and four out of 29 known sites).

For the processing sites with PEC/PNEC ratios above one, the PEC calculations are essentially based on default calculations. Therefore, an improvement of exposure data is possible for the wet polymerisation scenarios, e.g. by performing sufficiently detailed effluent measurements. However, keeping in mind reported year-to-year variations of used MMA tonnages by factors of up to 27, it seems questionable if appropriate effluent monitoring data can be achieved with reasonable expenditure of time and money. Reliable data have to meet the requirement of being representative for all possible utilisation factors (related to used MMA tonnage) of a specific site's overall capacity for wet polymerisation processes.

On the effects side of the risk assessment data improvement is possible because an assessment factor of 50 is used for the PNEC derivation and it might be possible to lower the PNEC by further testing, i.e. the assessment factor can be lowered to 10 if a long-term fish test is performed. But regarding the locally limited risks that are identified due to the specific scenario this kind of data improvement is not proposed.

It is concluded, that local risk reduction measures have to be considered, if the MMA processing capacity exceeds 5,000 t/a at one single site. It should be noted that wastewater reutilization / recycling systems are applied by some known polymerisation sites, avoiding any significant MMA emission to hydrosphere. Sites applying such advanced process engineering would not require further consideration of risk reduction measures.

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

Conclusion (ii) applies for effects on wastewater treatment plants, sediment, atmosphere, soil, and secondary poisoning. It also applies to the aquatic compartment regarding all production sites, the processing scenarios esterification and dry polymerisation, and the relevant use scenarios formulation of paints, private use of paints, and paper recycling.

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

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.

There is a need for limiting the risks of MMA concerning skin sensitisation and respiratory tract irritation at several workplaces in the chemical industry, industrial area and skilled trade and during use of casting resins. For certain inhalation exposure scenarios systemic toxicity gives in addition rise to concern. Risk reduction measures at the community level are recommended.

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)

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.

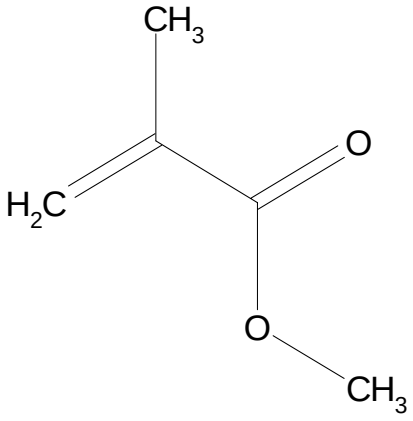
CONTENTS

TABLES

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS no: 80-62-6
EINECS no: 201-297-1
IUPAC name: 2-Methyl-propenoic acid, methyl ester
Molecular weight: 100.12 g/mol
Molecular formula: $C_5H_8O_2$
Structural formula:



Synonyms: Methyl methacrylate (MMA)

1.2 PURITY/IMPURITIES, ADDITIVES

A typical commercial sample of methyl methacrylate (MMA) has a specified purity of ≥99.8% w/w and may contain the following impurities: water (≤0.05% w/w) and methacrylic acid (≤0.005% w/w). Light fractions (typically 800 ppm maximum) may include: acetone, methyl acetate, methanol, methacrylonitrile, methyl isobutyrate and methyl propionate. Heavy fractions (400 ppm maximum) may include ethyl acrylate, butanols, methylhydroxy isobutyrate and succinic acid methyl ester (at ppm levels); diacetyl may be present at <1 ppm (company data sheets; ECETOC, 1995).

To prevent polymer formation, MMA is stabilized by the addition of inhibitors such as 2,4-dimethyl-6-tert-butylphenol (10-30 ppm), hydroquinone (HQ) (25-100 ppm) and the monomethylether of hydroquinone (MeHQ, synonym p-methoxy phenol) (2-100 ppm) (ECETOC, 1995).

1.3 PHYSICO-CHEMICAL PROPERTIES

MMA is a clear colourless liquid (at room temperature and normal pressure) with a pungent, fruity odour. Data on the physical and chemical properties are given in **Table 1.1**.

Table 1.1 Physico-chemical properties

Melting point	- 48°C (approx.)	Weast et al., 1988
Boiling point	100-101°C at 1.013 hPa	Weast et al., 1988
Relative density	0.9440	Weast et al., 1988
Vapour pressure	36-47 hPa at 20°C [1)]	Kirk-Othmer, 1984; Weast et al., 1988
Surface tension	61 mN/m	Röhm GmbH, 1996
Water solubility	16 g/l at 20° C (approx.)	Kirk-Othmer, 1984
Partition coefficient	log Pow 0.67-0.7 [2)] log Pow 1.38 [3)] at 20°C	Fujisawa and Masuhara, 1981 Tanii and Hashimoto, 1982
Flash point	10°C	Chemsafe, 1994
Autoflammability (ignition temperature)	430°C	Chemsafe, 1994
Flammability	highly flammable [4)]	Chemsafe, 1994
Explosive properties	not explosive [5)]	Chemsafe, 1994
Oxidising properties	no oxidising properties [5)]	Chemsafe, 1994
Henry's law constant	26.3 · Pa · m^3 · mol^{-1}	

1) There is no information about the used methods. The average value 42 hPa is used for the risk assessment
2) HPLC method
3) Flask shaking method; this value is used in the risk assessment
4) A.12 not conducted because of structural reasons
5) No test conducted because of structural reason

1.4 CLASSIFICATION

Classification and labelling according to the 28th ATP of Directive 67/548/EEC[4]:

Classification:	F; R11	Highly flammable
	Xi; R37/38	Irritating to respiratory system and skin
	R43	May cause sensitisation by skin contact
Labelling:	F; Xi	
	R: 11-37/38-43	S: (2-)24-37-46

Specific concentration limits: None

Note: D

[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

2.1 PRODUCTION

2.1.1 Production processes

MMA is produced commercially via the acetone cyanohydrin (methacrylamide sulphate) route or through oxidation of isobutene or *tert*-butanol (C_4 route), the former route is more important. A third, minor method uses ethylene as feed stock (C_2 route) (ECETOC, 1995). Methacrylic acid produced by other routes also serves as key intermediate to MMA (Bauer, 1993, cited in ECETOC, 1995).

2.1.2 Production capacity

In 1993, ca. 79,000 t MMA (17.3% of 1993 production) were exported outside the EU (CEFIC, 1995). Import tonnages were given only for a few single companies. Recent publications (Anonymus, 1998) indicate significant dynamics of the methacrylate-chemistry market with increasing trends, at least in Germany. According to CEFIC (1997) the total production volume within the EU amounted to 468,579 t/a in 1996 and the cumulated capacities were 632,000 t/a. As input for the exposure calculations, an annual tonnage of 470,000 was chosen.

2.2 PROCESSING/APPLICATION (CATEGORIES OF USE, AMOUNTS)

In **Table 2.1** the use of methyl methacrylate in the EU has been broken down to a number of main applications with specific regard to monomer containing preparations available to industry and skilled trade (CEFIC, 1995). Only small amounts of methyl methacrylate are sold to non-professional, consumer type markets.

The main use for methyl methacrylate is as an intermediate for the production of polymers. Minor amounts are distributed and used as monomer, e.g. in reactive resins, but even in these applications the MMA monomers eventually will be polymerised; the final polymerisation step takes place at the site of use.

Table 2.1 Methyl methacrylate use pattern in Europe (CEFIC 1995)

Type of use/application	by Producers [%]	by Customers [%]	Total [%]
MMA export outside the EU			17.3
Cast acrylic sheet production	22.0	3.6	25.6
Production of moulding and extrusion compounds	28.0	0.7	28.7
Methacrylate ester production	7.8	0.7	8.5
Productions of emulsions/ dispersions; solvent polymerisation	7.7	7.2	14.9
Reactive resins with monomer (resins, coatings, adhesives, dental products etc.)	2.4	0.8	3.2
Other polymers/resins or unknown	0.0	1.7	1.7
MMA monomer in products available to the public (e.g. reactive adhesives, embedding resins)	0.02	0.04	0.07
	67.9	14.7	100

Due to recent information, about one third of the total methyl methacrylate production is used by the methyl methacrylate producers as internal intermediate (captive use) for the production of polymers / co-polymers (96.5% of captive use) and reactive resins (3.5% of captive use).

Approximately two thirds of the methyl methacrylate production are forwarded to external processing sites and sold to customers, mainly for production of emulsion / dispersion / solvent polymers and of acrylic sheet type polymers.

A small fraction of the annual production (0.07% = ca. 300 t) of methyl methacrylate is sold to consumers, e.g. in form of reactive adhesives and embedding resins (2-component systems). Consumers also may get in contact with MMA as a component in paints, in floor coatings, in dental and medical applications as well as in other polymers used for consumer products.

According to the Danish Product Register (June 1996), the main MMA containing products are intermediates, paints, lacquers and varnishes, binding agents, adhesives and printing inks (no MMA production in DK). **Table 2.2** displays reported numbers of products and respective MMA contents.

Table 2.2 MMA content in products and amount sold in Denmark

Content of MMA in the product (range)	Number of products	Quantity of MMA sold in Denmark [t/a]
0 – 1%	1122	19
1 – 10%	61	22
10 – 80%	85	250
80 – 100%	52	6,219
Not determined	34	

Production of other Methacrylic acid esters (Transesterification)

MMA is reacted with alcohols to give the corresponding methacrylic ester and methanol. The latter of which is removed by azeotropic distillation. Reactions are carried out in closed batch reactors within the primary manufacturing site or by industrial users.

Production of cast acrylic sheet

MMA is widely used to produce polymeric MMA-sheet. The manufacturing process involves polymerisation of the monomer between silicate glass sheets in a batch process, which is only partially contained.

Production of extrusion and moulding polymers

MMA is used as backbone monomer or co-monomer in a suspension polymerisation process to yield polymer beads. The reactions are carried out in closed semiautomatic batch reactors. A second process is a continuous fully contained, automated process, resulting in polymer granulates.

Production of emulsion, suspension and solvent polymers

MMA is used as backbone polymer or co-polymer in emulsion, suspension and solvent polymerisation processes to yield polymers that are marketed in aqueous emulsions or powders

or as dissolved polymers for paints and varnishes. The reactions are carried out in closed semiautomatic batch reactors.

Reactive resins

Reactive resins are prepared by mixing monomers and/or pre-polymers together with fillers and other additives in closed batch processes. These resins are used as floor coatings or other speciality reactive resins like adhesives (e.g. glues for acrylic sheets), road markings, or in dental and medical applications with a certain content of MMA as a reactive diluent. Cold curing of these resins is carried out by specialised companies. Most of these applications should be regarded as non-closed systems.

Special products

MMA polymers and polymer mixtures have a broad area of applications in various products, such as plastics, printing colours and blocks, lacquers, paints, glues, the manufacture of dental prosthesis and tooth fillings, in the attachment of orthopaedic prosthesis and splints, soft lenses, in histological preparations, floor waxes and coatings, surface treatment of leather, textiles and paper products etc.

Recycling of acrylic scrap

Acrylic scrap may be recycled by thermal depolymerisation. The process is carried out in closed systems. The depolymerisation product is monomeric methyl methacrylate, which will be used by the producers of MMA.

The following **Table 2.3** gives an overview about the main, industrial and use categories according to the Technical Guidance Document (TGD) (EC, 1996). Due to uncertainties about the amounts of MMA assignable to these categories no quantitive information or percentages can be given.

Table 2.3 Main, industrial and use categories according to the TGD

Main category (MC)	Industrial category (IC)	Use category (UC)
Isolated intermediate (1b, 1c)	Chemical industry (3)	Intermediate (33)
Matrix-inclusion (2), Non dispersive use (3)	Polymers industry (11)	Intermediate (33)
Non dispersive use (3)	Pulp, paper. Board industry (12)	Intermediate (33)
Non dispersive use (3)	Paints, lacquers and varnishes industry (14)	Intermediate (33)
Wide dispersive use (4)	Personal / domestic (5), public domain (6)	Adhesives, binding agents (2)
Wide dispersive use (4)	Public domain (6)	Others (0)

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Environmental releases

Releases to the environment are to be expected mainly during production and processing of MMA with wastewater and exhaust gas as well as during the use of water based emulsion polymers, e.g. paints and varnishes.

Direct releases to agricultural or natural soil are not expected to a relevant extent.

Residual monomeric MMA-contents, which are the basis for release estimations from different polymeric products, are given in the following table for the most important polymers:

Table 3.1 Residual MMA-content in polymeric products

Application	Residual MMA-content (%)
Cast sheets	0.5 – 1.1
Extruded polymers	0.1 – 0.3
Aqueous dispersions	0.005 – 0.05

3.1.2 Environmental fate

3.1.2.1 Degradation

Hydrolysis

Hydrolysis is not significant at neutral or acid pH (Mabey and Mill, 1978). The hydrolysis half-life was estimated to be 3.9 years at pH 7, and 14 days at pH 9 (Ellington et al., 1987). These data were confirmed by Archer (1990) who found a hydrolysis half-life of 143 min (=2.4 h) at pH 11 and 1,600 days (= 4.4 a) at pH 7.

Photolysis

The absorption maximum for MMA is 231 nm (IARC, 1979), so it is unlikely to be significantly photolysed by radiation >290 nm.

Photooxidation

Free radicals formed in natural waters by the action of light could react with MMA, but there are no estimates of the rates of these reactions.

When released into the atmosphere, MMA reacts with photochemically produced hydroxyl radicals primarily by addition to the double bond, and with atmospheric ozone, resulting in estimated half-lives of 21 h and 1.0 d respectively, assuming a hydroxyl radical concentration of

500,000 molecules/cm³ and an ozone concentration of 7.10^{11} molecules/cm³ (AOP V.1.65-calculation).

Howard et al. (1991) calculated an atmospheric half-life of 1.1 – 9.7 hours for MMA, based on an estimated rate constant for reactions with hydroxyl radicals and ozone in air (Atkinson, 1987).

Biodegradation

For the evaluation of the biodegradability of MMA the following test results are considered:

- Closed-Bottle-Test (OECD GL 301 D): 88% degradation after 28 days but the 10-days window criterion was not fulfilled (Douglas & Bell, 1992).

- MITI-I-Test (OECD GL 301): 94% degradation after 14 days. Although the results are not described in detail from this test ready biodegradability might be deduced (CITI, 1992).

- In two modified MITI-I-Tests MMA showed biodegradation rates of 32% after 19 days and >30% after 14 days and did not reach the pass level for ready biodegradability (Röhm, 1988; Sasaki, 1978).

Taking all results into account MMA can be considered as ready biodegradable in water. Although it is not shown that the criterion of the 10-d window is fulfilled the biodegradation rate is set at $k = 1\ h^{-1}$ for the WWTP model for the following reasons:

- The high degradation rate of 94% within 14 days in MITI-I-Test indicates that the criterion of the 10 d-window is likely fulfilled.

- Similar substances like Acrylic Acid (CAS-No. 79-10-7) and Methacrylic Acid (CAS-No. 79-41-4) are readily biodegradable with fulfilment of the 10-d window.

For the biodegradation in soil a test with soil microorganisms, performed according to a US-EPA guideline is available (Hawkins et al., 1993). From the testdesign (e.g. C^{14}-labelling of the substance), the test could be considered as a simulation test, but the extrapolation to other soil groups needs to be made subject to further comparative research. Due to the highly variable influence of pH, cation exchange capacity or organic carbon content, the biodegradation of MMA remains to be elucidated.

Although the greatest amount of the applied MMA evaporated during the test duration of 28 days biological degradation was observed in the above-mentioned test. With the lower test concentration of 100 mg/kg soil the mineralisation was 28%. Although this test is not valid it supports the biodegradation results from the above-mentioned aquatic standard tests on which the calculation of the biodegradation in soil has to be based therefore. With $k_{p\ soil} = 1$ l/kg this leads to a rate constant of $k = 0.023\ d^{-1}$ for soil.

There is no study concerning the degradation by anaerobic microbes.

In **Table 3.2** the biodegradation rate constants are summarised for the different compartments. For WWTPs and surface water they are taken from Tables 4 and 5 of Chapter 3 in the TGD. For sediment and soil they are calculated using formulas 14 and 15 of Chapter 3 of the TGD (EC, 1996).

Table 3.2 Biodegradation rate constants for different compartments

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 = 26.3 · $Pa \cdot m^3 \cdot mol^{-1}$ suggests that MMA is moderate volatile and therefore evaporates from surface waters to the atmosphere. From the Henry's law constant, an average "half-life" of 6.3 h can be estimated for evaporation of MMA from a water body of 1 m depth, with a 1 m/s current and 3 m/s wind speed (Lyman et al., 1982).

The adsorption of MMA to soil was investigated using 5 different types of soil and six concentrations of ^{14}C-MMA from 0.5 to 8.9 µg/ml. The study included an adsorption cycle followed by 3 desorption cycles. The soil partition coefficients (K_p) ranged from 0.063 to 0.89 l/kg for adsorption and 0.22 to 3.24 l/kg for desorption (Hardies, 1991). According to these low K_p-values a high mobility in soils has to be expected. Once adsorbed, MMA was less readily desorbed from soil. The K_{oc}-values calculated in the study showed no positive correlation between adsorption and soil organic carbon content. For this reason, the default approach (as calculated in Appendix A1) proposed in the TGD (assuming a linear dependence of K_p from OC) for calculating specific K_p-values for the different compartments according to their different OC contents has not been used for the risk assessment. It was preferred to use an uniform partition coefficient Kp = 1 l/kg for all compartments (soil, sediment, suspended matter, and activated sludge), which is very close to the value of 1.103 as exactly calculated from the given absorption and desorption ranges.

Using the fugacity model of Mackay (level 1), the theoretical distribution of MMA at equilibrium can be estimated (calculated with EQC Model V. 1.0).

Table 3.3 Equilibrium distribution according to fugacity model of Mackay (level 1)

Compartment	%
Air	84.2
Water	15.6
Soil/Sediment	0.14

Based on the physico-chemical properties of MMA, the air and to a much lower extent the hydrosphere are the preferred target compartments for distribution.

Elimination in WWTPs

Based on the above-cited physical chemical properties (vapour pressure 4,200 Pa, solubility 16 g/l; Kp = 2 l/kg; log Pow = 1.38), 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. Due to this calculation model, the total elimination in the WWTP is 89%; 82% is covered by

biological degradation and 7% by volatilisation into the atmosphere; 11% is discharged to surface waters. **Table 3.4** summarises the elimination pathways:

Table 3.4 Elimination in WWTPs

Evaporation to air (%)	7
Release (dissolved) to water (%)	10.8
Adsorption to sewage sludge (%)	0.1
Biodegradation (%)	82.2
Total elimination from water (%)	89.2

3.1.2.3 Accumulation

No experimental results on bioaccumulation are available. The measured logPow of 0.7 to 1.38 does not indicate a potential for bioaccumulation.

According to the TGD (EC, 1996), using a SAR-approach, a maximal BCF of 3 $l \cdot kg^{-1}$ can be estimated for fish.

The experimentally determined Kp-values and the biodegradability indicate negligible geoaccumulation. Residual MMA may leach with seepage to the groundwater.

3.1.3 Aquatic compartment (incl. sediment)

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

The TGD proposes a generic (i.e. non site-specific) calculation (Emission Scenario Document – ESD) for the release of intermediates into surface water during production and processing. The following calculation is based on 200,000 t/a MMA production capacity. This value appears as reasonable mean with respect to the largest production site (185,000 t/a) and to the quite high upper limit of the respective range in IUCLID (100,000 – 500,000 t/a).

A $Clocal_{water}$ of **139 µg/l** is estimated under the following conditions: Default emission factors: 0.3% for production and 0.7% for processing; days of emission: 300 d/a; default river flow rate according to ESD: 60 m^3/s (see Appendix A2 for calculation).

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

Using the available specific data for several production sites, more reliable estimations of local MMA concentrations in water can be performed (**Table 3.5**). Concerning allocation of releases to production and processing on site, the data provided are fragmentary. There are sites without any on site processing of the monomer, just as well as production sites processing more than 95% on site. The main route of MMA processing is polymerisation. Therefore, if no site-specific data were available, a default emission factor of 0.3% for production was used, whereas processing of amounts not allocated to production sites was considered separately in a generic approach (cf. Section 3.1.3.3).

Table 3.5 Basic data and results of local release estimations into the hydrosphere

Site	Size of wwtp	Flow of receiving water	Release to wwtp-infl. [t/a]	Release via wwtp effl. [t/a]	Direct release [t/a]	$Clocal_{water}$ [µg/l]	Specific data used for exposure estimation
A	Site specific	Site specific	1.2	0.13	-	0.007	Estimated annual emission (by industrial expert) with process specific data; specific STP and specific river flow
B	No wwtp	Site specific, discharge into estuary	-	-	11.4*)	40 (Fresh water) *) 15.4 (marine) *)	Release estimation based on measured effluent concentrations *)
C	Default	Site specific	20	2.16	-	1.39	Strictly confidential release given by CEFIC Methacrylates Toxicology Committee; specific river flow
D	Default	Site specific	216	23.4	-	0.9	Maximum release calculated with measured COD-value (several acrylates included); specific river flow
E	Default	Site specific	0.724	0.08	-	0.004	Rrelease calculated with process specific data by industrial expert; specific river flow
F	Site specific, only physico-chemical wwt	Discharge into sea, default dilution factor	-	-	2.8	360	Estimated annual emission (by industrial expert); specific wastewater volume
G	Site specific	-	-	-	-	0	Waste residues are incinerated
H	Default	Default river flow	29.6	3.2	-	2	-
Σ			267	29	14.2		

*) The release amount is calculated on the basis of effluent monitoring performed during the years 1999 and 1998. Weekly composite samples (1998 complete: n = 52; 1999 till October: n = 41) were analysed with a detection limit of 1 mg/l. Concentrations in the positive samples (1998: n = 12; 1999: n = 12) ranged between 1 mg/l - 62 mg/l in 1998 and between 2 mg/l and 17 mg/l in 1999 with an average of 3.15 mg/l (1998) and 1.8 mg/l (1999 till October). The calculation of the annual release is based on the 1998 average concentration, assuming a concentration of 1 mg/l in the negative samples.

The calculation of $Clocal_{water}$ is based on a release concentration of 4 mg/l. This value has been measured in two weekly composite samples in 1999 was exceeded significantly during three weeks in 1998 and during one week in 1999. 4 mg/l is therefore 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 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 $Clocal_{water}$: Processing and use

The most important use of MMA is the production of polymers for a complex use pattern as described above. To a much smaller extent it is also used to react with alcohols to yield other methacrylic esters (cf. **Table 2.1**).

Basically four different polymerisation techniques are used:

- Mass polymerisation which is used e.g. for cast acrylic sheet
- Emulsion polymerisation used e.g. for dispersion paints and other emulsion products
- Bead polymerisation (suspension polymerisation) used e.g. for extrusion polymers and solvent based coatings
- Solvent polymerisation mainly used for solvent based coatings

For all types of processing considerable amounts of MMA are used as external intermediate, i.e. at sites different to those considered in **Table 3.5**. Due to information given 1998/99 on inquiry by the eight producer companies, about 32% of the overall EU production volume are confirmed to be processed at the production sites. For the remaining portion of ca. 68% (i.e. 320,000 t/a) external processing by downstream user sites is assumed.

In order to perform generic calculations using the emission tables of the TGD (IC = 11), the applications given in **Table 2.1** are related to the four polymerisation techniques listed above. The resulting percentage use pattern is displayed in **Table 3.6.**

Table 3.6 Polymerisation techniques and assigned process types (external processing tonnage)

Polymerisation technique (application)	Estimated percentage [%]	Process considered
Bead polymerisation (moulding and extrusion polymers)	35 (112,000 t/a)	1. Polymerisation: wet process 2. Shaping
Mass polymerisation (cast acrylic sheet)	30 (96,000 t/a)	Polymerisation: dry process, no further release during shaping considered
Emulsion polymerisation (emulsion polymers)	20 (64,000 t/a)	Polymerisation: wet process
Ester production	10 (32,000 t/a)	Processing as intermediate
Solvent polymerisation (reactive resins)	5 (16,000 t/a)	Polymerisation: dry process

The following section (Section 3.1.3.3.1) gives estimates of releases to hydrosphere based on comprehensive site-specific release data. Subsequently, Section 3.1.3.3.2 covers either generic scenarios for the estimation of releases due to processing and use and specifically calculated results for known external processing sites.

3.1.3.3.1 Estimation of $Clocal_{water}$ / Site-specific approach: processing

Four known mere processing sites are considered in this section. For two sites specific release data were provided (cf. **Table 3.7**). The other two sites confirmed zero emission to hydrosphere, justified by a concise description of process engineering applied. Specific release data cover a sum of 76,000 t/a MMA, used for wet and dry processes.

Table 3.7 Basic data and results of local release estimations into the hydrosphere (known mere processing sites)

Site	Size of STP	Flow of receiving water	Release to wwtp-influent [t/a]	Release to hydrosphere [t/a]	$Clocal_{water}$ [µg/l]	Data used for exposure estimation
P	Site specific	Default dilution factor	1.0	0.108	10.9	Estimated annual emission (by industrial expert) with process specific data; specific STP
Q	Site specific	Default dilution factor	1.3	0.14	1.04	Estimated annual emission (by industrial expert) with process specific data; specific STP; confirmation by MMA-concentration measurement in STP (50% of the estimated release)

3.1.3.3.2 Estimation of $Clocal_{water}$ / Processing of monomer and use of polymers

Ester production

A tonnage of 32,000 t/a MMA is assumed to be used externally for esterification. As a worst case, releases due to processing at one single external site are calculated, based on default settings according to the TGD, ESD IC-3 (release factor 0.007, see Appendix A3):

$$\mathbf{Clocal_{water} = 15.6\ \mu g/l}$$

Dry polymerisation

For an assumed amount of 51,000 t/a MMA polymerised in dry processes, no specific release data are known. Since the default release factor for dry polymerisation is set to zero (TGD Table A3.10), no relevant MMA emissions to hydrosphere are expected.

Wet polymerisation

According to **Table 3.6** and considering the tonnage covered by specific release data, an amount of 161,000 t/a MMA polymerised in wet processes is taken as basis for further calculation. On recent inquiry, specific information on processing sites has been received, covering a processing volume of 84,000 t/a, distributed to 29 individual sites. Ranges of plant size according to MMA tonnage handled, are indicated in the following table:

Table 3.8 Ranges of plant size according to MMA tonnage handled

Plant size: annual use of MMA [t/a]	No. of plants
> 10,000	2
5,000 ... 10,000	4
1,000 ... 5,000	5
500 ... 1,000	5
100 ... 500	11
50 ... 100	2

It should be noted, that a number of 1997 figures had been updated for 1998, in most cases increasing, at some sites by factors of about five, at one site by a factor of 27.

For eleven sites processing > 1,000 t/a each, a calculation of the $Clocal_{water}$ is performed based on site-specific tonnages, incorporating site-specific information on wastewater treatment and dilution as far as available and default release factors if necessary. The underlying site-specific data are confidential. The results are compiled in **Table 3.9**.

Table 3.9 Specific $Clocal_{water}$ calculated for known external processing sites applying wet polymerisation

Site	$Clocal_{water}$ [µg/l]
EP1	1.4
EP2	10.9
EP3	30.6
EP4	39.5
EP5	175
EP6	252
EP7	990
EP8	1,008
EP9	1,188
EP10	2,340
EP11	1.9

For the remaining tonnage of 77,000 t/a not covered by specific information, a $Clocal_{water}$ has to be calculated for a generic processing site. Applying the default parameters according to the TGD, including a fraction of main source of 0.05 (Table B3.9) gives a processing volume of 3,900 t/a for the generic site, resulting in (see Appendix A4):

$$\mathbf{Clocal_{water} = 693\ \mu g/l}$$

Considering received site-specific information, a processing volume of 10,000 t/a has to be assumed for one site as realistic worst case. It should be noted, that used MMA tonnages significantly exceed this value at two known sites. For 10,000 t/a MMA polymerised in wet processes at one generic site, the default calculation results in (see Appendix A5):

$$\mathbf{Clocal_{water} = 1{,}800\ \mu g/l}$$

Use of polymer

For the processing of polymers only the shaping process for bead polymers is considered: Based on 112,000 t/a MMA polymerised in dry processes and on the assumption of 0.3% residual

monomeric MMA content in the polymeric products, an amount of 336 t/a (112,000 · 0.003) monomeric MMA is considered for the shaping process. The default calculation according to the TGD, Tables A.3.11 (release factor 0.0005) and B3.9 (fraction of main source 0.05, emission period 300d/a) is resulting in (see Appendix A6):

$$\mathbf{Clocal_{water} = 0.15\ \mu g/l}$$

A lot of other processes for the *end-use of polymer products* are relevant for environmental exposure. In the following only three estimations for the hydrosphere are presented which possibly may not represent a main source of release for the local assessment. For other applications of MMA polymers data are not available.

The calculations are based on residual MMA contents which are given for the most important polymers listed in **Table 3.1** (cf. Section 3.1.1).

a) Formulation of paints

The release of monomeric MMA is possible during the formulation of paints. The emission scenario document for paints, lacquers and varnishing industry (ESD IC-14) does not provide appropriate tables for emulsion/dispersion paints. Therefore, the respective **A-** and **B-Tables** are used for the release estimation.

The following data are taken for an estimation of annual release:

- Percentage of consumption as emulsion/dispersion (related to the EU production volume of 470,000 t/a): 20%
- Assumed percentage of emulsion/dispersion which is formulated to paints: 90%
- Residual MMA-content in aqueous emulsion/dispersion: 0.05% (final product)
- Percentage of polymerised MMA in aqueous emulsion/dispersion: 50% (final product)

Residual MMA: 470,000 t/a · 0.2 · 0.9 · 0.0005 · 2 = 84.6 t/a

The emissions during formulation are estimated with the default-emission tables presented in Appendix I of the TGD (Table A 2.1 – emission factor: 0.003; Table B 2.3 – fraction of main source: 0.4; flow of WWTP 2,000 m^3/d; number of days: 300; dilution factor: 10 – see Appendix A7 for calculation).

The estimated $\mathbf{Clocal_{water}}$ amounts to **1.83 µg/l**.

b) Private use of paints

The estimation of MMA-release during private use of paints is based on the following calculation:

- Percentage of consumption as emulsion/dispersion (related to the EU production volume of 470,000 t/a): 20%
- Assumed percentage of emulsion/dispersion which is formulated to paints: 90%
- Residual MMA-content in aqueous emulsion/dispersion: 0.05% (final product)
- Percentage of polymerised MMA in aqueous emulsion/dispersion: 50% (final product)

Residual MMA for the whole continent: 470,000 t/a · 0.2 · 0.9 · 0.2 · 0.0005 · 2 = 84.6 t/a

10% of this amount (8.46 t/a) is taken for calculation of the local scenario. Classifying the private use of paints as "do it yourself", according to the default-emission tables presented in Appendix I of the TGD of WWTP 2,000 m^3/d; number of days: 300; dilution factor: 10) a **C_{local} = 0.015 µg/l** is calculated (see Appendix A8 for calculation).

c) Paper recycling

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

The following data are taken for an estimation of annual release:

- Percentage of consumption as emulsion/dispersion (related to the EU production volume of 470,000 t/a): 20%
- Assumed percentage of emulsion/dispersion which is used for paper coating: 20%
- Percentage processed within a standard region of the EU: 20%
- Residual MMA-content in aqueous emulsion/dispersion (final product): 0.05%
- Percentage of polymerised MMA in aqueous emulsion/dispersion (final product): 50%

Residual MMA: 470,000 t/a · 0.2 · 0.2 · 0.2 · 0.0005 · 2 = 3.76 t/a

The result of PEC-estimation according to the emission scenario document of the TGD (emission scenario document IC-12 for paper, see appendix A9 for calculation) is **$Clocal_{water}$ = 0.73 µg/l**.

3.1.3.4 Monitoring data

No actual data on measured aquatic concentrations are available.

3.1.3.5 Sediment

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

3.1.4.1 Estimation of $Clocal_{air}$ / Generic approach: production and processing

No emission scenario document for the release into the atmosphere of intermediates during production and processing is available at the moment. The emissions are therefore estimated with the emission tables presented in Appendix I of the TGD.

A production and processing volume of 200,000 t/a is used for the generic approach (cf. Section 3.1.3.1). According to the TGD (EC, 1996), Appendix I, Tables A 1.2 and A 3.3, with MC = 1b

for production and processing, the vapour pressure at 20 °C set at 4,200 Pa, a release fraction of 0.0011 is proposed.

For the default exposure assessment ($F_{mainsource}$ = 1, $T_{emission}$ = 300 d/a, $Fstp_{air}$ = 7%, $Fass_{air}$ = $2.4 \cdot 10^{-8}$), a release of 220 t/a is therefore assumed for the OPS-calculation (Appendix A10). The results are:

$$\mathbf{Clocal_{air,ann} = \quad 0.168\ mg\ m^{-3}}$$

$$\mathbf{DEPtotal_{ann} \quad = \quad 0.393\ mg\ m^{-2}\ d^{-1}}$$

3.1.4.2 Estimation of $Clocal_{air}$ / Site-specific approach: production and processing

For most production sites data on emission of MMA to atmosphere are given by industry, for two sites the release is calculated on the basis of default values. The annual emissions for all sites, including three mere processing sites, are summarised in **Table 3.10** being clearly below the release of the generic calculation above.

Table 3.10 Estimation of release to atmosphere from specific local sites

Site	Release to atmosphere [t/a]	Data used for exposure estimation
A	64	specific emission data
B 1	125	specific emission data
B 2	137	specific emission data
C	50	specific emission data
D	3.36	specific emission data
E	<0.2	specific emission data
F	29.8	default calculation
G	45	specific emission data
H	11	default calculation
Total	465	production and processing
P	22	specific emission data
Q	7	specific emission data
EP12	<0.05	specific emission data
Total	29	mere processing

The overall sum of 494 t/a represents the atmospheric releases from all production sites and covers as well the releases from known processing sites, if comprehensive site-specific data on releases to atmosphere had been provided.

3.1.4.3 Estimation of $Clocal_{air}$: processing of monomer and use of polymers

Corresponding to respective estimations for the aquatic compartment (cf. Section 3.1.3.3), a set of three processing type related generic exposure scenarios is calculated for air, using the OPS-model and proceeding on the same assumptions as explained in Section 3.1.3.3.

Ester production

A tonnage of 32,000 t/a MMA is assumed to be used externally for esterification. As a worst case, releases due to processing at one single external site are calculated, based on default settings according to the TGD (Table A3.3: release factor 0.001, see Appendix A11):

$$\mathbf{Clocal_{air,ann} = 24\ \mu g\ m^{-3}}$$

$$\mathbf{DEPtotal_{ann} = 52\ \mu g\ m^{-2}\ d^{-1}}$$

Dry polymerisation

For an assumed amount of 51,000 t/a MMA polymerised in dry processes, no specific release data are known. A default calculation according to the TGD, Tables A3.10: release factor 0.05 and B3.9: fraction of main source 0.05, 300d/a, gives (see Appendix A12):

$$\mathbf{Clocal_{air,ann} = 97\ \mu g\ m^{-3}}$$

$$\mathbf{DEPtotal_{ann} = 140\ \mu g\ m^{-2}\ d^{-1}}$$

Wet polymerisation

No comprehensive site-specific release data are available for an amount of 161,000 t/a MMA polymerised externally in wet processes. On recent inquiry, confidential site-specific information (mainly MMA tonnages, no further details regarding releases to atmosphere) has been received, covering a processing volume of 84,000 t/a, distributed to 29 individual sites (cf. respective Section 3.1.3.3 on wet polymerisation).

Applying the default parameters according to the TGD, including a fraction of main source of 0.05 (Table B3.9) gives a processing volume of 8,050 t/a for the generic site. Considering received site-specific information, a processing volume of 10,000 t/a has to be assumed for one site as a realistic worst case. It should be noted, that used MMA tonnages significantly exceed this value at two known sites. For 10,000 t/a MMA polymerised in wet processes at one generic site, the default calculation results in (see Appendix A13):

$$\mathbf{Clocal_{air,ann} = 381\ \mu g\ m^{-3}}$$

$$\mathbf{DEPtotal_{ann} = 560\ \mu g\ m^{-2}\ d^{-1}}$$

Use of polymers

Among the large number of processing types for the end-use of polymer products which may be relevant for environmental exposure, only the shaping process for polymers, formulation of paints and private use of paints are considered here. For other applications of MMA polymers data are not available.

Considering residual MMA contents as listed in **Table 3.1**, the calculations resulted in overall annual releases of 3.7 t/a for polymer shaping, of 423 kg/a for the formulation of paints and of 846 kg/a for private use of paints (see **Table 3.11**).

Table 3.11 Estimation of release to atmosphere from processing and use of polyMMA

Scenario	Total tonnage [t/a] times residual MMA content [%]	Total tonnage of residual MMA [t/a]	Release factor (A-table)	Total annual release [t/a]
Polymer shaping	123,000 · 0.3 %	370	0.01 (A3.11)	3.7
Formulation of paints	84,600 · 0.05 % · 2 [1)]	84.6	0.005 (A2.1)	0.423
Private use of paints (do it yourself)	84,600 · 0.05 % · 2 [1)]	84.6	0.01 (A4.5)	0.846

[1)] Residual MMA percentage is related to final product and final product contains 50% MMA emulsion / dispersion

Due to wide dispersion, these minor amounts are not relevant for the local scenarios, but were added to the regional / continental releases.

3.1.5 Terrestrial compartment

The release of MMA to soil is expected to occur through atmospheric deposition after local release to the atmosphere at the production and processing sites. Due to the distribution of MMA in WWTPs with a very low percentage of 0.1% in sludge (see Section 3.1.2.2) a further loading of soil through sludge application is neglected. However, for regional exposure calculation the actual distribution rate of 0.1% to sludge is considered in SimpleBox.

With the generic annual deposition rate of 393 $\mu g \cdot m^{-2} \cdot d^{-1}$ for production and processing (Section 3.1.4.1), the equilibrium soil concentration in close vicinity to a production/processing plant can be estimated according to the TGD (non-default input data: $K_{soil,water}$ = 3.2; $K_{air,water}$ = 0.011). Additionally calculated are the local soil concentrations for a generic site applying wet polymerisation. The annual deposition rate calculated for this scenario (560 $\mu g.m^{-2}.d^{-1}$, cf. Appendix A13) exceeds all other respective figures.

Table 3.12 Local exposure concentrations for soil

	Production/processing, generic approach	Wet polymerisation, generic approach
$Clocal_{soil}$ [mg/kg]	0.029	0.041
$Clocal_{agr,soil}$ [mg/kg]	0.029	0.041
$Clocal_{agr,soil\_porew}$ [mg/l]	0.029	0.041

(cf. Appendix A14, A15)

Since residual MMA may through seepage, as other chemicals with a potential to leach, reach groundwater, it should be considered to rule out possible groundwater contamination from local sources by means of appropriate data. However, as for aquatic compartment, no monitoring data are available.

3.1.6 Secondary poisoning

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

3.1.7 Regional exposure concentration

For determination of a regional background concentration all releases, from both point and diffuse sources, are considered. 20% of the total exposure quantity from point sources is taken into account for the defined regional EU standard model (densely populated area of 200·200 km with 20 million inhabitants), since MMA is produced and processed in large tonnages at local sites. Therefore, the default value for the fraction related to the region of 0.1 has been set to 0.2 for a more realistic regional scenario. This assumption is confirmed by the specific information recently provided by downstream users.

From diffuse sources, the default of 10% is considered for the standard region. The rest (80% from point sources and 90% from diffuse sources) of the total exposure quantity is taken into account for the continental model.

No direct release into the soil was identified. Diffuse release only occurs as a result of dispersal processes. Release is therefore to be expected as a result of deposition from the air (see Section 3.1.5).

Since not all of the previously mentioned releases arising from use of the substance enter the hydrosphere directly, but instead primarily via the wastewater which is possibly purified in municipal wastewater treatment plants, a 70% connection to wastewater treatment plants, in which 89.2% of the substance is eliminated and 7% evaporated, is assumed for this scenario. The remaining 30% of the water is discharged directly into the hydrosphere.

Point releases

In **Table 3.5** the total annual release of 267 t/a MMA to WWTPs and of 14.2 t/a directly into hydrosphere are allocated to all production sites. For consideration in the continental and regional models, the sum of releases to atmosphere is 465 t/a for known production and processing sites.

Table 3.13 Point releases due to external processing and use

Scenario	Total annual MMA tonnage [t/a]	f_r to hydrosphere (A-table)	Release to wastewater [t/a]	f_r to atmosphere (A-table)	Release to atmosphere [t/a]
Specific processing sites	76,000	specific	2.3	specific	29
Dry polymerisation	51,000	0 (A3.10)	0	0.05 (A3.10)	2,550
Esterification	32,000	0.007 (ESD IC-3)	224	0.001 (A3.3)	32
Wet polymerisation	161,000	0.01 (A3.10)	1 610	0.05 (A3.10)	8,050
Shaping of polymers	336 (0.3% residual MMA from 112,000 t/a)	0.0005 (A3.11)	0.168	0.01 (A3.11)	3.4

All releases are compiled in **Table 3.15**.

Diffuse releases:

For the diffuse releases a conservative estimation is carried out, using the available data on the consumption sectors (cf. **Table 3.7**) and the residual MMA-monomeric content (cf. **Table 3.1**). The calculated amounts of monomeric MMA for diffuse releases are given in the following **Table 3.14** (a total amount of 470,000 t/a is taken as a basis for calculation).

Table 3.14 Estimation of monomeric MMA put on the market via polymeric products

Application	Formula (tonnage.percentage of application.residual MMA-content)	Calculated max. MMA-amount [t/a]
Moulding and extrusion polymers	470,000 t/a · 0.35 · 0.003	494
Mass polymerisation	470,000 t/a · 0.3 · 0.011	1,551
Emulsion polymerisation	470,000 t/a · 0.2 · (0.0005 · 2) [1)]	94
Total		2,139

[1)] Factor 2 considers that the ratio of polymeric MMA in final emulsion amounts to 50%

During handling, use and disposal of the polymeric products the residual monomeric MMA may be released into different compartments of the environment. It is unknown how much of the monomeric MMA-content can be released during the life span of different products. Furthermore, no information about the annual emission rate is available. For the resulting monomer amount of 2,140 t/a it is assumed as a rough estimate that 80% of the monomer (1,712 t/a) is released during formulation, use and disposal, and that 20% remains in products which are incinerated. For an initial estimation it is assumed that the most polymeric products are not used in prolonged contact with water. Therefore, it is assumed that 90% of the whole amount (i.e. 1,541 t/a) is released directly to the atmosphere and the remaining amount of 10% (171 t/a) via wastewater. With a connection rate to WWTPs of 70%, 51 t/a would be released directly and 120 t/a into WWTPs.

As mentioned at the beginning of this section, for production, processing and formulation 20% of the point-source releases are assumed to occur into a region whereas according to the TGD from the diffuse releases only 10% are considered for the region.

The individual environmental releases are summarised in **Tables 3.15** and **3.16**.

Table 3.15 Summary of environmental releases

Field of application	Regional / continental	Release into hydrosphere [t/a]			Release into atmosphere
	[% / %]	direct	via wwtp	into wwtp	[t/a]
Production/processing of MMA	20 / 80	14.2	28.8	267	465
Processing of MMA, specific	20 / 80	/	0.25	2.3	29
Polymerisation of MMA (dry)	20 / 80	/	/	/	2,550
Ester production	20 / 80	/	24.2	224	32
Polymerisation of MMA (wet)	20 / 80	/	174	1,610	8,050
Shaping of polymers	20 / 80	/	0.02	0.168	3.6
Formulation of paints and lacquers	20 / 80	/	0.03	0.25	0.423
Sum (20 / 80)		14.2 *)	227.3	2,104	11,130
Private use of paints and lacquers ('do it yourself')	10 / 90	1.27	0.3	2.96	0.85
Diffuse releases during handling and use of polymeric products	10 / 90	51	12.9	120	1,541
Sum (10 / 90)		53.2	13.2	123	1,542

*) Sites B and F are emitting into a river estuary and directly to the sea, respectively. The releases are not assumed to occur in the region to avoid an unrealistic worst case. However, at least site B is located in a highly industrialised region and the releases are considered for the continent. This is done to be consistent with the TGD approach for freshwater, where the continental contribution of releases into one certain river to the regional background concentration of another river is not dependant on the geographic connections between these rivers. In addition, it seems not appropriate to link the decision of whether or not considering releases for the continent to a fixed distance between point of discharge and mouth of the river.

Table 3.16 Environmental releases in the calculation of the continental and regional model

	Continental model [t/a]	Regional model [t/a]
Air	10,292 [(0.8 · 11,130) + (0.9 · 1,542)]	2,380 [(0.2 · 11,130) + (0.1 · 1,542)]
Soil	/	/
Water – direct	61 *) [14.2 + (0.9 · 52.3)]	5.2 *) [0.1 · 52.3]
Water – into WWTPs	1,794 [(0.8 · 2104) + (0.9 · 123)]	433 [(0.2 · 2104) + (0.1 · 123)]

*) See footnote of Table 3.15

The input data for the model calculations are presented in detail in Appendix A16. The following regional environmental concentrations result from the calculations:

$PEC_{regional_{aquatic}}$ = 0.14 µg/l

$PEC_{regional_{air}}$ = 0.05 µg/m3

$PEC_{regional_{agr.,soil}}$ = 0.01 µg/kg (wwt)

$PEC_{regional_{agr.,soil,porewater}}$ = 0.01 µg/l

$PEC_{regional_{natural,soil}}$ = 0.004 µg/kg (wwt)

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

3.2.1 Aquatic compartment (incl. sediment)

Available effects data

Only few acute tests with aquatic organisms and one chronic study on invertebrates are relevant for the effects assessment of methyl methacrylate which are listed below. These are preferably flow through tests where concentrations were measured as MMA is moderate volatile. Several other fish species were tested as well, but the LC_{50}-values are not reliable because they are based on nominal concentrations from open static tests (Pickering and Henderson, 1966).

Table 3.17 Toxicity data for aquatic organisms

Species	Endpoint	Effect Conc.	Reference
Lepomis macrochirus	96h LC_{50}	191 mg/l	Bailey et al., 1985
Oncorhynchus mykiss	96h LC_{50} 96h NOEC	>79 mg/l 40 mg/l	Bowman, 1990
Daphnia magna	48h EC_{50} 48h EC_0	69 mg/l 48 mg/l	Burgess, 1990
Daphnia magna	21d NOEC	37 mg/l	SLI, 1997
Selenastrum capricornutum	96h EC_{50} 96h NOEC	170 mg/l 100 mg/l	Forbis, 1990
Selenastrum capricornutum	72h EC_{50} 72h NOEC	>110 mg/l 49 mg/l (biomass) 110 mg/l (growth rate)	Zeneca, 1999
Scenedesmus quadricauda	8d EC_3	37 mg/l	Bringmann & Kühn, 1978a,b, 1980a
Microcystis aeruginosa	8d EC_3	120 mg/l	Bringmann & Kühn, 1976, 1978a,b

The acute toxicity of MMA to *Lepomis macrochirus* was investigated in a flow-through system according to an US EPA guideline (Bailey et al., 1985). After 96 hours a LC_{50} of 191 mg/l was derived, after 72 hours the LC_{50} was 264 mg/l. The effect concentrations were calculated as mean of the measured concentrations at the beginning and the end of the test. The pH was not monitored.

In another acute flow-through test with *Oncorhynchus mykiss* no LC_{50} could be derived after 96 hours at the highest measured concentration of 79 mg/l MMA (Bowman, 1990). Referring to abnormal behaviour the NOEC was 40 mg/l. The test was performed according to an US EPA guideline, pH was measured between 7.7 and 7.9.

For *Daphnia magna* acute toxicity was investigated in a flow-through test with US EPA standard conditions (Burgess, 1990). The EC_{50} for immobilisation was 69 mg/l MMA after 48 hours (measured concentration). At 100 mg/l all daphnids were immobile after 48 hours. After 24 hours the same concentration was without visible effect. The pH values were measured as 7.8 - 7.9.

In two other publications EC_{50} values of 720 and 1,760 mg/l MMA were reported for *Daphnia magna* after 24 hours (Bringmann & Kühn 1977, 1982). These nominal values are not valid as static open systems were used and volatilisation of MMA has to be assumed.

In an OECD test with *Selenastrum capricornutum* after 96 hours an EC_{50} of 170 mg/l and a NOEC of 100 mg/l were derived for the reduction of biomass measured by cell counts (Forbis, 1990). The 24-, 48- and 72-hour EC_{50}-values were estimated to be > 200 mg/l. These are given as nominal concentrations because at the end of the test MMA concentrations were below the detection limit of 0.1 mg/l (pH = 7.0 – 7.7). In contrast in control samples with test aquaria water alone the average recovery of MMA was 98% after 96 hours.

According to a critical re-evaluation of the respective test report (Nyholm, 1999), the applied US EPA/ASTM testing protocol implies a possible limitation of phosphorus supply by day 3, whereas the test duration is four days. Due to limiting conditions on the third day, expressed as reduced increase in the original cell count data, higher pH values have to be assumed on day 3 than have been measured at the end of the present test. Since hydrolysis half-life decreases considerably with increasing pH (4.4 h at pH 7, 2.4 h at pH 11), this pathway may be an important cause of MMA loss. Considering the physicochemical properties of MMA, volatilisation and adsorption are expected to be of less relevance, but can no more be excluded than incorporation into the algae. In sum, duration and extent of algal exposure to MMA is virtually unknown and therefore the reported EC values should not be regarded as valid.

In 1999, a 72h-test with *Selenastrum capricornutum* has been conducted according to OECD guideline 201. The test vessels were completely filled glass bottles, with airtight, teflon faced disc/crimp closures. MMA concentrations have been measured at the beginning and after 72-h test duration in parallel blank solutions without algae. The percentage MMA loss in the measured concentrations over the test period ranged from 6 to 13%. However, no measured MMA concentrations are reported for the actual treatments comprising algae, thus leaving some remaining uncertainty regarding the “true” algal exposure to MMA. At the start of the test, pH ranged from 8.31 to 8.39 and at the end the range was 6.76 (110 mg/l treatment) to 9.3 (control treatment).

Cell multiplication inhibition tests were performed with *Scenedesmus quadricauda* and *Microcystis aeruginosa* (Bringmann & Kühn 1976, 1978a,b). The test vessels were covered with metal caps which fitted not very tightly. Besides it has to be kept in mind that the test duration of 8 days is longer than the exponential growth phase of the algae, which might have influenced the test results. Therefore the EC_3-values of 37 mg/l and 120 mg/l (nominal) have to be treated with care.

The report on a long-term daphnid study (SLI, 1997) has become available in 1998. This fully valid flow-through test reveals a 21-d NOEC of 37 mg/l, derived from measured MMA concentrations.

Determination of **$PNEC_{aquatic}$**

Results from acute tests with species from three trophic levels are available for which the LC/EC_{50}-values are in the same order of magnitude. Regarding the new algae test results as valid, the derivation of $PNEC_{aquatic}$ can be based on two long-term NOECs from species representing two trophic levels. Therefore, according to the TGD, an assessment factor of 50 has to be applied to the lowest NOEC of 37 mg/l for Daphnia magna. Since there is no specific evidence, that chronic MMA toxicity to fish might be lower than to daphnids, lowering of the assessment factor to 10 is rejected.

$PNEC_{aquatic}$ = 37 mg/l / 50 = 740 µg/l

Determination of the $PNEC_{microorganisms}$

For the derivation of the $PNEC_{microorganisms}$ the following data from non-standard tests with protozoa and bacteria are relevant. These are nominal values and the test media were neutralised.

Table 3.18 Toxicity data of organisms relevant for wastewater treatment plants

Species	Effect concentration	Reference
Chilomonas paramaecium	48h EC_5 = 178 mg/l	Bringmann et al. 1980
Entosiphon sulcatum	72h EC_5 = 447-450 mg/l	Bringmann and Kühn, 1980a, Bringmann, 1978
Uronema parduczi	20h EC_5 = 556 mg/l	Bringmann and Kühn, 1980b
Pseudomonas putida	16h EC_3 = 100 mg/l	Bringmann and Kühn, 1976, 1980a

The toxic threshold concentrations (EC5-values) for different species of protozoa were derived in cell multiplication inhibition tests showing less sensitivity than for *Pseudomonas putida*, which was assessed in a cell multiplication inhibition test as well. The test vessels were covered with metal or plastic caps.

The lowest NOEC was derived in the test with *Pseudomonas putida* which must be numbered among the more sensitive ones according to the TGD. Therefore the **$PNEC_{microorganisms}$ amounts to 100 mg/l**.

3.2.2 Atmosphere

Data on biotic or abiotic effects in the atmosphere are not available. From its chemical structure it can be assumed that MMA has no specific adverse effects in relation to global warming or ozone depletion.

3.2.3 Terrestrial compartment

To assess the effects of MMA on terrestrial organisms, only a test on the respiration inhibition of natural soil microflora is available (Hossack et Thomas, 1992). After two days incubation it appeared to be a dose-related inhibition of respiration. But at the end of an exposure duration of 28 days even for the highest concentration of 1,000 mg/kg this effect was no longer significant.

Determination of $PNEC_{soil}$

Based on the data available for the soil compartment, no PNEC can be derived. For an indicative risk assessment, the aquatic PNEC of 740 µg/l can be used and compared to the concentration in soil pore water.

Therefore: **$PNEC_{soil,porewater}$ = 740 µg/l**

3.2.4 Secondary poisoning

MMA 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

All calculated or measured wastewater concentrations of MMA in influents or effluents of wastewater treatment plants are far below the PNECmicroorganisms of 100 mg/l. Therefore, a risk to wastewater treatment plants is not to be 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 3.19** the comparison between PEC and PNEC for all relevant exposure scenarios is presented (PNEC = 740 µg/l). The regional background concentration (0.14 µg/l), being low compared to the PNEC of MMA in surface water, has no significant impact on the local PEC/PNEC ratios.

Table 3.19 $PEC_{localwater}$ and PEC/PNEC-ratios for local scenarios

Scenario / site	$PEClocal_{water}$ [µg/l]	PEC/PNEC
Production and processing		
generic site	139	0.2
Site A	0.147	< 0.1
Site B	40 (freshwater)	< 0.1
	15.5 (marine water)	< 0.1
Site C	1.53	< 0.1
Site D	1.04	< 0.1
Site E	0.144	< 0.1
Site F	360	0.5
Site G	0.14	< 0.1
Site H	2.14	< 0.1
External processing		
Site P	11	< 0.1
Site Q	1.2	< 0.1
ester production, generic site	15.7	< 0.1
dry polymerisation, default	0.14	< 0.1
wet polymerisation, default	6,931,800	0.94
wet polymerisation, generic site	1.5	2.4
wet polymerisation, site EP1	11	< 0.1
wet polymerisation, site EP2	30.7	< 0.1
wet polymerisation, site EP3	39.6	< 0.1
wet polymerisation, site EP4	175	0.1
wet polymerisation, site EP5	252	0.5
wet polymerisation, site EP6	990	0.7
wet polymerisation, site EP7	1,008	1.3
wet polymerisation, site EP8	1,188	1.4
wet polymerisation, site EP9	2,340	1.6
wet polymerisation, site EP10	2.0	3.2
wet polymerisation, site EP11		< 0.1
Processing and use of polymers		
shaping of polymers	0.29	< 0.1
formulation of paints	2.0	< 0.1
private use of paints	0.16	< 0.1
paper recycling	0.9	< 0.1

Based on the present data configuration, PEC/PNEC ratios exceeding one are calculated for wet polymerisation, default calculation, generic site and known sites EP7 to EP10.

Therefore, a risk has to be deduced from the present data configuration. There is a need for further testing and gathering of exposure information or for limiting the risk.

Producers / importers

Based on the updated site-specific data (effluent monitoring, site-specific dilution models), all producing sites reveal PEC/PNEC ratios clearly below 1. There is at present no need for further information gathering or for limiting the risk beyond those measures which are already being applied (**conclusion (ii)**).

External processing, use of polymers

For four out of 29 known downstream users sites where MMA is used for wet polymerisation processes, as well as for the generic site scenarios of wet polymerisation, PEC/PNEC ratios above one are calculated and a risk for the aquatic compartment has to be deduced on the basis of the present data configuration.

During a comprehensive consultation of downstream user industry, all 29 sites declaring themselves, represented a good half of the externally processed MMA tonnage, and provided figures concerning their individual MMA use tonnages. Some sites provided further details with regard to flow rates of receiving wwtps or rivers. Two sites demonstrated to apply processing techniques without any releases to hydrosphere. None of the remaining 27 sites provided any data which could serve as basis for deriving reliable and representative specific emission factors for the wet polymerisation scenario.

For the processing sites with PEC/PNEC ratios above one, the PEC calculations are essentially based on default calculations. Therefore, an improvement of exposure data is possible for the wet polymerisation scenarios, e.g. by performing effluent measurements. However, keeping in mind reported year-to-year variations of used MMA tonnages by factors of up to 27, it seems questionable if appropriate effluent monitoring data can be achieved with reasonable expenditure of time and money. Reliable data have to meet the requirement of being representative for all possible utilisation factors (related to used MMA tonnage) of a specific site's overall capacity for wet polymerisation processes.

On the effects side of the risk assessment data improvement is possible because an assessment factor of 50 is used for the PNEC derivation and it might be possible to lower the PNEC by further testing, i.e. the assessment factor can be lowered to 10 if a long-term fish test is performed. But regarding the locally limited risks that are identified due to the specific scenario this kind of data improvement is not proposed by the rapporteur.

It is concluded, that local risk reduction measures have to be considered, if the MMA processing capacity exceeds 5,000 t/a at one single site (**conclusion (iii)**). Based on default calculation, this MMA tonnage gives a PEC/PNEC ratio significantly above one. It should be noted, that wastewater reutilisation / recycling systems are applied by some known polymerisation sites, avoiding any significant MMA emission to hydrosphere. Sites applying such advanced process engineering would not require further consideration of risk reduction measures.

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

The use of polymers, containing residual MMA, covers a wide range of applications, different products and used technologies making it nearly impossible to calculate a resulting PEC for each application. Only in special cases like paint formulation, private use of paints and paper recycling, release estimations were possible, leading to PEC/PNEC-ratios in surface water clearly below 1 (**conclusion (ii)**). Since environmental releases during the use of MMA polymers are determined by the low residual MMA contents, a risk to the environment is assumed to be low for the local assessment (**conclusion (ii)**).

The release assessment for the regional model was carried out with default values for the residual MMA-amount in polymers. But as the $PEC_{regional}$ is low compared to the local concentrations and therefore does not contribute to a significant extent to the PEC/PNEC-ratios, there is no need for an improvement of the input data for this estimation.

Sediment

Neither monitoring data on concentrations of MMA in sediment nor experimental results with benthic organisms are available. As there is no evidence for relevant adsorption of MMA onto sediment, the assessment is covered by the aquatic evaluation (cf. TGD, chapter 3 – 3.5.2) (c**onclusion (ii)**).

3.3.2 Atmosphere

As MMA reveals a short half-life for atmospheric photooxidation (21-24 hours) a risk to the atmosphere by abiotic or biotic effects is not to be expected (**conclusion (ii)**).

3.3.3 Terrestrial compartment

Based on a $PNEC_{soil,porewater}$ of 740 µg/l and the maximum calculated concentration in soil porewater of 41 µg/l the PEC/PNEC-ratio amounts to 0.06 and there is no risk identified for the terrestrial compartment (**conclusion (ii)**).

Due to its leaching potential, residual MMA may reach groundwater through seepage. It should be considered to rule out possible groundwater contamination from local sources by means of appropriate data. However, as for the aquatic compartment, no monitoring data are available.

3.3.4 Secondary poisoning

MMA 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

Methyl methacrylate is primarily used as a chemical intermediate which is further processed to polymers. Main products are acrylic sheets, methacrylate esters, moulding, extrusion, emulsion and dispersion–polymers as well as reactive resins.

The substance is used in reactive resin preparations which are applied in industrial and skilled trade sectors e.g. as floor coatings (app. 20%), adhesives (app. 60%) and dental products (app. 80%). Methyl methacrylate may be a residual component in paints, lacquers and varnishes (app 0.5%).

Methyl methacrylate has a characteristic odour. The odour threshold is 0.21-1.4 mg/m^3 (0.05 - 0.34 ml/ m^3) (IUCLID data sheet 1994).

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

Oral intake of small amounts of residual monomer migrating from food packaging materials may be an additional route for consumer exposure. For methacrylates including MMA a group-TDI has been defined at 100 µg/kg bw/d (EEC, Synoptic Document No. 7, 1994).

Consumers may be exposed to methyl methacrylate via variable amounts of residual methyl methacrylate monomers in a wide range of applications.

From plastic products containing the methyl methacrylate-monomer migration of methyl methacrylate takes place.

4.1.1.2 Occupational exposure

Methyl methacrylate is primarily used as a chemical intermediate which is further processed to polymers. Main products are acrylic sheets, methacrylate esters, moulding, extrusion, emulsion and dispersion – polymers and reactive resins.

The formulations applied in the industrial and skilled trade sector contain up to 80% MMA as a reactive component or as a diluent, e.g. adhesives, floor coatings and resins. Other formulations like paints and varnishes contain residual MMA up to max 0.5%.

The following occupational exposure limits (8-h TWA) are established for methyl methacrylate (ILO 1994):

AUS, B, FIN, F, USA (NIOSH/OSHA)	410 mg/m^3	100 ml/m^3		
USA (ACGIH)	410 mg/m^3	100 ml/m^3	since 2000: 205 mg/m^3	50 ml/m^3
DK	307 mg/m^3	75 ml/m^3		
D	210 mg/m^3	50 ml/m^3		
NL	200 mg/m^3	50 ml/m^3	1.5.1999: 100 mg/m^3	25 ml/m^3
Sweden	200 mg/m^3	50 ml/m^3		
Switzerland	210 mg/m^3	50 ml/m^3		
UK	208 mg/m^3	50 ml/m^3		

Within the EU, the lowest short-term level (D) amounts to 210 mg/m^3 (50 ml/m^3) and the highest (F) to 820 mg/m^3 (200 ml/m^3).

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

Production

The production of methyl methacrylate is carried out in highly contained systems in a continuous process. Control measures are maintained with respect to workplace exposures to more hazardous chemicals e.g. acetone cyanohydrin (CEFIC, 1995).

High standards of control are practised in areas where the containment may be breached, e.g. during maintenance and the taking of process samples as well as during cleaning and repair works. Inhalation exposure in other areas is minimised by purpose-designed tanker filling stations and the use of local extraction ventilation around drum filling stations (CEFIC, 1995).

About 220 employees are exposed during MMA production (Röhm, 1998, data of three companies).

Workplace measurements

Table 4.1 Exposure to MMA in workplace air
(Röhm, 1998, Company data of 5 European producers; CEFIC, 1995, Company data of 7 European producers)

Job category	Year of measu-rement	No. of samp.	8-h TWA Range [mg/m³]	Mean 8-h TWA [mg/m³]	50th percentile [mg/m³]	90th percentile [mg/m³]	Short term conc. [mg/m³] (min)
MMA production [1]							
- All activities	1993-98 1991-93 1993	59 54 3	0.0 – 93.5 [2] 0.04 – 247	- - -	5 - -	18 - -	- - 13 – 87 (15 min)
- Production	1992-93 1992-93	24 14	0.4 – 41 -	5 -	- -	- -	- 27 (50 min)
- Maintenance	1993-98 1993	6 4	1.7 – 14 [2] 1.5 – 5.0	- -	- -	- -	- -
- Packaging	1993-98 1993	13 2	0.7 – 93.5 [2] 32.5 / 44	- -	- -	- -	- -
PMMA production [1],[2]							
- Production of extrusion polymers dry process	1993-98	20	0.0 – 4.6 [2]	-	0.4	2.5	-
- Production of extrusion and moulding polymers manufacture tank farm bead polymers	 1991-94 1989-94 1989-94 1992-94	 33 6 42 12	 0 – 12.5 0.4 – 0.8 0.4 – 54 -	 - - - -	 - - - -	 - - - -	 - - - 7.9 (5 min)
- Solvent polymerisation	1993-98 1991-93 1991-93	7 15 31	0.0 – 11 [2] 0.4 – 32 -	- 5.8 -	- - -	- - -	- - 79 (5 min)
- Dispersion polymerisation	1991-94 1991-94 1991-94	7 7 7	0.4 – 3.3 1.2 – 10 -	0.3 1.6 -	- - -	- - -	- - 22 (8 min)
- Bead and emulsion polymerisation production/packaging maintenance	 1993-98 1993	 34 4	 0.0 – 24 [2] 1.2 – 24	 - -	 1.2 -	 7.1 -	 - -
- Substance polymersiation	1995-97	24	0.0 – 135 [2]	-	2.1	28	-
- Polymerisation	1989-94	31	>0.4 – 10	1.4	-	-	-
- Production of emulsion, dispersion, plastic additives	1992	4	0.2 – 9.2	-	-	-	-

[1] According to the producers PPE is generally worn during activities with high exposure potential
[2] New data from Röhm 1998

Table 4.1 continued overleaf

Table 4.1 continued Exposure to MMA in Workplace Air

Job category	Year of measu-rement	No. of samp.	8-h TWA Range [mg/m³]	Mean 8-h TWA [mg/m³]	50th percentile [mg/m³]	90th percentile [mg/m³]	Short term conc. [mg/m³](min)
Transesterification [1),2)]							
- Filling / production	1993-98	36	0.0 –55 [2)]	-	2.1	10	-
	1993-94 1993-94	48 14	0.4 – 84 -	9.2 -	- -	- -	- 33 (5 min)
Cast sheet production [1),2)]							
- All activities	1990-93 1992-93 1993 1992-93	21 15 2 5	0.8 – 225 1.4 – 62	- - - -	- - - -	- - - -	 121 – 749 (15 min) 23 – 233 (7-15 min)
- Cast production	1993 1993-94 1993-94 1993-94 1993-94 1993-94	- 21 26 22 19 163	2.1 – 686 4.2 – 50 25 – 112 37 – 141 33 – 283 -	92 21 67 91.5 146 -	- - - - - -	- - - - - -	- - - - 75 – 412 (5 min)
- Cast filling / assembly	1993-98	127	2,3 –714 [2)]	-	48	148.5	-
- Syrup production	1993-98	119	2.1 – 618 [2)]	-	42	106	-
- Waste handling	1995-97	7	1.1 – 147 [2)]	-	-	-	-
Coatings, resins [1)]							
Adhesives production production/packaging	1993-98	15	5 – 60 [2)]	-	23	57	-
- Production of reactive resins (incl. Dental resins, reactive and floor coatings)	1993-98	33	1.7 – 264 [2)]	-	28	119	-
- Production of floor coatings	1995-97	5	1.5 – 25	-	-	-	-
- Production of reactive coatings	1995-98	21	5 – 264 [2)]	-	-	-	-
- Production of dental resins	1996-97	7	3 – 84	-	-	-	-

[1)] According to the producers PPE is generally worn during activities with high exposure potential
[2)] New data from Röhm 1998

In European companies exposure concentrations during the production of methyl methacrylate (8-hour TWA) regarding all activities (probably including filling, maintenance, repair, sampling, storage) the exposure levels during the years 1993 – 1998 are up to 93.5 mg/m³ (up to 22.5ml/ m³). The 90th percentile is 18 mg/ m³ (4.3 ml/ m³) (Röhm, 1998). Short-term measurements are up to 87 mg/m³ (21 ml/ m³, 15 min) (CEFIC, 1995, cf. **Table 4.1**).

The applied analytical method is unknown. A recommended method comprises GC with FID detection after absorption the substance to a special scavenger (XAD – 2) and desorbing with

carbon disulphide (NIOSH No. 2537). The detection range is located between 10 and 1,100 mg/m^3 (sampling volume 3 l).

The submitted measurement results are regarded as valid although workplaces and activities upon which the results are based, are in part only described in general terms.

Further processing as a chemical intermediate

Methyl methacrylate is predominantly further processed at the site of the producers. The remaining quantity (app. 75,000 t) is further processed at sites of customers, which may belong to the large-scale chemistry as well as to the plastics industry and smaller formulation companies.

The only use for methyl methacrylate is the use as a chemical intermediate for the production of polymers. This is also true for applications where the final polymerisation step takes place at the site of use, e. g. reactive resins. Main products are extrusion, moulding, dispersion and emulsion polymers, acrylic sheets and reactive resins. These products contain only residual monomeric methyl methacrylate except reactive resins, which may contain up to 80% of the monomer.

The further processing of MMA to prepolymers is not described separately. It is assumed that the exposure scenario and the exposure level are the same as during the production and further processing of MMA.

PMMA production

Production of extrusion and moulding polymers

MMA is used as a monomer or copolymer in a suspension polymerisation process to yield polymer beads. The reaction can be carried out in semiautomated batch reactors. Another process is a continuous, automated process in closed systems. Dermal and inhalation exposures are to be expected during handling the monomer, e.g. during transfer, filling and dosing operations.

The polymerisation reactions can be carried out in semiautomated batch reactors or as a continuous, automated process in closed systems. Dermal and inhalation exposures are to be expected during handling the monomer, e.g. during transfer, filling and dosing operations.

Individual measurements during production of extrusion polymers are up to 4.6 mg/m³ (1.1 ml/m³) (8-h TWA) for all activities involved in the dry process. The 90th percentile is 2.5 mg/m^3 (0.6ml/m³) (Röhm, 1998).

Production of solvent, dispersion, emulsion and substance polymers

Methyl methacrylate is used as a monomer or copolymer in solvent, dispersion, emulsion and substance polymerisation processes to yield polymers that are marketed in aqueous emulsions or powders (beads) or blocks (substance polymers) or as dissolved polymers for paints and varnishes.

The reactions are carried out in semiautomated batch reactors. Most production steps are performed within a closed system. Exposure may occur during handling, filling, sampling operations and waste treatment.

Personal monitoring data from the bead and emulsion polymerisation are up to 24 mg/m³ (up to 5.7 ml/m³) (8-h TWA) for all activities involved in production (packaging, maintenance). The

90th percentile is 7.1 mg/m3 (1.7 ml/m³) (Röhm, 1998). Short-terms measurements with the mean of 79 mg/m³ (19 ml/m³) were observed (5 min) (cf. **Table 4.1**) during the solvent polymerisation (CEFIC, 1995).

Production of methacrylic acid esters (Transesterification)

The transesterifications are carried out in closed batch reactors within the primary manufacturing site or by industrial users.

MMA is reacted with alcohols to give the corresponding methacrylic acid esters and methanol. Exposure may occur during handling, sampling, filling, cleaning, maintenance, repair work and waste treatment. Workplace concentration levels are up to 55 mg/m³ (up to 13.3 ml/m³, 8-h TWA, cf. **Table 4.1**). The 90th percentile is 10 mg/m³ (2.5 ml/m³) (Röhm, 1998).

Production of cast acrylic sheet

The production process of cast acrylic sheet consists of four independent production steps with different exposure potential:

1. Production of syrup (monomer mixture containing all pigments, colourants, fillers and aids for polymerisation): The components are mixed in a batch reactor at room temperature. This production step results in a viscous pre-polymer.

2. Cell filling (syrup/pre-polymer is filled into cells consisting of two sheets of silicate glass separated by a plastic seal which determines the thickness of the acrylic sheet): In this semi-automated process the syrup is filled manually into the cells which are finally sealed and transported to the polymerisation unit. Due to the high exposure potential purpose-designed LEV is used according to the producers during this production step.

3. Polymerisation: The sealed cells are stored for several hours at increased temperature in large incubators or in a water bath.

4. Tempering: At the end of the step 3 when the polymerisation process is almost complete, the cells are slowly heated to temperatures up to or above 100 °C in order to remove most of the residual monomer by final polymerisation. The high temperature is maintained for several hours. It is needed because the diffusion of the remaining MMA is very slow at this stage and, as a consequence, the availability for the polymerisation process would otherwise be too low.

Finally, the cells are slowly cooled down to room temperature and the silicate glass sheets and the plastic seals are removed. Step 1 and especially 2 are the steps with the highest exposure potential during the production process. They are performed at room temperature. For activities with a high exposure potential PPE is used. Step 3 and 4 are performed at increased temperature but they have only a low potential because the containment (cells) is not breached until the polymerisation process is complete (Röhm, 1998).

According to new information provided by Röhm (1998), personal monitoring data for the single process steps involved in cast sheet production (cast filling, assembly, syrup production and waste handling) exposure values (8-h TWA, cf. **Table 4.1**) range from 1.1 – 714 mg/m³ (0.3 - 172 ml/m³). The 90th percentile is 148.5 mg/m³ (35.7 ml/m³). Short-term measurements of this time range were not available.

Older single full-shift measurements range from 0.8 to 686 mg/m³ (0.2 – 165 ml/ m³) with peak exposures (short-term measurements) up to 750 mg/m³ (180 ml/ m³, 15 min) (cf. **Table 4.1**) (CEFIC, 1995).

About 190 employees were reported to be exposed in this production process (Röhm, 1998). For activities with a high probability of exposure personal protective equipment is used.

Coatings, resins

Production of reactive resins (incl. Dental resins, reactive and floor coatings) and adhesives

Reactive resins are prepared by mixing monomers and/or pre-polymers with fillers and other additives in closed batch processes.

The resins containing 20 – 80% MMA are used in floor coatings or other speciality resins like adhesives (e.g. glues for acrylic sheets), road markings, polymer concrete or dental and medical application.

Exposure is possible during sampling and analysis, filling and drumming, as well as during cleaning, maintenance and repair works.

According to information provided by the producers of MMA, personal monitoring data for MMA in reactive resins (incl. Dental resins, reactive and floor coatings) production range from 1.7 – 264 mg/m³ (0.4 to 63.4 ml/m³) (8-h TWA, c. f. **Table 4.1**) for all activities in manufacture. The 90th percentile is 119 mg/m³ (28.5 ml/m³) (Röhm, 1998).

Individual measurements during production of adhesives range from 5-60mg/m³ (1.2 – 14.4 ml/m³) (8-h TWA, c. f. **Table 4.1**) for activities involved in the production and packaging. The 90th percentile is 57 mg/m³ (13.8 ml/m³) (Röhm, 1998).

Acrylic scrap recycling

Several European companies recycle acrylic scrap by thermal depolymerisation within closed systems. Since the recycling product is methyl methacrylate, it must be assumed that exposure-intensive activities are comparable to those involved during manufacture. The MMA product is delivered to manufacturers of MMA polymers for further processing.

No data are available on exposure during recycling. However, in view of the nature of the process, it is assumed that exposure will be at least as high as during the manufacture of MMA. Exposure is possible during sampling and analysis, during filling activities as well as during repair, maintenance and cleaning work.

Dermal exposure within the chemical industry (manufacture and further processing)

Dermal exposure in the large-scale chemical industry is estimated considering that MMA is manufactured and further processed primarily in closed systems and that the use of gloves is highly accepted within the chemical industry. The extent of protection depends inter alia on the suitability of the recommended personal protective equipment (here gloves) with regard to the permeation of methyl methacrylate. Since most producers give no information about appropriate glove types or recommend glove materials providing only limited protection, dermal exposure during production and further processing of MMA has to be considered. The exposure level is assessed using the EASE model.

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

According to **Table 4.1**, further processing of methyl methacrylate is mainly performed at the sites of the producers, but a considerable quantity is further processed by customers. It is to be assumed that further processing is performed not only in the large-scale chemical industry but also in companies with lower levels of protection belonging to the further processing industry. Generally, in these areas, it cannot be excluded that the substance is handled in open systems during certain tasks, e.g. metering and filling activities or application works, and that suitable technical measures (local exhaust ventilation (LEV)) and personal protective equipment (PPE), here gloves, are not used (Voullaire, Kliemt, 1995).

Further processing of MMA in the further processing industry

Methyl methacrylate is also processed to prepolymers and reactive (or casting) resins, emulsion and suspension polymers which are used to formulate products like adhesives, floor coatings as well as paints and lacquers (for description see following sections).

Exposure is expected to occur mainly during further processing of the monomer and when the formulations contain high amounts of monomeric MMA like reactive resins for dental products (up to 80% MMA), adhesives (up to 60%) and special coatings (20%) are used.

Production of adhesives, casting resins and floor coating materials

Adhesive formulators may purchase methyl methacrylate as a polymer in resin form, as a prepolymer or as a monomer, which they polymerise or process further on site.

Industrial polymerisation of MMA is usually conducted by batch process in closed reactors equipped with release vents. Released gases are condensed and returned to the process or to a scrubber. Worker exposure during polymerisation is most likely to occur during handling the monomer (filling, metering) but also during handling the adhesives or resins, which contain considerable amounts of the monomer (EPA, 1986).

Adhesives are manufactured either quasi continuously or batchwise in both closed and partially open systems (lidded mixer). For the USA it is described that the plants have typically general ventilation only (EPA, 1986). The formulated adhesive may contain up to 60% methyl methacrylate.

It is assumed that floor coating materials and casting resins are produced similar to adhesives.

Exposure is possible during handling the monomeric MMA or during handling the products. Relevant tasks are sampling and analysis, filling and drumming as well as cleaning, maintenance and repair tasks. Since no workplace measurements are available, inhalation and dermal exposure is assessed in application of the EASE model. The duration of exposure is assumed to be 4 hours daily because there is no detailed information.

Production of paints and varnishes containing residual methyl methacrylate

Paint formulators may purchase methyl methacrylate as a polymer in resin form (PMMA) or as a monomer which they polymerise or process further on site. Industrial polymerisations are usually conducted by batch process in closed reactors equipped with release vents. Released gases are condensed and returned to the process or to a scrubber. Worker exposure during polymerisation

is most likely to occur during handling the monomer (filling, metering). The produced polymers contain only residual monomer (up to 1.5%).

In the paint industry, fully automatic production lines are seldom used (e.g. for white dispersion paints). In view of the wide range of varieties, batch production may be assumed for most paint varieties (Goldschmidt et al., 1984). Paint dispersions are manufactured both in closed (e.g. stirrer mills) and open dispersers (e.g. three-roll mills), either continuously or in batch processes (Harnisch et al., 1982). Often, the pigment is premixed with binder, thinner and additives to produce a coarse dispersion which is then charged to a mill or a high speed disperser. After dispersion, a thinning step follows in which the paint is mixed with additional solvent (EPA, 1986). Since paints contain max. 30% of PMMA and app. 0.5% of residual monomer it can be concluded, that exposure occurs mainly during the polymerisation of the monomer (see above) and less during the handling and further processing of the polymers.

Workplace measurements regarding filling, weighing and mixing inter alia in the area of paint production have been provided by the German workers compensation funds (BGAA, 1995) from 1990-1995 (n = 28). The 50^{th} percentile amounts to 24 mg/m³ (5.8 ml/m³) without LEV and 9mg/m³ (2.2 ml/m³) with LEV. The corresponding 95^{th} percentile amount to 120 mg/m³ (29 ml/m³) and 146 mg/m^3 (35 ml/m³), respectively.

It is stated that during filling activities (paint production, wholesale) the exposure levels are located near to the 50^{th} percentile and that higher exposures above the 90^{th} percentile of 72 mg/m³ (17.3 ml/m³, without LEV) and 123 mg/m³ (29.3 ml/m³, with LEV) arise during manual mixing of paints (BGAA, 1995).

It is revealed that the level of exposure to methyl methacrylate is, in part, independent of the use of ventilations systems. This is explained by the fact that technical measures (inter alia, for the purpose of adherence to the occupational exposure limit) are taken in particular in cases where the specific work situation leads to a higher release of the substance. With regard to methyl methacrylate, this might, for example, be the case when large quantities of the substance are handled or when processing involving large areas is carried out.

It it not clear, whether the measurements also include the handling of the monomeric MMA and the use of less suitable LEV which is assessed at the reasonable worst case for this exposure scenario. For comparison model calculations applying EASE are used.

Use of formulations containing MMA

Formulations containing MMA are applied in different industrial and skilled trade sectors. Generally in these areas it cannot be excluded that the substance is handled in open systems during certain tasks, e.g. metering and filling activities and that suitable technical measures (LEV) and PPE, here gloves, are not used (Voullaire, Kliemt, 1995).

Use of extrusion and moulding polymers within the further processing industry

During the extrusion or moulding procedure when PMMA beads are heated in closed systems to melting temperatures (usually above 250°C), the polymer may depolymerise to a limited extent. Extruders are often not equipped with local exhaust ventilation, so that during cooling of the formed parts residual methyl methacrylate (0.3%) may be released.

CEFIC (1995) has provided data indicating a 8-h TWA range from 0.4-9 mg/m³ (0.1 – 2.2 ml/m³, mean values: 0.4, 0.8 mg/m³, 0.1, 0.2 ml/m³).

The producers have provided exposure data from the German workers compensation funds concerning the extrusion of plastics. 13 samples were taken in 7 companies. The 95th percentile amounts to 25.4 mg/m³ (6 ml/m³). It was stated, that in the mean 27 workers are exposed per company.

Dermal exposure through touching contaminated surfaces (indirect exposure) is expected to be low.

During extrusion and moulding processes about 200 workers in the MMA producer companies and an additional number of more than 300 employees in a major company using moulding compounds (and an unknown number of workers in other companies buying extrusion and moulding compounds) are intermittently exposed (CEFIC, 1995).

Use of adhesives in the further processing industry

MMA is used in reactive adhesive preparations (one- and two-package polymerisation adhesives) which are used in the industrial area and for skilled trade applications being a potential source of exposure (Franck, 1988; Habenicht, 1986). The quantity of MMA is only known for a 2-package polymerisation adhesive used in the automotive industry. One component contains 60% MMA.

MMA containing adhesives are applied in many different branches like plastics industry, automotive industry, electric industry, wood processing and shoe manufacturing.

In the field of engineering, device and tool construction industries, anaerobic and radiation-hardening adhesives are used to bond metals or metal and glass during assembly. Automatic or semi-automatic bonding machines are employed within continuous production processes (production lines). After the bonding step, the workpiece 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.

Workplace measurements

Table 4.2 MMA exposures during application of adhesives at workplaces belonging to different industries

Work area / activities	Year of measure-ments	Number of measure-ments	Exhaust ventilation	Range of measurement data [mg/m³]	Mean value [mg/m³]	95th percentile [mg/m³]	Source
- Adhesives	1992	--		8.3 – 13.1	11.1	--	CEFIC, 1995*
Bonding e.g. plastics industry, electric industry, shoe manufacture	1990 – 1995	106 34	no yes	--	11 3	132 83	BGAA, 1995

*) calculated from ppm to mg/m³ (factor 4.16)

For the use of adhesives, 8-h TWA values in the range of 8.3 to 13.1 mg/m³ (2 – 3.2 ml/m^3) were reported with short-term values up to 135 mg/m³ (33 ml/m³; 120 min) for a different application (CEFIC, 1995). During bonding metallic stripes, lower exposures were observed (confidential information).

Measurement results obtained in different industries were provided from the German workers compensation funds (cf. **Table 4.2**), mainly from plastics industry, e.g. bonding of acrylic sheet, and also electric industry and manufacturing of shoes, in total 70 companies. During

bonding small areas (electric industry, manufacturing of shoes), exposure levels were located <11 mg/m³ (2.6 ml/m³, 50th percentile) for workplaces without LEV and <3 mg/m³ (0.7 ml/m³, 50th percentile) for workplaces equipped with LEV. The corresponding 95th percentile amount to 132 mg/m³ (32 ml/m³, without LEV) and 83 mg/m³ (20 ml/m³, with LEV), respectively. Exposure levels higher than the 90th percentile of 80 mg/m³ (19.2 ml/m³) without LEV and 46 mg/m³ (20 ml/m³) with LEV were observed when large areas were bonded. It is stated, that exposure levels are in the area of 11 mg/m³ (2.6 ml/m³, 50th percentile, see above) when small areas are bonded. Short-term exposure levels lie in the area of 195 mg/m³ (46.9 ml/m³).

In the case of handling adhesives, frequent immediate skin contact has to be taken into consideration. Generally workers only avoid immediate skin contact with adhesives that can be removed only with difficulties. But the corresponding adhesives harden only slowly on the skin. Possibly, these adhesives are removed later with the aid of skin cleaning agents which are also employed following contact with paints and thus have the opportunity to penetrate the skin. Dermal exposure as a result of drumming or handling adhesives has to be taken into account (Kliemt, 1995). The corresponding exposure level is assessed by the EASE model (see Section 4.1.1.2.4).

Use of paints, lacquers and varnishes containing residual MMA within the further processing industry

MMA containing emulsion polymers used in water-based dispersion paints have unpolymerised MMA present in a range of 0.005 to 0.05% (Röhm et al., 1994). ECETOC reports residual monomer content of dispersions to be below 0.1% (ECETOC, 1995).

In solvent-based paints MMA-containing polymers and co-polymers are dissolved in volatile aliphatic or aromatic solvents (e.g. petroleum, butyl acetate and other esters, acetone or similar ketones, propanol or similar carbinols or diols etc.). The polymers present in lacquers and varnishes may have unpolymerised MMA present up to a maximum of 1.5% in solvent and block polymers.

Assuming that the polymer content in the finished formulations of the solvent-based paints is app. 30%, the maximum content of MMA monomer will be app. 0.5%.

In industrial sectors, paints and varnishes are often applied by painting or spraying, e.g. in the wood and furniture industry and in the automotive industry. Often spray-painting is performed in spray booths.

Exposure levels regarding painting and casting works were provided from the German workers compensation funds. The 50th percentile amount to 1 mg/m³ (0.24 ml/m³, with and without LEV) and the 95th percentile are 187 mg/m³ (45 ml/m³) without LEV and 61 mg/m³ (15 ml/m³) with LEV. It is stated that the 50th percentile of 1 mg/m³ (0.23 ml/m³, with and without LEV) regard to the use of paints and lacquers, the higher levels were observed during works with casting resins. Workplace measurements of MMA during spray painting are not available.

For comparison by analogy, substances with comparable physico-chemical properties being components of paints have been considered:

Table 4.3 Comparison to substances with similar physico-chemical properties

Substance	Vapour pressure [Pa]	Molecular weight [g/mol]
2-propanol	4,300	60.1
n-heptane	4,800	100.2
methylcyclohexane	4,800	99.2
methyl methacrylate	4,700	100.1

For spray-painting work, measured values of 0.4 – 125 mg/m³ (0.1 – 51 ml/m³) and 1 – 84 mg/m³ (0.3 – 21 ml/m³) have been reported. (Triebig, 1992; Whitehead, 1984; Bau-BG, 1994; de Rosa, 1985). For spray-painting work in the furniture industry, values up to 59 mg/m³ (24 ml/ m³) were measured, though most values lay between 9 and 29 mg/m³ (4 – 12 ml/ m³) (Schäcke, 1984).

The concentration of solvents in paints are in general app. >10%, the evaluation of app.180 security data sheets of automotive paints show that 2-propanol is often contained at ≥25% and n-heptane at 2.5–10%; much higher than the concentrations of residual MMA momomer (app. 0.5%). Predicted exposure levels for MMA during spray-painting may therefore be assumed to lie at or even below the lower end of these concentration ranges of about 0.4 – 16.6 mg/m³ – 4 ml/m³).

It is assumed that paints are often and regularly used. Therefore regular and frequent skin contact is expected when dispersion paints and solvent-based paints are used.

Dermal exposure during filling, mixing, painting as well as cleaning activities has to be considered. The corresponding exposure level is assessed applying the EASE model (see Section 4.1.1.2.4).

Release of MMA through thermal processes of PMMA

Methyl methacrylate may be released as a decomposition product during the thermal processing of PMMA.

Auffarth et al. (1989) investigated MMA emissions during laser-beam cutting of acrylic sheet. PMMA depolymerises in the intense heat of the laser and emits MMA vapour. Using local exhaust ventilation at the workplace, concentrations of 0.8 mg/m³ (0.2 ml/m³) were determined by stationary and personal measurements.

Vainiotalo et al. (1989) reported MMA exposure during PMMA processing operations (extrusion, moulding and thermoforming) in four plants using polymers of different origin. The duration of the stationary measurements (app. 0.5 m from source) was 2 – 3.5 h which was considered representative for the exposure situation. At these workplaces with local exhaust ventilation mean MMA concentrations of 0.05 to 4.6 mg/m³ (0.01-1.1 ml/m³) were observed.

Because MMA is released during thermal processes, normally no immediate skin contact occurs. The dermal exposure level caused by touching of MMA contaminated surfaces (indirect exposure) is regarded as being low.

4.1.1.2.3 Occupational exposure in the skilled trade sector

Formulations containing MMA are applied in different skilled trade sectors. Generally, in these areas, it cannot be excluded that the substance is handled in open systems during certain tasks, e.g. metering and filling activities, and that suitable technical measures (LEV) and personal protective equipment (PPE, here gloves) are not used (Voullaire, Kliemt, 1995).

Use of adhesives in the skilled trade sector

Adhesives which contain MMA are inter alia used to repair metal workpieces. During repair works, which may involve rather small areas, workers may be subjected to inhalation and dermal exposure. It may be assumed that exhaust ventilation systems are absent, and that suitable personal protective equipment is not worn if adhesives are handled.

Neither workplace measurements nor information on the duration and frequency of exposure or on the exposed group are available. For exposure assessment it is assumed that the exposure scenario in the skilled trade sector is comparable to that within the further processing industry. Therefore the given value for bonding small areas without local exhaust ventilation is used (11 mg/m³, 2.6 ml/m³, 50th percentile, see Section 4.1.1.2.2, paragraph "Use of adhesives in the further processing industry"). Immediate dermal contact has to be taken into account, especially when adhesives which harden slowly, e.g. anaerobic or radiation-hardening adhesives are used.

Use of MMA containing floor coatings in skilled trade sectors

One important open application of reactive resins is floor coatings. Preparations containing up to 20% MMA are used by specialised companies. The applied mixture is polymerised within approx. 30 – 60 min dependent on temperature and initiator concentration. However, a certain amount of MMA may evaporate from the reaction mixture before it is fully polymerised. The evaporation of MMA is reduced to a certain extent by a cover layer of paraffin forming a film on the surface of the coating.

In the CEFIC data collection (CEFIC, 1995, cf. **Table 4.4**) only a limited number of data were available: 8-h TWA of 125 – 424 mg/m³ (30–102 ml/m³) and short-term exposure up to 832 mg/m³ (200 ml/m³).

Table 4.4 Concentration of MMA in air at the workplace, uses of reactive resins during coating works

Work area / activities	Year of measu-rements	Number of measure-ments	Exhaust ventilation	Mean value * (no TWA) [mg/m³]	Mean 8-h TWA [mg/m³]	95th percentile [mg/m³]	Source
Floor coating	1990 1993	3 4	-- --		399 204	-- --	CEFIC, 1995 **
- Priming	--	4 3	no yes	605 196		--	Kersting et al, 1995, German BIA/BAU-BG
- Mixing	--	16	no	715		--	
		4	yes	381		--	
		20	outside	174		--	
- Transport	--	15	no	615		--	
- Covering	--	47	no	610		--	
		13	yes	601		--	
- Sealing	--	40 10	no yes	687 774		--	
Floor coating	1990 – 1995	78 34	no yes	--	241*** 141***	1045 625	BGAA, 1995

* Exposure duration not known
** Calculated from ppm to mg/m³ (factor 4.16)
*** 50th percentile of the measurement collective

Data provided from the German workers compensation funds were obtained mainly within the production of industry floors (see **Table 4.4**, BGAA). During floor coating high exposure levels were observed: the mean 50th percentile amounts to 241 mg/m³ without LEV (51 ml/m³, n = 78 within 7 enterprises) and 141 mg/m³ with LEV (34 ml/m³, n=34 within 2 enterprises). The corresponding 95th percentile are 1,045 mg/m³ (251 ml/m³, without LEV) and 625 mg/m³ (152 ml/m³ with LEV). It is stated that exhaust ventilation is rather seldom applied. The 95th percentile of short-term exposures (<1h) of 683 mg/m³ (164 ml/m³; n = 50) was measured during floor coating.

Additional measurements were provided (Bau-BG, 1993, available through German GISBAU (information system of Bau-BG)) and recently published (Kersting et al., 1995, see **Table 4.4**). Data available from this project indicate that without technical and organisational measures the occupational exposure concentrations vary considerably and high exposures (up to 774 mg/m³ (186 ml/m³)) have been observed at several occasions.

In the area which, in part, belongs to the building trade, it has to be considered that gloves possibly are not worn and that dermal exposure occurs not daily.

Technical measures may reduce exposure to MMA. Kersting et al. (1995) and Christensen (1990) presented evidence that suitable ventilation and accompanying reorganisation of working methods ("working in line") may significantly reduce MMA exposure below 210 mg/m³ (50 ml/m³) and possibly to mean values of <20 mg/m³ (<5 ml/m³).

A method of personal protection to reduce occupational exposure is the use of an "airstream helmet" where filtered air is pumped into the breathing zone. With this method also a significant reduction of exposure to values below 40 mg/m³ (10 ml/m³) may be obtained in areas with high MMA concentrations (Kersting et al., 1995).

Additional uses of MMA in polymer concrete and in road marking materials are mentioned by the producers. It is assumed that the exposures are in the same range or even lower than observed for floor coating works.

Use of paints, lacquers and varnishes containing residual MMA within the skilled trade sector

MMA containing emulsion polymers used in water-based dispersion paints have unpolymerised MMA present in a range of 0.005 to 0.05% (Röhm et al., 1994). ECETOC reports residual monomer content of dispersions to be below 0.1% (ECETOC, 1995), in solvent-based paints max. 30% PMMA is assumed with a residual content of 0.5% MMA.

Model calculations were performed by the producer applying the SCIES model which is used when consumer exposures are estimated. It can be assumed that the working conditions of consumers are similar to those during skilled trade use of paints. Calculations were made for painting of two rooms (20 m³ and 40 m³) with a dispersion paint containing 15% polymer and 0.015% residual MMA monomer (0.1% of 15%). The quantity of paint used was set at 200 g/m², and the painted surfaces set at 31 m² and 53 m² for the two model rooms. Assuming natural air ventilation rate, the highest concentration was estimated to be approximately 7 mg/m³ (1.7 ml/m^3).

MMA exposure values resulting from the model calculation are in the same order of magnitude as the measurement results regarding the use of paints and lacquers in the industrial area (1 mg/m^3, 0.23 ml/m³, with and without LEV) (cf. Section 4.1.1.2.2, paragraph “Use of paints, lacquers and varnishes containing residual MMA within the further processing industry”). It is assumed that this measurement set comprises the use of either dispersion and solvent-based paints, so the result is used for the risk assessment.

It is assumed that paints are often and regularly used. Therefore regular and frequent skin contact is expected when dispersion paints and solvent-based paints are used.

Exposure levels of spray painting in companies belonging to the skilled trade sectors e.g. car repair shops are assessed using the EASE model. Automobile lacquering in car repair shops without spray booths are limited. In general, the lacquering is carried out in a more separate area. The process itself may be limited to a few minutes (Auffarth et al., 1997).

Dermal exposure during filling, mixing painting as well as cleaning activities has to be considered.

Use of casting resins

MMA is applied in casting resins, which are used in dental laboratories, for orthopaedic purposes, embedding, lense manufacturing and ornament manufacturing. The resin preparations are often prepared at the use site (Forster, 1987). The concentrations of MMA in the resins are not known for all applications. It is to be assumed that the reactive resins with concentrations up to 80% MMA may be handled (mixing, dosing).

Medical application of casting resins

MMA is employed medically as a component of bone cement (mixture of MMA and its polymer) for orthopaedic purposes and for fixing metal and plastic protheses. Short-term inhalation exposure (a few minutes during an operation) is possible when these cements are prepared for application. It can be assumed that during medical applications protective gloves will be employed for reasons of medical hygiene. In assessing the dermal exposure it has to be

born in mind that the producers recommend gloves which provides only limited protection. Therefore the EASE model is applied to calculate dermal exposure levels.

In a study regarding the exposure of hospital operating personnel during operations where MMA was used in surgery only in 4 of 27 cases MMA concentrations above the detection limit (1.2 mg/m³ = 0.29 ml/m³) were found (3.7; 4.0; 4.0; 55.3 mg/m³ = 0.9; 1.0; 1.0; 13.3 ml/m³; Sass-Kortsak et al., 1992). Darre et al. (1992) reported workplace concentrations between 210 and 420 mg/m³ (50 – 100 ml/m³) of MMA during hip and knee replacement operations under conventional operating conditions without laminar airflow. Measurements were made in the breathing zone of the surgeons. The concentrations remained at the measured levels for a maximum of 10 minutes.

Orthopaedic workshops, dental laboratories and surgeries

In dental laboratories and in dental surgeries liquid MMA (assumed 80%) and powdery MMA prepolymers are used inter alia to construct orthodontic components, fillings and inlays. Use of MMA can also be assumed for orthopaedic workshops. Exposure relevant activities like filling, dosing, mixing, bonding and humidifying with liquid MMA (see below) may be performed on different time scales as several times for a short duration or regularly over a longer period of time, possibly over the whole shift. It may be assumed that suitable ventilation equipment is not always employed.

Measurement results obtained in dental laboratories are provided (German federal monitoring authorities and the German workers compensation fund provided by the producers).

Exposure data (n = 112) from 1990 – 1995 have been provided for the coating with casting resins, lacquers and paints (German workers compensation funds). At present it is not possible to differentiate the data further. It is stated that exposure levels during the use of paints and lacquers are near the detection limit and during the use of casting resins e.g. for orthopaedic purposes are near 187 mg/m³ (45 ml/m^3) without LEV and 61 mg/m³ (14.7 ml/m³) with LEV, which is the 95th percentile for all activities (painting and use of resins).

Exposures in dental laboratories and surgeries at workplaces with local exhaust ventilation are usually between 3 and 6 mg/m³ (0.7-1.4 ml/m³) (data from the German workers compensation fund in 1990 – 1994). From the federal monitoring authorities single exposure levels in dental surgeries of <62 mg/m³ (15 ml/m³), 7.5 mg/m³ (1.8 ml/m³) and “not detected” are provided. According to the federal monitoring authority Hamburg the short-term values at workplaces with suitable LEV are below 42 mg/m³ (10 ml/m³).

Exposures of 197.5 mg/m³ (47 ml/m³), 155 mg/m³ (37 ml/m³) and 125 mg/m³ (30 ml/m³) for some hours without LEV (federal monitoring authorities) and shift averages of 110 mg/m³ (26.4 ml/m³) and 14 mg/m³ (3.4 ml/m³) under unfavourable conditions (small room, no ventilation, workers compensation fund) have been observed. Short-term exposures (30 min, n = 4) up to 144 mg/m³ (35 ml/m³) without LEV and 600 mg/m³ (144.2 ml/m³) under unsuitable ventilation conditions have been measured. The federal monitoring authority Hamburg shows significant differences depending on the use of LEV. Especially during a specific task (alternately humidifying orthodentic components with liquid MMA and strewing with powdery prepolymerised MMA) the short-term values (5 min) measured at workplaces without LEV in six laboratories were between 420 – 840 mg/m³ (100 – 200 ml/m³) or sometimes even higher (FID measurement 1989/90).

Dermal exposure has to be considered during filling, mixing and coating activities, which are assumed to be performed repeatedly on a daily basis.

Other exposure data

In a preliminary screen of 27 "establishments", 8-h TWA exposure levels were as follows:

Table 4.5 Exposure levels in 27 "Establishments" (Cromer and Kronoveter, 1976)

Establishment	Concentration (8-h TWA, mg/m³)*
Monomer production	< 21
Refining	42
Resin manufacturing	< 21
Sheet manufacturing	42 – 541
Reinforced sheet manufacturing	8.3 – 166
Lens manufacturing	< 4.2- 42
Ornament manufacturing	83 – 374
Acrylic contact product	< 208
Dental laboratory	< 21 – 42

*Calculated from ppm to mg/m³ (factor 4.16)

In the literature, exposure levels of <4.2 – 42 mg/m³ (< 1.0 – 10 ml/m³) during the manufacturing of lenses and 83 – 374 mg/m³ (20 – 90 ml/m³) during ornament manufacturing are reported (Cromer and Kronoveter, 1976).

HSE (1994) reported results of workplace measurements for different job categories: Aerospace manufacture and repair, artificial teeth production and use of moulding and extrusion polymers (pooled data; personal and static, short and long-term): geometric mean 43 ± 9.75 mg/m³ (10.2 ml/m³ ± 2.32 (range 0.8 – 109 ml/m³; 87 samples)). 64 long-term (sample duration > one hour) personal exposure from the above data set had a geometric mean of 55.8 ± 10.1 mg/m³ (13.3 ml/m^3 ± 2.4 (range 0.8 – 109 ml/m³)). Of these values 42% were less than 84 mg/m³ (20 ml/m³) and 93% were less than 210 mg/m³ (50 ml/m³).

FIN has provided data (mean values) regarding bone cement use (13 mg/m³, 3.2 ml/m³), production of acrylic cement for road markings (21 mg/m³, 5.2 ml/m³), floor coating with acrylic cement (545 mg/m³, 133 ml/m³), impregnating of parquet material (47 mg/m³, 11.5 ml/m³) and working on PMMA (49 mg/m³, 12 ml/m³).

4.1.1.2.4 Estimation of the exposure according to the EASE model

Estimation of inhalation and dermal exposure from the EASE model yields the following results:

Inhalation exposure

All calculations have been done assuming exposure to pure substance. Only for spray painting an estimated percentage of MMA in the aerosol has been considered.

1. Chemical industry: manufacture and further processing in the chemical industry (including transesterification, production of polymers and reactive resins, moulding and extrusion compounds) and when recycling acrylic scrap (local exhaust ventilation).

Further processing industry: manufacture of acrylic sheet, further processing of MMA in the further processing industry (including polymerisation), recycling of acrylic sheet and when using reactive resins and adhesives.

Input parameters:	T = 20°C closed system and significant breaching / non dispersive use LEV present
Estimated exposure:	42 – 210 mg/m³ (10 – 50 ml/m³)

2. Further processing of MMA (including polymerisation) in the further processing industry, using formulations containing MMA in industrial sectors e.g. during painting, using adhesives and reactive resins (incl. Dental fields).

Input parameters:	T = 20°C non dispersive use dilution ventilation and direct handling
Estimated exposure:	420 – 840 mg/m³ (100 – 200 ml/m³)

3. Using formulations containing MMA in skilled trade sectors, e.g. during use of adhesives, interior painting, floor coating work.

Input parameters:	T = 20°C wide dispersive use direct handling and dilution ventilation
Estimated exposure:	840 – 2,100 mg/m³ (200 – 500 ml/m³)

4. Spraying dispersion paints and solvent-based paints.

Input parameters:	T = 20°C non dispersive use aerosol formation is true local exhaust ventilation
Estimated exposure:	410 – 840 mg/m³ (100 – 200 ml/m³)

Considering that the content of MMA in dispersion paints and solvent-based paints is max. 0.5%, that the liquid content of the paint (50% assumed) will evaporate completely and that the modelled value is based on an average molecular weight for solvents of app. 100 g/mol, the exposure level is estimated to:

4.1 - 8.4 mg/m³ (1 – 2 ml/m³)

5. Spraying dispersion paints and solvent-based paints.

Input parameters:	T = 20°C non/wide dispersive use aerosol formation is true dilution ventilation and direct handling
Estimated exposure:	2,100 – 4,200 mg/m³ (500 – 1,000 ml/m³)

Considering that the content of MMA in dispersion paints and solvent-based paints is max. 0.5%, that the liquid content of the paint (50% assumed) will evaporate completely and that the modelled value is based on an average molecular weight for solvents of app. 100 g/mol, the exposure level is estimated to

21 – 42 mg/m³ (5 – 10 ml/m³)

Dermal exposure

1. Manufacture of methyl methacrylate and further processing in the chemical industry, manufacture of cast sheet, recycling acrylic scrap.

Input parameters:	T = 20°C non dispersive use direct handling intermittent
Estimated exposure:	0.1 – 1 mg/cm^2/day

2. Immediate dermal exposure to monomeric MMA during the manufacture of formulations (adhesives, resins, paints, varnishes) outside the chemical industry.

Input parameters:	T = 20°C non dispersive use direct handling intermittent
Estimated exposure:	0.1 – 1 mg/cm^2/day

3. Dermal exposure when painting, varnishing or spray painting and when using reactive resins for floor coatings.

Input parameters:	T = 20°C wide dispersive use direct handling intermittent
Estimated exposure:	1 – 5 mg/cm²/day

Considering a content of MMA in paints and varnishes and when spray-painting is apparently 0.5% as a worst case, the exposure level is estimated to:

0.005 – 0.025 mg/cm²/day

Considering a content of MMA in reactive resins used for floor coatings is apparently 20% as a reasonable worst case, the exposure level is estimated to:

0.2 – 1.0 mg/cm²/day

4. Dermal exposure during use in the medical, orthopaedic field when using other casting resins.

Input parameters:	T = 20°C non dispersive use direct handling incidental
Estimated exposure:	0 – 0.1 mg/cm²/day

Considering the content of MMA in preparations used for medical applications is apparently 80% as a reasonable worst case, the exposure level is estimated to:

0 – 0.08 mg/cm²/day

5. Dermal exposure during use in the orthopaedic and dental field and when using reactive resins and adhesives.

Input parameters:	T = 20°C non dispersive use direct handling intermittent
Estimated exposure:	0.1 – 1 mg/cm²/day

Considering the content of MMA in adhesives is apparently 60% as a reasonable worst case, the exposure level is estimated to:

0.06 – 0.6 mg/cm²/day

Considering the content of MMA in preparations used for dental applications and when using other casting resins is apparently 80% as a reasonable worst case, the exposure level is estimated to:

0.08 – 0.8 mg/cm²/day

4.1.1.2.5 Integrated assessment

Methyl methacrylate is primarily used as a chemical intermediate which is further processed to polymers. This is also true for applications where the final polymerisation step takes place at the site of use (e.g. use of adhesives). Main products are cast acrylic sheets, moulding, extrusion, emulsion and dispersion polymers, methacrylate esters and reactive resins. The further processing of MMA is predominantly performed at the site of the producers. The remaining quantity (approx. 75.000 t) is further processed at sites of customers, which may belong to the large-scale chemistry as well as to the plastics industry and smaller formulation companies.

The substance is used in reactive resin preparations up to 80% MMA which are applied in industrial and skilled trade sectors e.g. as floor coatings, adhesives, and dental products. Methyl methacrylate may be a residual component in paints and varnishes and may be released during thermal processing of PMMA.

Manufacture and further processing in the chemical industry and acrylic scrap recycling

The exposure scenarios in the chemical industry comprise the:

- production of MMA,
- production of PMMA,
- transesterification,
- cast sheet production,
- production of adhesives,
- production of reactive resins.

Within the chemical industry the scenarios can be summarised with regard to inhalation and dermal exposure (with the assumption that the protection standards are comparable).

During the MMA production, the duration and frequence of exposure is assumed to be 8 hours daily, for the other areas in the chemical industry 4 hours daily.

For the production of MMA an 8-h TWA value of 18 mg/m³ MMA (4.3 ml/m³, 90th percentile, derived from given data) for inhalation exposure should be assumed. In the case of filling activities and similar works, short-term higher exposures of up to 87 mg/m³ MMA (21 ml/m³, 15 min) are possible.

In further processing especially for the *production of cast sheet* higher exposure levels are to be considered, since this process is only partially performed in closed systems. For the purpose of risk characterisation, inhalation exposure is taken to have a value of 148.5 mg/m³ MMA (36 ml/m³, 90th percentile, derived from given data). A short-term value of 412 mg/m³ MMA (99 ml/m³, 5 min) is to be assumed for the estimation of exposure.

For the areas “production of PMMA”, “transesterification”, “production of adhesives and reactive resins”, see detailed information about the inhalation exposure levels in **Table 4.6**.

When acrylic scrap is recycled, MMA is produced by thermal depolymerisation. Inhalation and dermal exposure may be expected in the same order of magnitude as during MMA and PMMA manufacture.

Dermal exposure in the large-scale chemical industry

Dermal exposure in the large-scale chemical industry is estimated considering that MMA is manufactured and further processed primarily in closed systems and that the use of gloves is highly accepted within the chemical industry. The extent of protection depends inter alia on the suitability of the recommended personal protective equipment (here gloves) with regard to the permeation of methyl methacrylate. Since most producers give no information about appropriate glove types or recommend glove materials providing only limited protection, dermal exposure has to be considered.

Supposing that gloves with limited protection are worn, a worst-case estimation of the daily dermal exposure according to the EASE model on the basis of dermal contact without using protective gloves is made. The estimation results in a dermal exposure level of 0.1 – 1 mg/cm² per day. Considering an exposed area of 420 cm² (palms of two hands) the exposure level amounts to 42 – 420 mg/person/day.

In December 1998 the MMA producers submitted new results of permeation tests of gloves determined according to the European standard (EN 374). The results confirm that different glove types have different resistances against the permeation of MMA. They also indicate that

butyl and nitrile gloves may provide a better protection than natural rubber or latex, which is at present recommended mainly.

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

Further processing of methyl methacrylate is not limited to the large-scale chemical industry but occurs in companies with lower levels of protection standards belonging to the further processing industry, too. Generally, in these areas, it cannot be excluded that the substance is handled in open systems during certain tasks, e.g. metering and filling activities, and that suitable technical measures (LEV) and PPE (here gloves) are not used (Voullaire, Kliemt, 1995).

Production of adhesives, casting resins and floor coating materials

Adhesive formulators may purchase methyl methacrylate as a polymer in resin form or as a monomer which they polymerise or process further on site. Industrial polymerisations are usually conducted by batch process in closed reactors equipped with release vents. Subsequently, the adhesives are formulated by mixing in both closed and open systems, either continuously or in batch processes. It is assumed that casting resins and floor coating materials are produced similarly.

Workers may be exposed during the handling of the monomer (filling, dosing, mixing) as well as during handling the products, which may contain up to 80% MMA. A daily duration of 4 hours is assumed.

Workplace measurements are not available, consequently inhalation and dermal exposures are estimated in using the EASE model. For assessing the risk of inhalation exposure an 8-h TWA of 21 – 105 mg/m³ (5 – 25 ml/m³, with LEV) and 210 – 420 mg/m³ (50 – 100 ml/m³, without LEV) should be used.

For the further processing of MMA in the industrial sector it cannot be excluded that gloves are not worn and that immediate dermal contact occurs. Therefore dermal exposure is assessed using the EASE model. The exposure level results to 0.1 – 1 mg/cm² /day. Considering an exposed area of 420 cm², dermal exposure amounts to 42 – 420 mg/p/day.

Production of paints and varnishes

Paint formulators may purchase methyl methacrylate as a polymer in resin form or as a monomer which they polymerise or process further on site. Industrial polymerisations are usually conducted by batch process in closed reactors equipped with release vents. Subsequently, the paints are formulated by mixing in both in closed and open reactors, either continuously or in batch processes.

Worker exposure is most likely to occur during the polymerisation step, when the monomer is handled (filling, metering). The produced polymers may contain residual monomer (up to 1.5%), the finished formulations may contain 0.5% MMA monomer.

Workplace measurements regarding filling, weighing and mixing inter alia in the area of paint production have been provided by the German workers compensation funds (BGAA, 1995) from 1990 – 1995 (n = 28). The corresponding 95th percentile amount to 120 mg/m³ (29 ml/m³) without and 146 mg/m^3 (35 ml/m³) with LEV.

Because it is not clear whether the provided data regarding the production of paints include measurements during handling (filling, dosing, mixing, see Section 4.1.1.2.2) monomeric MMA before polymerisation, an EASE calculation has been made for this exposure scenario (see Section 4.1.1.2.4).

Considering a daily duration of app. 2 hours, exposure levels 10.4 – 52 mg/m³ (2.5 – 12.5ml/m³ with LEV) and 104 – 208 mg/m³ (25 – 50 ml/m³ without LEV) are obtained.

It is obvious that the measurement results for the scenario without LEV are in good agreement with EASE estimates. On the contrary, for the scenario with LEV, the workplace measurements are higher than the EASE estimates. Because no information about the suitability of the LEV was submitted, the measurements may include LEVs with less efficiency than assumed by EASE Therefore, the measured values were used as the reasonable worst case for this scenario. The following exposure levels should be taken for assessing the risks of daily inhalation exposure in the paint production: 146 mg/m³ (35 ml/m³) with LEV and 120 mg/m³ (29 ml/m³) without LEV (95th percentile of measurement collectives comprising results inter alia from paint production, wholesale and manual mixing of paints).

For the further processing of MMA in the industrial sector it cannot be excluded that gloves are not worn and that immediate dermal contact occurs. Therefore dermal exposure is assessed using the EASE model. The exposure level results to 0.1 – 1 mg/cm²/day. Considering an exposed area of 420 cm², dermal exposure amounts to 42 – 420 mg/p/day.

Use of formulations containing MMA

Formulations containing MMA are applied in different industrial and skilled trade sectors. Generally, in these areas, it cannot be excluded that the substance is handled 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, Kliemt, 1995).

Use of extrusion and moulding polymers within the industrial sector

During the extrusion or moulding procedure when PMMA beads are heated in closed systems to melting temperatures (usually above 250°C) the polymer may depolymerise to a limited extent. Extruders are often not equipped with local exhaust ventilation, so that during cooling of the formed parts methyl methacrylate may be released.

For the purpose of assessing the risks as a result of exposure the 95th percentile of a measurement collective of 25.4 mg/m³ (6 ml/m³) is to be considered as the 8-h time-weighted average for daily exposure.

Dermal exposure may occur when the finished products are handled as well as through touching contaminated surfaces (indirect exposure). Dermal exposure by touching contaminated surfaces, caused by depolymerisation of PMMA in MMA-monomer during the moulding and extrusion process is regarded as being low (expert judgement).

Use of adhesives in the further processing industry

It is to be assumed that, in the further processing industry (e.g. plastics, automotive and electric industry, wood processing and shoe manufacturing), the reactive adhesives (one- and two-package polymerisation; containing up to 60% MMA) are sometimes handled in open systems

during certain activities such as dosage, filling and bonding. Further, MMA which has not reacted during the (UV) hardening process could evaporate if the warm workpiece is stored openly.

For assessing the risks of daily inhalation exposure the 95th percentile of measurement collectives 83 mg/m³ (20 ml/m³) with LEV and 132 mg/m³ (32 ml/m³) without LEV should be used. If small areas are bonded, exposure levels may be lower (cf. Section 4.1.1.2.3).

As concerns dermal exposure, the EASE model yields a dermal exposure of 0.1 – 1 mg/cm²/day. Assuming that skin contact occurs to preparations containing up to 60% MMA and an exposed area of 210 cm² (fingers) an exposure level of 12.6 – 126 mg/p/day is used.

Use of paints, lacquers and varnishes in the further processing industry

Solvent-based paints may contain a maximum of 0.5% MMA. In industrial sectors, paints and varnishes are often applied by painting and spraying, e.g. in the wood and furniture industry and in the automotive industries.

Workplace measurements for spray-painting are not available, consequently inhalation and dermal exposures are estimated in using the EASE model. For spray-painting an 8-h TWA of 4.2 – 8.4 mg/m³ (1 – 2 ml/m³) according to the EASE calculations (assumption: 0.5% MMA with LEV, liquid content of the paint (50%) evaporates completely, average molecular weight of solvents the model scenario based on assumed as 100 g/mol) and 21 – 42 mg/m³ MMA (5 – 10 ml/m³) (no LEV) should be used. The exposure range with LEV is in good agreement with the results obtaining by comparison with analogues of about 0.4 – 16.6 mg/m³ (0.1 – 4 ml/m³). Higher short-term exposures are possible.

For painting works (painting, filling, mixing) the 50th percentile of a measurement set of 1mg/m³ (0.24 ml/m³) should be used.

It may be assumed that suitable PPE is not always used during painting and spray-painting works. In application of the EASE model and considering a maximum MMA content of 0.5%, a dermal exposure of 0.005 – 0.025 mg/cm²/day is obtained. Assuming an exposed area of 1,300 cm² (hands and parts of the forearms) an exposure level for MMA of 6.5 - 32.5 mg/p/day is used during painting, varnishing and spray painting.

Release of MMA through thermal processing of PMMA

Methyl methacrylate may be released as a decomposition product during the thermal processing of PMMA.

For assessing the risks of daily inhalation exposure 4.6 mg/m³ (1.1 ml/m³, Vainiotalo et al., highest value) should be used.

Because MMA is released during thermal processes, normally no immediate skin contact occurs. The dermal exposure level caused by touching of MMA contaminated surfaces (indirect exposure) is regarded as being low (expert judgement).

Occupational exposure in the skilled trade sector

Applications of MMA containing formulations occur also in the skilled trade sector. Generally, in this area, it cannot be excluded that the substance is handled in open systems during certain tasks, e.g. metering and filling activities, and that suitable technical measures (LEV) and PPE (here gloves) are not used (Voullaire, Kliemt, 1995).

Use of reactive adhesives in the skilled trade sector

Workers will be subject to inhalation and dermal exposure during open handling of adhesives (e.g. during repair work) which contain MMA up to 60%.

For the use of adhesives in the skilled trade sector, it has to be taken into account that the overall duration of open handling of adhesives is probably much shorter than the shift duration. Measurement results obtained during bonding works in the skilled trade sector are not available, but information provided by the German workers compensation funds reveal, that during bonding small areas in the further processing industry, exposures of 11 mg/m³ (2,6 ml/m³; 50th percentile of a measurement collective regarding bonding of large and small areas without LEV) are observed. Assuming that in the skilled trade sector rather small areas are bonded and that the duration of exposure is generally shorter than shift length, this exposure level should be taken for assessing the risks of inhalation exposure.

The dermal exposure levels may be in the same order of magnitude or even lower than assessed for the use of adhesives in the industrial sector: 0.1 – 1 mg/cm²/day. Assuming that skin contact occurs to preparations containing up to 60% MMA and an exposed area of 210 cm² (fingers) an exposure level of 12.6 – 126 mg/p/day is used.

Use of floor coatings in the skilled trade sector

MMA floor coatings are applied by specialised companies. The coating materials used are sticky and viscous, and generally contain up to 20% MMA. In floor coating work, the workers continually change the location of their activity and it may be assumed that there is in general, no adequate ventilation and that suitable personal protective equipment is not used.

For the risk characterisation of inhalation exposure, an 8-h TWA of 1,045 mg/m³ MMA (251 ml/m³, 95th percentile of a measurement collective) should be used.

As concerns dermal exposure, the EASE model considering a MMA content of 20% in the reactive resins used yields a dermal exposure of 0.2 – 1 mg/cm²/day. Assuming an exposed area of 840 cm² (hands) an exposure level of 168 – 840 mg/p/day should be used for assessing the risks. Exposure is assumed over the shift length but not daily.

Use of paints, lacquers and varnishes in the skilled trade sector

Solvent-based paints contain a maximum of 0.5% MMA. It is assumed that conventional spray works within the skilled trade sector are comparable to those within the further processing industry (see Section 4.1.1.2.3).

For the purpose of assessing the risks as a result of exposure regarding the use of paints and lacquers, 1 mg/m³ (0.23 ml/m³, 50th percentile) is to be considered as the 8-h TWA for daily exposure. It is assumed that paints are often and regularly used. Therefore regular and frequent skin contact is expected when dispersion paints and solvent-based paints are used. This level is in good agreement with exposure levels calculated with the SCIES-model for consumer exposure during painting works (see Section 4.1.1.2.3).

If spray-painting is performed within the skilled trade sector, daily exposure levels are assessed using the EASE model under consideration of a duration of 2 hours to 5.2 – 10.4 mg/m³ (1.25 - 2.5 ml/m³).

It may be assumed that suitable personal protective equipment is not always used during painting and spray-painting work. In using the EASE model and considering a maximum

MMA content of 0.5% a dermal exposure level of 0.005 – 0.025 mg/cm²/day is obtained. Assuming an exposed area of 1,300 cm² (hands and parts of the forearms) an exposure level for MMA of 6.5 – 32.5 mg/p/day should be used for painting, varnishing and spray painting.

Use of casting resins

MMA is applied in casting resins, which are used in dental laboratories, orthopaedic purposes, embedding, lense manufacturing and ornament manufacturing. The resin preparations are often prepared at the use site (Forster, 1987). The concentrations of MMA in the resins are not known for all applications. It is to be assumed that the reactive resins with concentrations up to 80% MMA may be handled.

Medical applications of casting resins

In a study of the exposure of hospital operating personnel during operations where MMA was used in surgery, only in 4 of 27 cases MMA concentrations above the detection limit (1.2 mg/m³, 0.29 ml/m³) were found (Sass-Kortsak et al., 1992, see Section 4.1.1.2.3). For assessing the risk of daily inhalation exposure, 4 mg/m³ (1 ml/m³) should be used. Short-term exposures of 420 mg/m³ (100 ml/m³, 10 min) were observed during hip and knee replacement operations in conventional operating theatres without laminar air flow.

It can be assumed that during medical applications protective gloves are employed for reasons of medical hygiene. In assessing the dermal exposure it has to be born in mind that the producers recommend gloves which provide only limited protection. Therefore the EASE model is applied to calculate dermal exposure levels. Dermal exposure amounts to 0 – 0.1 mg/cm²/day. Considering an amount of 80% MMA and an exposed area of 210 cm² (fingers) dermal exposure is assessed to 0 – 16.8 mg/p/day.

Orthopaedic workshops, dental laboratories and surgeries

Significant differences in the level of exposure are strongly depending on the use of LEV. For assessing the risk during tasks in orthopaedic workshops 187 mg/m³ (45 ml/m³) without LEV should be used and 61 mg/m³ (14.7 ml/m³) with LEV.

In dental laboratories MMA-containing prepolymers are used to construct fillings and inlays. Exposure may occur during dosing, mixing and application. For assessing the risks 6 mg/m³ (1.4 ml/m³, 8-h TWA) and a short-term value of 42 mg/m³ (10 ml/m³, short-term) with LEV as well as 110 mg/m³ (26.4 ml/m³, 8-h TWA) and 600 mg/m³ (140 ml/m³, short-term) under unfavorable conditions without LEV should be used.

As regards dermal exposure in the orthopaedic and dental fields, the EASE model yields a dermal exposure of 0.1 – 1 mg/cm²/day. Assuming that skin contact occurs to preparations containing up to 80% MMA and an exposed area of 420 cm² (palms of two hands) for orthopaedic applications and of 50 cm² (fingertips) for dental application an exposure level of 34 – 336 mg/p/day respectively 4 – 40 mg/p/day is used.

Other uses of casting resins

In the literature exposure levels of <4.2 - 42 mg/m³ (<1 – 10 ml/m³) during the manufacturing of lenses and 83 – 374 mg/m³ (20 – 90 ml/m³) during ornament manufacturing are reported and should be used for the risk assessment (Cromer and Kronoveter, 1976). As regards dermal exposure the EASE model amounts to 0.1 – 1 mg/cm²/day. Since the concentrations of MMA are

not known, dermal exposure is assumed to be similar to that of dental surgeries. Assuming that skin contact occurs to preparations containing up to 0% MMA and an exposed area of 50 cm² (fingertips) for lens manufacturing and of 420 cm² (palms of two hands) for ornament manufacturing, an exposure level of 4 – 40 mg/p/day respectively 34 – 336 mg/p/day should be used.

4.1.1.2.6 Summary of exposure data relevant for the workplace risk assessment

Table 4.6 shows the exposure data of methyl methacrylate which are relevant for occupational risk assessment.

Table 4.6 Summary of exposure data of methyl methacrylate which are relevant for occupational risk assessment

Area of production and use	Form of exposure	Activity	Duration and frequency	Inhalation exposure		Dermal exposure			
				Shift average [mg/m³]	Method	Level of exposure [mg/cm²/day]	Exposed area [cm²]	Shift average [mg/p/day]	Method
Chemical industry									
1. MMA production	vapour (liquid)	production, packaging, drumming maintenance	shift length / daily and short term	18 87 [6)]	90th percentile workpl. measur. short-term (15 min) measur.	0.1- 1	420 (palms of two hands)	42 – 420	EASE [2)]
2. PMMA production	vapour (liquid)	polymerisation , maintenance packaging	4 hours / daily and short term	28 79 [6)]	90th percentile workpl. measur. short-term (5 min) measur.	0.1- 1	420 (palms of two hands)	42 – 420	EASE [2)]
3. Transesterification	vapour (liquid)	production, filling	4 hours / daily and short term	10 33 [6)]	90th percentile workpl. measur. short-term (5 min) measur.	0.1- 1	420 (palms of two hands)	42 – 420	EASE [2)]
4. Cast sheet production	vapour (liquid)	cast filling, waste handling	4 hours / daily and short term	148.5 412 [6)]	90th percentile workpl. measur. short-term (15 min) measur.	0.1- 1	420 (palms of two hands)	42 – 420	EASE [2)]
5. Production of adhesives	vapour (liquid)	production, packaging	4 hours / daily	57	90th percentile workpl. measur.	0.1- 1	420 (palms of two hands)	42 – 420	EASE [2)]
6. Production of reactive resins	vapour (liquid)	mixing, packaging, maintenance	4 hours / daily	119	90th percentile workpl. measur.	0.1- 1	420 (palms of two hands)	42 – 420	EASE [2)]

Table 4.6 continued overleaf

Table 4.6 continued Summary of exposure data of methyl methacrylate which are relevant for occupational risk assessment

Area of production and use	Form of exposure	Activity	Duration and frequency	Inhalation exposure		Dermal exposure			
				Shift average [mg/m³]	Method	Level of exposure [mg/cm²/day]	Exposed area [cm²]	Shift average [mg/p/day]	Method
Industrial area									
7. Production of adhesives, casting resins and floor coating materials		filling, mixing, cleaning	4 hours / daily (assumed)	21 – 105 (with LEV) 210 – 420 (without LEV)	EASE EASE	0.1 – 1	420 (palms of two hands)	42 – 420	EASE
8. Production of paints and varnish	vapour (liquid)	filling sampling mixing	no information / daily	146 (with LEV) 120 (without LEV)	95th percentile workpl. measur.“	0.1 – 1	420 (palms of two hands)	42 – 420	EASE
9. Use of moulding and extrusion compounds	vapour	cooling of formed parts	shift length / daily (assumed)	25.4	95th percentile workpl. measur.	Low	low	low	exp. Judg.[3])
10. Use of adhesives in plastics, electronics and glass industry (60 % MMA)	vapour (liquid)	mixing bonding coating	shift length / daily (assumed)	83 (with LEV) 132 (without LEV)	95th percentile workpl. measur. “	0.06 – 0.6	210 (fingers)	12.6 – 126	EASE
11. Use of paints (residual MMA <0.5%)	aerosol	spray painting painting	shift length / daily (assumed)	4.2 – 8.4 (with LEV) 21 – 42 (without LEV) 1	EASE 50th percentile [4])	0.005 – 0.025	1300 (hands and part of forearms)	6.5 – 32.5	EASE
12. Thermal processing of PMMA	vapour		shift length / daily (assumed)	4.6	literature data	low		low	exp. Judg.[3])

Table 4.6 continued overleaf

Table 4.6 continued Summary of exposure data of methyl methacrylate which are relevant for occupational risk assessment

Area of production and use	Form of exposure	Activity	Duration and frequency	Inhalation exposure		Dermal exposure			
				Shift average [mg/m³]	Method	Level of exposure [mg/cm²/day]	Exposed area [cm²]	Shift average [mg/p/day]	Method
Skilled trade area									
13. Use of adhesives (bonding small areas) (60 % MMA)	vapour (liquid)	mixing, coating, bonding	shorter than shift length, not daily (assumed)	11	50 % percentile [5]) workpl. measur.	0.06 – 0.6	210 (fingers)	12.6 – 126	EASE
14. Floor coating (20 % MMA)	vapour (liquid)	Priming, transfer, mixing, covering, sealing	shift length / not daily	1,045	95 % percentile workpl. measur.	0.2 – 1	840 (hands)	168 – 840	EASE
15. Use of paints (residual MMA < 0.5 %) Spray-painting	vapour (liquid) aerosol	mixing, filling, painting spraying	< shift length / daily (assumed) 2 hours, not daily (assumed)	1 5.2 – 10.4	analogy to use of paints in industrial area EASE	0.005 – 0.025	1300 (hands and parts of forearms	6.5 – 32.5	EASE
Use of casting resins									
16. Medical applications	vapour (liquid)	filling, mixing, applicating	about 2 h / daily (assumed) and short term	4 420 [6])	literature data short-term,(10 min) measur.	0 – 0.08	210 (fingers)	0 – 16.8	EASE
17. Orthopaedic workshops	vapour (liquid)	filling, mixing, applicating	shift length / daily	61 (with LEV) 187 (without LEV)	expert judg. [1]) expert judg. [1])	0.08 – 0.8	420 (palms of two hands)	34 – 336	EASE

Table 4.6 continued overleaf

Table 4.6 continued Summary of exposure data of methyl methacrylate which are relevant for occupational risk assessment

Area of production and use	Form of exposure	Activity	Duration and frequency	Inhalation exposure		Dermal exposure			
				Shift average [mg/m³]	Method	Level of exposure [mg/cm²/day]	Exposed area [cm²]	Shift average [mg/p/day]	Method
Use of casting resins									
18. Dental laboratories and surgeries	vapour (liquid)	filling mixing applicating	about 2 h / daily	6 (with LEV)	expert judg. [1])	0.08 – 0.8	50 (fingertips)	4 – 40	EASE
			short term	42 (with LEV)	short-term (10 min) measurement				
			about 2 h / daily	110 (without LEV)	expert judg. [1])				
			short term	600 (without LEV)	short-term (10 min) measurement				
19. Manufacturing of lenses	vapour (liquid)	filling mixing applicating	no information / not daily	4.2 – 42	literature data	0.08 – 0.8	50 (fingertips)	4 – 40	exp. judg. analogous to dental
20. Ornamental decoration	vapour (liquid)	filling mixing applicating	no information / not daily	83 – 374	literature data	0.08 – 0.81	420 (palms of two hands)	34 – 336	exp. judg. analogous to ortho-paedic

[1]) expert judgement of a reasonable worst case from the given /measured data
[2]) worst case, immediate skin contact because of unsuitable glove material
[3]) release of MMA as a thermal decomposition product, secondary contact with contaminated surfaces (<1 mg/m³)
[4]) measurement collective comprises uses of paints (<0.5% MMA) and works with formulations containing higher amounts of MMA
[5]) measurement collective comprises bonding large and small areas, for skilled trade sector bonding small areas is assumed
[6]) short-term concentration, no shift average value

4.1.1.3 Consumer exposure

Inhalation exposure

The EPA computer model SCIES was used to estimate the inhalation exposure of consumers to methyl methacrylate from the use of dispersion paints and 2-component adhesives. The content of methyl methacrylate 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

All scenarios for inhalation exposure of consumers using dispersion paints are based on a 15% polymeric methyl methacrylate concentration in formulations and an absorption rate of 100%. The producer assumes a residual monomer content of polymeric MMA used in dispersion paints of less than 0.02%.

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 0.5 room air exchanges/h; user inhalation rate 1.3 m^3/h), the resulting MMA (monomer) exposure of the consumer by the inhalation route was calculated to be 4.8 µg/kg bw/d as yearly average dose rate (lower microgram/kg bw and day range). During application of the dispersion paint the consumer may be exposed by the inhalatory route to a maximum (peak) concentration per event of 2.8 mg/m^3. This calculation is based on a weight fraction of 0.00003 as due to producer information.

2-Component adhesives

Methyl methacrylate is used as a component in 2-component adhesives. For the calculation of inhalation consumer exposure to methyl methacrylate using the SCIES model the following conditions for an appropriate use were applied.

Assuming the appropriate use (frequency of use 4 events/year; mass of product 1.0 gram; room size 40 m^3; duration of use 1 h; house air exchange rate 0.2 room air exchanges/h; user inhalation rate 1.3 m^3/h), inhalation consumer exposure calculation results in an average dose rate of 2.4 µg/kg bw/d (lower microgram/kg bw/d range). Peak concentrations of up to 6.8 mg/m^3 (per event) have been estimated by this modelling.

Taking into consideration that most of the monomeric MMA will polymerise immediately during use, the concentration of residual monomers of MMA available for inhalation is much lower. Thus, the concentration that can lead to an acute exposure is essentially lower than the calculated average value of 5.3 mg/m^3. Thus, the calculation represents an overestimation. Moreover, taking into account the short-term exposure by use of 2-component adhesives the acute exposure by inhalation to MMA can therefore be neglected.

Dermal exposure

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

Table 4.7 Estimation of dermal exposure using dispersion paints (worst case)

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 MMA in paints	15	%
Amount of MMA in contact with skin	0.400	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 1,360 cm² which is rather similar to the area of both forearms. Taking this amount of paint, the exposure to MMA will result in an amount of 0.400 mg. Direct dermal exposure due to uncontrolled splash of paint to skin in relation to bodyweight is then ~5.8 µg/kg per event.

Dermal exposure by contact of air with skin can be calculated taking the estimated air concentration of 1 mg/m³. If the hypothetical area of contact is the total body surface and the thickness of layer 0.01 cm, the volume in contact with skin is 194 cm³ resulting in a value of 0.194 µg of MMA, which is negligible.

Oral exposure

Plastic products

Methyl methacrylate is used as a component in plastic products, e.g. lenses, glasses, plastics coming into contact with foodstuffs.

In the EU methyl methacrylate is listed in the positive list for monomers used for plastics and coatings coming into contact with foodstuffs without any restrictions concerning the migration limits (90/128/EEC and amendments). The scientific committee for foodstuffs recommended a group tolerable daily intake for methacrylates of 0.1 mg/kg based on a 2-year oral study in rats and several other studies with methyl methacrylate. Inoue et al. (1981) measured the migration of unpolymerized methyl methacrylate from polymethyl methacrylate based articles containing 0.03-1% residual methyl methacrylate into food simulants. Migration to water and acetic acid was not detected (detection limit 0.05 ppm). Migration of methyl methacrylate into 20% ethanol (solvent extraction) was 1 ppm after 1 day and 10 ppm after 90 days.

Based on the low migration rate, consumer methyl methacrylate exposure by skin contact with polymethyl methacrylate or oral intake from use of polymethyl methacrylate articles is regarded to be negligible.

Conclusion

Polymers manufactured with methyl methacrylate are used in consumer products for private use. The sum of all types of exposure is expected to be in the range of 1 – 10 µg/kg bw/d (lower microgram/kg body weight and day range when the products are used as intended.

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 through food, drinking water and air is estimated for a local and a regional approach. For the local approach the annual average of the concentration estimated on the basis of the generic scenario for wet polymerisation was chosen, since this processing type revealed the highest exposure rates. This is compared to an average intake due to exposure via the regional background concentration (see appendix A17 for calculations).

The following input data were selected:

Annual average local PEC in surface water:	1.48 mg l^{-1}
Annual average local PEC in air:	0.381 mg m^{-3}
Local PEC in grassland:	0.058 mg kg^{-1}
Local PEC in porewater of agricultural soil:	0.041 mg l^{-1}
Local PEC in porewater of grassland:	0.058 mg l^{-1}
Local PEC in groundwater under agricultural soil:	0.041 mgl^{-1}
Regional PEC in surface water:	$1.44 \cdot 10^{-4}$ mg l^{-1}
Regional PEC in air:	$5.49 \cdot 10^{-5}$ mg m^{-3}
Regional PEC in agricultural soil:	$1.03 \cdot 10^{-5}$ mg kg^{-1}
Regional PEC in porewater of agricultural soil:	$1.03 \cdot 10^{-5}$ mg l^{-1}

The resulting total daily doses are:

$$\mathbf{DOSE_{tot,local} = 0.132\ mg \cdot kg_{bw}^{-1} \cdot d^{-1}}$$

$$\mathbf{DOSE_{tot,regional} = 1.7 \cdot 10^{-5}\ mg \cdot kg_{bw}^{-1} \cdot d^{-1}}$$

The calculated doses comprise the following routes:

Table 4.8 Calculated doses routes

Route	Regional model, percentage of total dose	Point source model; percentage of total dose
Drinking water	25	32
Fish	4	5
Stem	0.6	0.6
Root	0.4	0.2
Meat	0	0
Milk	0	0
Air	70	62

The main route of exposure is the air.

Because the input concentration for the local scenario is based on a default calculation the total daily dose resulting from the local model may be overestimated.

4.1.1.5 Combined exposure

A person who is exposed indirectly to methyl methacrylate through the environment may also be exposed through different applications via residual methyl methacrylate monomers from polymethyl methacrylate containing products. Taking into account the sum of all types of consumer exposure (1-10 µg/kg bw/d) and the indirect exposure via the environment (local scenario, 0.128 mg/kg bw/d) a combined exposure of about 0.14 mg/kg bw/d will be expected. Considering the regional exposure ($2.2 \cdot 10^{-5}$ mg/kg bw/d) a combined exposure in the range of 1 - 10 µg/kg bw/d can be estimated.

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

4.1.2.1 Toxico-kinetics, metabolism and distribution

Toxicokinetics

Studies in animals

After oral or i.v. administration of ^{14}C-labeled methyl methacrylate (oral: 5.7 or 120 mg/kg bw; i.v.: 5.7 or 6.8 mg/kg bw) in rats, 76 – 88% of the radioactivity is found in expired air within 10 days, 4.7 – 7.2% is in urine, 1.7 – 3.0% in faeces and the remainder being retained in liver and fat tissues (Bratt and Hathway, 1977; ICI, 1977a).

Rapid changes of rat blood serum methacrylic acid concentration were observed after administration of a single dose of methyl methacrylate by the stomach tube (approximately 8 mmol/kg bw, equivalent 800 mg/kg bw) (Bereznowsky, 1995). The maximum concentration (0.8 mM) was reached between 10 and 15 min after methyl methacrylate administration and decreased over the next 50 min.

After inhalatory exposure with 100 ppm methyl methacrylate to rats for 1, 2, 3, and 4 hours, concentrations of methyl methacrylate were found to be about 11 mg/100 ml in blood, about 21 µg/g in lungs and about 25 µg/g in brain (independent of the exposure time) (Raje et al., 1985) at the end of exposure.

After i.v. administration to seven dogs at a total dose of 0.05 ml/kg over a 4-min period pulmonary excretion of methyl methacrylate accounted only for a maximum of 3% of the administered dose. Methyl methacrylate levels in the expired air were maximal within 2-4 min of the start of the infusion and became negligible after 7 min. After 9 min no methyl methacrylate could be detected in the blood (Derks et al., 1977).

Tissue distribution of radioactivity after i.v. administration of labeled methyl methacrylate to three rats was studied by whole body autoradiography. Irrespective of the time of sacrifice the greatest concentrations were determined in blood, heart, lungs, liver, kidneys and salivary glands. Some of the radioactivity was located in the seminal vesicles. It was not possible to determine whether the radioactivity in any of the tissues was due to the presence of methyl methacrylate or its metabolites (ICI, 1983).

After infusion of the substance (33 mg MMA/kg·min for 3 min) the substance disappeared very rapidly from the blood of the experimental animals (rabbit and dog). The half-life was less than 30 s in rabbit and 41 s in dog (Paulet et al., 1979).

After i.p. administration of ^{14}C-methyl methacrylate to rats within 24 hours 80% of the radiolabel was exhaled as $^{14}CO_2$, 7-14% was excreted in the urine and approximately 3% was retained in tissues at this time (Crout et al., 1982).

Clearance of methyl ^{14}C-methacrylate from blood was determined in beagle dogs after simulated hip arthroplasty and after subsequent i.v. administration of 25, 50 or 75 mg/kg bw. Following hip arthroplasty, venous blood concentrations reached a maximum after 3 min and decreased over the next 16 min. Only 0.5% of the total amount of implanted monomer was detected in the venous circulation and no radioactivity could be detected in the arterial blood. After i.v. administration of 25 or 50 mg/kg bw maximum arterial levels were found at 30 s, but were below the limit of detection after 3 min (McLaughlin et al., 1973).

Studies in humans

Five min after the insertion of the bone cement into the femoral cavity both methyl methacrylate and its metabolite methacrylic acid (MAA) were detected in significant quantities, concentrations of MAA tending to lag behind those of methyl methacrylate. The authors therefore conclude that the initial step of methyl methacrylate metabolism *in vivo* is hydrolysis to MAA catalysed by nonspecific serum esterases (Crout et al., 1979).

The amount of exhaled methyl methacrylate was dependent on the surgical technique (Eggert et al., 1980).

Arterial blood levels were lower than venous blood levels. Maximum venous methyl methacrylate blood levels in nine patients 2 to 10 min after tourniquet release during knee arthroplasty ranged between 0.1 and 1.44 µg/ml. The half-life of methyl methacrylate in blood was reported to be 47 – 55 min (Svartling et al., 1986).

Concentrations of methyl methacrylate in blood of patients with a hip arthroplasty, receiving about 48 g of a half-cured methacrylate bone cement, varied widely. Maximum blood levels were obtained between 30 and 60 s after implantation with mean concentration of 0.8 – 1.2 µg/ml. In samples taken after 3 and 6 min, methyl methacrylate could not be detected (Gentil et al., 1991). From these data, an initial half-life of 0.3 min and a terminal half-life of 3 min (Gentil et al., 1991) were calculated which is in contrast to the data reported earlier (Svartling et al., 1986).

Metabolism

After oral administration (gavage; 5.7 or 120 mg/kg bw) of radiolabeled methyl methacrylate to Wistar rats, 65% of the dose was exhaled as CO_2 within 2 hr, 76-88% within 10 days. Pulmonary excretion of unchanged methyl methacrylate accounted for less than 1.4% of the dose. Metabolites excreted with urine (4.7-6.0%) were methacrylic acid (0.8% of the dose), methyl malonic acid (1.4%), succinic acid (0.2%), 2 minor metabolites co-eluating with β-hydroxyisobutyric acid and methylmalonic semialdehyde. The authors conclude that methyl methacrylate is metabolised via physiological pathways and enters into the citric acid cycle via methylmalonyl-CoA and succinyl-CoA, which is a part of the valine pathway. After a single i.v. administration to rats of ^{14}C-labeled methyl methacrylate (5.7 or 6.8 mg/kg bw) the metabolism and excretion of methyl methacrylate were qualitatively the same as after oral administration (Bratt and Hathway, 1977; ICI, 1977a).

These studies were corroborated by Crout et al. (1982), who found similar distribution patterns after i.p. administration of ^{14}C-labeled methyl methacrylate to rats.

Delbressine et al. (1981) studied the formation of thioether conjugates after i.p. administration of methyl methacrylate to rats with and without pretreatment with tri-o-tolyl phosphate (TOTP), an inhibitor of tissue esterases. After a single dose of 0.14 mmol/kg bw thioether excretion did not differ significantly from that of controls. After pretreatment with TOTP (0.34 mmol/kg bw), 11% of the administered dose was excreted in urine as thioether within 24 h.

These results are corroborated by studies of Elovaara et al. (1983). Following i.p. administration of 1,000 mg methyl methacrylate/kg bw on 3 consecutive days to rats no significant effects were seen on liver and kidney GSH levels 1, 5 or 12 days after the last injection. After i.p. administration of a single dose of 2,000 mg/kg bw, a decrease in GSH levels was reported 3 hours after administration (20% of control in liver and 48% of control in kidney). At both levels no changes in total cytochrome P-450 levels or viability of liver cells were observed.

Deposition of methyl methacrylate vapors in the surgically isolated upper respiratory tract (URT) of urethane anaesthetised rats was studied after inhalation of 90, 437, 2,262 mg methyl methacrylate/m³. Two inspiratory flow conditions were used: constant velocity unindirectional flow or cyclic flow. Uptake of methyl methacrylate by the URT was determined in rats without pretreatment and with bis-nitrophenylphosphate (BNPP, a carboxylesterase inhibitor) pretreatment to determine the influence of metabolic ester hydrolysis by the nasal carboxylesterases. URT deposition efficiencies of the rats without pretreatment averaged 10-20% under both flow conditions. Deposition of methyl methacrylate was less efficient at the high than at the low and mid exposure concentrations. BNPP-pretreatment significantly reduced URT methyl methacrylate deposition by 2-8% under both flow regimens (Morris, 1992).

Andersen et al. (1998) developed a steady-state PBPK model with the aim to predict the local nasal tissue concentrations of inhaled methyl methacrylate as a function of pulmonary ventilation rate taking into consideration the anatomical specificities of the rat nose cavity, air to liquid phase permeation coefficients, the portion of total cardial output perfusing the upper respiratory tract and the metabolism of methyl methacrylate in the rat nose. This model assumes three regions in air flow paths through the rat nose cavity. In the model, nose tissue is constructed to contain a mucus layer at the surface, an epithelial tissue compartment, and a blood exchange region. Metabolism is assumed to occur in the epithelial tissue compartment and in the blood exchange region as well. The authors used equations describing the mass transport processes for uptake and metabolism in the rat nose, which have been developed by Kimbell (1993) using formaldehyde. Computational solutions show that the tissue dose for methyl methacrylate is related to flow, diffusion coefficients, metabolic parameters and blood flow, respectively (Andersen and Sarapagani, 1998). Nasal metabolism of methyl methacrylate was parameterized with data derived from *in vitro* esterase activity in nasal homogenates of both species rat and man and from *in vitro* esterase activity in human liver tissue (as surrogate for nasal tissue activity) (Green, 1996). Methyl methacrylate demonstrates non-linear extraction in the rat nose, which might be explained by capacity limited metabolism. The extraction at low concentration (approximately 1 ppm) is about 20%, the extraction at high concentrations (approximately 600 ppm) falls to about 10%. This is in agreement with measured data from Morris (1992) and Morris and Frederick (1995).

The rat model was applied to the situation in man assuming differences in the nasal tissue metabolism of methyl methacrylate in rats and humans and taking into consideration species differences in ventilation rates (ventilation rates for a rat at rest 197 ml/min, for a human at light exercise 13,800 ml/min). Based on the model of the human nose it seems that the metabolic clearance is limiting for deposition and that airflow has little impact (Andersen et al., 1998). The interspecies-extrapolation rat-human is based on *in vitro* data for tissue homogenates as

described above (Green, 1996). Bogdanffy and al. (1998) provided evidence that measured by histochemical means esterase was differently distributed within the different layers of the olfactory tissue and that the distribution pattern was different between rat and man. Model calculations of methyl methacrylate metabolites in the tissue ("tissue dose") of both species were used to estimate the dosimetric adjustment factor (DAF). The estimated DAFs were concentration-dependent, varying between 2.4 and 4.76 for a concentration range from 1 to 400 ppm MMA (Andersen et al., 1998).

In vitro studies

Following addition of methyl methacrylate to human blood (0.184 µl/ml), concentrations in blood cells were twice as high as plasma concentrations. Disappearance from plasma was very rapid, while the rate constant in the cells was about 10 times lower. The half-life of methyl methacrylate in whole blood was determined to be 3 h at 20°C (Rijke et al., 1977). In another study, distribution of methyl methacrylate between plasma and erythrocytes in human blood was calculated to be 1:1.4 (Eggert et al., 1974).

Blood samples from ten individuals were incubated with 10 µg labeled methyl methacrylate/ml at 37°C for 90 min. Disappearance of methyl methacrylate from human blood followed pseudo first-order kinetics. Half-lifes varied from 18 to 40 min (Corkill et al., 1976).

The second order rate constants for the spontaneous reaction of methyl methacrylate with GSH *in vitro* was determined to be 0.325 l/mol min. The ester concentration required to deplete 20% of rat red blood cell GSH (EC 20) was 2.5 mM for methyl methacrylate and was higher than that of methylacrylate (0.063 mM) (McCarthy and Witz, 1991).

Following the addition of 0, 2, 5 and 10 mM methyl methacrylate to isolated rat hepatocyte preparations and incubation for 2 h at 37°C, a concentration- and time-dependent depletion of reduced glutathione (GSH) in the cells was observed (Elovaara et al., 1983).

A skin absorption study has been conducted with methyl methacrylate using heat separated human epidermis and a static diffusion cell model. The obtained data indicate that methyl methacrylate can be absorbed through human skin, absorption being enhanced under occluded conditions. Under unoccluded conditions only a small amount of the applied dose (0.56%) penetrated the skin suggesting that evaporation from the surface of the skin is a significant factor when assessing the amount of methyl methacrylate that could be absorbed in any given human exposure scenario (CEFIC, 1993).

It has been demonstrated that olfactory epithelium has the highest carboxylesterase activity of all tissues in the upper respiratory tract in rats and humans (Bogdanffy and Frame, 1995; Green, 1996). The findings of Green concerning the relative activity of the carboxylesterase activity in rat and man communicated in the same paper (Green, 1996) have to be interpreted with caution because of experimental limitations. The determinations show wide variation which in conjunction with limited number of data results in wide confidence intervals for the estimates. The experimental conditions do not assure that the data are true estimates of Vmax.

Thus, in conclusion it cannot be accepted to infer a higher NOAEL/LOAEL in man compared to rat because the assumption of the different carboxylesterase activity is confounded by experimental pitfalls and by the anatomical differences between the two species at the site of adverse action which were not appropriately taken into account.

Conclusions

After oral or inhalatory administration, methyl methacrylate is rapidly absorbed and distributed. *In vitro* skin absorption studies in human skin indicate that methyl methacrylate can be absorbed through human skin, absorption being enhanced under occluded conditions. However, only a very small amount of the applied dose (0.56%) penetrated the skin under unoccluded conditions. After inhalation exposure to rats 10 to 20% of the substance is deposited in the upper respiratory tract where it is metabolised. Activities of local tissue esterases of the nasal epithelial cells may be lower in man than in rodents.

Toxicokinetics seem to be similar in man and experimental animal. After arthroplasty using methyl methacrylate-based cements, exhalation of unchanged ester occurs to a greater extent than after i.v., i.p. or oral administration. After oral or parenteral administration methyl methacrylate is further metabolised by physiological pathways with the majority of the administered dose being exhaled as CO_2. Conjugation with GSH or NPSH plays a minor role in methyl methacrylate metabolism and only occurs at high tissue concentrations.

Concerning the PBPK model it can be stated that the experimental work used within the model is well performed. The rat nose model may give simulation data which are in conformity with the limited experimental data on concentration-dependent tissue extraction. However, as the authors stated, further esterase distribution studies in the nasal tissue are necessary. Furthermore interspecies extrapolation does not seem to be sufficiently supported by the available data in humans as no measurements were done on the extraction. Hence, the conclusions the authors draw from their model concerning safe levels of exposure still remain speculative and need further experimental support.

4.1.2.2 Acute toxicity

Studies in animals

Oral

Oral LD50 values for methyl methacrylate have been reported in the range of 8.0 to 10.0 ml/kg (7,552-9,440 mg/kg) in rats and about 5,000 mg/kg body weight in mice and rabbits. A dose of 5.0 ml/kg (4,720 mg/kg) killed ½ dogs. (Spealman et al., 1945; Deichman, 1941; Lawrence et al., 1974; Schwach and Hofer, 1978). The main clinical signs of methyl methacrylate toxicity are increased rate of respiration in about 2-5 minutes, followed by motor weakness and decreased respiration in 15-40 minutes, discoloration and piloerection. At necropsy degenerative changes in the tubules of the kidney were observed in dogs (Spealman et al., 1945). None of the tests were conducted according to OECD Guideline 401 but nevertheless an assessment was possible.

Inhalation

The inhalation LC_{50} value for methyl methacrylate in the rat has been reported to be about 29.8 mg/l for a 4-hour exposure (Tansy et al., 1980). Acute inhalation toxicity for mice is described by LC_{50} values of >25 mg/l/4 hours (Spealman et al., 1945; Lawrence et al., 1974). The main clinical signs were depression, ataxia, excessive salivation (Spealman et al., 1945).

Local and systemic effects of single inhalation exposures of rats to methyl methacrylate were reported in two other studies. Interalveolar congestion/hemorrhage, pulmonary vasodilatation and oedema were observed with rats exposed to 100 ppm (~0.410 mg/l) for 2, 3 and 4 hours, but

not for 1 hour. No histopathologic changes were seen in the brain of any of the exposed rats (Raje et al., 1985). In the other study it was demonstrated that only the lateral hypothalamic and ventral hippocampal nuclei showed any significant alterations in multi-unit neuronal activity during one-hour inhalation exposure of rats to 400 ppm (~1.64 mg/l) vapour in room air. The alteration in neuronal activity was marked by slowing of the neuronal firing rate, which turned towards the pre-exposure level when the animal returned to room air. It was concluded that the cerebellum was reflecting the decreased motor activity associated with the anesthetic and not the vapour (Innes, 1988). None of the tests were conducted according to OECD Guideline 403 but nevertheless an assessment was possible.

Dermal

The LD50 value of methyl methacrylate in rabbits by dermal route, using an occlusive dressing, has been reported as being greater than 5,000 mg/kg body weight (Spealman et al., 1945; Lawrence et al., 1974; Rohm and Haas, 1982). Clinical signs at 40 ml/kg (37,760 mg/kg): irritation and temporary central nervous system depression (Spealman et al., 1945). None of the tests were conducted according to OECD Guideline 402 but nevertheless an assessment was possible.

Studies in humans

A fall in blood pressure was noted in the first 3 min following the application of the bone cement and an increase in pulmonary artery pressure was noted during the first 10 min. There was no correlation between the concentration of methyl methacrylate and either of the reported effects (Wenda et al., 1988).

Conclusion

Acute toxicity of methyl methacrylate by the oral, dermal, and inhalation routes is low as judged by several reported tests with different species: The oral LD_{50} for rats, mice, and rabbits is found to exceed 5,000 mg/kg body weight. Acute inhalation toxicity for rats and mice is described by LC_{50} values of >25 mg/l/4 hours. Acute dermal toxicity is reported for rabbits to exceed 5,000 mg/kg.

4.1.2.3 Irritation

Studies in animals

Skin

After a 4-hour exposure with 0.5 ml test substance (purity: 99.8%) a range finding study with two rabbits resulted in erythema scores between 2 and 2.5 within 72 hours. After 7 days the erythema score was 2. Oedema scores ranged from 1.5 to 1 within 72 hours and were 0.5 after 7 days. In addition, blanching, eschar formation and desiccation was observed (Rohm and Haas, 1982).

Groups of 2 male rabbits were treated dermally with MMA at doses of 0.2, 2 or 5 g/kg bw under occluded conditions for 24 hours. Well-defined to severe erythema with blanching and moderate to severe oedema with pocketing were observed at 24 hours. The skin irritation was still present at day 14 in the animals treated at 2 or 5 g MMA/kg bw but was not present after day 3 in the animals treated at 0.2 g/kg bw. Eschar was observed at day 2 in animals treated at the 2 or 5 mg/kg bw dose levels and some eschar was observed to be sloughing off with new hair growth on the underlying

skin at day 12 in animals dosed at 2 or 5 g/kg bw. Desiccation was also observed after day 4 in animals treated at all 3 dose levels (Rohm and Haas, 1982).

Eye

Eye irritation was investigated in two studies. A dose of 0.1 ml to 2 rabbits (Rohm and Haas, 1982) or 6 rabbits (Röhm, 1978) of undiluted methyl methacrylate showed in all rabbits no effects on iris and cornea. Grade 2 conjuctival redness was observed only at 24 hours (Rohm and Haas, 1982) or no effects were detected (Röhm, 1978).

Respiratory system

Raje et al. (1985) tested the local and systemic effects following inhalation of 100 ppm (~0.410 mg/l) of methyl methacrylate by rats using different exposure periods. The changes observed were interalveolar congestion/hemorrhage, pulmonary vasodilatation and edema, observed after an exposure time of 2 hours or 4 hours, but not after an exposure of 1 hour. The authors conclude that this indicates that MMA has a direct irritant action on pulmonary capillaries as well as on alveolar capillaries. This interpretation of the findings seems plausible.

Studies in humans

Methyl methacrylate is clearly irritating to human skin. Nyquist et al. (1958) reported erythema and eczematous dermatitis in 18/20 human volunteers to methyl methacrylate (5% in paraffin or olive oil). No skin reactions were reported in a 48-hour patch test on the same individuals with heat-cured acrylic resin containing 5-6% residual monomer (Nyquist et al., 1958).

Spealman et al. (1945) reported mild erythema, limited to the area of application, in approximately one third of 50 volunteers after a 48-hour exposure (forearm) with saturated MMA cotton pellets (Spealman et al., 1945).

Karpov (1954, 1955) reported irritation of the respiratory tract, weakness, fever, dizziness, nausea, headache, and sleepiness after 20-90 minutes inhalation of MMA vapors at concentrations between 48-480 ppm (~0.197-1.968 mg/l). A threshold limit for changes in the electrical activity of the brain (EEC changes after light impulse during exposure of 5 individuals to 0.02 or 0.04 ppm MMA for 5 minutes) was reported to be 0.04 ppm.

In denture laboratories in Manitoba (Canada) concentrations of MMA from 4.09 to 30.64 mg/m³ were measured in the breathing zone of workers (n=8) (Korczynski, 1998). In 16 cases, concentrations in ambient air were found that ranged from 3.68 to 38.41 mg/m³. These data show quick exchange of MMA concentrations in the air directly surrounding workers and other parts of the room. Persons manufacturing MMA over 20-30 minutes complain about irritations at skin and mucous membranes as well as at the eyes.

Conclusion

Skin and respiratory irritation are reported for subjects exposed to monomer methyl methacrylate: Nyquist et al. (1958) reported erythema and eczematous dermatitis in 18/20 human volunteers exposed to a 5% solution of methyl methacrylate in paraffin or in olive oil. Karpov (1954, 1955) reported irritation of the respiratory tract, weakness, fever, dizziness, nausea, headache, and sleepiness after 20-90 minutes inhalation of MMA vapors at concentrations between 48-480 ppm (approx. 0.197-1.968 mg/l).

Pure methyl methacrylate has been shown to produce severe skin irritation when tested undiluted on rabbits skin using a 4-hour and up to a-24 hour exposure period. There are indications from studies in animals that methyl methacrylate can be irritating to the respiratory system.

In contact with eyes methyl methacrylate has shown to produce only weak irritation of the conjunctivae not to be labelled according to EU regulations. The available data indicate that methyl methacrylate is not corrosive to skin or eyes. Based on the data presented above methyl methacrylate is classified as irritating to respiratory system and to the skin (R 37/38).

4.1.2.4 Corrosivity

Animal data

Methyl methacrylate is not corrosive in animals.

Human data

Methyl methacrylate is not corrosive in humans.

4.1.2.5 Sensitisation

4.1.2.5.1 Studies in animals

A number of skin skin sensitisation studies in guinea pigs are reported in the literature.

In a Guinea Pig Maximization Test, using an intradermal induction concentration of 5% methyl methacrylate, topical induction with 100% and challenge with 1% and 5%, showed a 10% and a 50% positive sensitisation rate respectively (Cavelier et al., 1981). Results from other Magnusson Kligman tests showed positive reactions between concentrations of 50-100%, but also not sensitising effects**.** The reported negative results are mainly due to lower MMA concentration used. Non adjuvant tests gave negative responses. A summary of all available 36 test results is published by ECETOC (1995).

4.1.2.5.2 Studies in humans

a) Skin sensitisation

Methyl methacrylate is a widely used substance to which many people have had repeated inhalation and dermal exposure. Numerous case reports of skin sensitisation in certain occupational environments, where frequent and prolonged unprotected skin contact with monomer containing preparations was common practice exist. Single cases were also reported in some medical and cosmetic applications.

Repeated exposure to undiluted MMA may lead to skin sensitisation in susceptible persons. The incidence of sensitisation seems to vary widely and reactions to impurities, stabilizers, etc. should also be taken into consideration.

Volunteer studies

When 20 female volunteers without reported previous contact to MMA were patch tested with 5% MMA in liquid paraffin or olive oil (purity, stabilizer content not indicated), 18 responded with skin reactions varying from erythema to delayed eczematous dermatitis. A distinct differentiation between sensitisation and irritation reactions was not made by the author. In a follow-up patch test of the same subjects with small plates of heat-cured acrylic resin containing 5.2% to 6.4% of residual MMA monomer no skin reactions were observed (Nyquist, 1958).

A 48-hour occlusive patch test with undiluted MMA, containing 1% hydroquinone, was conducted with 30 volunteers. After 2 days, one case of erythema was observed, at day 10 no skin reaction were observed in the 27 volunteers who returned. At day 19, 20 of the volunteers were challenged using the same procedure at a different part of the back. In 2 cases, a positive skin reaction (irritation) was seen after 48 hours. A third case of a positive reaction was observed 10 days after the second application. In this case, lymphocyte infiltration of the skin area was observed. Two of the volunteers with skin reactions were subsequently tested with hydroquinone 1% in petrolatum, and did not show any reaction. Forty-five volunteers were patch tested with 20% MMA in olive oil (stabilizer content 1%) for 48 to 72 hours (Finn Chamber). No skin reactions were observed after 2, 10, 20 and 30 days. A challenge application after 30 days did not reveal any skin reactions 2 days later (Cavelier et al., 1981).

Following exposure of 50 medical students to pellets of cotton saturated with MMA (purity, stabilizer content not indicated) sealed with elastic bandages for 48 hours on one forearm, 21 individuals showed a mild skin irritation after removal of the patches. After 10 days the same individuals were exposed in a similar way on the other forearm. No skin reactions were seen immediately after removal of the patches at 48 hours, but a few hours to 4 days later, skin erythema occurred in 10 of the individuals (Spealman et al., 1945).

Occupational studies

Orthopedic surgeons

Fisher (1978) reported 2 cases of contact dermatitis of surgeons using bone cements. Paraesthesia of finger tips in the form of burning sensation, tingling and slight numbness persisting for several weeks after dermatitis had subsided were observed. The nature of the effects is not certain. Neither the exposure period nor the composition of bone cement mixture was indicated.

Fries et al. (1975) reported a case of a surgeon with a contact dermatitis to acrylic bone cement. Positive patch test results were obtained only with MMA (purity, stabilizer content not reported). The authors reported another 13 cases of dermatitis in handlers of bone cement, 7 of them giving positive patch test results with MMA (10% in olive oil; purity and stabilizer content not reported).

Darre et al. (1983) reported one case of contact dermatitis to bone cement in an orthopedic nurse, with a positive patch test result to MMA (5%) (purity and stabilizer content not indicated). Contact was prevented by using butyl rubber gloves. These results are also reported by Vedel et al. (1983).

Kassis et al. (1984) reported 2 cases of contact dermatitis to bone cements in orthopedic nurses, 1 case had already been reported by Darre et al. (1983, see above). The reaction to other ingredients of the bone cement preparation was not tested in this case. The authors admit that the monomer used for the patch testing was of unknown purity. The second patient did not react to MMA or initiators and stabilizers in a patch test on the back. However, an occluded application

of undiluted monomer (stabilizer, purity not indicated) to the fingers, where the patient experienced the reactions, led to a weak positive reaction after 24 hours.

One case of a surgeon experiencing contact dermatitis to acrylic bone cements was reported by Pegum and Medhurst (1971). Positive patch test results were obtained with undiluted monomer and the initiator benzoyl peroxide (10% in petroleum jelly). Patch tests with the stabilizers, dimethyl-*p*-toluidine (2% in petroleum jelly) and ascorbic acid (2% in water) gave negative results.

Dentists and dental technicians

Of 106 dental technicians responding to a questionnaire designed to investigate the incidence of hand dermatitis in dental technicians, 19% reported irritant reactions of the hand, the incidence of atopic dermatitis was 15%. Half of the cases with hand dermatitis related the problem to handling acrylic monomer liquids without using protective gloves. The skin problems were considered to be mild. Four technicians reported allergic contact hand eczema due to MMA. Seven patients with eczema of the irritant type participated in a clinical investigation. None of them showed a positive patch test reaction to acrylic monomers. The authors concluded that the frequency of contact allergy to MMA among dental technicians handling monomers is relatively low, presumably below 10%. Other ingredients of the acrylic preparations may contribute to the observed skin reactions and the problems may be resolved by using adequate hand protection (Estlander et al., 1984).

A group of 293 dental technicians, technical assistants and students handling preparations containing acrylic monomers, including MMA were surveyed in a questionnaire study. Eighty-one percent were handling acrylic monomers daily without skin protection. Current hand dermatitis or previous local dermatological problems were reported by 17%. Other finger symptoms, numbness, whitening, feeling of coldness and pain were reported by 25%. Frequency of symptoms increased with the frequency of handling acrylic monomers and the duration of occupation. Only 2% reported a previously diagnosed allergy against acrylates. Persons with current dermatitis reported atopic skin disease during childhood or allergic rhinitis and conjunctivitis more often than the others. The role of MMA with respect to the skin reactions remains unclear (Rajaniemi and Tola, 1985).

One hundred and seventy-five dental technicians or students, with and without previous experience of handling MMA containing dental materials, were patch tested with MMA (2%). No positive reactions were observed (Marx et al., 1982).

Four cases of occupational hand contact dermatitis caused by working with dental prostheses observed between 1974 and 1992 were described by Kanerva et al. (1993). Three of them revealed a positive patch test reaction with MMA (1-10% in petrolatum). Concomitant sensitisation with butyl acrylate, ethyl acrylate and hydroxypropyl methacrylate was also observed.

Fisher (1954, 1956) reported 4 cases of dentists or dental technicians with hand dermatitis due to handling of self-curing methacrylate preparations. The same cases were reported in both publications. All 4 showed positive patch test reactions with the monomer (purity, stabilizer content not indicated), the self-curing monomer preparation and to a self-cured disk. No reactions were observed with heat-cured polymers or polymer powder.

A case of a dentist is reported who used new materials containing mono- and di-methacrylates and benzoyl peroxide. A patch test with 1% MMA, 0.5% benzoyl peroxide and the original resins showed only positive reactions to the resins, but not to MMA or benzoyl peroxide. The

patient also reacted to triethylene glycol dimethacrylate, a constituent of both tested resins (Riva et al., 1984).

46 dental technicians or dentists with hand dermatitis were tested for allergic contact dermatitis to methyl methacrylate and other (meth) acrylates. Patch testing was conducted with 10% or 2% monomer in petrolatum. Four of the patients reacted positively to methyl methacrylate. Concomitant sensitisation to other (meth) acrylates was observed (Kanerva et al., 1988).

Six dental nurses and 1 dentist with an allergic contact dermatitis to dental composite resins containing a variety of (meth)acrylate and other components were patch tested with several (meth)acrylates. Two of the 7 reacted positively with MMA (purity 99.5%, stabilizer content not indicated, 2-10% in petrolatum) and also showed positive reactions to some of the other test substances (Kanerva et al., 1989).

Van Ketel (1977) reported a case of contact dermatitis of a dentist who reacted positively to a catalyst used for the preparation of dental resins (chemical nature not mentioned), but who did not give a positive patch test reaction with MMA (10% in petrolatum).

Two dental technicians with chronic hand eczema revealed positive patch test reactions to MMA (5% in petrolatum), and ethyleneglycol dimethacrylate (2% in petrolatum). One of the patients also reacted to the catalyst p-toyldiethanol amine and the cross-linking agents triethyleneglycol dimethacrylate and tetraethyleneglycol dimethacrylate. Neither of them reacted to the stabilizer hydroquinone monobenzylether (1% in petrolatum) (Farli et al., 1990).

Kanerva et al. (1992) reported a case of a dentist exposed to acrylic denture materials who experienced pharyngitis but no asthmatic symptoms or symptoms of rhinitis or conjunctivits at work. Patch tests with 18 of 30 acrylates or methacrylates, including MMA (2% in petrolatum) were positive.

In 1997, Kanerva et al. published a summary of patch tests reports of subjects with previous exposure to (M)MA; 7.4% of the subjects showed a positive reaction.

Among 82 patients suspected of occupational sensitisation to acrylates from either exposure to dental materials or anaerobic sealants, 11 were identified as having been sensitised to acrylates over a 5-year period. One patient reacted positively in a patch test with MMA (5% in petrolatum) (Guerra et al., 1993).

Other occupational exposures

Seven workers exposed to a self hardening acrylic sealant of unknown composition developed a hand dermatitis. All 7 showed a positive patch test reaction to the unpolymerised sealant (undiluted), 2 of them showed a positive patch test reaction with MMA (1% in methylethyl ketone) (Magnusson and Mobacken, 1972; Mobacken, 1983).

Six patients with skin dermatitis after occupational use of anaerobic sealants without skin protection, were investigated for contact allergic reactions to monomers. Three of them showed positive patch test results to MMA (10% in petrolatum) and hydroxyethyl methacrylate (2% in petrolatum) and 2 also to ethyleneglycol dimethacrylate (1% in petrolatum). The purity and stabilizer content of the monomers were not reported. Reactions to stabilizers or initiators have not been investigated (Condé-Salazar et al., 1988).

Clinical examinations of 20 employees handling 2 industrial sealing agents based on MMA for 1 month to 5 years and 56 volunteers assessed for allergic contact dermatitis did not reveal any evidence of contact dermatitis. Occluded and unoccluded patch tests were conducted with the

sealing agents. No further details concerning the composition of the preparations is given in the article (Pasricha and Gupta, 1985).

Mikulecký et al. (1962) described 4 cases of slight skin reactions of occupationally exposed patients to MMA (1 or 5%, purity, stabilizer content not indicated). It is not clear if the reactions were of an irritant or allergic nature.

Patients

Patients with limb prothesis

In patients with limb prothesis, sensitisation to MMA seems to be a very rare event compared to the widespread use of MMA containing bone cements in arthroplastic surgery. This is understandable because this way of administration bypasses antigen presenting cells in the skin.

Fisher (1986) stated that patients receiving prosthesis very rarely, if ever, become sensitised.

Monteny et al. (1978a) tried to link cardiovascular reactions observed in patients undergoing hip arthroplasty to possible immunological reactions involving the complement system. He monitored 25 patients for changes in serum concentrations of the hemolytic complement components 3 and 4. The introduction of the bone cement did not induce activation of the complement. Only anesthesia with flunitrazepam, fentanyl or pancuronium induced significant activation of the complement system prior to the induction of the bone cement.

Monteny et al. (1978b) reported one case of a positive patch test reaction to 20 or 40% MMA in olive oil out of 42 patients with hip arthroplasty. No reaction was observed when a 2-5% solution of MMA was used for the patch test (stabilizer content and purity not indicated).

Foussereau et al. (1989) reported a positive patch test reaction to MMA (2% in petrolatum) in a patient with a knee prothesis. No reactions occurred to stabilizers, initiators and other constituents of the prothesis or to antibiotics.

A positive patch test result with MMA (2% in petrolatum) and several acrylates and methacrylates was reported in a patient with an incompatibility reaction to a surgical prothesis (Romaguera, 1985). Another case of eczematous allergic contact dermatitis to a limb prothesis was reported by Romaguera et al. (1990). Positive patch test reactions were obtained with potassium dichromate and cobalt salts as well as with MMA (2% in petrolatum) and some other methacrylates.

Casati et al. (1986) claim that an anaphylactic systemic reaction with sudden fall in blood pressure and a bronchospasm in an asthmatic patient undergoing arthroplastic surgery and receiving different medications and blood transfusions was due to the methacrylate containing blood cement used. The authors admitted that this was a very rare event in their experience.

Romaguera et al. (1985) reported a positive patch test result with 2% MMA in petrolether in an individual with an osteomyelitis from a hip prosthesis.

Dental patients

Bradford and Sheff (1948) described a case of a inflammation of the mucoperisteum due to a methacrylate containing denture. A skin test with the denture material resulted in a skin rash 48 hours after application. The reaction cannot clearly be attributed to MMA and may be due to a

mechanical effect as Fisher (1954) obtained similar skin reactions by stripping other inert materials to the forearms of patients.

Fisher (1954) examined 20 patients with a stomatitis which had been attributed to acrylic dentures. One case of allergic hypersensitivity to MMA (purity, stabilizer content not indicated) was identified by a positive patch test reaction.

Kanzaki et al. (1989) reported a case of contact stomatitis resulting from a large amount of residual MMA in a denture. A positive patch test reaction to MMA (0.1-5% in acetone) was observed in the patient.

Four cases of a burning mouth syndrome following the use of denture materials were reported. In 2 patients, the allergens could not be identified, 1 patient reacted positively to MMA (25% in petrolatum, no indication of stabilizer content, purity) in a patch test and one reacted to epoxy resin (Van Joost et al., 1988).

Positive patch test reactions to MMA (10% in olive oil, purity not indicated) were obtained in four patients who reported discomfort due to dental prostheses. Clinical findings did not reveal any changes of the mucous membranes of the mouth (Bäuerle, 1982).

Nealey and Del Rio (1969) described one case of allergic contact stomatitis to a self curing acrylic resin used for the preparation of a partial denture. A patch test revealed a positive reaction to MMA monomer or to one of its additives. (No indication was given of the exact nature and concentration of the monomer used for the testing.)

Four cases of positive patch test results to MMA (purity, stabilizer not indicated) were reported in patients with stomatitis from denture materials (Crissey, 1965).

Fifty-three denture-wearing patients with a burning mouth syndrome were investigated for potential allergic reactions to compounds of the denture materials. Two of the patients showed positive patch test reactions to MMA (30% in petrolatum, no indication of purity, stabilizer content). These 2 patients did not react to hydroquinone (1% in petrolatum), p-phenylene diamine (1% in petrolatum), dimethyl-p-toluidine (30% in petrolatum) or other test substances, such as metal salts, possibly present in the dentures (Kaaber et al., 1979).

Of 131 patients with stomatitis from dentures who underwent a skin patch test 1 reacted positively to an undiluted monomer (chemical nature not indicated) and 10 reacted positively to benzoyl peroxide (10%). According to the authors, both reactions could be of an irritant rather than of an allergic type (Marx et al., 1982).

Corazza et al. (1992) reported a case of a positive patch test reaction with MMA monomer (25% and 2% in petrolether) persisting up to 30 days in a patient suffering from a stomatitis due to a dental prothesis.

Use of artificial nails

Fisher et al. (1957) reported 4 cases of onychia, paronychia and dermatitis following the use of monomer/polymer preparations as sculptured artificial nails. Positive patch test reactions were seen in all patients with the liquid monomer. The nature of the monomer used for the patch testing is not clear from the article and it may well have been the liquid part of the preparation containing initiators, and other substances.

Another case of a severe reaction following the application of an artificial nail preparation containing MMA (composition of the preparation not specified) was reported by the same

author. The patient experienced swelling, redness, pain, paraesthesia of the fingers and a loss of the fingernails. A patch test with MMA (5% in olive oil) was positive. After 6 years the nails had not regrown and the patient still suffered from oedema of the paronychial tissues and paraesthesia of the finger tips (Fisher, 1980a).

Marks et al. (1979) reported the case of a 50-year-old woman with dermatitis after using an artificial nail preparation containing monomers. Positive patch test results were obtained with MMA, ethyl methacrylate, and *n*-butyl methacrylate (5% monomer in petrolatum). Stabilizer content and purity were not indicated.

A patient developing contact dermatitis to self curing denture materials was reported to have used artificial nail preparations before suffering from similar skin reactions (Nealey and Del Rio, 1969).

Four dermatitis patients using artificial nail preparations showed a positive skin patch test reaction to MMA (1% in petrolatum, purity, stabilizer content not indicated). No cross-reactions to *n*-butyl methacrylate or ethyl methacrylate were observed in these patients (Maibach et al., 1978).

Condé-Salazar et al. (1986) reported the case of a woman who had been working in manufacture and application of artificial nails for 6 months. She experienced skin dryness and fissures at the hands. Patch tests with some of the ingredients of the preparation showed severe reactions with the primer and minor reactions with MMA in 10% petrolatum.

Other cases

Meding and Ringdahl (1990) reported 4 positive patch test reactions to MMA (2% in petrolatum, stabilizer content, purity not indicated) out of 22 patients with dermatitis from hearing aids containing residual monomeric MMA.

Guill and Odom (1978) reported a case of an allergic contact dermatitis in a hearing aid containing large amounts of residual MMA. Patch test results with 10% MMA in olive oil were positive (purity and stabilizer content not indicated).

Three of 45 patients with a shoe dermatitis gave positive patch test reactions with MMA (purity, stabilizer content, concentration and vehicle not indicated; Grimalt and Romaguera, 1975).

Kuzelová et al. (1985) reported 3 cases of allergic eczema in people occupationally exposed to 30-300 mg MMA/m³ (7.2-72 ppm) for an average of 10 years (no further data, abstract only).

Kanerva and Verkkala (1986) developed an immuno-histochemical profile on 2 individuals who were allergic to MMA. The immunological changes were similar to those of other allergens but there were few details of the study.

Cross reactivities

Cross reactivity to MMA was reported in one patient handling anaerobic sealants without skin protection and being sensitised to polyurethane dimethacrylate. The patient also reacted to glycidyl methacrylate and ethyl methacrylate (Dempsey, 1982). Cross reactivity has also been demonstrated in a laboratory technician sensitised to hydroxyethyl methacrylate (Mathias et al., 1979) and in patients sensitised by artificial nail preparations to hydroxyethyl methacrylate, ethyl methacrylate, propyl and isopropyl methacrylate (Fisher, 1980b). However no cross reactivity with MMA was demonstrated in patients sensitised to 2-ethylhexyl acrylate or N-tert-butyl maleamic acid from commercial adhesive tape (Jordan, 1975) or polyethyleneglycol dimethacrylate from acrylic sealants (Mathias and Maibach, 1984). Similarly, no cross-reaction

to MMA was observed in workers sensitised to printing inks containing urethane acrylate and pentaerythritol triacrylate (Nethercott, 1978; Nethercott et al., 1983) or trimethylolpropane triacrylate, pentaerythrytol triacrylate, and epoxydiacrylate (Björkner and Dahlquist, 1979).

From 1992-1995 an organisation of German dermatological hospitals (IVDK) has reported 4,221 results of human patch tests. Of these cases, 1.2% (51 patients) have been tested positive with MMA (2% in petrolatum). In 1996 additional 1,161 test results have been reported by the IVDK, 0.8% (9 patients, 4 of these patients were dental technicians) were tested positive with MMA. Only in a few cases the occupation of the patients have been reported (IVDK, 1997).

b) Respiratory sensitisation

In addition to the recognised respiratory irritation caused by exposure to MMA, a small number of case studies have attempted to link MMA exposure to occupational asthma.

Burchman and Wheater (1976) reported dizzy spells, difficulty in breathing, nausea and vomiting in staff in an operating theater where MMA was used. No details were provided on atmospheric concentrations of MMA, work practices or potential exposure to other chemicals.

A second year dental student while working with MMA had exacerbations of long-standing asthma which were corroborated by inhalation challenge. In a study the past histories and symptoms associated with usual lab activities of 502 dental students were determined by a multiple choice questionnaire. Of those students exposed, 6% reported respiratory symptoms with methyl methacrylate and 5% while working with high-speed drills. Eighty percent of these students had histories of either asthma or allergic rhinitis. Less than 1% reported symptoms with other materials (Andrews et al., 1979).

The respiratory health of workers at the Rohm and Haas Knoxville facility in the USA was examined by Rohm and Haas (1981). The protocol included a self-administered questionnaire on respiratory symptoms and smoking history, pulmonary function tests and a chest X-ray. Of the 826 workers at this facility, 780 volunteered to participate. Of these, 68 had been exposed to MMA. In this small sub-cohort there was no evidence of clinically abnormal pulmonary function.

In a follow-up study of a subcohort (workers exposed to MMA that had never smoked) 11 of the original 17 were still employed at the US Knoxville facility and their pulmonary tests were repeated. The results confirmed that these workers exposed to MMA showed normal lung function (Monroe et al., 1981).

In a study of olfactory function, Schwartz et al. (1989) examined 731 workers from a Rohm and Haas plant manufacturing acrylates and methacrylates. The testing involved the administration of the University of Pennsylvania smell identification test (UPSIT) and a questionnaire concerning shift and job profile. In the original cross-sectional (prevalence) study no association was found between chemical exposure and olfactory test scores. A nested case control study was then performed on 77 of the workers who scored at or below the tenth percentile (for their age) on the UPSIT and 77 control workers (matched for age, gender and ethnic group) to assess the cumulative effect of exposure. An association was found between cumulative exposure and olfactory dysfunction, the association appeared to be dose-related. Exposure odds ratios of 2.8 and 13.5 were calculated, by logistic regression analysis, for all workers and those that had never smoked, respectively. A decreasing odds ratio was observed between olfactory dysfunction and time since last exposure, indicating reversibility of the effect. Although the study indicates a reverse association between acrylate-methacrylate exposure and decreased olfactory function, the changes were physiological rather than clinical. The full significance of this study is unclear.

Jedrychowski (1982) and Jedrychowski et al. (1982) studied respiratory symptoms in an industrial population consisting of 454 males exposed to MMA (up to 95 ppm) and styrene, and 683 control males who were not exposed to either material. The workers were evaluated by standardized interviews on chest symptoms and by lung function testing (measurement of FEV_1). The authors reported no difference in the prevalence of chronic chest symptoms between the 2 groups of workers, but did observe that the frequency of lung obstruction was twice as high in the group of workers exposed to MMA and styrene compared to the control group. Surprisingly, a large proportion of the cases of lung obstruction did not show any chronic chest symptoms, however, because of the mixed exposure, it is considered that the effects cannot be attributed to any single chemical.

A standardised questionnaire and spirometry study was conducted on a group of 4,717 male chemical industry workers in Poland. The prevalence of chronic bronchitis, bronchial asthma and obstructive syndrome was evaluated in relation to the variety of chemicals used on the chemical plants. As expected, increased levels of chronic bronchitis, asthma and obstructive syndrome were found in groups of subjects of advanced age and amongst smokers. The frequency on asthma and obstructive syndrome was higher in the chemical industry workers than in the general Polish population, but the frequency of chronic bronchitis was comparable in the 2 groups. The authors concluded that exposure of 1 group of the workers to styrene, benzene and MMA was responsible for the increased prevalence of the pulmonary symptoms observed (Jedrychowski and Fonte, 1984). Due to the mixed nature of the exposures to these agents, it is not possible to attribute the effects observed to any single chemical.

No change of lung function was observed in 10 floor layers regularly exposed to MMA concentrations between 62 and 601 ppm for intervals of approximately 20 minutes followed by a period of no exposure between 30 and 60 minutes. Three of the persons experienced irritation of the nose or throat (Lindberg et al., 1991).

Lozewicz et al. (1985) reported two cases of sensitisation in connection with MMA exposure: A 40-year-old dental assistant used MMA in the manufacture of prosthetic trays. Asthmatic symptoms were related to occupational exposure and a challenge test resulted in an immediate response. It is not demonstrated if the asthmatic responses were due to an immunological mechanism or due to the irritant effects of MMA. In a second case, a 52-year-old railway cable joiner, who smoked cigarettes for many years used an acrylic curing system containing MMA. Symptoms of headache, sweating and lassitude occurred in relation to exposure of MMA but not frequent attacks of cough and wheeze. These two cases demonstrate a relationship of clinical symptoms and MMA exposure but a relationship to the occurrence of respiratory sensitisation cannot be deduced.

There is a report of a 56-year-old theatre sister, who smoked 10-20 cigarettes daily, had worked in an orthopedic operating theatre for 11 years. During this period she had regularly handled bone cement, over the last seven years making about 12 mixes weekly. Before presentation she had handled a new cement mixed by the use of liquid methyl methacrylate, and developed respiratory symptoms characterized by a persistent cough with wheezing and breathlessness. The association between her symptoms and work became apparent. A challenge test with MMA resulted in late asthmatic reactions. The asthmatic symptoms were due to exposure of transient and high levels of MMA vapour. Pulmonary function tests, when she was not working, yielded normal results (Pickering et al., 1986).

A 39-year-old orthopedic theater nurse developed breathing difficulties during the course of mixing cement to seal prostheses. She had previously complained of rhinitis, conjunctivitis and a spasmodic “cold”. Spirometry and chest X-rays were normal. Provocative exposure to the

MMA-containing cement resulted in a fall of 25% in VEMS within 30 minutes of exposure. Respiration returned to normal following the application of b-2-mimetics. Bronchial reaction to acetylcholine was positive, typical of an asthmatic subject (Reynaud-Gaubert et al., 1991). It is therefore considered that it cannot be concluded that MMA was acting other than in an irritant and non-specific manner.

Savonius et al. (1993a) reported 3 cases of respiratory sensitisation that they have linked with exposure to MMA. The nomenclature used in the original publication was confusing and indicated that the individuals in question were exposed to methyl cyanoacrylates rather than to MMA. The authors have, however, recently published an erratum (Savonius et al., 1993b) in which they specify that 3 of the individuals were exposed to MMA. Patient M1, a 48 year old female, is alleged to have been exposed to MMA during the use of a glue (composition unspecified) during plate engraving and is reported to have developed respiratory distress at work, strain, sneezing, rhinorrhoea and stuffiness. Challenge to the implicated glue caused a maximal 24% fall in PEF values and her symptoms persisted on transfer to the use of a cyanoacrylate glue. Patient M2, a 32-year-old male involved in the assembly of hearing devices, showed a small maximal 15% decrease in PEF values following the grinding of "a piece of methacrylate" in an exposure chamber. The third patient, M3, was a 46-year-old female who had worked for about 20 years as a dental technician. She developed paraesthesia on the unular side of both hands but not dermatitis. She subsequently experienced a feeling of tickling in her throat, yawning, cough, tiredness and chest tightness; the symptoms subsided on sick leave and vacations but recurred within a week at work. Simulated occupational exposed to "methacrylate powder and methacrylate liquid" for 30 minutes resulted in a maximal fall of 26% in PEF value. Skin prick test to "methacrylate" was negative. Although this case report appears to show an association between occupational exposure to "methacrylate liquid" and the respiratory symptoms observed it is not possible from the data provided to conclude that the symptoms resulted from exposure to MMA. Therefore consideration of the available data from the 3 cases reported by Savonius et al. (1993a,b) do not show sufficient evidence of respiratory sensitisation by MMA.

Six of 32 male workers exposed to 0.4-112 ppm of MMA (8-h TWA) complained of frequent cough and sputa and 4 of throat irritation. All cases were related to the high exposure group (exposures between 5 and 112 ppm) (Mizunuma et al., 1993). It is however not reported in this paper, if short-term high exposure levels beyond 100 ppm were observed in this work force.

Pickering et al. of the North West Lung Centre, Manchester, UK conducted 2 studies on workers involved in the manufacture of polyMMA acrylic sheet and liquid MMA composites at the ICI Acrylics sites at Darwen in the UK (ICI, 1993). Worker turnover at the sites was reported by ICI to be low and exposure to MMA as high as 100 ppm (8-h TWA) in the past years. The first study was a cross-sectional study involving 384 (89.1%) of a total workforce of 412 and consisted of an assessment of lung function (using simple spirometry to measure FEV_1 and FVC) and a health questionnaire. The second study was a follow-up on the those individuals not available for the first study, a population of past leavers and those workers identified as having 2 or more work related respiratory symptoms in the first study.

In the first study one individual was identified by the authors to have a medical history and peak expiratory flow measurements which are suggestive of occupational asthma. A number of individuals in the study reported symptoms of irritation to the eyes and respiratory system particularly following high, transient exposure to MMA.

In the second study (Pickering et al., 1993) no evidence of respiratory sensitisation was observed in the remainder of the current workforce. From a total past leaver population of 140 individuals, 83 (59.3%) participated in the follow-up which represented 80% of the available target

population. These individuals were investigated by means of a respiratory health questionnaire and spirometry measurements. Based on these data the past leavers population showed work related respiratory symptoms similar to those observed for the current working population in the first study. One individual in the population of leavers was judged by the authors to have been respiratory sensitised to MMA. However, the clinical symptoms reported for this individual indicate the development of pneumonia followed by exposure to a respiratory irritant which could have acted as a provocation to a predisposed condition. From these studies there is no convincing evidence that MMA is acting as a respiratory sensitiser, however, there is clear evidence of acute respiratory irritation, at high exposure levels.

Piirilä et al. (1998) state that in dental workers acrylates can cause respiratory hypersensitivity that is probably not IgE-mediated. Three groups of acrylates are important in dentistry: (a) monofunctional methacrylates such as methyl methacrylate (MMA) and 2-hydroxyethyl methacrylate (2-HEMA), (b) multifunctional methacrylates such as ethyleneglycol dimethacrylate (EDGMA) and trietyleneglycol dimethacrylate (TREGDMA), and (c) acrylated and methacrylated prepolymers such as 2,2-bis(4-(2-hydroxy-3-methacryloxy)phenyl)propane (BIS-GMA) and urethane dimethacrylate. The 12 subjects were exposed to various methacrylate mixtures. Ten subjects were exposed to various methacrylate mixtures and two patients to MMA. None of the patients reacted to prick tests and only 5/12 patients had an elevated total IgE (>100 kU/l). The mean duration of exposure to acrylates was 22 years, and the duration of respiratory symptoms was 8 years. One patient exposed to MMA had an elevated IgE (200 kU/l) and PEF monitoring showed a strong reaction. The clinical symptoms consisted of asthma, rhinitis and pharyngitis. The second patient exposed to MMA had laryngitis only and no alterations in the parameters cited for the first patient were demonstrated. It is stated that the long exposure time before the appearance of the symptoms may be one reason why the number of published cases is low.

Summary

Acute occupational exposure to MMA at high concentrations is recognized to result in respiratory irritation in a proportion of exposed workers and this has been confirmed by the studies and case reports reviewed above. One case report (Pickering et al., 1986) reported a delayed asthmatic response following challenge with MMA which would implicate MMA as a potential respiratory sensitiser. One of two patients exposed to MMA showed clinical signs of respiratory hypersensitivity (Piirilä et al., 1998).

4.1.2.5.3 Conclusion on sensitisation

There have been numerous reports on skin sensitisation in certain occupational environments, where frequent and prolonged unprotected skin contact with monomer containing preparations was common practice. In the literature cases of sensitisation of patients with implanted acrylic bone cement, of patients with hearing aids and of persons using synthetic fingernails have been reported. In skin sensitisation studies guinea pigs showed a positive sensitisation rate. It was concluded that methyl methacrylate has a moderate to strong sensitising potential in experimental animals**.** Methyl methacrylate is classified as R 43 (May cause sensitisation by skin contact).

A small number of case studies have attempted to link MMA exposure with occupational asthma. Authors reported only immediate responses which are most likely due to an airways irritation. While an immunological mechanism may be deduced in a few cases, the majority of cases do not seem to indicate a mechanism resulting in respiratory sensitisation but due to irritative reactions. It was concluded that there is no convincing evidence that methyl methacrylate is a respiratory sensitiser in humans. Thus, the R-phrase R 42 is not warranted,

however, possible non-specific asthmatic responses due to respiratory tract irritation cannot be excluded and labelling with R 37 is sufficient for the protection of humans.

4.1.2.6 Repeated dose toxicity

4.1.2.6.1 Studies in animals

Effects on the respiratory tract from inhalation studies

Male and female F344/N rats and B6C3F1 mice (5 animals/sex/group) were exposed to 0, 500, 1,000, 2,000, 3,000 or 50,000 ppm MMA on 6 hours/day for 10 exposures in a 11-day period (NTP, 1986). Animals were repeatedly weighed and necropsy was performed on all surviving animals. Histologic examination was done on tissues from the heart, lung, kidneys, salivary gland, mammary gland, and nose on one or two male mice from each dose group (not reported to be done in rats). – All rats exposed at 5,000 ppm (on days 1-3) and 2/5 females exposed at 3,000 ppm (on days 4 and 6) died before the end of the study. Ruffled fur of surviving animals and lower final mean weights of rats exposed to 2,000 ppm or 3,000 ppm were the only compound-related effects. – In mice, deaths occurred in all exposed groups of male mice. All animals exposed at 5,000 ppm died on day 1-2 of the treatment. Four 3,000 ppm males died between day 1 and 8 of the study, at 2,000 ppm 3 males died on 6-10, at 1,000 ppm 1 male was found dead on day 8, and two deaths occurred at 500 ppm on days 8 and 9. Dyspnoe and redness and swelling of the nasal region were compound-related effects (no further data reported).

Another shortly reported study of the NTP report (1986) was a 10-day study on male and female F344/N rats and B6C3F1 mice (5 animals/sex/group) which were exposed to 0, 75, 125, 500, or 1,000 ppm MMA on 6 hours/day for 9 exposures over 10 days. Animals were repeatedly weighed and necropsy was performed on all surviving animals. Histologic examination on the nasal cavity, nose, lung, and kidneys kiwas only performed on five mice of the control and 1,000 ppm groups, five male mice from the 125 ppm group, and one mouse of each sex from the 500 ppm group. In rats, no early deaths and no other compound-related clinical signs or gross pathologic effect were seen. The final mean body weights were within a 6% limit of the control values. The mice study did not reveal any MMA-related effect on the mortality rate, final mean body weights, gross or microscopic pathology.

Groups of 45 female F344 rats (five animals per time point, 5-6 weeks old) were exposed whole body for 6 hours per day to 0, 110 or 400 ppm methyl methacrylate (99.9%) (app. 0, 0.017 and 1.68 mg/l) for 1, 2, 5, 10 or 28 consecutive days (CEFIC, 1997). In addition, four satellite groups of the 28-day exposure groups were retained for a period of 1, 3, 6 or 9 months following exposure to assess reversibility of any nasal tissue effects. Clinical observations were made, bodyweights were measured and at the end of the scheduled period, the animals were killed and subjected to an examination post mortem. From the groups of all exposure periods and from 1 and 3-month recovery groups, specified tissues (lung, trachea, nose (6 sections were examined but not separately reported)) were preserved for subsequent histopathology examination, but only the nose was reported being examined. The study was not in conformance to the OECD guideline 413 (only one sex, no examinations on hematology and clinical chemistry, histopathological examination exclusively conducted on the respiratory tract, no lung perfusion, the minimal recovery period exceeded the standard recovery duration for the 28-day study). There were no deaths or adverse clinical symptoms during either the exposure or recovery period. Bodyweights were slightly reduced in animals exposed to 400 ppm methyl methacrylate

during the first week of the exposure period. There were no gross findings at necropsy. Microscopic findings associated to methyl methacrylate exposure consisted of a damage of the olfactory epithelium at 110 ppm and 400 ppm. Beginning at day 1 of exposure, there was degeneration/necrosis of the olfactory epithelium of minimal severity at 110 ppm and of mainly moderate severity at 400 ppm. At 400 ppm, intraluminal inflammatory excudate and submucosal inflammatory cell infiltration were evident in all exposure and recovery groups. There was also indication of early epithelial regeneration with a single layer of large, polygonal cells overlying the basal lamina in some areas, beginning at the 400 ppm exposure level at day 2 of exposure and at the 110 ppm exposure level at day 5 of exposure. After 28 days of exposure, rats of the 110 ppm groups did not show any lesions in the nasal cavities. Animals of the 400 ppm group showed minimal degeneration/necrosis of the olfactory epithelium and disorganized/regenerated olfactory epithelium. Four out of five females of this exposure group showed minimal respiratory metaplasia and three of them had adhesions between the septum and turbinate. The adhesions were reported to consist of fibrinous exudate/fibrous tissue connecting the submucosa of the septum to the submucosa of the turbinate or turbinate to turbinate with apparent loss of the basement membrane. Recovery groups revealed that no lesions persisted in the 110 ppm exposure groups. Minimal disorganization of the olfactory epithelium and minimal inflammatory changes, respiratory metaplasia and adhesions persisted in rats exposed to 400 ppm methyl methacrylate and maintained without treatment on 28 days or 13 weeks of recovery. Systemic effects after methyl methacrylate inhalation were not investigated, also a dose without effects (NOAEC) was not estimated. The LOAEC for local effects on the respiratory tract was 110 ppm.

Inhalation studies in F344 rats and B6C3F1 mice of 14-week duration revealed signs of irritation of ocular and nasal membranes in dosage of 8.3 mg/l (equivalent to 2,000 ppm) or more (Battelle, 1980; NTP, 1986). In these studies used for dose-selection, 10 male and 10 female rats were exposed to 0, 500, 1,000, 2,000, 3,000 or 5,000 ppm (0, 2.1; 4.2, 8.3, 12.5, and 20.8 mg/l) of methyl methacrylate. Complete histopathology (including nasal turbinates, lungs, liver, kidneys, brain, vagina, heart, thymus, skin, large intestine, small intestine, adrenal glands, urinary bladder) were performed on all rats exposed at 3,000 and 5,000 ppm, and on all controls and unscheduled deaths. Nasal turbinates (except 1,000 ppm males), larynx, trachea, lungs, and brain were examined for all 1,000 ppm rats and survivors of the 2,000 ppm rats. There were no data on histopathologic examinations at 500 ppm rats. Compound-related clinical signs observed during the first 2 days included listlessness in all animals of all dose groups, from 2,000 ppm serious ocular discharge, nasal discharge, and incoordination occurred, in addition prostation was seen at 5,000 ppm. All rats exposed at 5,000 ppm (week 1-2), 1/10 males and 9/10 females exposed at 3,000 ppm (week 2-3), and 1/10 males (week 11) and 3/10 females (week 2-5) exposed at 2,000 ppm died before the end of the study. Final mean body weights were 20%, resp. 25% lower for males and females exposed to 3,000 ppm, and 7% and 11% lower for males and females exposed to 2,000 ppm. Inflammation in the nasal cavity associated with necrosis and loss of olfactory epithelium occurred in exposed males at 3,000 ppm or higher and in females at 2,000 ppm or higher. (Other results see in Section: “Systemic effects from inhalation studies”). In contrast to the above cited findings from the NTP report, the incidences of the microscopic lesions were different to that reported in the Battelle report. Although not cited, we assume a peer review at least of the nasal lesions by the NTP peer reviewer. However, it seems noteworthy that the Battelle group found acute laryngitis in 1 female at 2,000 ppm and the control group, 1 male and 3 females at 3,000 ppm, 2 males and 2 females at 5,000 ppm. Acute tracheitis was seen in one female at 2,000 ppm, 2 females at 3,000 ppm, and 2 females at 5,000 ppm versus none in the control groups. Lung lesions were not reported in the NTP report, but Battelle found congestion and hemorrhage of the lung of 1-3 males in all dose groups from 1,000 ppm except the 5,000 ppm group in which all males showed congestion. In females, congestion was observed

in 3 controls, 2 rats at 2,000 ppm, 5 at 3,000 ppm, and 9 at 5,000 ppm. Corresponding to this, the redness of the lung was seen in all dose groups from 2,000 ppm.

Unscheduled deaths also occurred in mice exposed to the same dose groups like rats. Complete histopathology on mice at 5,000 ppm included nasal turbinates, lungs, liver, kidneys, brain, vagina, testes, and ovaries. Nasal turbinates (females only), lung, and liver (males only), of surviving mice were examined from surviving mice at 3,000 ppm. At 2,000 ppm, histopathology was performed on nasal turbinates, lung, and brain (males only). The sections from the nasal turbinates and brain (males only) were examined at 1,000 ppm. Microscopic examination of any group included the trachea or pharynx/larynx. Compound-related clinical signs observed during the first 1 or 2 days included listlessness in all animals of all dose groups, from 2,000 ppm serious ocular discharge and incoordination occurred at the first two days. Listlessness persisted up to day 10 at 3,000 ppm, all symptoms persisted during the entire study at 5,000 ppm. Additionally the 5,000 ppm mice suffered from nasal discharge. Males and females exposed to 5,000 ppm (week 1-10, 6 males and 5 females of which died in week 1-2), 4/10 males exposed at 3,000 ppm (week 2) and 2/10 males and 1/10 females exposed at 2,000 ppm (week 1-2) died before the end of the study. The final mean body weights of all groups were dose-dependently lower than that of the controls (males 13-27%, females 6-18%). Gross lesions were increased redness of the external surface of the lungs in exposed groups (males >1,000 ppm, females >2,000 ppm), most frequently in the highest concentrations. Opacity of the eyes was evident in 1-3 animals of all groups, but the incidences did not show dose-relationship. Pale liver foci were observed in two 5,000 ppm males. In the NTP report, all male and female mice exposed to methyl methacrylate were reported showing metaplasia of the nasal epithelium. However, the incidence table did only include the microscopic findings at doses at or higher than 2,000 ppm. In both sexes, an inflammation of the nasal turbinates was evident in 4 or 5/10 animals per group at 2,000 ppm and 3,000 ppm, and in 8/10 mice at 5,000 ppm. Overall, there was an inconsistency of the summaries on the microscopic lesions from the original study report of Battelle to the NTP report. We assumed that at least the sections of the nasal turbinates, livers, and kidney were reevaluated by the peer reviewers of the NTP. Additionally, the study of Battelle found lung congestion in exposed males (1 at 2,000 ppm, 2 at 3,000 ppm, 3 at 5,000 ppm) and females (2 at 3,000 ppm and 5 at 5,000 ppm). 3 females of the 5,000 ppm group also presented hemorrhage of the lungs. (Other results see in Section: “Systemic effects from inhalation studies”).

Damage to the tracheal mucosa of rats exposed to 0.5 mg/l (equivalent to 116 ppm) for six months were observed by light microscopy. Rats exposed to 0.5 mg/l (equivalent to 116 ppm) for three months showed similar results in scanning electron microscopical examination consisting in tracheal mucosa denuded of cilia and covered with reduced number of microvilli (Tansy et al., 1980b).

The combined chronic toxicity/carcinogenicity study of methyl methacrylate in F344 rats (Rohm and Haas, 1979a; the nasal tissues were reevaluated by Lomax, 1992; Lomax et al., 1997) was assessed for the requirements of the regulation 793/93/EEC as a valid study with restrictions. In comparison to the minimal requirements of a 28-day inhalation study (OECD 412), the list of organs to be weighted did not include the liver and the heart. 70 male and 70 female F344 rats were exposed to vapor concentrations of 0, 25, 100 or 400 ppm methyl methacrylate for two years. Ten male and ten female rats from all groups were sacrificed after 13 and 52 weeks of exposure and all surviving rats were killed during week 104-106. Histological examination was conducted on more than 35 tissues including 3-4 cross-sections of the nasal cavity. Tissues from the trachea and the pharynx/larynx were not preserved for histopathologic examination. Mortality rates of treatment and control groups did not show significant differences. No compound-induced clinical signs were observed. After week 52, mean body weight of high dose females was generally lower than controls gaining intermittently significance. Reduced growth

represented the only adverse effect outside the respiratory tract. Evaluation of hematology, clinical chemistry and urinalysis data did not reveal any methyl methacrylate associated effect. At the end of the study, there were weight changes of some organs in males or females without any consistent relationship to the treatment. Similarly, no treatment-related macroscopic findings were observed in any of the dose groups. No histomorphological lesions other than nasal lesions were attributable to methyl methacrylate exposure of any exposed group. The examination of nasal cavities from male and female rats exposed to 400 ppm for 13 weeks or 52 weeks revealed a degeneration of the neuroepithelial olfactory cells lining the dorsal meatus of the anterior portions of the nasal cavities in conjunction with atrophy of Bowman's glands and focal basal cell hyperplasia. Chronic active inflammation, respiratory epithelial hyperplasia and squamous metaplasia characterized the lesions on the tips of the maxilloturbinate and nasoturbinats and focally along the nasal septum in more anterior regions of the nose. At the final sacrifice, nasal lesions were evident in males and females of the 100 ppm and 400 ppm exposure groups characterised by inflammatory degeneration of nasal epithelium. The primary target tissue was the olfactory epithelium with degeneration and/or atrophy of neurogenic epithelium and submucosal (Bowman's) glands lining the dorsal meatus, hyperplasia of basal cells, replacement of olfactory epithelium with ciliate (respiratory like) epithelium (metaplasia), and inflammation of the mucosa and/or submucosa. The severity of the lesions varied from minimal to slight at 0.4 mg/l (equivalent to 100 ppm) to moderate at 1.7 mg/l (equivalent to 400 ppm). At 0.1 mg/l (equivalent to 25 ppm) no pathological effects on the olfactory epithelium were reported, representing the NOAEC for local effects on the respiratory tract. Slight to moderate changes in respiratory epithelium occurred at 1.7 mg/l (equivalent to 400 ppm) and were characterized as hyperplasia of submucosal glands and/or goblet cells in the anterior regions of the nasal cativy. In the respiratory epithelium, there was inflammation of the mucosa and/or submucosa in males and females exposed to 400 ppm. **Table 4.9** summarises the incidences of degenerative, hyperplastic, metaplastic and inflammatory lesions observed in this study. The NOAEC for systemic effects was considered to be 100 ppm for female rats and 400 ppm for male rats.

Table 4.9 Frequency of nasal lesions in F344 rats exposed to methyl methacrylate(MMA) vapor for two years (cited from Lomax, 1992)

	Males				Females			
MMA concentration (ppm)	0	25	100	400	0	25	100	400
Olfactory epithelium								
No. of animals exam.	39	47	48	38	44	45	41	41
Degeneration/atrophy	0	0	86%	100%	0	0	59%	95%
Basal cell hyperplasia	13%	6%	69%	87%	0%	2%	44%	76%
Inflammation (chronic, mucosal & submucosal)	0%	0%	35%	76%	0%	0%	12%	61%
Olfactory replaced by ciliated (metaplasia)	0%	0%	2%	39%	0%	0%	17%	51%
Respiratory epithelium								
No. of animals exam.	44	47	48	42	45	45	41	42
Hyperplasia, submucosal gland & goblet cell	2%	0%	2%	60%	0%	0%	2%	21%
Inflammation, (chronic, mucosal & submucosal)	9%	0%	4%	60%	4%	0%	0%	21%

The cancer studies of the National Institutes of Health (NTP, 1986) revealed toxicological effects regarding the respiratory tract in male and female rats and mice. Groups of 50 male F344 rats and 50 B6C3F1 mice of each sex were exposed 6 hours per day, 5 days per week to air containing methyl methacrylate at target concentrations of 0, 2.1 or 4.2 mg/l (equivalent to 500 or 1,000 ppm) for 102 weeks. Groups of 50 female rats were exposed at concentrations of 0, 1.0 or 2.1 mg/l (equivalent to 250 or 500 ppm) on the same schedule. Increased incidences of serous and suppurative inflammation of the nasal cavity were observed in male and female rats. Degeneration of the olfactory sensory epithelium characterized by loss of neuroepithelial cells was also observed in male and female rats. In exposed male and female mice inflammation of the nasal cavity, epithelial hyperplasia in the nasal mucosa and degenerative changes of the olfactory sensory epithelium were reported. In addition methyl methacrylate caused interstitial inflammation of the lung in high dose male mice. The trachea and larynx were also included in the histopathology, but no compound-related effects on these tissues were reported for rats and mice of each dose and sex. A NOAEC could not be established either from rats or mice.

In a 78-week carcinogenicity study Golden hamsters were exposed to 0, 25, 100 or 400 ppm (equivalent to 0, 102.5, 410 or 1,640 mg/m³) methyl methyacrylate for 6 hours daily for 5 days a week (Lomax et al., 1997). No exposure-related microscopic changes were observed in the nasal cavities including the olfactory epithelium or other organs (>35 tissues examined). Two to four cross sections of the nasal cavity were examined per animal.

Systemic effects from inhalation studies

Treatment-related systemic effects in a short-term inhalation study (7 days) on rats showed reduced concentrations/activities of albumin, glucose, blood urea nitrogen, ASAT, ALAT, and albumin-glucose ratio at 4.2 mg/l (equivalent to 1,000 ppm) compared to the controls (Tansy et al., 1980b).

Systemic toxic effects of the 14-week inhalation studies on rats and mice (NTP, 1986, already cited above) were observed in the liver, kidneys, central nervous system and spleen. The incidences of liver necrosis (3 males at 5,000 ppm) and renal cortical necrosis and cortical tubular degeneration (1, 3, resp. 5 males at 2,000, 3,000, resp. 5,000 ppm) were increased in treated mice. In rats extensive cerebellar congestion and hemorrhage in the cerebellar peduncles occurred in the early death females in the 12.5 and 20.8 mg/l (equivalent to 3,000 and 5,000 ppm) group. Malacia and gliosis of the brain were found in surviving females at 3,000 ppm (12.5 mg/l) and in females at 5,000 ppm (20.8 mg/l) which died late in the study. Malacia and gliosis were observed in 5/9 females exposed at 2,000 ppm (8.3 mg/l) and 1/8 females at 1,000 ppm (4.2 mg/l). Although there is only one case of brain toxicity at 1,000 ppm, in the context of an increased incidence of the same lesion at 2,000 ppm it was interpreted as a treatment-induced adverse effect. Follicular atrophy of the spleen in male rats and bone marrow atrophy in females occurred at 20.8 mg/l (equivalent to 5,000 ppm). As commented above, the findings of the NTP report were inhomogenous to the original study report of Battelle (1980, which did not report these findings). According to the NTP report, the NOAEC for systemic effects was 1,000 ppm in mice, and 500 ppm in rats.

In a not sufficiently documented study effects on the endocrine system of female Wistar rats have been reported at 0.05 and 0.5 mg/l (equivalent to 12.6 and 126 ppm). The content of the gonadotropin-releasing hormone (GnRH) in different parts of the hypothalamus, the serum concentration of gonadotropic hormones LH and FSH, and of estradiol and progesterone after inhalation exposure for 4 h/d for 1 or 4 months were examined (Stepanov et al., 1991). According to the translation from Russian, there were no data on the number of animals per group exposed, the number of animals examined for endocrine effects, on the time point of the

hormonal determinations, no exact descriptions of the markers and methods used, and a high variability of serum hormone levels in controls comparing values at 1 month versus 4 months. After 1 month of treatment, the serum levels of LH, FSH, and progesterone were increased at 0.05 mg/l compared to control values, but the response was not related to the dose and was obviously controversial to that after 4 months. At that time, the serum levels of estradiol were reported to be unchanged, the progesterone concentrations were lower than those of the controls. The weights of the ovaries were increased after 1 month of treatment and decreased at 4 months of treatment (no numerical data), at 4 months the ovary to body weight ratio was slightly increased (no data on 1 month of treatment). After 4 months, several areas of the hypothalamus were reported to contain less GnRH in high dose animals than in controls, LH levels were higher than control values, and the FSH did not show a difference to the control. According to this publication, no clear adverse effect on the endocrine function could be demonstrated.

A 3-month inhalation study in Beagle dogs revealed no significant differences to the control in cardiovascular performance parameters, various blood parameters, urinary components and body and organ weights up to the high dose level of 1.7 mg/l (equivalent to 400 ppm) (Rohm and Haas, 1979b).

After 6-month inhalation of MMA vapour (concentration 0.5 mg/l, equivalent to 116 ppm) reduced intestinal motor activities and smooth muscle tonus in the conscious rat occurred (Tansy et al., 1976a, 1976b). In another 6-month inhalation study using 116 ppm vapour concentration of MMA no significant exposure-related systemic effects were observed in tissue sections from heart, kidney, spleen, stomach, small intestine, adrenals, and lungs (Tansy et al., 1980b).

In two-year chronic inhalation studies of methyl methacrylate mean body weights of 500 ppm and 1,000 ppm male and female mice (equivalent to 2.1 and 4.2 mg/l) were about 10% lower than those of controls throughout most of the study; mean body weights were also lower in female rats at 500 ppm after week 73 (NTP, 1986). In the combined chronic toxicity/carcinogenicity study (Rohm and Haas, 1979a) reduced body weights have been reported in female rats after week 52 at high-dose level (1.7 mg/l, equivalent to 400 ppm). No other adverse systemic effects were reported in these studies including histopathology.

Information from studies with other exposure routes

In an insufficiently documented 21-day oral study on rats, methyl methacrylate impaired locomotoric activity and learning ability, and for a brief period gait and rear leg function at 500 mg/kg body weight. Neurotransmitter levels were slightly changed (Husain et al., 1986).

An early 2-year chronic study on Beagle dogs and Wistar 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).

Groups of 25 male and 25 female rats were administered with 6, 60 and 2,000 ppm MMA in the drinking water (app. 0.6, 6, and 200 mg/kg bw/d, calculated on water consumption of 10% of bw), the low and medium doses increased to 7 and 70 ppm after five months. The rats were weighed once weekly, food and water consumption was measured after week 1 and 4, and thereafter monthly, hematologic values (Hct, Hb, WBC, differential cell counts) of 5 rats were examined at 3-month intervals and semiquantitative urinalysis of reducing agents and protein was performed at 3-month intervals. At 2-year sacrifice, organ weights of heart, spleen, kidney, liver, and testes were obtained and 15 tissues/organs (including the kidneys) were preserved for histopathology, which was only done in high dose rats. The growth was unaffected by treatment, fluid consumption was reduced in high dose male and female rats compared to the controls. No other

treatment-related effect was seen in orally treated rats except increased kidney ratios in female rats at 2,000 ppm. Because altered kidney weight was not corroborated by other findings, the NOAEL for rats was considered to be 2,000 ppm (200 mg/kg bw/d).

Additionally, two male and two female dogs received gelatin 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. Hematologic studies and urinalysis (as reported for the rats above) were made prior to the treatment begin, at 2, 4, and 13 weeks and at 3-month intervals. At sacrifice, organ to body weight ratios and the same tissues as for rats (see above) were obtained, histopathologic studies were made from all dogs. No treatment-related effect was observed in the dogs. Because of the low numbers of animals this study was not used for the derivation of a NOAEL.

4.1.2.6.2 Studies in humans

There are many reports, which describe adverse effects on human health on occupationally exposed people (cf. Section 4.1.2.5.2 “Studies in humans”). Considering the lack of important details and the unclear exposure situation, it is often not possible to link these effects alone to methyl methacrylate or to particular methyl methacrylate concentrations.

Marez et al. (1993) investigated the lung function parameters in eight workers with more than five and less than 10-year exposure and 32 workers with more than 10-year exposure to methyl methacrylate in two factories with mean concentrations of 18.5 and 21.6 ppm (ranges of 9-32 ppm and 11.9-38.5 ppm). 13 of the 40 workers were non-smokers, 11 were ex-smokers and 16 were smokers. An increased incidence of chronic cough was observed in 8 out of 40 exposed workers and 2 out of 45 controls with similar smoking habits. Spirometric values did not differ before the workshift, but decreased in controls and exposed workers during the workshift. The decrease of two parameters out of nine, the maximum expiratory flow (MEF) when 50% of the forced vital capacity remained to be exhaled and the ratio of MEF to maximal expiratory flow, were significantly higher in the exposed workers. There was no interaction of smoking habit and methyl methacrylate exposure related to the functional parameters. The increased cough incidence and the mild airway obstruction were correlated to the methyl methacrylate exposure.

In this study, only a small population was investigated (including 13 workers without smoking history). There are no data whether the exposed people had ever had longtime exposure to other respiratory irritants. Monitoring time to estimate the methyl methacrylate concentration using a passive sampling technique on activated charcoal was eight hours. Two single respiratory measurements were done, one before and the second during the workshift. Data collection was not repeated, no data are available on the correlation of the findings to the mean or peak concentrations. There are some doubts therefore on the accuracy of the exposure values that have been presented. In addition this technique would not detect short-term high-level exposure.

The occupational exposure study of Cromer and Kronoveter (1976) with a group of 91 exposed and 43 non-exposed workers did not reveal any significant differences between the exposed and non-exposed groups to 4-49 ppm methyl methacrylate (8-h TWA exposure level). Parameters on acute effects included symptomatology, blood pressure and pulse rate, parameters on chronic effects included symptomatology, blood pressure, respiratory function testing, haemoglobin and white blood count, urinalysis, and blood chemistry. There were significant differences between the control group and the <5 ppm-group for cough which was explained with a higher percentage of smokers in this group than in the control group. In groups with higher mean exposure (mean

exposure 5-25 ppm and 25-50 ppm) the cough incidence decreased. Methyl methacrylate (incl. 1-2% additives) was the only monomer in four plants, one plant used also ethyl acrylate.

In an acrylic sheet production plant 211 male workers exposed to methyl methacrylate were examined in a medical survey consisting of a self questionnaire about lifestyle, occupation and medical history with emphasis on complaints of nose, throat and respiratory system failures, and allergic reactions including skin and asthmatic reactions (Röhm, 1994a). The questionnaire was supplemented by a detailed anamnesis and aterior rhinoscopy using a speculum. The workers (mean age 37 years) spent an average of 8.8 years (<1 until >20 years) in acrylic sheet production. 55 subjects starting to work in the factory during the report period without any prior exposure to methyl methacrylate were examined in the same manner. Present exposures to methyl methacrylate varied between <3 and 40 ppm (<12 and 160 mg/m³) (8-hour average value). Past exposures were between 10 and 70 ppm (4 and 290 mg/m³) methyl methacrylate. Occasional short-term peak concentrations of 100 – 680 ppm (410 and 2,800 mg/m³) had also been recorded. No case of methyl methacrylate exposure related respiratory or skin sensitisation was observed in the exposed groups. Observation of irritation in the eyes and the upper respiratory tract was reported to be limited to acute and reversible reactions after short-term peak exposures at concentration levels exceeding 100 ppm (410 mg/m³) (without any proof for the correlation). There were no indications for clinical symptoms of a work-related rhinopathy or any substance related abnormalities in the nasal cavity in the exposed group. The study did not include data on the exposure to other chemicals; there was no control group, no statistical evaluation was performed.

In a cross-sectional study with Rhino-Test, a smell test with 6 aromas to detect hyposmia or anosmia, prevalence of smell disorders of 175 MMA-exposed workers (smokers 58.3%, non-smokers 32.6% and former smokers 9.1% was comparable to 88 non-exposed controls (smokers 34.1%, non-smokers 42% and former smokers 23.9%). In the group of exposed workers only one case (0.6%) of hyposmia was observed. The mean duration of exposure was 9.6 + 7.1 years (minimum 1 year, maximum 33 years). Time weighted average concentrations of MMA were reported to be up to 50 ppm during the past 6 years and up to 100 ppm the time before. From 1987 to 1992, repeated short-term (<1 hour) and long-term (>1 hour) average concentrations of MMA during the workshift were monitored at the body of workers from different work areas according to the German Technische Regel für Gefahrstoffe 402. With few exceptions, workers were reported to be exclusively exposed to MMA. The smell test was performed either before, during or just after the shift (no exact data) (Muttray et al., 1997; Röhm, 1994b).

Furthermore, effects on the respiratory tract (breathing difficulties) (Burchman et al., 1976), cardiovascular system (Marez et al., 1992; Dorofeeva, 1976), endocrine system (Makarov, 1983) and gastrointestinal system (Sharova, 1989) appeared in epidemiological studies and/or case reports with limited reliability (as mentioned above). Lang et al. (1986) reported (only abstract available) dose-dependent increases in the incidences of neurasthenia, laryngitis and hypotension in a group of workers inhalation exposed to methyl methacrylate for periods between 3 months and 26 years.

In several studies unspecific symptoms including headaches, vertigo, nervousness, concen-tration difficulties and poor memory (Blagodatin et al., 1971; Raines et al., 1957; Christiansen, 1987) have been reported from occupationally exposed people via the inhalation or dermal routes.

Local neurotoxicity, but no disturbance of the lung function, has been reported in form of reduced peripheral nerve function in arms and legs of inhalation exposed floor layers (Lindberg et al., 1991). Estimated exposure concentrations were between 62 and 601 ppm for intervals of approximately 20 min followed by non-exposure periods of 30-60 min. Total exposure time of the

workers varied between 0.7 and 12 years. Three workers had eye irritation at least once a week, another three one to three times a month, indicating an acute response to high peak concentrations. Exposure to substances other than MMA during the floor laying process was not estimated.

Generalized sensomotoric peripheral neuropathy (Donaghy et al., 1991) and slower distal sensory conduction velocities in the fingers (Seppalainen et al., 1984) have been reported from methyl methacrylate exposed dental technicians.

4.1.2.6.3 Summary of toxic effects after repeated exposures

In subacute, subchronic and chronic inhalation studies on rats and mice, the predominant target organ was the respiratory tract. In rats, the primary target tissue was the olfactory epithelium of the nasal passages showing degeneration/necrosis at methyl methacrylate concentrations of 100 ppm and higher. At higher doses or with prolongation to chronic exposure, inflammatory infiltrates were also evident in the olfactory and the respiratory epithelium. Occasionally, rodent studies indicated irritative effects on the trachea (at 116 ppm), but findings were not confirmed by other studies.

Interstitial pneumonia was observed in a mouse cancer study (NTP, 1986) at a high dose (1,000 ppm), but treatment-related effects on the lung were absent in other repeated dose studies up to a concentration of 400 ppm. Long-term exposed mice also showed damage of the olfactory epithelium, however at methyl methacrylate concentrations of 500 ppm or higher (NTP, 1986). No adverse effects of chronic methyl methacrylate exposure were observed in the respiratory tract of hamsters.

No adverse effect was observed at 25 ppm (equivalent to 0.1 mg/l) (NOAEC). Slight degenerative and regenerative lesions of the olfactory epithelium were obvious at 110 ppm independent whether the exposure duration was 1, 2, 5, or 28 days in the CEFIC study (1997) and 100 ppm in the 2-year study conducted by Rohm and Haas (1992). In both studies, the severity of the lesions observed at 100 ppm was in the same range of gradation, described to be minimal to slight with respect to the degeneration of olfactory epithelium. In addition, the 2-year study revealed inflammatory lesions of the olfactory epithelium at concentrations of 100 ppm and higher, whereas inflammatory lesions were only found at 400 ppm in the subacute study of CEFIC (1997). Whereas induced lesions were confined to the olfactory epithelium after subacute exposure up to 28 days, irritative effects were also seen at 400 ppm of methyl methacrylate for 2 years inducing hyperplasia of submucosal glands and/or goblet cell hyperplasia and inflammation of the mucosa and/or submucosa in the anterior regions of the nasal cavities lined by the respiratory epithelium. This means that the LOAEC from rat data was constant in short- and long-term studies, however the long-term inhalation led to an exacerbation with an increase of the multiplicity of lesions and the locations affected.

Nasal lesions seen at 100 ppm methyl methacrylate were reversible after 4 weeks and 13 weeks of recovery (CEFIC, 1997), however the duration of the recovery period was prolonged in comparison to standard methods (2 weeks after a 28-day exposure is the regular time). As early as on the second day of exposure hyperplasia of basal cells was seen indicating an early attempt to regenerate/reparate the loss of differentiated olfactory epithelial cells (CEFIC, 1997). A replacement of olfactory epithelium by respiratory like epithelium (metaplasia) was first evident at day 28 of exposure and in 400 ppm rats only, and persisted in the groups at 4 weeks and 13 weeks of recovery. Consistently, metaplasia was also observed in both sexes of the 400 ppm group in the 2-year study with incidences of 39% for males and 51% in females and in 100 ppm females at 17% (Lomax, 1992). Respiratory metaplasia of the olfactory epithelium is known to occur spontaneously in old rats (and humans); the incidences were reported to be low in rats of

old age (mean values 4% in F344 males (range: 0-12%), 1% in F344 females (0-4%) (Nagano et al., 1996). Although it is known that sensory cells of the olfactory epithelium have the ability to regenerate with a 28- to 30-day turnover rate in the rat (Harkema, 1991), the respiratory epithelium metaplasia in the area of destroyed olfactory cells represents tissue repair. This means there was no full regeneration with return to a complete olfactory function.

At a concentration of 116 ppm methyl methacrylate, Tansy et al. (1980b) reported a damage of the tracheal mucosa in rats exposed to 116 ppm (equivalent to 0.5 mg/l) for 6 months (by light microscopy) or 3 months (by electron microscopy). Laryngitis and tracheitis were also found after a 14-week exposure of rats at MMA concentrations of 2,000 ppm and higher (Battelle, 1980). Due to the absence of histopathologic examination, no data on effects on the trachea were described in other reports. In contrast to this, no abnormal findings were reported in the trachea and larynx in a 2-year cancer study on rats and mice up to 1,000 ppm MMA (NTP, 1986).

Other relevant toxic effects outside the respiratory tract were reported to occur in the liver, kidneys, spleen, bone marrow and central nervous system. After a 14-week inhalation, mice had lower body weight gain $\geq$500 ppm/2.1 mg/l, cellular necrosis in liver and renal cortices $\geq$2,000 ppm/8.3 mg/l and rats showed splenic follicular atrophy and bone marrow atrophy at 5,000 ppm/20.8 mg/l. Higher mortality rates were seen in rats at high doses of MMA (>2,000 ppm, 14-week study, NTP, 1996), however early deaths in mice were seen at doses of 500 ppm and higher (11-day study, NTP, 1986). The most sensitive effect outside the respiratory tract was the retardation of growth in rats (>400 ppm, Rohm & Haas, 1979a) and in mice (>500 ppm, NTP, 1986). It may be assumed that lower body weight gains may be related to the nasal irritation via lower consumption of food. Since there were no data on a reduction of food consumption, the reduction of growth was considered to be a direct compound-related effect.

MMA vapour produced smooth muscle relaxation of the intestine *in vivo* (rat) and *in vitro* (guinea pig).

The depressive heart and blood flow effects found in the isolated rabbit heart were not confirmed by other findings in the 3-months dog study.

There are a number of findings which may indicate an effect on the nervous system. In an oral subacute rat study, effects on behaviour (listlessness, locomotoric activity, learning ability, gait and rear leg function), and changes in brain chemistry and peripheral nervous system were observed. Malacia and gliosis of the brain occurred at doses $\geq$4.2 mg/l (equivalent to $\geq$1,000 ppm) in rats which inhaled methyl methacrylate vapour for 14 weeks. These neurotoxic effects could not be confirmed in chronic inhalation studies up to concentrations of 400 ppm.

The studies in humans were of limited validity mainly due to defaults in the exposure data and the possible mixed exposure to other relevant substances. It cannot be excluded that adverse effects on the respiratory tract, the central and peripheral nervous system, the cardiovascular system, and the gastrointestinal system were attributable to the repeated exposures to MMA. No disturbance of the olfactory function was detected in MMA exposed workers showed normosmia with a standardized smell test.

At the moment, there is no indication of any serious clinical health effect on humans after prolonged exposure up to 50 ppm of MMA vapour concentration (8-h TWA). At the present state of data (within the limits of quality) it seems that there is no consistent evidence of a disturbed respiratory tract function in humans at this dosage level. However, the NOAEC for humans of 50 ppm is not verified until now. That means that the occurrence of morphologic alterations cannot be excluded, even when no clinical symptoms or altered smell functions could be related to MMA concentrations up to 50 ppm.

Relevance of animal data

Besides interspecies differences in the nasal anatomy and breathing physiology a much greater percentage (approximately 50%) of the nasal cavity is lined by olfactory epithelium in the rat than in humans where it is limited to an area of about 500 mm² or 3% of the surface area of the nasal cavity (Harkema and Morgan, 1996). The types of nasal epithelial cells in rats are similar to those of other mammalian species, including humans where olfactory dysfunction is well known in some diseases (Talamo et al., 1994, Nakashima et al., 1991). Although there are species-specific differences in nasal structure and breathing physiology, it is not reasonable to claim a species-specific phenomenon. Currently there is no adequate knowledge on morphological and/or functional lesions of the olfactory mucosa in humans. It is assumed that the principal mechanism of action of vapours per mm² of olfactory mucosa following long-term exposure is similar in rats and in humans.

Currently there is only little knowledge on species differences in the susceptibility of the olfactory mucosa of man and rodents to xenobiotic injury. Repeated dose studies revealed that the rat was more sensitive than the mouse to methyl methacrylate induced nasal lesions, whereas the hamster was not sensitive. In rats, the olfactory epithelium has high activities of esterases and seems to be more sensitive to toxic effects of many esters compared to the respiratory epithelium. Whether the absence of nasal lesions in hamsters is related to differences in the metabolic capacity of the olfactory epithelium is at present unknown. The interpretation of the relevance of these observations with respect to the human health is unclear. Unless the database is insufficient, the most sensitive species should be used for risk assessment procedures.

MMA is cleaved by unspecified carboxylesterases in the respiratory and olfactory epithelium (see Section 4.1.2.1). The preferable site of MMA damage is the olfactory epithelium. Until recently, it was thought that higher carboxylesterase activity in the olfactory epithelium than in the respiratory mucosa which was demonstrated in the rat and human nose (Bogdanffy et al., 1987) is related to a higher susceptibility for rat olfactory tissue to degenerate during MMA exposure. But new data using an *in vitro* gas uptake method on organ explants from rat turbinates or sections of intact nasal tissue from humans demonstrated similar esterase activity of the olfactory sustentacular cells to that of the respiratory epithelial cells (Bogdanffy et al., 1998). Activities of the rat olfactory enzymes were about equivalent to those of humans. This leads to the conclusion that the damage of the olfactory epithelium, which is particularly susceptible to the MMA toxicity, is probably not associated to the metabolic activity of enzymes. Otherwise it would be expected that the respiratory epithelium would show a similar susceptibility. If the metabolic activity is of less relevance, the significance of quantitative interspecies differences is only minor or even absent.

Since there are no consistent results from the studies on the adverse effects in humans especially on the lower respiratory tract, the toxicologic relevance of the effects in experimental animals remains unclear. For health protection purposes animal data were considered predictive for possible adverse effects in exposed people unless no better database is available.

Other information

Effects on smooth muscle, heart and nervous system were confirmed by some additional *in vitro* tests:

- *In vitro* exposure of strips of rat small intestine and guinea pig ileum resulted in reduced spontaneous motor activity and tonus (Mir et al., 1973b). Exposure of isolated rabbit heart

showed an irreversible effect on cardiatic rate (negative chronotrop), force of contraction (negative inotrop), and reduced coronary flow rate (Mir et al., 1973a).

- Dose-dependent effects on the desheated myelinated nerve and on the node of Ranvier of frogs were reported (Böhling et al., 1977). With MMA concentrations above 10 mM the action potential decreased and membrane hyperpolarization was increased. Nerve depolarization by reduced Ca solutions or veratrine pretreatment was reversed by MMA. 50 mM MMA induced a decrease of the Na and K currents in voltage clamp experiments on the node of Ranvier.

No-observed-adverse-effect-level (NOAEL)

From the 2-year inhalation study on chronic toxicity/carcinogenicity on rats (Rohm and Haas, 1979a; Lomax, 1992):

- NOAEC for local effects on the respiratory tract: 25 ppm (equivalent to 0.1 mg/l) 6 h/d, 5 d/wk,
- NOAEC for systemic effects: 100 ppm (equivalent to 0.4 mg/l),
- NOAEL for oral administration: 2,000 ppm in drinking water (equivalent to 200 mg/kg bw/d) 2-year chronic toxicity study on rats (Borzelleca, 1964).

Although there are indications on possible adverse effects outside the respiratory tract, they were observed at very high concentrations which are not considered to be relevant for prolonged exposure of humans. Nonneoplastic findings from animal carcinogenicity studies (Rohm and Haas, 1979a; Lomax et al., 1997) did not reveal any serious effect up to concentrations of 400 ppm methyl methacrylate.

4.1.2.7 Mutagenicity

Bacterial systems

Bacterial gene mutation tests with methyl methacrylate were negative with and without S-9 mix in Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 (Zeiger et al., 1987; Waegemaekers and Bensink, 1984; Lijinsky and Andrews, 1980; Hachiya et al., 1982; Barsky, 1975). Pre-incubation methodology – which is appropriate for volatile substances – was used for doses up to 10,000 µg/plate by Zeiger et al. (1987), Waegemakers and Bensink (1984; only TA100), for doses up to 4,700 µg/plate by Hachiya et al. (1982) and for doses up to 1,000 µg/plate by Lijinsky and Andrews (1980). Standard-plate methodology was employed for doses up to 10,000 µg/plate by Waegemakers and Bensink (1984; five strains), by Lijinsky and Andrews (1980) and Barsky (1975).

Poss et al. (1979) reported on a gene mutation assay with Salmonella typhimurium TM677 in which forward mutations to azaguanine resistance were analysed. With a pre-incubation methodology, doses ranging from 10 to 100 mmol/l were tested with and without S-9 mix. The result was negative in absence of S-9 mix. In presence of S-9 mix, a weak effect was obtained: in the negative control 6 to 8 mutants per 10^5 surviving bacteria were found, at 100 mmol/l mutation frequencies were approximately 16 to 24 mutants per 10^5 surviving bacteria, accompanied by approximately 10% survival. This finding is evaluated as equivocal.

In vitro systems with mammalian cells

In a cytogenetic test with CHO cells induction of chromosomal aberrations was bound to high doses which are assumed to be strongly cytotoxic (Anderson et al., 1990). With S-9 mix treatment was for 2 h followed by 8 to 10 h recovery. Doses up to 1,600 µg/ml were negative, at 5,000 µg/ml the frequency of aberrant cells was 30%; only one experiment was performed. Without S-9 mix, treatment time was 8 hours with 2.0 to 2.5 h recovery. Doses up to 500 µg/ml were negative, at 1,600 and 3,000 µg/ml aberration frequencies ranging from 5 to 10% were found. Data on cytotoxic effects were not given, however, it can be assumed from the data presentation and the general approach of the authors that the highest doses tested led to strong cytotoxic effects, see also data from further mammalian cell culture assays. Thus, methyl methacrylate seems to be a high toxicity clastogen, i.e., the induction of chromosomal aberrations is bound to highly toxic doses.

According to Moore et al. (1988) methyl methacrylate induced chromosomal aberrations in L5178Y mouse lymphoma cells in the absence of S-9 mix; no test was run in presence of S-9 mix. After 4-h treatment with doses ranging from 1,000 to 3,000 µg/ml and 14-h recovery aberration frequencies between 16 and 39% were recorded without dose-effect relationship. In the negative control, an unacceptable high "spontaneous" frequency of 15% aberrant cells was found. Furthermore, during the recovery period cells were exposed to the (co-)clastogen BrdUrd. Information on cytotoxic effects was not given within this assay. In a mouse lymphoma assay which was run in parallel under very similar conditions relative survival was approximately 20% to 30% for a dose of 2,202 µg/ml and decreased to 12% at 3,000 µg/ml. Altogether, this finding is of low reliability and significance.

In parallel to the chromosomal aberration test with L5178Y cells (Moore et al., 1988) an *in vitro* micronucleus test was conducted using the CB technique (cytokinesis block by exposure to cytochalasin B). Using this non-standard methodology, at 8 doses ranging from 2,202 to 3,000 µg/ml micronucleus frequencies from 1.2% to 2.2% were observed without dose-effect relationship (negative control 0.9%). Information on cytotoxic effects was not given within this assay. In a mouse lymphoma assay which was run in parallel under very similar conditions relative survival was approximately 20% to 30% for a dose of 2,202 µg/ml and decreased to 12% at 3,000 µg/ml. The finding is evaluated as equivocal.

A test for induction of sister-chromatid exchanges (SCE) in CHO cells led to a marginally positive finding with and without S-9 mix after treatment for 2 h. With S-9 mix, methyl methacrylate was negative for doses up to 500 µg/ml and marginally positive at 5,000 µg/ml (2/2 experiments) and 1,600 µg/ml (1/2 experiments) with the maximum SCE frequency being 1.4 fold over control level. Without S-9 mix, a weak but dose-dependent increase in SCE frequencies was observed in the dose range 16 to 1,250 µg/ml with the maximum effect being less than a doubling of the negative control level. Data on cytotoxicity were not given. Small increases in SCE frequencies might well be induced by cell cycle delay (prolongation of S-phase) rather than by direct interaction with DNA.

Three mouse lymphoma assays were described for methyl methacrylate.

According to Myhr et al. (1990) methyl methacrylate was weakly positive with and without S-9 mix. With S-9 mix a dose-dependent increase in mutation frequencies was obtained for doses ranging from 250 nl/ml (doubling of control level, 72% relative total growth) to 1,500 nl/ml (more than 3-fold the control level, relative total growth 25%). Without S-9 mix the substance was positive in 1 out of 2 experiments for doses ranging from 500 to 1,000 nl/ml; 1,500 nl/ml led to total toxicity. In a second experiment a weak positive response was obtained at 1,500 nl/ml.

Clear and reproducible increases in mutation frequencies were bound to high toxicity below 20% relative total growth.

Rohm and Haas (1985) reported on a mouse lymphoma assay which was weakly positive in presence and negative in absence of S-9 mix. Without S-9 mix doses up to 100 nl/ml were tested, higher doses led to total toxicity. With S-9 mix methyl methacrylate was positive in the dose range 100 nl/ml to 250 nl/ml, however, clear effects were observed only at doses with high toxicity below 20% relative growth.

In a third mouse lymphoma assay which was only run without S-9 mix, weak effects were obtained for doses producing high toxicity (Moore et al., 1988). According to the authors, 2,000 µg/ml was positive in both experiments (92 and 98 mutants per 10^6 survivors vs. 54 and 68 in the negative controls), relative survival was approximately 20% and 30%; in one experiment the highest dose of 2,499 µg/ml induced 143 mutants at 10% relative survival; in the second experiment the highest dose of 3,100 µg/ml induced 220 mutants with 11% relative survival. The vast majority of induced colonies were small ones (indicating that the genetic effect was derived from clastogenicity and not from gene mutations).

In vivo systems with mammals

Hachiya et al. (1982) reported on a negative bone marrow micronucleus assay with mice. In an acute test methyl methacrylate was given by gavage in doses ranging from 1,130 to 4,520 mg/kg, in a subacute assay daily doses of 1,130 mg/kg were given on 4 consecutive days. All groups consisted of 6 animals, sampling was done 24 h after (last) administration. There was no increase in the frequency of micronucleated polychromatic erythrocytes. The percentage of reticulocytes from all bone marrow cells was not affected; data on general toxicity were not given.

Three bone marrow chromosomal aberration tests with rats led to inconclusive findings.

Fedyukov and Egorova (1991) tested the effect of intraperitoneal administrations of 650 to 1,300 mg/kg methyl methacrylate (single exposure) or 650 mg/kg in a subacute test with 2 administrations per week for 2, 4, 6 or 8 weeks. The acute LD_{50} is given as 2,600 mg/kg, further toxicity data were not described. Five animals were used per group, 50 metaphases per animal were analyzed. In the acute test methyl methacrylate was negative for doses of 650 and 900 mg/kg, with 1,300 mg/kg an aberration frequency of 17.5% was found (negative control, 1.8%; no mention whether gaps were included or not). In the subacute test positive effects are described for treatment times of 2 and 4 weeks (12. 0% and 7.2% aberrant cells), negative effects occurred at treatment times of 6 and 8 weeks. There is no plausible explanation for this unusual time-effect relationship. Therefore, the findings are of relatively low reliability.

Two chromosomal aberration tests were conducted by ICI (1976a; 1979) investigating the effect of inhalation exposure to methyl methacrylate for doses ranging from 100 to 9,000 ppm. In both tests acute exposure was for 2 h (sampling 24 h after treatment) and subacute exposure for 5 h a day on 5 consecutive days (sampling 24 h after last treatment). Data on toxicity were not given. Group sizes varied from 2 to 9; as far as possible 50 metaphases were analysed per animal. The first study was negative for chromosomal aberration frequencies when – as usual – gaps were excluded. Including gaps and combining two acute experiments conducted independently some increases in aberration frequency were statistically significant. In the second study frequencies of chromosomal aberrations excluding gaps were not given. Including gaps increases were recorded at some experimental entries. Furthermore, combined data on chromosomal aberration frequencies exclusively gaps from both studies were given, then weak increases were obtained for 400 and 700 ppm in the acute study (not for 100, 1,000 or 9,000 ppm) and 9,000 ppm in the

subacute study. Both studies suffer from inadequate description; esp. the second study demonstrates severe methodological problems, e.g., analysis of 50 metaphases was not possible for 10 out of 27 animals in the acute and 10 out 26 in the subacute test. Altogether, a clear conclusion cannot be drawn from theses studies.

A dominant lethal assay on male mice was negative after inhalation exposure to doses ranging from 100 to 9,000 ppm (ICI, 1976b). Specific data on toxicity were not given, however, in the 9,000 ppm group 6 out 20 males died. Treated males were mated to 2 females each for 8 periods of 1 week each, females were killed 13 days after assumed dates of fertilization. There was no significant increase in dominate lethal mutations.

Studies in humans

In two studies the effect of exposure of male workers to methyl methacrylate was investigated by use of cytogenetic methods with peripheral lymphocytes.

Seiji et al. (1994) investigated 38 subjects exposed to methyl methacrylate with respect to chromosomal aberrations and SCE. The exposure concentration was 7.35 ppm for 8 hours per day (geometric mean, range 0.9 to 71.9 ppm); the exposure period was not given. A control group consisted of 38 non-exposed persons, the smoking habit was considered. For chromosomal aberrations a clearly negative result was obtained, with respect to SCE a marginal increase was found (6.11 vs. 4.90 SCE per cell), however, this effect was considered to be age-related (and not dependent on MMA exposure).

Marez et al. (1991) reported on SCE frequencies of 31 male workers from 4 factories with mean daily exposures of 2.71, 18.5, 0.70 and 21.6 ppm, individual exposure periods varied from 2.1 to 22.14 years. As compared to negative control groups negative results were found for the whole group of 31 workers as well as for the 4 sub-groups representing different factories. However, in a sub-group of 6 persons exposed to MMA peaks ranging from 114 to 400 ppm a weak increase was found (10.0 vs. 7.48 SCE per cell). According to the authors this effect is due to a low number of cells with high SCE frequencies (hfc). Since negative results were obtained for all pre-defined groups (total of 31 workers and workers from each of the 4 factories), the weak effect described for the 6 persons exposed to high MMA peaks is not considered to be meaningful.

Summary of mutagenicity data and conclusion

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 the negative dominant lethal assay indicate that this potential is probably not expressed *in vivo*.

4.1.2.8 Carcinogenicity

Experimental animal data

Inhalation

The combined chronic toxicity and carcinogenicity study on methyl methacylate of Rohm and Haas (1979a, reevaluated by Lomax, 1992) reported in Section 4.1.2.6 did not reveal any significant incidence of tumors or increase of tumor incidence. One male each out of a total of 49, respectively 47 males exposed to 100 and 400 ppm methyl methacrylate had a small solitary polypoid mass attached to the lateral wall of one side of the anterior nasal cavity. Both masses were composed of well-differentiated pseudoglandular structures arising from respiratory epithelium diagnosed as adenomas. Both animals had chronic inflammation of the respiratory epithelial region. An association of the nasal adenomas to methyl methacrylate inhalation was considered to be unlikely, because the incidence was not significantly increased in comparison to controls without any nasal tumor and the findings were not confirmed by other studies. However, historical data show that adenomas from respiratory epithelium are very rare tumors in rats with a spontaneous rate of 0-0.1% for F344 male and female rats (Haseman et al., 1990).

Groups of 50 male F344/N rats were exposed to methyl methacrylate (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 hours a day, 5 days a week for 102 weeks (NTP, 1986; Chan et al., 1988). Animals were killed at 111-112 weeks (rats) or 113-114 weeks (mice) of age. No significant differences of the survival rates were observed between any groups of rats and 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 with groups of 53-56 males and 56-59 females 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 (no interim sacrifice). At the high-dose, body weight decreased and mortality increased in high dose males (Rohm and Haas, 1979c, cited from Chan et al. 1994; Lomax et al., 1997). After week 60, males exposed to 400 ppm and to 25 ppm had significantly lower body weight during some weeks. There were no clinical signs or hematological effects attributable to exposure to methyl methacrylate at either the 52- or 78- week sampling times. No gross hematological changes indicative for a possible exposure-related effect were observed.

Oral

An early 2-year chronic study on 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 gelatin 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.

This studies on 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 methyl methacrylate, low percentages of ethyl acrylate (EA) and volatile by-products of the methyl methacrylate 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 methyl methacrylate 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 (1994) colorectal cancer was as expected (17 observed deaths versus 16.9 expected) and respiratory cancer mortality 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.

Conclusion on carcinogenicity

There is no relevant concern on carcinogenicity in humans and animals. Epidemiology data on increased tumor rates in exposed cohorts were of limited reliability and cannot be related to MMA as the solely causal agent. Therefore there are no reasons to assume that MMA should be considered to be carcinogenic in humans.

4.1.2.9 Toxicity for reproduction

Studies in animals

Impairment of fertility

At present no guideline concerning generation studies or fertility studies are available for methyl methacrylate.

Data of limited relevance for the evaluation of possible fertility impairment can be obtained from a dominant lethal study. Groups of 20 male CD-1 mice were exposed 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, 1976b). However, the exposure period of 5 days is too short, in view of the length of the spermatogenesis cycle in mice (35 days).

Developmental toxicity

Methyl methacrylate has been tested in a series of developmental toxicity studies in rats and rabbits.

In a developmental toxicity study according to OECD 414 and conducted in compliance with GLP standards (Rohm and Haas, 1991; Solomon et al., 1993) 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/m^3) for 6 hr/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 euthanized and the thoracic and abdominal cavities were examined for gross changes. Each uterus was weighed and corpora lutea, implantation sites and resorptions were counted. 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 concentration 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 groups 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 of fetal toxicity was evident and no increase in the incidence in the 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 on 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 of late resorptions in only one experiment was observed. They derived a NOAEL of 100 ppm for methyl methacrylate from their results (ICI, 1977b). This study, however, suffers from methodological difficulties (insufficient randomization of test animals, insufficient test protocol, poor documentation of results), so that the authors' interpretations of their 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 vapor (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 g.d. 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, 1976c). 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 was observed at the top dose only. There were no increases in soft tissue or skeletal abnormalities.

Studies in humans

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 in comparison to those involved in workplace concentrations of <10 mg/m^3 or to a not further described nonexposed control group. The evaluation of a total of 319 deliveries resulted in the finding of a higher rate of late abortions and of complications during pregnancy for those which had been assigned to the higher workplace concentrations. According 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 of 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 risk assessment.

Sexual disorders (not further specified) in male and female workers occupationally exposed to both methyl methacrylate and to 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 risk assessment.

In Germany methyl methacrylate is assigned to the MAK-pregnancy category "C" (DFG, 1998) denoting that there is no fear of a risk for adverse developmental effects when workplace conditions are kept to the MAK-value (maximum workplace concentrations) which is for methyl methacrylate: 210 mg/ m³ (DFG, 1998).

Conclusion on toxicity for reproduction

The available human data on sexual disorders in male and female workers are not considered for risk assessment of reproductive toxicity due to the uncertain validity of these studies.

Definite assessment of possible impairment of fertility will be provided from a 2-generation inhalation study planned in the USA for the near future. At present only data of limited value from a dominant lethal study with short-term inhalation exposure are available. With this study design methyl methacrylate did not reveal any effect on male fertility in mice when animals had been exposed to up to 9,000 ppm for a period of 5 days before mating.

As for developmental toxicity investigations, from a series of studies following inhalation exposure the most definitive study is that of Solomon et al. (1993), conducted to a rigorous protocol in accordance with current OECD guideline and under GLP conditions. No teratogenicity, embryotoxicity or fetotoxicity has been observed at exposure levels up to and including 2,028 ppm (8,425 mg/m^3). The studies using the intraperitoneal route of administration that produced some inconsistent results, are of questionable significance, also since this route of administration is not considered to be an appropriate or relevant route of exposure.

4.1.3 Risk characterisation

4.1.3.1 General aspects

Methyl methacrylate is a water-soluble substance showing remarkable volatility. After oral or inhalatory administration, methyl methacrylate is rapidly absorbed and distributed. Methyl methacrylate can be absorbed through human skin, absorption being enhanced under occluded conditions. Toxicokinetics seem to be similar in man and experimental animal. It may be concluded that the substance is metabolized via physiological pathways entering into the citric acid cycle.

After arthroplasty using methyl methacrylate-based cements, exhalation of unchanged ester seems to be of major importance, while after i.v., i.p., or oral administration metabolism occurs to a greater extent. After inhalatory exposure to rats 10 to 20% of the substance is deposited in the upper respiratory tract where it is metabolized. Experiments with ^{14}C labelled methyl methacrylate show that 80 to 90% of the radioactivity was found in expired air. Thus the main route of elimination of methyl methacrylate and its metabolites is exhalation in the breath, urinary excretion is of minor importance, slight faecal excretion also occurs.

Acute toxicity of methyl methacrylate by the oral, dermal, and inhalation routes is low as judged by several reported tests with different species: the oral LD_{50} for rats, mice, and rabbits is found to exceed 5,000 mg/kg body weight. Acute inhalation toxicity for rats and mice is described by LC_{50} values of >25 mg/l/4 hours. Acute dermal toxicity is reported for rabbits to exceed 5,000 mg/kg.

Methyl methacrylate causes irritation if inhaled and severe skin irritation in humans and animals. It produces only slight irritation to the conjunctivae of eyes. Skin and respiratory irritation are reported for subjects exposed to monomer methyl methacrylate.

Subjects occupationally exposed to monomeric methyl methacrylate showed allergic contact dermatitis. There is no convincing evidence that methyl methacrylate is a respiratory sensitiser in humans. Skin sensitising properties for the substance are demonstrated in experimental animals.

Assessment of the available animal toxicological data indicates that the lead effect caused by methyl methacrylate is a degeneration of the olfactory region of the nose being the most sensitive target tissue. For this effect a NOEC of 104 mg/m^3 (= 25 ppm) in a two-year inhalation study in rats was identified but only slight effects on the olfactory tissues have been observed at 416 mg/m^3 (=100 ppm). The animal data showing degeneration/atrophy/replacement of the olfactory epithelium are considered to be relevant for predicting possible health effects on humans.

The most sensitive adverse effect considered to be compound-related was lower final body weights in rats at MMA doses of 400 ppm and higher and in mice at 500 ppm and higher. In subchronic inhalation studies systemic toxic effects were seen in rats >1,000 ppm, respectively in mice >500 ppm including degenerative and necrotic lesions in liver, kidney, brain, and atrophic changes in spleen and bone marrow. These effects were not seen in chronic studies up to 1,000 ppm. Higher mortality rates were seen in rats subchronically exposed to high doses of MMA (>2,000 ppm), however early deaths in mice were seen in a subacute study at doses of 500 ppm and higher.

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. The negative *in vivo* micronucleus test and the negative dominant lethal assay indicate that this potential may not be expressed *in vivo*.

Studies on experimental animals indicate that methyl methacrylate is not an animal carcinogen. There is inadequate evidence in humans for the carcinogenicity of MMA. At the moment MMA is not considered a carcinogen to humans.

In a dominant lethal study in mice with only short-term exposure no adverse effects on fertility and preimplantation development were detected; no effects on reproductive organs in experimental animals have been observed. More definite information related to fertility will be provided from a 2-generation inhalation study planned in the USA in the near future. From the available developmental toxicity studies it can be concluded that there is at present no concern regarding possible developmental effects of methyl methacrylate (NOAEC 2,028 ppm).

There are many reports, which describe adverse effects on human health in occupationally exposed people. Considering the lack of important details and the unclear exposure situation, it is often not possible to link these effects only to methyl methacrylate or to particular methyl methylacrylate concentrations. The health studies in workers indicate that the main effect in humans is local irritation (skin, respiratory tract) after acute exposure. In certain individuals skin contact may result in contact allergic dermatitis and cross reactions to other esters of acrylic and methacrylic acid. The pungent, characteristic odor of the substance (odour threshold: 0.208 – 1.4 mg/m^3 (0.05-0.34 ppm) acts as a warning for limiting the exposure.

Some studies with limited validity on the health situation of workers exposed to methyl methacrylate are available. From studies with limited reliability there is some concern that effects on the respiratory tract, the central and peripheral nervous system, the cardiovascular system, the endocrine system, and the gastrointestinal system may be associated to the repeated exposures to methyl methacrylate.

At the moment, there are no valid data which indicate any serious health effect on humans up to 50 ppm of methyl methacrylate vapour concentration. At the present state of data (within the limits of quality) it seems that there is no consistent evidence of a disturbed lung function in humans at this dosage level.

4.1.3.2 Workers

4.1.3.2.1 General remarks on calculations and extrapolations relevant for workplace risk assessment

The toxicity profile of methyl methacrylate is mainly determined by its tissue damaging properties at the site of entry. The concentration-dependent severity of skin and airways irritation is thus the main subject of quantitative evaluation during risk assessment at the workplace.

For methyl methacrylate short and long-term inhalation data from rats and mice are available. Thus data adjustment for the purposes of workplace risk assessment concentrates on species extrapolation from animal data to humans. One main discussion point in the past addressed the question whether rats are more sensitive to lesions in the olfactory region of the nose than humans according to species differences in site-specific metabolic capacity and local air-flow characteristics.

For methyl methacrylate a PBPK-model was developed, which allows to address local concentrations in the nose of different species but until now the model is not sufficiently validated for a founded quantification of species differences between rats and humans. As outlined during the effects assessment in Section 4.1.2 for the time being data from rat inhalation

studies are thus judged to be relevant for humans. This includes systemic toxicity as well as local effects. Calculation of MOS values therefore does not include species specific adjustment factors.

MOS values concerning inhalation toxicity are calculated by directly using experimental data. Nevertheless they can be considered as adjusted to humans. The situation is different for dermal MOS values which could not be calculated directly because dermal data are missing. Thus route-to-route adjustment was necessary.

4.1.3.2.2 Summary of effects relevant for workplace risk assessment

Table 4.10 Summary of effects relevant for occupational risk assessment of MMA

	Inhalation	Dermal
Acute toxicity	LC50 (rat, 4h): 30,000 mg/m³ (ca 7,220 ppm)	LD50 (rabbits): greater than 5,000 mg/kg bw
Irritation/Corrosivity	Upper respiratory tract irritant. NAEC [1)] (acute irritation effects): 25 ppm (100 mg/m³)	Formulations containing ≥5 % MMA: irritating to the skin
Sensitisation	Isolated cases of asthma reported, but no convincing evidence that MMA is acting as a respiratory sensitiser.	Formulations containing ≥1% MMA: sensitising to the skin
Repeated dose toxicity: Local	NAEC [1)] (degeneration of olfactory epithelium) 25 ppm (100 mg/m³)	see Irritation/Corrosivity
Systemic	NAEC[1)] (retardation of growth) 100 ppm (410 mg/m³) Early deaths at doses of 500 ppm (2,050 mg/m³) and higher	NAEL[2)] (adjusted) 4,100 mg/person/day
Mutagenicity	Not considered to be mutagenic *in vivo*	
Carcinogenicity	Not considered to be carcinogenic	
Reproductive toxicity: Fertility impairment	2-generation study in preparation at present no indication for fertility impairment	
Developmental toxicity	NOAEC from animal studies 2,028 ppm (8,300 mg/m³)	

[1)] Effects observed in animal studies, no special adjustment step for humans necessary
[2)] Inhalation animal data used for adjustment to dermal application route

4.1.3.2.3 Acute toxicity

Inhalation

From single inhalation exposures of rats to air concentrations of about 410 mg/m^3 (100 ppm) for 2 or more hours local effects at the airways are reported. These effects are evaluated in Section *Irritation, inhalation*. The LC_{50}-value (4h) for rats has been reported to be about 30,000 mg/m³

(≈ 7,200 ppm). The value is judged to be directly relevant for human risk assessment purposes considering acute toxicity.

Short-term inhalation exposure is identified during production and further processing in the chemical industry with exposure levels up to 400 mg/m^3 (100 ppm) for an undefined short-time period. In addition during use of casting resins for medical applications and dental laboratories and surgeries short-term inhalation values up to 600 mg/m^3 (150 ppm) are reported. The highest measured shift average value for inhalation exposure (floor coating work, skilled trade sector, 95th percentile, shift average value) is 1,045 mg/m³ (255 ppm).

Based on the LC_{50}-value the lowest MOS value results for floor coating and is calculated to about 30 (30,000/1,045). For short-term inhalation exposure a MOS value of 50 (30,000/600) is derived from the use of casting resins in dental laboratories and surgeries. These high values signal that lethality due to acute inhalation exposure is not anticipated to occur in occupational settings: **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

The acute dermal toxicity (LD_{50}) is reported to exceed 5,000 mg/kg for rabbits. For comparison, oral LD_{50} values for rats, mice and rabbits can be cited, which are reported to be greater than 5,000 mg/kg as well. A dose of 5,000 mg/kg for rabbits corresponds to 2,500 mg/kg for humans based on metabolic rate scaling (adjustment factor: $(70/4):(70/4)^{0.75}$ = 2, with bodyweight human: 70 kg, bodyweight rabbit: 4 kg).

The highest estimated dermal exposure is 840 mg/p/day (=12 mg/kg/d) during floor coating works in the skilled trade area. Comparing this level of exposure with the LD_{50}-values reveals an MOS >200, which indicates that lethality due to occupational skin contact is not anticipated to occur: **conclusion (ii)**.

4.1.3.2.4 Irritation/Corrosivity

Eyes

In contact with the rabbit eye MMA has shown to produce only weak irritation of the conjunctivae, which does not fulfill the criteria for classification and labelling. Eye contact at workplaces is therefore not anticipated to result in relevant irritation: **conclusion (ii)**.

Dermal

MMA has been shown to produce severe skin irritation when tested undiluted on rabbit skin. A 5% methyl methacrylate preparation resulted in skin irritation in human volunteers. From the available data the concentration of a dilution without irritating effects cannot be estimated, but for risk assessment purposes it is assumed that preparations containing ≥5% MMA are irritating to human skin.

Skin contact has to be considered in all working areas. Even in the large-scale chemical industry with a high acceptance of the use of gloves dermal exposure has to be anticipated because most producers of MMA give no information about appropriate glove types or recommend unsuitable glove materials with limited protection. In industrial areas and skilled trade applications it cannot

be excluded that gloves are not worn and that immediate dermal contact occurs. It is concluded, that in all cases with skin contact against concentrated MMA or preparations containing ≥5% MMA skin irritation at the workplace might occur.

Skin irritation is a reversible adverse effect which can be immediately recognised, experienced and prevented. Contrary to the above risk characterisation conclusion (iii) is therefore not recommended because the resulting risks by their nature are considered to be of lower concern relative to other toxicological endpoints and do not require specific risk reduction measures beyond those already applied: **conclusion (ii)**.

Inhalation

From human case reports it is demonstrated, that acute occupational exposure to high air concentrations of methyl methacrylate might result in signs of airway irritation. An air concentration without irritating effects cannot be derived from this data.

In rats single inhalation exposures to 410 mg/m^3 (100 ppm) for 2 or more hours resulted in irritating effects in the respiratory tract. In this acute study a level without effects was not identified, but studies with repeated application indicate that the irritation threshold for short-term exposure does not significantly differ from that for long-term exposure. Therefore the chronic irritation threshold of 25 ppm (100 mg/m³) is used as NAEC for the purpose of risk assessment.

From the exposure assessment several scenarios with short-term inhalation are identified (**Table 4.6**) which are compared to the NAEC in **Table 4.12**. In addition exposure situations which are of longer duration throughout a shift but do not occur daily are evaluated in **Table 4.12**.

A range of MOS values from about 20 to 0.1 is calculated for the different exposure scenarios in **Table 4.12**. In each case that exposure levels exceed the inhalation threshold, resulting in MOS values below 1, acute respiratory irritation is anticipated to occur. Because of sufficient information on dose-response-relationship MOS values greater than 1 are not considered of concern (see Section *Repeated dose toxicity, inhalation).*

For the evaluation of risks by acute irritation scenarios with long-term repeated exposures are equally relevant. The evaluation of respiratory irritation for these scenarios is explicitly addressed under Section *Repeated dose toxicity, inhalation* (compare with **Table 4.14**). Consequently **conclusion (iii)** concerning acute respiratory irritation additionally applies for all scenarios that come up with conclusion (iii) in **Table 4.14**. A summary of all exposure scenarios which give rise to conclusion (iii) under the aspect of acute respiratory irritation is listed in detail in **Table 4.11**.

Table 4.11 Scenarios giving rise to conclusion (iii) for acute respiratory irritation

Chemical industry:	(4)	Cast sheet production
	(6)	Production of reactive resins
Industrial area:	(7)	Production of adhesives without LEV
	(8)	Production of paints with and without LEV
	(10)	Use of adhesives without LEV
Skilled trade area:	(14)	Floor coating
Use of casting resins:	(16)	Medical applications
	(17)	Orthopaedic workshops without LEV
	(18)	Dental laboratories and surgeries without LEV
	(20)	Ornamental decoration

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

Table 4.12 Short-term or not daily inhalation scenarios and MOS concerning acute respiratory irritation (NAEC = 100 mg/m³)

Nr [1]	Area of production and use	Duration of exposure	Exposure level [2] [mg/m³]	MOS [3] (local)	Conclusion [4]
Short-term inhalation scenarios					
18	*Use of casting resins* Dental laboratories and surgeries	short term	600 (without LEV)	0.2	iii
16	*Use of casting resins* Medical applications	short term	420	0.2	iii
4	*Chemical industry* Cast sheet production	short term	412	0.2	iii
1	*Chemical industry* MMA production	short term	87	1.1	ii
2	*Chemical industry* PMMA production	short term	79	1.3	ii [4]
18	*Use of casting resins* Dental laboratories and surgeries	short term	42 (with LEV)	2.4	ii
3	*Chemical industry* Transesterification	short term	33	3.0	ii

Table 4.12 continued overleaf

Table 4.12 continued..Short-term or not daily inhalation scenarios and MOS concerning acute respiratory irritation (NAEC = 100 mg/m³)

Nr [1]	Area of production and use	Duration of exposure	Exposure level [2] [mg/m³]	MOS [3] (local)	Conclusion [4]
Inhalation scenarios which are not daily (shift average values)					
14	*Skilled trade sector* Floor coating (20 % MMA)	shift length, not daily	1,045	0.1	iii
20	*Use of casting resins* Ornamental decoration	no information, not daily	83 – 374	1.2 – 0.3	iii
19	*Use of casting resins* Manufacturing of lenses	no information, not daily	4.2 – 42	24 – 2.4	ii
13	*Skilled trade sector* Use of adhesives (bonding small areas) (60 % MMA)	shorter than shift length, not daily	11	9	ii
15	*Skilled trade sector* Use of paints (residual MMA < 0.5 %), Spray painting	2 hours, not daily	5.2 – 10.4	19 – 10	ii

[1] Exposure scenarios according to Table 4.6, further information refer to this table
[2] In the upper part of the table short term values are given, in the lower part shift average values are listed
[3] MOS = NAEC / Exposure level, with NAEC = 25 ppm (100 mg/m³)
[4] MOS <1 leads to conclusion (iii)

4.1.3.2.5 Sensitisation

Dermal

MMA may cause sensitisation by skin contact. This assessment is based on experimental animal data and supported by human experience. The data do not allow to estimate sensitisation potency, thus the concentration of a dilution without sensitising properties cannot be identified, but it is known by the nature of the effect that even low exposures might lead to sensitisation.

According to the concentration limit for classification and labelling it is assumed for risk assessment purposes that preparations containing ≥1% MMA are sensitising to human skin.

Methyl methacrylate and its preparations containing ≥1% MMA are classified and labelled as skin sensitising. However at several workplaces relevant dermal exposure cannot be excluded (see **Table 4.6** and Section *Irritation, dermal)* thus rising the possibility of skin sensitisation by occupational exposure against concentrated MMA or preparations containing ≥1% MMA.

In some exposure scenarios the MMA content of the formulation which leads to skin contact is below 1% or dermal exposure levels are expected to be low for other reasons. These are the only scenarios which do not give rise to concern under the aspect of skin sensitisation. Discussion might be started for scenarios with skin contact which is not repeated daily, but by the nature of the effect intermittent exposures appear to be relevant too.

Allergic contact dermatitis is considered to be a severe health problem. For MMA case reports of skin sensitisation underline the fact that risk reduction measures beyond those already applied have to be considered.

All dermal exposure scenarios except (9), (11), (12), (15): **conclusion (iii)**.

Inhalation

The literature reports isolated cases of asthma in the context of MMA exposure. Substance-specific bronchoconstriction or delayed asthmatic responses respectively were confirmed only in very few cases. Asthmatic reactions seem to be restricted to exposure levels which primarily result in respiratory tract irritation. With reference to Section 4.1.2.5 from the reported data no convincing evidence was found that MMA acts as a respiratory sensitiser in humans.

Scenarios which are considered of concern against the background of primary irritation are described in sSection *Irritation/Corrosivity, inhalation*. Based on the available medical evidence, taking into account the wide use of MMA, a specific risk of respiratory sensitisation at the workplace additional to respiratory irritation is not anticipated to occur: **conclusion (ii)**.

4.1.3.2.6 Repeated dose toxicity

Inhalation, local effects

For the assessment of repeated dose toxicity per inhalation, both animal and human data are available.

The primary effect in experimental animals is respiratory tract irritation and degeneration, the olfactory epithelium of the nasal cavity being the most sensitive target tissue. Comparison of the subacute and chronic rat inhalation studies with methyl methacrylate supports the conclusion that long term inhalation leads to an increase of multiplicity of lesions and locations affected, however the respiratory tract irritation threshold does not substantially change with duration of exposure.

In a 2-year study in rats, a NOAEC of 25 ppm (100 mg/m^3) was established for nasal irritation, only slight adverse effects were observed at 100 ppm (410 mg/m^3). There were no experimental exposure levels between 25 and 100 ppm and therefore it is impossible to be more precise.

The main problem in methyl methacrylate risk assessment is species extrapolation from rodents to humans. Rodents show a nasal anatomy and respiratory physiology different from man. These differences will influence the toxicokinetics of methyl methacrylate in the upper respiratory tract. PBPK modelling suggests that humans are less sensitive than rodents. The PBPK data on methyl methacrylate generated todate are not considered robust enough to be used as a quantitative basis for establishing a human NOEL for nasal effects (see Sections 4.1.2.1, 4.1.2.6 and 4.1.3.2.1).

It should be recognised that human health studies are available for the specific exposure scenario of acrylic cast sheet production in the chemical industry (see scenario 4). These worker health data indicate that exposure levels up to 50 ppm MMA (TWA) are not associated with respiratory symptoms or olfactory dysfunction. Short-term exposure to higher levels of MMA vapour caused increased incidences of cough, throat irritation and mild airway obstruction.

The comparison of the rat and human health data does not point to a substantial difference in species sensitivity. The rat irritation threshold level of 25 ppm or somewhat higher (slight nasal

histopathology at 100 ppm) is not contrary to the human evidence indicating no olfactory or respiratory dysfunction up to 50 ppm.

The worker health data from acrylic cast sheet production nevertheless seem to indicate that the human NAEC is slightly higher than the experimental NOAEC of 25 ppm. However, the relevance of these human health data is not considered to be sufficient to justify the assumption of an overall human NAEC of 50 ppm. Due to the understandable limitations of the human health studies the occurrence of morphological alterations in the upper respiratory tract of exposed workers cannot be excluded with certainty.

Overall assessment of the toxicity of methyl methacrylate places central weight on the experimental animal data. Thus for risk assessment purposes a human NOEL of 25 ppm is assumed. Taking into account the PBPK data and available human health studies the possibility of a human NOEL slightly higher than 25 ppm cannot be totally excluded.

In **Table 4.14** the anticipated human NAEC is compared with the scenario-specific information on long-term inhalation exposure. Since there is considerable knowledge on the toxicity of MMA, MOS values greater than 1 are not considered of concern. There are certain working areas in production and use of MMA where MOS values <1 indicate concern.

Special attention should be given to scenario 4, which describes exposure to methyl methacrylate during acrylic cast sheet production. As outlined and evaluated above, workers involved in acrylic cast sheet production did not experience olfactory or respiratory dysfunction. The exposure level of 148 mg/m³ (90^{th} percentile) for this scenario slightly exceeds the level of 100 mg/m³ which finally is proposed to be used as anticipated human NOEL. **Conclusion (iii)** is reached for scenario 4 because adverse effects other than olfactory or respiratory dysfunction (e.g. morphological changes of nasal epithelium) cannot be excluded with sufficient certainty.

Table 4.13 Scenarios giving rise to conclusion (iii) for repeated dose toxicity, inhalation local effects

Chemical industry:	(4)	Cast sheet production
	(6)	Production of reactive resins
Industrial area:	(7)	Production of adhesives without LEV
	(8)	Production of paints with and without LEV
	(10)	Use of adhesives without LEV
Use of casting resins:	(17)	Orthopaedic workshops without LEV
	(18)	Dental laboratories and surgeries without LEV

Conclusion (iii).

Table 4.14 Long-term inhalation scenarios and MOS concerning chronic respiratory irritation (NAEC = 100 mg/m³)

Nr [1]	Area of production and use	Shift average value (mg/m³)	MOS (local) [2]	Conclusion [3]
7	*Industrial area* Production of adhesives, casting resins and floor coating materials	210 – 420 (without LEV)	0.5 – 0.2	iii
17	*Use of casting resins* Orthopaedic workshops	187 (without LEV)	0.5	iii
4	*Chemical industry* Cast sheet production	148.5	0.7	iii
8	*Industrial area* Production of paints and varnishes	146 (with LEV)	0.7	iii
10	*Industrial area* Use of adhesives in plastics, electronics and glass industry (60 % MMA)	132 (without LEV)	0.8	iii
8	*Industrial area* Production of paints and varnishes	120 (without LEV)	0.8	iii
6	*Chemical industry* Production of reactive resins	119	0.8	iii
18	*Use of casting resins* Dental laboratories and surgeries	110 (without LEV)	0.9	iii
7	*Industrial area* Production of adhesives, casting resins and floor coating materials	21 – 105 (with LEV)	4.8 – 1	ii
10	*Industrial area* Use of adhesives in plastics, electronics and glass industry (60 % MMA)	83 (with LEV)	1.2	ii
17	*Use of casting resins* Orthopaedic workshops	61 (with LEV)	1.6	ii
5	*Chemical industry* Production of adhesives	57	1.8	ii
11	*Industrial area* Use of paints (residual MMA <0.5 %)	21 – 42 (without LEV)	4.8 - 2.4	ii
2	*Chemical industry* PMMA production	28	3.6	ii
18	*Use of casting resins* Dental laboratories and surgeries	6 (with LEV)	17	ii
9	*Industrial area* Use of moulding and extrusion compounds	25.4	3.9	ii
1	*Chemical industry* MMA production	18	5.6	ii
3	*Chemical industry* Transesterification	10	10	ii
11	*Industrial area* Use of paints (residual MMA < 0.5%)	4.2 - 8.4 (with LEV)	24 - 12	ii
12	Industrial area Thermal processing of PMMA	4.6	22	ii
16	Use of casting resins Medical applications	4	25	ii
11	*Industrial area* Use of paints (residual MMA < 0.5%)	1	100	ii
15	*Skilled trade area* Use of paints (residual MMA < 0.5%)	1	100	ii

[1] Exposure scenarios according to Table 4.6, for further information refer to this table
[2] MOS = NAEC / Exposure level, with NAEC = 25 ppm (100 mg/m³)
[3] MOS <1 leads to conclusion iii

Inhalation, systemic effects

From repeated inhalation studies in rats and mice the most sensitive toxic effect besides the effect in the respiratory tract is reported to be dose-dependent growth retardation starting at air concentrations of 400 ppm (1,640 mg/m^3) in female rats. Beginning with exposures of 500 ppm for just a few days lethality occurred in mice and at higher air concentration also in rats. In other studies however lethality was not observed to the same extent. The NOAEC for systemic effects was estimated to 100 ppm (410 mg/m^3, see Section 4.1.2.6).

For risk assessment purposes a systemic NAEC of 100 ppm (410 mg/m^3) is anticipated to be relevant for humans (compare with Section 4.1.3.2.1). In **Table 4.15,** the MOS values for systemic effects by repeated inhalation are calculated. Long-term exposure scenarios are used as outlined in **Table 4.6**. In addition in the lower part of **Table 4.15** shift average values are included which occur repeatedly but not every day. Assessment of these scenarios seems justified with reference to the time schedule of the early deaths in the animal studies.

Table 4.15 Inhalation exposure scenarios and MOS values concerning systemic toxicity by repeated exposure (NAEC = 410 mg/m^3)

Nr [1]	Area of production and use	Shift average value [2] (mg/m^3)	MOS [3] (systemic)	Conclusion [4]
Long-term inhalation scenarios				
7	*Industrial area* Production of adhesives, casting resins and floor coating materials	210 – 420 (without LEV)	1.9 – 1	iii
17	*Use of casting resins* Orthopaedic workshops	187 (without LEV)	2.2	iii
4	*Chemical industry* Cast sheet production	148.5	2.8	iii
8	*Industrial area* Production of paints and varnishes	146 (with LEV)	2.8	iii
10	*Industrial area* Use of adhesives in plastics, electronics and glass industry (60% MMA)	132 (without LEV)	3.1	ii
8	*Industrial area* Production of paints and varnishes	120 (without LEV)	3.4	ii
6	*Chemical industry* Production of reactive resins	119	3.4	ii
18	*Use of casting resins* Dental laboratories and surgeries	110 (without LEV)	3.7	ii
7	*Industrial area* Production of adhesives, casting resins and floor coating materials	21 – 105 (with LEV)	20 – 3.9	ii
10	*Industrial area* Use of adhesives in plastics, electronics and glass industry (60% MMA)	83 (with LEV)	4.9	ii
17	*Use of casting resins* Orthopaedic workshops	61 (with LEV)	6.7	ii

Table 4.15 continued overleaf

Table 4.15 continued Inhalation exposure scenarios and MOS values concerning systemic toxicity by repeated exposure (NAEC = 410 mg/m³)

Nr [1]	Area of production and use	Shift average value [2] (mg/m³)	MOS [3] (systemic)	Conclusion [4]
5	*Chemical industry* Production of adhesives	57	7.2	ii
11	*Industrial area* Use of paints (residual MMA <0.5%)	1 – 42 (without LEV)	20 - 9.8	ii
2	*Chemical industry* PMMA production	28	15	ii
18	*Use of casting resins* Dental laboratories and surgeries	27	15	ii
9	*Industrial area* Use of moulding and extrusion compounds	25.4	16	ii
1	*Chemical industry* MMA production	18	23	ii
3	*Chemical industry* Transesterification	10	41	ii
11	*Industrial area* Use of paints (residual MMA <0.5%)	4.2 - 8.4 (with LEV)	98 - 49	ii
18	*Use of casting resins* Dental laboratories and surgeries	6 (with LEV)	68	ii
12	*Industrial area* Thermal processing of PMMA	4.6	89	ii
16	*Use of casting resins* Medical applications	4	103	ii
11	*Industrial area* Use of paints (residual MMA <0.5%)	1	410	ii
15	*Skilled trade area* Use of paints (residual MMA <0.5%)	1	410	ii
Inhalation scenarios with repeated exposure but not daily				
14	*Skilled trade area* Floor coating (20% MMA)	1,045	0.4	iii
20	*Use of casting resins* Ornamental decoration	83 - 374	4.9 - 1.1	iii
19	*Use of casting resins* Manufacturing of lenses	4.2 - 42	98 - 9.8	ii
13	*Skilled trade area* Use of adhesives (bonding small areas) (60% MMA)	11	37	ii
15	*Skilled trade area* Use of paints (residual MMA <0.5%), Spray painting	5.2 - 10.4	79 - 39	ii

[1] Exposure scenarios according to Table 4.6, further information refer to this table
[2] In the upper part of the table long-term inhalation scenarios are given, in the lower part inhalation scenarios with repeated but not daily exposure are listed, in each case: shift average values
[3] MOS = NAEC / Exposure level, with NAEC = 100 ppm (410 mg/m³)
[4] MOS <3 leads to conclusion iii

Discussion could be started on the level of margin of safety that should give rise to concern. For respiratory tract irritation with a NAEC of 25 ppm and marginal local effects starting at 100 ppm a MOS of less than 1 was judged critical. Relative to this the difference between NAEC and LAEC for systemic toxicity (100 ppm and 400 ppm, respectively) at the first view seems similar, however at air concentrations of 500 ppm early deaths occurred which cannot be excluded to be substance related und thus have to be taken into consideration. In summary MOS values below 3 are judged to be of concern for systemic toxicity in occupational risk assessment.

The highest value for chronic inhalation exposure is estimated for floor coating in the skilled trade area with an exposure level of 1,045 mg/m³ resulting in a MOS value of about 0.4 thus clearly leading to concern even though exposure is not reported to be daily. For details concerning the other scenarios at risk compare with **Table 4.15.**

Table 4.16 Scenarios giving rise to conclusion (iii) for repeated dose toxicity, inhalation systemic effects

Chemical industry:	(4)	Cast sheet production
Industrial area:	(7)	Production of adhesives without LEV
	(8)	Production of paints with LEV
Skilled trade area:	(14)	Floor coating
Use of casting resins:	(17)	Orthopaedic workshops without LEV
	(20)	Ornamental decoration

Conclusion (iii).

Dermal, local effects

MMA is irritating to the skin. Experimental data describing skin effects after repeated dermal application are not available. Occasionally from human case reports paraesthesia of fingers or finger tips have been reported especially in connection with skin sensitisation. This effect is not further substanciated by experimental data and for the time being its association with MMA is unclear. Therefore it cannot be used as basis for risk assessment.

Acute skin irritation effects are evaluated in Section *Irritation/Corrosivity, dermal.* A different or additional risk concerning local dermal effects after repeated exposure is not anticipated: **conclusion (ii)**.

Dermal, systemic effects

Dermal animal studies of sufficient validity are not available. From a 2-year drinking water study in rats the highest dose of 200 mg/kg/d is reported as NOAEL. This dose corresponds to a NAEL of 50 mg/kg/d for humans based on metabolic rate scaling (adjustment factor: $(70/0.25):(70/0.25)^{0.75} = 4$, with bodyweight human: 70 kg, bodyweight rat: 0.25 kg).

For comparison the systemic NOAEC of 100 ppm (410 mg/m^3) of the 2-year inhalation study is used to calculate a corresponding daily dose for humans, assuming a breathing volume of 10 m^3 per shift. The so determined NAEL results in 59 mg/kg/d (NAEC · respiratory volume / body weight = 410 mg/m^3 · 10 m^3 / 70 kg). At higher air concentrations inhalation studies revealed growth retardation (400 ppm) and early deaths (500 ppm), compare with Section *Inhalation, systemic effects*.

Dermal absorption seems to be significantly lower than oral absorption or absorption via the respiratory tract. According to Section 4.1.2.1 only a very small amount of the applied dose (0.56%) penetrated the skin under unoccluded conditions. The actual dermal NAEL may thus be substantially higher as the above-calculated values. For risk assessment purposes the NOAEC from the inhalation study is used to calculate a dermal NAEL of 4,100 mg/p/d (410 mg/m^3 · 10 m^3).

This NAEL is compared to the level of repeated dermal exposure (for MOS values see **Table 4.17**). Exposures which occur repeatedly but not every day are included in the assessment because of the time schedule of the early deaths in the inhalation studies. On the background of systemic toxicity by inhalation a MOS of 3 was considered to be critical (see Section *Repeated dose toxicity, Inhalation, systemic effets*).

The highest level of repeated dermal exposure is estimated to be 840 mg/p/day during floor coating, more common scenarios reach maximally 420 mg/p/d (e.g. in the chemical industry and in the industrial area). The according MOS values calculate to 4.9 and 9.8 respectively. Taking into account that the actual MOS values are probably substantially higher than calculated because dermal absorption is most likely lower than assumed this values do not give rise to concern. Similarly all the other scenarios with lower exposure levels are not anticipated to result in systemic effects by mere skin contact: **Conclusion: (ii)**.

Combined exposure (inhalation and dermal contact)

In addition to route-specific risks health effects due to combined exposure (inhalation and dermal contact) are to be assessed. Concerning local effects combined exposure is not assumed to contribute to an increase in risk levels either at the respiratory tract or at the skin. For systemic effects however a combined risk assessment is meaningful.

The MOS values for combined exposure can be calculated according to the formula (Darschnik et al., 1998):

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

There are several workplace activities which lead to combined dermal and inhalation exposure. All scenarios with long-term inhalation are evaluated under the aspect of combined risks with the exception of those for which dermal exposure is reported to be low (i.e. use of moulding and extrusion compounds and thermal processing of PMMA). In addition the assessment includes exposures which occur repeatedly but not every day because of the time schedule of the early deaths in the repeated dose studies (see Section *Repeated dose toxicity*, *Inhalation, systemic effects*). The results are presented in **Table 4.17.**

Table 4.17 MOS values concerning systemic toxicity after repeated exposure for combined exposure scenarios

Nr [1]	Area of production and use	MOS [2] inhalation	MOS [3] dermal	MOS [4] combined	Conclusion [5]
Long-term inhalation scenarios					
7	*Industrial area* Production of adhesives, casting resins and floor coating materials	1.9 – 1 (without LEV)	98 - 9.8	1.9 -0.9	iii
17	*Use of casting resins* Orthopaedic workshops	2.2 (without LEV)	120 - 12	2.2 - 1.9	iii
4	*Chemical industry* Cast sheet production	2.8	98 - 9.8	2.7 - 2.2	iii
8	*Industrial area* Production of paints and varnishes	2.8 (with LEV)	98 - 9.8	2.7 - 2.2	iii
10	*Industrial area* Use of adhesives in plastics, electronics and glass industry (60% MMA)	3.1 (without LEV)	325 - 33	3.1 - 2.8	ii
8	*Industrial area* Production of paints and varnishes	3.4 (without LEV)	98 - 9.8	3.3 - 2.5	ii
6	*Chemical industry* Production of reactive resins	3.4	98 - 9.8	3.3 - 2.5	ii
18	*Use of casting resins* Dental laboratories and surgeries	3.7 (without LEV)	1,025 - 103	3.7 – 3.6	ii
7	*Industrial area* Production of adhesives, casting resins and floor coating materials	20 - 3.9 (with LEV)	98 - 9.8	17 - 2.8	ii
10	*Industrial area* Use of adhesives in plastics, electronics and glass industry (60% MMA)	4.9 (with LEV)	325 - 33	4.8 - 4.3	ii
17	*Use of casting resins* Orthopaedic workshops	6.7 (with LEV)	120 - 12	6.3 - 4.3	ii
5	*Chemical industry* Production of adhesives	7.2	98 - 9.8	6.7 - 4.2	ii
11	*Industrial area* Use of paints (residual MMA < 0.5%)	20 - 9.8 (without LEV)	630 - 126	19 - 9	ii
2	*Chemical industry* PMMA production	15	98 - 9.8	13 - 5.9	ii
18	*Use of casting resins* Dental laboratories and surgeries	15	1,025 - 103	15 - 13	ii
1	*Chemical industry* MMA production	23	98 - 9.8	19 - 6.9	ii
3	*Chemical industry* Transesterification	41	98 - 9.8	29 - 7.9	ii
11	*Industrial area* Use of paints (residual MMA < 0.5 %)	98 – 49 (with LEV)	630 - 126	85 - 35	ii
18	*Use of casting resins* Dental laboratories and surgeries	68 (with LEV)	1,025 - 103	64 - 41	ii

Table 4.17 continued overleaf

Table 4.17 continued MOS values concerning systemic toxicity after repeated exposure for combined exposure scenarios

Nr [1]	Area of production and use	MOS [2] inhalation	MOS [3] dermal	MOS [4] combined	Conclusion [5]
16	*Use of casting resins* Medical applications	103	244	103 - 72	ii
11	*Industrial area* Use of paints (residual MMA < 0.5%)	410	630 - 126	248 - 96	ii
15	*Skilled trade area* Use of paints (residual MMA < 0.5%)	410	630 - 126	248-96	ii
Inhalation scenarios with repeated exposure but not daily					
14	*Skilled trade area* Floor coating (20 % MMA)	0.4	24 - 4.9	0.4 - 0.4	iii
20	*Use of casting resins* Ornamental decoration	4.9 - 1.1	120 - 12	4.7 - 1	iii
19	*Use of casting resins* Manufacturing of lenses	98 - 9.8	1,025 - 103	89 - 8.9	ii
13	*Skilled trade area* Use of adhesives (bonding small areas) (60 % MMA)	37	325 - 33	33 - 17	ii
15	*Skilled trade area* Use of paints (residual MMA < 0.5 %), Spray painting	79 - 39	630 - 126	70 - 30	ii

[1] Exposure scenarios according to Table 4.6, further information refer to this table
[2] MOS = NAEC / Exposure level, with NAEC = 100 ppm (410 mg/m³)
[3] MOS = NAEC / Exposure level, with NAEL = 4,100 mg/p/d

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

[5] MOS <3 leads to conclusion iii, except scenarios 8, 10: without LEV and 6, 7: with LEV

Based on the calculated dermal MOS values the dermal contribution to the combined MOS values in most cases is small, as could be expected from Section *Repeated dose toxicity, Dermal, systemic effets* already. Given a critical MOS value of 3 as outlined in Section *Repeated dose toxicity*, *Inhalation, systemic effects* the scenarios of concern appear almost similar to those identified before. In addition only four borderline scenarios (10 without LEV), (8 without LEV), (6) and (7 with LEV) result in a range of combined MOS values which extend to values below 3. If it is taken into account that the actual dermal MOS values are probably substantially higher than estimated (see Section *Repeated dose toxicity, Dermal, systemic effets)* the summary assessment should rely on dermal MOS values taken from the upper end of their individual ranges. As a result the actual combined MOS values for the four borderline scenarios most probably lie above 3, thus not leading to concern.

In summary the combined risk assessment for inhalation and dermal exposure did not identify exposure scenarios at risk additional to those already determined during inhalation risk assessment. The detailed list below is thus identical to that in Section *Repeated dose toxicity*, *Inhalation, systemic effects*.

Table 4.18 Scenarios giving rise to conclusion (iii) for repeated dose toxicity, inhalation and dermal, systemic effects.

Chemical industry:	(4)	Cast sheet production
Industrial area:	(7)	Production of adhesives without LEV
	(8)	Production of paints with LEV
Skilled trade area:	(14)	Floor coating
Use of casting resins:	(17)	Orthopaedic workshops without LEV
	(20)	Ornamental decoration

Conclusion (iii).

4.1.3.2.7 Mutagenicity

In vitro methyl methacrylate has the potential for induction of mutagenic effects (clastogenicity); however this potential seems to be limited to high doses with strong toxic effects. The negative *in vivo* micronucleus test, and to some extent the negative dominant lethal test, indicate that this potential is probably not expressed *in vivo*. Corresponding occupational risks are not anticipated to occur: **conclusion (ii)**.

4.1.3.2.8 Carcinogenicity

Carcinogenicity assessment of methyl methacrylate relies upon epidemiology data and experimental animal data. Based on these data methyl methacrylate is not considered to be a carcinogen. Corresponding risks at workplaces are not anticipated to occur: **conclusion (ii)**.

4.1.3.2.9 Reproductive toxicity

Fertility

At present no sufficiently validated study on fertility is available. From preliminary animal data no indication of fertility impairment has been obtained. A 2-generation inhalation study is in preparation.

For risk assessment purposes at the workplace for the time being no concern is rised considering fertility impairment: **conclusion (ii)**.

Developmental toxicity

There are some epidemiological data reported which as a whole are not considered validated enough to be a basis for risk assessment. Animal studies by inhalation revealed that there is at present no concern regarding possible developmental effects of methyl methacrylate. The NOAEC was determined to 2,028 ppm (about 8,300 mg/m^3), which is about 80 or 20 times higher than the NOAEC for local or systemic toxicity, respectively.

For risk assessment purposes the MOS value for the most critical exposure scenario of floor coating (scenario 14) is calculated. For general systemic effects combined exposure during floor coating may result in a MOS value of 0.4 (see **Table 4.17**). Because the NOAEC for

developmental toxicity is 20 times higher than the NOAEC for general systemic effects, a lowest combined MOS for developmental toxicity of 8 is calculated. MOS values for all other scenarios are greater than 8.

Against the background of available information (methyl methacrylate is not considered to be a developmental toxicant, lowest MOS of 8) a risk of developmental toxicity is not anticipated to occur at workplaces: **conclusion (ii)**.

4.1.3.2.10 Conclusions of the occupational risk assessment

The conclusions of the occupational risk assessment are summarised in **Table 4.19.**

Table 4.19 Conclusions of the occupational risk assessment of MMA [1)]

No [2)]	Area of production and use	Specification	Acute toxicity (inh. dermal)	Irritation/ Corrosivity (eyes, dermal) [3)]	Irritation/ Corrosivity (inh.) [4)]	Sensitisation (dermal)	Sensitisation (inh.)	Repeated dose tox. (inhalation local effects) [5)]	Repeated dose tox. (inhalation systemic effects) [6)]	Repeated dose tox. (dermal) [7)]	Repeated dose tox. (combined exposure) [8)]	Mutagenicity/ Carcinogenicity	Reprod. tox. (fert.) [9)]	Reprod. tox. (develop. tox.) [10)]
Chemical Industry														
1	MMA production					iii								
2	PMMA production					iii								
3	Transesterification					iii								
4	Cast sheet production				iii	iii		iii	iii		iii			
5	Production of adhesives					iii								
6	Production of reactive resins				iii	iii		iii						
Industrial area														
7	Production of adhesives, casting resins and floor coating materials	with LEV				iii								
		without LEV			iii	iii		iii	iii		iii			
8	Production of paints and varnishes	with LEV			iii	iii		iii	iii		iii			
		without LEV			iii	iii		iii						

Table 4.19 continued overleaf

Table 4.19 **continued** Conclusions of the occupational risk assessment of MMA

No [2]	Area of production and use	Specification	Acute toxicity (inh. dermal)	Irritation/ Corrosivity (eyes, dermal) [3]	Irritation/ Corrosivity (inh.) [4]	Sensitisation (dermal)	Sensitisation (inh.)	Repeated dose tox. (inhalation local effects) [5]	Repeated dose tox. (inhalation systemic effects) [6]	Repeated dose tox. (dermal) [7]	Repeated dose tox. (combined exposure) [8]	Mutagenicity/ Carcinogenicity	Reprod. tox. (fert.) [9]	Reprod. tox. (develop. tox.) [10]
Industrial area														
9	Use of moulding and extrusion compounds													
10	Use of adhesives in plastics, electronics and glass industry (60% MMA)	with LEV				iii								
		without LEV			iii	iii		iii						
11	Use of paints (residual MMA <0.5%)	spray painting with LEV												
		spray painting without LEV												
		painting												
12	Thermal processing of PMMA													

Table 4.19 continued overleaf

Table 4.19 **continued** Conclusions of the occupational risk assessment of MMA

No [2]	Area of production and use	Specification	Acute toxicity (inh. dermal)	Irritation/ Corrosivity (eyes, dermal) [3]	Irritation/ Corrosivity (inh.) [4]	Sensitisation (dermal)	Sensitisation (inh.)	Repeated dose tox. (inhalation local effects) [5]	Repeated dose tox. (inhalation systemic effects) [6]	Repeated dose tox. (dermal) [7]	Repeated dose tox. (combined exposure) [8]	Mutagenicity/ Carcinogenicity	Reprod. tox. (fert.) [9]	Reprod. tox. (develop. tox.) [10]
Skilled trade area														
13	Use of adhesives (bonding small areas) (60% MMA)					iii								
14	Floor coating (20% MMA)				iii	iii			iii [11]		iii [11]			
15	Use of paints (residual MMA <0.5%)	spray painting												

Table 4.19 continued overleaf

Table 4.19 **continued** Conclusions of the occupational risk assessment of MMA

No [2]	Area of production and use	Speci-fication	Acute toxicity (inh. dermal)	Irritation/ Corrosivity (eyes, dermal) [3]	Irritation/ Corrosivity (inh.) [4]	Sensitisation (dermal)	Sensiti-sation (inh.)	Repeated dose tox. (inhalation local effects) [5]	Repeated dose tox. (inhalation systemic effects) [6]	Repeated dose tox. (dermal) [7]	Repeated dose tox. (combined exposure) [8]	Muta-genicity/ Carcino-genicity	Reprod. tox. (fert.) [9]	Reprod. tox. (develop. tox.) [10]
Use of casting resins														
16	Medical applications				iii	iii								
17	Orthopaedic workshops	with LEV				iii								
		without LEV			iii	iii		iii	iii		iii			
18	Dental laboratories and surgeries	with LEV				iii								
		without LEV			iii	iii		iii						
19	Manufacture of lenses					iii								
20	Ornamental decoration				iii	iii			iii [11]		iii [11]			

[1] Blank fields: **conclusion (ii)** applies, **conclusion (iii)**: there is a need for limiting the risks; risk reduction measures which are being applied shall be taken into account
[2] Exposure scenarios are listed according to Table 4.6, further information refer to that table
[3] For several scenarios skin irritation is anticipated to occur, however specific risk reduction measures concerning this toxicological endpoint are not considered necessary
[4] MOS calculated with NAEC = 100 mg/m³, **conclusion (iii)** for MOS <1
[5] MOS calculated with NAEC = 100 mg/m³, **conclusion (ii)** for MOS <1
[6] MOS calculated with NAEC = 410 mg/m³, **conclusion (iii)** for MOS <3
[7] Neither from local nor from systemic effects, risks considered give rise to concern
[8] Only systemic effects considered, **conclusion (iii)** for MOS <3
[9] A 2-generation inhalation study is in preparation
[10] NOAEC (rat) = 8,300 mg/m³
[11] Scenarios with repeated but not daily exposure

4.1.3.3 Consumers

Acute Toxicity

Following the exposure assessment, consumers are not expected to be exposed to methyl methacrylate in the range of doses which can be derived from acute oral or dermal toxicity figures based on animal LD_{50} values (oral and dermal: >5,000 mg/kg body weight). Therefore the substance is of no concern in relation to acute oral or dermal toxicity.

The inhalation route of exposure should be of no concern, because in rats and mice methyl methacrylate has demonstrated LC_{50} values of >25 mg/l/4h. For using dispersion paints peak concentration up to 0.0028 mg/l have been estimated applying the SCIES model.

Conclusion (ii).

Irritation/Corrosivity

Following the exposure assessment, consumers may be exposed to low amounts of residual monomeric methyl methacrylate via infrequent applications of products containing polymethyl methacrylate.

Methyl methacrylate is reported to cause severe irritation if inhaled and severe skin irritation in humans and in animals. In rabbits, methyl methacrylate produced only slight irritation to the conjunctive of the eyes. Skin and respiratory irritation are frequently reported for subjects exposed to monomer methyl methacrylate.

According to the data presented methyl methacrylate is labelled with the following combination of R-phrases: Irritating to respiratory system and to the skin (R 37/38). The existing classification irritant (Xi) is confirmed.

Conclusion (ii).

Sensitisation

Following the exposure assessment, consumers may be exposed to low amounts of residual monomeric methyl methacrylate via infrequent applications of products containing polymethyl methacrylate.

Allergic contact dermatitis is reported for subjects occupationally exposed to monomeric methyl methacrylate.

In the literature cases of sensitisation of patients with implanted acrylic bone cement, of patients with hearing aids and of persons using synthetic fingernails have been reported, but the incidence seems low.

There is evidence from well-conducted studies in humans, that methyl methacrylate can cause sensitisation by skin contact (R43).

Conclusion (ii).

Remark

According to the Industrieverband Körperpflege- und Waschmittel (Industrial association for body care products and detergents) no information is available on the use of MMA-containing

adhesives for nail extension in Europe. Thus, without further exposure information on such use conclusion (iii) seems not to be justified.

Repeated dose toxicity

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

During the application of dispersion paints, consumers may be exposed to an average concentration of about 2.0 mg/m^3 (4.9 hours) with a possible peak value of 2.8 mg/m^3. The inhalation exposure resulting from residual monomeric methyl methacrylate does not reflect a realistic chronic exposure scenario. Nevertheless, this scenario represents a "worst case", therefore, a risk characterisation is performed.

In subacute, subchronic, and chronic inhalation studies in rats and mice the predominant target organ was the respiratory tract. MMA caused serious and suppurative inflammation of the nasal cavity and degeneration of the olfactory epithelium. Effects on the lung included oedema, fibrosis and emphysema like changes. Prolonged inhalation (over two years) of concentrations from 100 ppm or higher in rats (400 mg/m^3) induced degeneration of the olfactory epithelium. A NOAEC for local effects of 25 ppm (resp. 100 mg/m^3) was derived from this study on rats.

Animal studies revealed also treatment related effects on mean body weights, liver, kidney, smooth muscle, spleen, bone marrow, cardiovascular and endocrine system.

Effects on behavior (listlessness, locomotoric activity, learning ability, gait, and rear leg function) and changes in peripheral nervous system were observed in subacute and subchronic animal studies with inhalation and oral exposure. Malacia and gliosis of the brain occurred in doses of >1,000 ppm (>4,200 mg/m^3). However, these effects could not be confirmed in chronic inhalation studies.

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 the 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 recognized 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 studies cited above consistenly indicated degeneration of the nasal epithelium in several studies in rats and mice. From a well-performed 2-year inhalation study in rats a NOAEC for local effects of 100 mg/m^3 (25 ppm) was derived and the results were in conformity with the findings of the other studies.

A lower conformity of the effects outside the respiratory tract was observed in the inhalation and oral repeated dose studies. Especially, the occurrence and relevance of the neurotoxic effects at concentrations of > 4,200 mg/m^3 is at present unclear.

As neurotoxicity was only observed at high doses not relevant for human exposure and as it was a single finding not confirmed by other studies there are no reasons for the necessity of a higher MOS.

- 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 does not seem sufficiently supported by the limited data available on humans. Therefore, a lower MOS does not seem justified at present.

- Nature and severity of the effect

The main effects considered as "critical effects" are the degenerative and atrophic changes of the olfactory epithelium (irreversible, serious health effect).

There are no reasons to assume that the effects shown in the animal experiments are limited to the species tested, and therefore not relevant 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

In rats as well as in mice no steep dose-response-relationship is observed for the irritation effects at the olfactorium. At the LOAEC (400 mg/m^3, 100 ppm) only minimal to slight changes in the olfactory epithelium were observed. However, only insufficient data are available for the steepness of the dose-response-relationship for the questionable neurotoxic effects (>4,200 mg/m^3).

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 MMA 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 2-year inhalation study in rats. Because MMA acts primarily at the nasal cavity, systemic effects have not been considered. Moreover, the NOAEC for systemic effects was considered to be 420 mg/m^3 in the same study. In an oral 2-year drinking water study in rats a NOAEL of 200 mg/kg bw/d was established.

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.

MOS for Inhalation exposure scenario

During application of dispersion paints for 4.9 hours (6 times per year) the consumer may be exposed to an average concentration of 2.0 mg/m^3 with a possible peak value of 2.8 mg/m^3. This exposure does not reflect a real chronic exposure scenario. Therefore, the margin of safety between the

estimated exposure level of 2 mg/m^3

and the

NOAEC for local irritation effects of 100 mg/m^3

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*.

Conclusion (ii).

MOS for Oral and dermal exposure scenario

The oral and dermal uptakes are negligible.

Conclusion (ii).

Mutagenicity

Methyl methacrylate was negative in a bacterial mutation assay and positive in mammalian cell culture assays. An *in vivo* mouse bone marrow micronucleus test and an *in vivo* assay on germ cells (dominant lethal assay) led to negative results.

Due to the positive mammalian cell culture assays, MMA has a mutagenic potential. The negative *in vivo* micronucleus test and the negative dominant lethal assay - indicate that this potential may not be expressed *in vivo*. Taking into account the negligible exposure of the consumer, however, it can be concluded that there should be no concern regarding *in vivo* mutagenicity.

Conclusion (ii).

Carcinogenicity

Studies in experimental animals indicate that methyl methacrylate is not an animal carcinogen. There is inadequate evidence in humans for the carcinogenicity of methyl methacrylate.

Conclusion (ii).

Reproductive toxicity

Following the exposure assessment consumers may be exposed to methyl methacrylate via variable amounts of residual methyl methacrylate monomers in different applications (<0.01 mg/kg body weight).

At present a sufficiently validated study on fertility is not available. However, a 2-generation inhalation study is planned in the USA for the near future. From a dominant lethal study with

short-term inhalation exposure only data of limited value are available. With this study design methyl methacrylate did not reveal an effect on male fertility in mice when animals had been exposed to up to 9,000 ppm for a period of 5 days before mating. In a developmental toxicity study according to OECD Guideline 414 methyl methacrylate was administered by inhalation to groups of presumed pregnant rats (Crl:CDBR) at concentrations of 0, 99, 304, 1,178, and 2,028 ppm. No embryo or fetal toxicity was evident and no increase in the incidence of malformations or variations was noted at exposure up to and including 2,028 ppm (8,436 mg/m^3).

Following the exposure assessment, the consumer may be exposed to methyl methacrylate via inhalation, whereas oral and dermal exposures are assumed of minor importance.

Reproductive toxicity – fertility

A value of 9,000 ppm from a dominant lethal study in mice was used as NOAEC. Conversion of this value (9,000 ppm = 36,900 mg/m^3) to the inhaled amount of the substance (respiratory minute volume (mice) 1.3 l/min/kg; exposure duration: 6 h (360 min/day) to an oral dose yields.

36.9 mg/l · 1.3 l/min/kg · 360 min = 17,260 mg/kg bw.

The margin of safety between the

calculated exposure level of	0.01 mg/kg bw/d

and the

NOAEL (oral) of	17,260 mg/kg bw/d

is judged to be sufficient.

Conclusion (ii).

Reproductive toxicity – developmental toxicity

From the developmental toxicity study in rats a NOAEC of 2,028 ppm (8,436 mg/m^3) was derived for teratogenic and embryo-/fetotoxic effects. Conversion of the NOAEC of this study (8,436 mg/m^3) to the inhaled amount of the substance (respiratory minute volume (rat) 0.8 l/min/kg; exposure duration: 6 h (360 min/day) to an oral dose yields:

8.436 mg/l · 0.8 l/min/kg · 360 min = 2,430 mg/kg bw.

Thus, the margin of safety between the

calculated exposure level of	0.01 mg/kg bw/d

and the

NOAEL (oral) of	2,430 mg/kg bw/d

is judged to be sufficient.

Conclusion (ii).

4.1.3.4 Humans exposed via the environment

Indirect exposure to methyl methacrylate via the environment occurs mainly by air and drinking water. Following the local scenario data (at a point source) an intake of a total daily dose of 0.132 mg/kg body weight/d is calculated (as a worst case). This total daily dose may be overestimated because a default value was used as input concentration. For the regional scenario, the respective figure is smaller (0.017 µg/kg bw/d). From the two-year drinking water study in rats (Borzelleca et al., 1964) a NOAEL of 200 mg/kg bw/d (2,000 ppm) was derived.

Comparison indirect exposure (local) /NOAEL

$$\frac{\text{Indirect exposure}}{\text{NOAEL}} = \frac{0.132 \text{ mg/kg bw/d}}{200 \text{ mg/kg bw/d}}$$

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

Conclusion (ii).

Comparison indirect exposure (regional) /NOAEL

$$\frac{\text{Indirect exposure}}{\text{NOAEL}} = \frac{0.000017 \text{ mg/kg bw/d}}{200 \text{ mg/kg bw/d}}$$

The margin of safety expressed by the magnitude between the calculated exposure and the NOAEL is very low for the 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 consumer exposure (1-10 µg/kg bw/d) and the indirect exposure via the environment (local scenario, 0.132 mg/kg bw/d) a combined exposure of about 0.14 mg/kg bw/d was estimated.

Comparison combined exposure / NOAEL

$$\frac{\text{Combined exposure}}{\text{NOAEL}} = \frac{0.14 \text{ mg/kg bw/d}}{200 \text{ mg/kg bw/d}}$$

The margin of safety expressed by the magnitude between the estimated combined exposure and the NOAEL is very low for the combined scenario. Thus, there is no concern.

Conclusion (ii).

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

4.2.1 Exposure assessment

Refer to Section 4.1.1.1.

4.2.2 Effects assessment: Hazard identification

Explosive properties and oxidising properties of MMA are not considered to form a hazard. Since MMA is highly flammable, adequate worker protection measures must be observed.

4.2.3 Risk characterisation

4.2.3.1 Workers

MMA is highly flammable. Adequate worker protection measures must be observed.

MMA is suspectible to polymerisation initiated by prolonged heating or a catalyst. Heat, UV-light, peroxide, azo-compounds, alkalis and oxidising agents may cause polymerisation resulting in explosion. Uncontrolled exothermic polymerisation in closed bulk containers may lead to violent rupture caused by increasing pressure. This does not occur in drums or smaller quantities. To prevent polymerisation MMA is stabilised with approx. 25 - 100 ppm hydroquinone or another inhibitor like the monomethylether of hydroquinone (Röhm, 1995).

According to producers information following precautions must always be observed when storing MMA (Röhm, 1995):

- MMA must be stored under air as the stabiliser (for example hydroquinone monomethyl ether) is only effective in the presence of oxygen.
- Heat and direct sunlight must be excluded, as they promote polymerisation.
- MMA must be stored at temperatures preferably not exceeding 30°C; MMA can be stored without chemical inhibitor at low temperatures (<0°C).
- Care should be taken to prevent contamination, as contaminants can render the stabiliser ineffective or can react with MMA and promote polymerisation.

Conclusion (ii).

4.2.3.2 Consumers

There is no need for further information and/or testing with regard to the consumers.

Conclusion (ii).

4.2.3.3 Humans exposed via the environment

There is no need for further information and/or testing with regard to man exposed indirectly via the environment.

Conclusion (ii).

5 RESULTS

5.1 ENVIRONMENT

A potential risk to the local aquatic environment is identified from wet polymerisation processes by downstream users of monomeric MMA (default calculations for generic site and four out of 29 known sites).

For the processing sites with PEC/PNEC ratios above one, the PEC calculations are essentially based on default calculations. Therefore, an improvement of exposure data is possible for the wet polymerisation scenarios, e.g. by performing sufficiently detailed effluent measurements. However, keeping in mind reported year-to-year variations of used MMA tonnages by factors of up to 27, it seems questionable if appropriate effluent monitoring data can be achieved with reasonable expenditure of time and money. Reliable data have to meet the requirement of being representative for all possible utilisation factors (related to used MMA tonnage) of a specific site overall capacity for wet polymerisation processes.

On the effects side of the risk assessment data improvement is possible because an assessment factor of 50 is used for the PNEC derivation and it might be possible to lower the PNEC by further testing, i.e. the assessment factor can be lowered to 10 if a long-term fish test is performed. But regarding the locally limited risks that are identified due to the specific scenario this kind of data improvement is not proposed.

It is concluded, that local risk reduction measures have to be considered, if the MMA processing capacity exceeds 5,000 t/a at one single site. It should be noted, that wastewater reutilisation / recycling systems are applied by some known polymerisation sites, avoiding any significant MMA emission to hydrosphere. Sites applying such advanced process engineering would not require further consideration of risk reduction measures.

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

Conclusion (ii) applies for effects on wastewater treatment plants, sediment, atmosphere, soil, and secondary poisoning. It also applies to the aquatic compartment regarding all production sites, the processing scenarios esterification and dry polymerisation, and the relevant use scenarios formulation of paints, private use of paints, and paper recycling.

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 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.

There is a need for limiting the risks of MMA concerning skin sensitisation and respiratory tract irritation at several workplaces in the chemical industry, industrial area and skilled trade and during use of casting resins. For certain inhalation exposure scenarios systemic toxicity gives in addition rise to concern. Risk reduction measures at the community level are recommended.

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)

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

Distribution and Fate

$d := \text{Tag}$

Substance: MMA

vapour pressure:	$VP := 4200 \cdot Pa$	(293 K)
water solubility:	$SOL := 16000\,mg \cdot l^{-1}$	(293 K)
part. coefficient octanol/water:	$LOGP_{OW} := 1.38$	
moleculare weight:	$MOLW := 0.1 \cdot kg \cdot mol^{-1}$	
gas constant:	$R := 8.3143\,J \cdot mol \cdot K^{-1}$	
temperature:	$T := 285 \cdot K$	
conc. of suspended matter in the river:	$SUSP_{water} := 15 \cdot mg \cdot l^{-1}$	
density of the solid phase:	$RHO_{solid} := 2500\,kg \cdot m^{-3}$	
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 $SURF_{air}$:	$product := 10^{-4} \cdot Pa$	

distribution air/water: Henry-constant

$$HENRY := \frac{VP \cdot MOLW}{SOL} \qquad HENRY = 26.25 \cdot Pa \cdot m^3 \cdot mol^{-1}$$

$$\log\left(\frac{HENRY}{Pa \cdot m^3 \cdot mol^{-1}}\right) = 1.419$$

$$K_{air\_water} := \frac{HENRY}{R \cdot T} \qquad K_{air\_water} = 0.011$$

solid/water-partition coefficient Kp_{comp} and total compartment/water-partition coefficient K_{comp_water}

(default calculation)

$a := 0.49$ (a,b from chapter 4.3.4 TGD, p. 539)

$b := 1.05$ $K_{OC} := 10^{a \cdot LOGP_{OW} + b} \cdot l \cdot kg^{-1}$ $K_{OC} = 53.2 \bullet l \cdot kg^{-1}$

Suspended matter

$Kp_{susp} := 0.1 \cdot K_{OC}$ $Kp_{susp} = 5.324 \bullet l \cdot kg^{-1}$

$K_{susp\_water} := Fwater_{susp} + Fsolid_{susp} \cdot Kp_{susp} \cdot RHO_{solid}$ $K_{susp\_water} = 2.231$

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

$factor := 1 + Kp_{susp} \cdot SUSP_{water}$ $factor = 1$

Sediment

$Kp_{sed} := 0.1 \cdot K_{OC}$ $Kp_{sed} = 5.324 \bullet l \cdot kg^{-1}$

$K_{sed\_water} := Fwater_{sed} + Fsolid_{sed} \cdot Kp_{sed} \cdot RHO_{solid}$ $K_{sed\_water} = 3.462$

Soil

$Kp_{soil} := 0.02 \cdot K_{OC}$ $Kp_{soil} = 1.065 \bullet l \cdot kg^{-1}$

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

$K_{soil\_water} = 1.799$

Sludge

$K_{p\_sludge} := 0.37 \cdot K_{OC}$ $K_{p\_sludge} = 19.697 \bullet l \cdot kg^{-1}$

Elimination in STPs (SimpleTreat 3.0)

rate constant in STP: k = 1* h^{-1} elimination P = f (k, logpow, logH) = 89.2 %

fraction directed to surface water $Fstp_{water}$ = 10.8 %

biodegradation in different compartments

surface water

$kbio_{water} := 0.047 \cdot d^{-1}$ (cTGD, table 5)

soil

$DT50bio_{soil} := 30 \cdot d$ (cTGD, table 6)

$kbio_{soil} := \frac{\ln(2)}{DT50bio_{soil}}$ $kbio_{soil} = 2.31 \cdot 10^{-2} \cdot d^{-1}$

sediment

$kbio_{sed} := \frac{\ln(2)}{DT50bio_{soil}} \cdot Faer_{sed}$ $kbio_{sed} = 2.31 \cdot 10^{-3} \cdot d^{-1}$

degradation in surface waters

$khydr_{water} := 4.9 \cdot 10^{-4} \cdot d^{-1}$ ($t_{1/2}$ = 3.9 years)

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

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

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

Atmosphere

calculation of CONjunge * SURFaer for the OPS-model

$Fass_{aer} := \frac{product}{VP + product}$ $Fass_{aer} = 2.4 \cdot 10^{-8}$

degradation in the atmosphere

$kdeg_{air}$ = 8.2 h^{-1} (AOP)

Appendix A2 Calculation of C_{Local} for the aquatic compartment during production and processing of chemicals for the hydrosphere

Calculation of C_{local} for the aquatic Compartment during Production and Processing of Chemicals for the Hydrosphere

(Status: UCD-Scenario)

Methyl methacrylate CAS-No.: 80-62-6

default calculation: production and processing of 200 000 t/a,generic

$a := 365 \cdot Tag$

$d := 24 \cdot h$

$\mu g := 10^{-9} \cdot kg$

tonnage: $T := 200000 \cdot t \cdot a^{-1}$

emission factor: $f := 1 \cdot \%$

elimination in WWTP k= 1*h^{-1}: $P := 89.2 \cdot \%$

(logH:1,4 ;logPow:1,4)

flow rate of receiving river: $V := 60 \cdot m^3 \cdot s^{-1}$

duration of emission: $D := 300 \cdot d$

capacity of plant: $PK := \frac{T \cdot a}{D}$

$PK = 666.67 \cdot t \cdot d^{-1}$

factor for calculating C_{local_water} : $factor := 1$

$$C_{local\_water} := \frac{PK \cdot f \cdot (1 - P)}{V} \cdot \frac{1}{factor}$$

$$C_{local\_water} = 139 \cdot \mu g \cdot l^{-1}$$

$$C_{local\_water\_ann} := C_{local\_water} \cdot \frac{300}{365}$$

$$C_{local\_water\_ann} = 114.16 \cdot \mu g \cdot l^{-1}$$

Appendix A3 Default calculation of Clocal for aquatic compartment at one site

Default Calculation of C_{local} for aquatic compartment at one site

status: TGD, ESD, IC-3

$d := 86400\,s$

$a := 365 \cdot d$

$\mu g := 10^{-9} \cdot kg$

chemical: MMA
stage of life cycle: esterification, IC03/UC33

Total annual tonnage of chemical: $T := 32000\,t \cdot a^{-1}$

Release factor $f := 0.7 \cdot \%$

Duration of emission for processing $Temission_1 := 300 \cdot d \cdot a^{-1}$

Fraction of emission directed to water:
(SimpleTreat, k: 1 h-1; logH:1,4 ; $logK_{ow}$:1,38) $Fstp_{water} := 10.8 \cdot \%$

River flow rate $V := 60 \cdot m^3 \cdot s^{-1}$

Factor (1 + K_p * SUSPwater): $FACTOR := 1$

Emission per day:

$$Elocal_{water} := \frac{T \cdot f}{Temission_1} \qquad Elocal_{water} = 746.67 \bullet kg \cdot d^{-1}$$

Concentration in surface water:

$$Clocal_{water} := \frac{Elocal_{water} \cdot Fstp_{water}}{V \cdot FACTOR} \qquad Clocal_{water} = 15.56 \bullet \mu g \cdot l^{-1}$$

Release to hydrosphere:

$$RELEASE_{sw} := T \cdot f \cdot Fstp_{water} \qquad RELEASE_{sw} = 24.192 \bullet t \cdot a^{-1}$$

Appendix A4 Default exposure estimation of $C_{localwater}$, polymerisation, wet process

Default Exposure Estimation of $Clocal_{water}$

status: TGD, table A and B

$\mu g := 10^{-9} \cdot kg$

$d := 86400 \cdot s$

$a := 365 \cdot d$

$t := 1000 \cdot kg$

chemical : MMA

stage of life cycle: default processing (polymerisation), wet process
IC/UC/MC:11/33/III

Total annual tonnage of chemical: $TONNAGE := 77000 \cdot t \cdot a^{-1}$

Release factor (A-table: A3.10): $f_{emission} := 0.01$

Fraction of main source (B-table: B3.9): $Fmainsource := 0.05$

Waste water flow of wwtp: $EFFLUENT_{stp} := 2000 \cdot m^3 \cdot d^{-1}$

Duration of emission (B-table: B3.9): $Temission := 300 \cdot d \cdot a^{-1}$

Fraction of emission directed to water:
(SimpleTreat; k: 1 h^{-1}; logPow: 1.38; logH:1.4) $Fstp_{water} := 10.8 \cdot \%$

Dilution factor (TGD): $DILUTION := 10$

Factor (1+Kp * SUSPwater): $FACTOR := 1$

Emission per day:

$$Elocal_{water} := \frac{TONNAGE \cdot Fmainsource \cdot f_{emission}}{Temission} \qquad Elocal_{water} = 128.33 \cdot kg \cdot d^{-1}$$

Influent concentration:

$$Clocal_{inf} := \frac{Elocal_{water}}{EFFLUENT_{stp}} \qquad Clocal_{inf} = 6.42 \cdot 10^{4} \cdot \mu g \cdot l^{-1}$$

Effluent concentration:

$$Clocal_{eff} := Clocal_{inf} \cdot Fstp_{water} \qquad Clocal_{eff} = 6.93 \cdot 10^{3} \cdot \mu g \cdot l^{-1}$$

Concentration in surface water:

$$Clocal_{water} := \frac{Clocal_{eff}}{FACTOR \cdot DILUTION} \qquad Clocal_{water} = 693 \cdot \mu g \cdot l^{-1}$$

Annual average local concentration in water:

$$Clocal_{water\_ann} := Clocal_{water} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}} \qquad Clocal_{water\_ann} = 569.59 \cdot \mu g \cdot l^{-1}$$

Appendix A5 Default exposure estimation of $C_{localwater}$, polymerisation, wet process, generic site

Default Exposure Estimation of Clocal$_{water}$ -

status: TGD, table A and B

$:= 10^{-9} \cdot kg$

chemical : MMA

$d := 86400\,s \quad a := 365 \cdot d$

stage of life cycle: default processing (polymerisation), wet process, generic site

IC/UC/MC:11/33/III

Total annual tonnage of chemical: $TONNAGE := 10000\,t \cdot a^{-1}$

Release factor (A-table: A3.10): $f_{emission} := 0.01$

Fraction of main source (B-table: B3.9): $Fmainsource := 1$

Waste water flow of wwtp: $EFFLUENT_{stp} := 2000 \cdot m^3 \cdot d^{-1}$

Duration of emission (B-table: B3.9): $Temission := 300 \cdot d \cdot a^{-1}$

Fraction of emission directed to water:
(SimpleTreat; k: 1 h^{-1}; logPow: 1.38; logH:1.4) $Fstp_{water} := 10.8\,\%$

Dilution factor (TGD): $DILUTION := 10$

Factor (1+Kp * SUSPwater): $FACTOR := 1$

Emission per day:

$$Elocal_{water} := \frac{TONNAGE \cdot Fmainsource \cdot f_{emission}}{Temission} \qquad Elocal_{water} = 333.33 \cdot kg \cdot d^{-1}$$

Influent concentration:

$$Clocal_{inf} := \frac{Elocal_{water}}{EFFLUENT_{stp}} \qquad Clocal_{inf} = 1.67 \cdot 10^{5} \cdot \mu g \cdot l^{-1}$$

Effluent concentration:

$$Clocal_{eff} := Clocal_{inf} \cdot Fstp_{water} \qquad Clocal_{eff} = 1.8 \cdot 10^{4} \cdot \mu g \cdot l^{-1}$$

Concentration in surface water:

$$Clocal_{water} := \frac{Clocal_{eff}}{FACTOR \cdot DILUTION} \qquad Clocal_{water} = 1.8 \cdot 10^{3} \cdot \mu g \cdot l^{-1}$$

Annual average local concentration in water:

$$Clocal_{water\_ann} := Clocal_{water} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}} \qquad Clocal_{water\_ann} = 1.48 \cdot 10^{3} \cdot \mu g \cdot l^{-1}$$

Appendix A6 Default exposure estimation of $C_{localwater}$, processing (shaping)

Default Exposure Estimation of Clocal$_{water}$ -

status: TGD, table A and B

$\mu g := 10^{-9} \cdot kg$

$d := 86400\,s$

$a := 365 \cdot d$

chemical : MMA

stage of life cycle: processing (shaping)
IC/UC:11/33

Total annual tonnage of chemical: $TONNAGE := 336 \cdot t \cdot a^{-1}$

Release factor (A-table: A3.11): $f_{emission} := 0.0005$

Fraction of main source (B-table: B3.9): $Fmainsource := 0.05$

Waste water flow of wwtp: $EFFLUENT_{stp} := 2000 \cdot m^3 \cdot d^{-1}$

Duration of emission (B-table: B3.9): $Temission := 300 \cdot d \cdot a^{-1}$

Fraction of emission directed to water:
(SimpleTreat; k: 1 h^{-1}; logPow: 1.38; logH:1.4) $Fstp_{water} := 10.8 \cdot \%$

Dilution factor (TGD): $DILUTION := 10$

Factor (1+Kp * SUSPwater): $FACTOR := 1$

Emission per day:

$$Elocal_{water} := \frac{TONNAGE \cdot Fmainsource \cdot f_{emission}}{Temission} \qquad Elocal_{water} = 0.03 \cdot kg \cdot d^{-1}$$

Influent concentration:

$$Clocal_{inf} := \frac{Elocal_{water}}{EFFLUENT_{stp}} \qquad Clocal_{inf} = 14 \cdot \mu g \cdot l^{-1}$$

Effluent concentration:

$$Clocal_{eff} := Clocal_{inf} \cdot Fstp_{water} \qquad Clocal_{eff} = 1.51 \cdot \mu g \cdot l^{-1}$$

Concentration in surface water:

$$Clocal_{water} := \frac{Clocal_{eff}}{FACTOR \cdot DILUTION} \qquad Clocal_{water} = 0.15 \cdot \mu g \cdot l^{-1}$$

Annual average local concentration in water:

$$Clocal_{water\_ann} := Clocal_{water} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}} \qquad Clocal_{water\_ann} = 0.12 \cdot \mu g \cdot l^{-1}$$

Appendix A7 Default calculation of C_{local} for the hydrosphere, formulation of paints

Default-Calculation of C_local for the Hydrosphere

(Status: TGD for Existing Substances / EUSES)

Methyl methacrylate

formulation of paints

tables: A2.1, B2.3

tonnage: $T := 84.6 \cdot tonne$

release factor (A2.1): $r := 0.003$

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

waste water flow of the WWTP: $Q := 2000 \cdot m^3 \cdot d^{-1}$

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

$d := 86400 \cdot s$

$\mu g := 10^{-9} \cdot kg$

$$C_{inf} := \frac{T \cdot r \cdot f}{Q \cdot d} \qquad C_{inf} = 0.169 \cdot mg \cdot l^{-1}$$

Elimination in WWTP related to SIMPLETREAT:

$P := 89.2 \cdot \%$ P = f (biodegradation, log pow, log H)

$$C_{eff} := C_{inf}(1 - P) \qquad C_{eff} = 0.018 \cdot mg \cdot l^{-1}$$

Calculation of C-local:

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

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

dilution factor for receiving surface water: $D := 10$

$$C_{local} := \frac{C_{eff}}{\left(1 + K_{p\_susp} \cdot c_{susp}\right) \cdot D}$$

$$C_{local} = 1.827 \cdot \mu g \cdot l^{-1}$$

Appendix A8 Default calculation of C_{local} for the hydrosphere, private use of paints

Default-Calculation of C_local for the Hydrosphere

(Status: TGD for Existing Substances / EUSES)

Methyl methacrylate

private use of paints

tables: A4.5 B4.4

tonnage: $T := 8.46 \cdot tonne$

release factor (A4.5): $r := 0.05$

fraction of main source (B4.4): $f := 0.002$

waste water flow of the WWTP: $Q := 2000 \cdot m^3 \cdot d^{-1}$

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

$d := 86400 \cdot s$

$\mu g := 10^{-9} \cdot kg$

$$C_{inf} := \frac{T \cdot r \cdot f}{Q \cdot d} \qquad C_{inf} = 1.41 \cdot 10^{-3} \ \circ mg \cdot l^{-1}$$

Elimination in WWTP related to SIMPLETREAT:

$P := 89.2 \cdot \%$ P = f (biodegradation, log pow, log H)

$$C_{eff} := C_{inf}(1 - P) \qquad C_{eff} = 1.523 \cdot 10^{-4} \ \circ mg \cdot l^{-1}$$

Calculation C-local:

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

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

dilution factor for receiving surface water: $D := 10$

$$C_{local} := \frac{C_{eff}}{\left(1 + K_{p\_susp} \cdot c_{susp}\right) \cdot D}$$

$$C_{local} = 0.015 \circ \mu g \cdot l^{-1}$$

Appendix A9 Exposure during paper recycling

Exposure during paper recycling
(Status: mod. UCD-Scenario)

Methyl methacrylate, CAS-No.: 80-62-6

$d := Tag \qquad a := 365 \cdot d$

$\mu g := 0.001 \cdot mg$

total annual consumption of the substance $Ws := 3760 \cdot kg \cdot a^{-1}$

rate of recycling $RR := 50 \cdot \%$

deinking rate $DR := 90 \cdot \%$

not absorbed quantity $NA := 20 \cdot \%$

number of working days $N := 250 \cdot d \cdot a^{-1}$

volume of waste water $V := 2000 \cdot m^3 \cdot d^{-1}$

number of plants $A := 10$

influent concentration

$$c_{infl} := \frac{Ws \cdot RR \cdot DR \cdot NA}{N \cdot V \cdot A}$$

$c_{infl} = 0.068 \cdot mg \cdot l^{-1}$

elimination in WWTP; k=1 * h^{-1}
(logH=1.4; logPow=1.4)

$P := 89.2 \cdot \%$

effluent concentration

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

$c_{eff} = 7.309 \cdot 10^{-3} \cdot mg \cdot l^{-1}$

dilution factor $D := 10$

Clocal:

$C_{local} := c_{eff} \cdot D^{-1}$

$C_{local} = 0.731 \cdot \mu g \cdot l^{-1}$

Appendix A10 Atmosphere (OPS-model). MMA generic calculation, production and processing

Atmosphere (OPS-model)

substance: MMA, generic calculation, production and processing

$d := 86400 \cdot s$

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

Calculation of Clocal $_{air}$

tonnage for specific scenario: $TONNAGE := 200000 \cdot t \cdot a^{-1}$

release factor (tables A1.2 and A3.3) : $f_{emission} := 0.0011$

fraction of main source: $Fmainsource := 1$

days of use per year: $Temission := 300 \cdot d \cdot a^{-1}$

release during life cycle to air: $RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 220 \bullet t \cdot a^{-1}$

local emission during episode to air: $Elocal_{air} := \frac{Fmainsource \cdot RELEASE}{Temission}$

$Elocal_{air} = 733.333 \bullet kg \cdot d^{-1}$

concentration in air at source strength of 1kg/d: $Cstd_{air} := 2.78 \cdot 10^{-4} \cdot mg \cdot m^{-3} \cdot kg^{-1} \cdot d$

fraction of the emission to air from STP: $Fstp_{air} := 7 \cdot \%$

local emission rate to water during emission episode: $Elocal_{water} := 6600 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode: $Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 462 \bullet kg \cdot d^{-1}$

local concentation in air during emission episode: $Clocal_{air} := wenn\left(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air}\right)$

$Clocal_{air} = 0.204 \bullet mg \cdot m^{-3}$

annual average concentration in air, 100m from point source: $Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$

$Clocal_{air\_ann} = 0.168 \bullet mg \cdot m^{-3}$

regional concentration in air: $PECregional_{air} := 0 \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air: $PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.168 \bullet mg \cdot m^{-3}$

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)

$$Fass_{aer} := 2.4 \cdot 10^{-8}$$

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

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

$$DEPtotal = 0.478 \cdot mg \cdot m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.393 \cdot mg \cdot m^{-2} \cdot d^{-1}$$

Appendix A11 Atmosphere (OPS-model). MMA, ester production

Atmosphere (OPS-model)

$d := 86400 \cdot s$

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

substance: MMA, ester production

Calculation of Clocal $_{air}$

tonnage for specific scenario: $TONNAGE := 32000 \cdot t \cdot a^{-1}$

release factor (A3.3) : $f_{emission} := 0.001$

fraction of main source: $Fmainsource := 1$

days of use per year: $Temission := 300 \cdot d \cdot a^{-1}$

release during life cycle to air: $RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 32 \cdot t \cdot a^{-1}$

local emission during episode to air: $Elocal_{air} := \frac{Fmainsource \cdot RELEASE}{Temission}$

$Elocal_{air} = 106.6667 \cdot kg \cdot d^{-1}$

concentration in air at source strength of 1kg/d: $Cstd_{air} := 2.78 \cdot 10^{-4} \cdot mg \cdot m^{-3} \cdot kg^{-1} \cdot d$

fraction of the emission to air from STP: $Fstp_{air} := 7 \cdot \%$

local emission rate to water during emission episode: $Elocal_{water} := 746.67 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode: $Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 52.2669 \cdot kg \cdot d^{-1}$

local concentation in air during emission episode: $Clocal_{air} := wenn\left(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air}\right)$

$Clocal_{air} = 0.0297 \cdot mg \cdot m^{-3}$

annual average concentration in air, 100m from point source: $Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$

$Clocal_{air\_ann} = 0.0244 \cdot mg \cdot m^{-3}$

regional concentration in air: $PECregional_{air} := 0 \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air: $PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.0244 \cdot mg \cdot m^{-3}$

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)

$$Fass_{aer} := 2.4 \cdot 10^{-8}$$

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

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

$$DEPtotal = 0.0636 \cdot mg \cdot m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.0523 \cdot mg \cdot m^{-2} \cdot d^{-1}$$

Appendix A12 Atmosphere (OPS-model). MMA, polymerisation (dry)

Atmosphere (OPS-model)

substance: MMA, polymerisation (dry)

$d := 86400 \cdot s$

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

Calculation of Clocal $_{air}$

tonnage for specific scenario: $TONNAGE := 51000 \cdot t \cdot a^{-1}$

release factor (A3.10) : $f_{emission} := 0.05$

fraction of main source (B3.9) : $Fmainsource := 0.05$

days of use per year: $Temission := 300 \cdot d \cdot a^{-1}$

release during life cycle to air: $RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 2.55 \cdot 10^{3} \ \cdot t \cdot a^{-1}$

local emission during episode to air: $Elocal_{air} := \frac{Fmainsource \cdot RELEASE}{Temission}$

$Elocal_{air} = 425 \cdot kg \cdot d^{-1}$

concentration in air at source strength of 1kg/d: $Cstd_{air} := 2.78 \cdot 10^{-4} \cdot mg \cdot m^{-3} \cdot kg^{-1} \cdot d$

fraction of the emission to air from STP: $Fstp_{air} := 7 \cdot \%$

local emission rate to water during emission episode: $Elocal_{water} := 0 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode: $Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 0 \cdot kg \cdot d^{-1}$

local concentation in air during emission episode: $Clocal_{air} := wenn\left(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air}\right)$

$Clocal_{air} = 0.1182 \cdot mg \cdot m^{-3}$

annual average concentration in air, 100m from point source: $Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$

$Clocal_{air\_ann} = 0.0971 \cdot mg \cdot m^{-3}$

regional concentration in air: $PECregional_{air} := 0 \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air: $PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.0971 \cdot mg \cdot m^{-3}$

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)

$$Fass_{aer} := 2.4 \cdot 10^{-8}$$

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

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

$$DEPtotal = 0.17 \bullet mg \cdot m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.1397 \bullet mg \cdot m^{-2} \cdot d^{-1}$$

Appendix A13 Atmosphere (OPS-model). MMA, polymerisation (wet), generic site

Atmosphere (OPS-model)

$d := 86400\,s$

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

substance: MMA, polymerisation (wet), generic site

Calculation of Clocal $_{air}$

tonnage for specific scenario: $TONNAGE := 10000\,t \cdot a^{-1}$

release factor (A3.10) : $f_{emission} := 0.05$

fraction of main source (B3.9) : $Fmainsource := 1$

days of use per year: $Temission := 300 \cdot d \cdot a^{-1}$

release during life cycle to air: $RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 500 \cdot t \cdot a^{-1}$

local emission during episode to air: $Elocal_{air} := \frac{Fmainsource \cdot RELEASE}{Temission}$

$Elocal_{air} = 1.6667 \cdot 10^{3} \cdot kg \cdot d^{-1}$

concentration in air at source strength of 1kg/d $Cstd_{air} := 2.78 \cdot 10^{-4} \cdot mg \cdot m^{-3} \cdot kg^{-1} \cdot d$

fraction of the emission to air from STP $Fstp_{air} := 7 \cdot \%$

local emission rate to water during emission episode $Elocal_{water} := 333.3 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode $Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 23.331 \cdot kg \cdot d^{-1}$

local concentation in air during emission episode: $Clocal_{air} := wenn\left(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air}\right)$

$Clocal_{air} = 0.4633 \cdot mg \cdot m^{-3}$

annual average concentration in air, 100m from point source $Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$

$Clocal_{air\_ann} = 0.3808 \cdot mg \cdot m^{-3}$

regional concentration in air $PECregional_{air} := 0 \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air $PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.3808 \cdot mg \cdot m^{-3}$

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)

$$Fass_{aer} := 2.4 \cdot 10^{-8}$$

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

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

$$DEPtotal = 0.676 \bullet mg \cdot m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.56 \bullet mg \cdot m^{-2} \cdot d^{-1}$$

Appendix A14 Exposure of soil, MMA, production and processing, generic site

Appendix A14

Exposure of Soil

$ppm := mg \cdot kg^{-1}$ $d := 86400\,s$

Substance: MMA, production and processing, generic site

$i := 1..3$ $a := 365 \cdot d$

Input:

annual average total deposition flux: $DEPtotal_{ann} := 0.393 \cdot mg \cdot m^{-2} \cdot d^{-1}$

soil-water partitioning coefficient: $K_{soil\_water} := 1.7$

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

air-water partitioning coefficient: $K_{air\_water} := 0.011$

rate constant for for removal from top soil: $kbio_{soil} := 2.3 \cdot 10^{-2} \cdot d^{-1}$

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

Defaults:

mixing depth of soil: $DEPTHsoil_i :=$

$0.2 \cdot m$
$0.2 \cdot m$
$0.1 \cdot m$

bulk density of soil: $RHO_{soil} := 1700 \cdot kg \cdot m^{-3}$

average time for exposure: $T_i :=$

$30 \cdot d$
$180 \cdot d$
$180 \cdot d$

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

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

partial mass transfer coefficient at soilwater-side of the air-soil interface: $kasl_{soilwater} := 4.8 \cdot 10^{-5} \cdot m \cdot d^{-1}$

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

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

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:

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

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:

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

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

	$\frac{Clocal_{soil_i}}{ppm}$
$Clocal_{soil}$ =	0.029
$Clocal_{agr.soil}$ =	0.029
$Clocal_{grassland}$ =	0.041

	$\frac{PEClocal_{soil_i}}{ppm}$
$PEClocal_{soil}$ =	0.029
$PEClocal_{agr.soil}$ =	0.029
$PEClocal_{grassland}$ =	0.041

concentration in pore water

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

	$\frac{Clocal_{soil\_porew_i}}{mg \cdot l^{-1}}$
$Clocal_{soil\_porew}$ =	0.029
$Clocal_{agr.soil\_porew}$ =	0.029
$Clocal_{grassland\_porew}$ =	0.041

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

	$\frac{PEClocal_{soil\_porew_i}}{mg \cdot l^{-1}}$
$PEClocal_{soil\_porew}$ =	0.029
$PEClocal_{agr.soil\_porew}$ =	0.029
$PEClocal_{grassland\_porew}$ =	0.041

concentration in ground water

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

Appendix A15 Exposure of soil, MMA, polymerisation, wet, generic site

Appendix A15

Exposure of Soil

$ppm := mg \cdot kg^{-1}$ $d := 86400\,s$

Substance: MMA, polymerisation, wet, generic site

$i := 1..3$ $a := 365 \cdot d$

Input:

annual average total deposition flux: $DEPtotal_{ann} := 0.56 \cdot mg \cdot m^{-2} \cdot d^{-1}$

soil-water partitioning coefficient: $K_{soil\_water} := 1.7$

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

air-water partitioning coefficient: $K_{air\_water} := 0.011$

rate constant for for removal from top soil: $kbio_{soil} := 2.3 \cdot 10^{-2} \cdot d^{-1}$

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

Defaults:

mixing depth of soil: $DEPTHsoil_i :=$

$0.2 \cdot m$
$0.2 \cdot m$
$0.1 \cdot m$

bulk density of soil: $RHO_{soil} := 1700 \cdot kg \cdot m^{-3}$

average time for exposure: $T_i :=$

$30 \cdot d$
$180 \cdot d$
$180 \cdot d$

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

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

partial mass transfer coefficient at soilwater-side of the air-soil interface: $kasl_{soilwater} := 4.8 \cdot 10^{-5} \cdot m \cdot d^{-1}$

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

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

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:

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

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:

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

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

		$\frac{Clocal_{soil_i}}{ppm}$
$Clocal_{soil}$	=	0.041
$Clocal_{agr.soil}$	=	0.041
$Clocal_{grassland}$	=	0.058

		$\frac{PEClocal_{soil_i}}{ppm}$
$PEClocal_{soil}$	=	0.041
$PEClocal_{agr.soil}$	=	0.041
$PEClocal_{grassland}$	=	0.058

concentration in pore water

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

		$\frac{Clocal_{soil\_porew_i}}{mg \cdot l^{-1}}$
$Clocal_{soil\_porew}$	=	0.041
$Clocal_{agr.soil\_porew}$	=	0.041
$Clocal_{grassland\_porew}$	=	0.058

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

		$\frac{PEClocal_{soil\_porew_i}}{mg \cdot l^{-1}}$
$PEClocal_{soil\_porew}$	=	0.041
$PEClocal_{agr.soil\_porew}$	=	0.041
$PEClocal_{grassland\_porew}$	=	0.058

concentration in ground water

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

Appendix A16 SimpleBox2.0a – calculation of continental and regional PEC's

Table A16 Adaptation to TGD (1996) / EUSES 1.00: Umweltbundesamt (06/98)

INPUT - MMA				
Parameter names acc. SimpleBox20	Unit	names	Input	Parameter names according Euses
Physicochemical properties				
COMPOUND NAME	[-]	input1	MMA	Substance
MOL WEIGHT	[g.mol-1]	input2	100,12	Molecular weight
MELTING POINT	[° C]	input3	-48	Melting Point
VAPOR PRESSURE(25)	[Pa]	input4	4200	Vapour pressure at 25°C
log K_{ow}	[log10]	input5	1,38	Octanol-water partition coefficient
SOLUBILITY(25)	[mg.l^{-1}]	input6	16000	Water solubility
Distribution - Partition coefficients				
- Solids water partitioning (derived from K_{oc})				
Kp(soil)	[l.kg_{d}^{-1}]	input7	1	Solids-water partitioning in soil
Kp(sed)	[l.kg_{d}^{-1}]	input8	1	Solids-water partitioning in sediment
Kp(susp)	[l.kg_{d}^{-1}]	input9	1	Solids-water partitioning in sudpended matter
- Biota-water				
BCF(fish)	[l.kg_{w}^{-1}]	input10	3	Biocentration factor for aquatic biota
Degradation and Transfromation rates - Characterisation and STP				
PASSreadytest	[y / n]	input11	y	Characterisation of biodegradability
- Environmental Total Degradation				
kdeg(air)	[d-1]	input12	1,72E+00	Rate constant for degradation in air
kdeg(water)	[d^{-1}]	input13	4,70E-02	Rate constant for degradation in bulk surface water
kdeg(soil)	[d^{-1}]	input14	2,30E-02	Rate constant for degradation in bulk soil
kdeg(sed)	[d^{-1}]	input15	2,30E-03	Rate constant for degradation in bulk sediment
Sewage treatment (e.g. calculated by SimpleTreat)				
- Continental				
$FR_{(volatstp)}$ [C]	[-]	input16	7,00E-02	Fraction of emission directed to air (STPcont)
$FR_{(effstp)}$ [C]	[-]	input17	1,08E-01	Fraction of emission directed to water (STPcont)
$FR_{(sludgestp)}$ [C]	[-]	input18	1,00E-03	Fraction of emission directed to sludge (STPcont)
- Regional				
FR(volatstp) [R]	[-]	input19	7,00E-02	Fraction of emission directed to air (STP_{reg})
FR(effstp) [R]	[-]	input20	1,08E-01	Fraction of emission directed to water (STP_{reg})
FR(sludgestp) [R]	[-]	input21	1,00E-03	Fraction of emission directed to sludge (STP_{reg})

Table A16 continued overleaf

Table A16 continued. Adaptation to TGD (1996) / EUSES 1.00: Umweltbundesamt (06/98)

Release estimation – Continental					
	$E_{direct(air)}$ [C]	[t.y^{-1}]	input22	10292	Total continental emission to air
	STP_{load} [C]	[t.y^{-1}]	input23	1794	Total continental emission to wastewater
	$E_{direct(water1)}$) [C]	[t.y^{-1}]	input24	61	Total continental emission to surface water
	$E_{direct(soil3)}$ [C]	[t.y^{-1}]	input25	0	Total continental emission to industrial soil
	$E_{direct(soil2)}$ [C]	[t.y^{-1}]	input30	0	Total continental emission to agricultural soil
- Regional					
	$E_{direct(air)}$ [R]	[t.y^{-1}]	input26	2380	Total continental emission to air
	STP_{load} [R]	[t.y^{-1}]	input27	433	Total continental emission to wastewater
	$E_{direct(water1)}$ [R]	[t.y^{-1}]	input28	5,2	Total continental emission to surface water
	$E_{direct(soil3)}$ [R]	[t.y^{-1}]	input29	0	Total continental emission to industrial soil
	$E_{direct(soil2)}$ [R]	[t.y^{-1}]	input31	0	Total continental emission to agricultural soil
OUTPUT - MMA					
Parameter names acc. SimpleBox20		Unit	names	Output	Parameter names according Euses
Physicochemical properties					
	COMPOUND NAME	[-]	input1	MMA	Substance
Output					
- Continental					
	$PEC_{surfacewater\ (total)}$	[mg.l^{-1}]	output1	8,72E-06	Continental PEC in surface water (total)
	$PEC_{surfacewater\ (dissolved)}$	[mg.l^{-1}]	output2	8,72E-06	Continental PEC in surface water (dissolved)
	PEC_{air}	[mg.m^{-3}]	output3	4,85E-06	Continental PEC in air (total)
	$PEC_{agr.soil}$	[mg.kg$_{wwt}^{-1}$]	output4	5,91E-07	Continental PEC in agricultural soil (total)
	$PEC_{porewater\ agr.soil}$	[mg.l^{-1}]	output5	5,91E-07	Continental PEC in pore water of agricultural soils
	$PEC_{nat.soil}$	[mg.kg$_{wwt}^{-1}$]	output6	3,85E-07	Continental PEC in natural soil (total)
	$PEC_{ind.soil}$	[mg.kg$_{wwt}^{-1}$]	output7	3,85E-07	Continental PEC in industrial soil (total)
	$PEC_{sediment}$	[mg.kg$_{wwt}^{-1}$]	output8	8,09E-06	Continental PEC in sediment (total)
- Regional					
	$PEC_{surfacewater\ (total)}$	[mg.l^{-1}]	output9	1,44E-04	Regional PEC in surface water (total)
	$PEC_{surfacewater\ (dissolved)}$	[mg.l^{-1}]	output10	1,44E-04	Regional PEC in surface water (dissolved)
	PEC_{air}	[mg.m^{-3}]	output11	5,49E-05	Regional PEC in air (total)
	$PEC_{agr.soil}$	[mg.kg$_{wwt}^{-1}$]	output12	1,03E-05	Regional PEC in agricultural soil (total)
	$PEC_{porewater\ agr.soil}$	[mg.l^{-1}]	output13	1,03E-05	Regional PEC in pore water of agricultural soils
	$PEC_{nat.soil}$	[mg.kg$_{wwt}^{-1}$]	output14	4,36E-06	Regional PEC in natural soil (total)
	$PEC_{ind.soil}$	[mg.kg$_{wwt}^{-1}$]	output15	4,36E-06	Regional PEC in industrial soil (total)
	$PEC_{sediment}$	[mg.kg$_{wwt}^{-1}$]	output16	1,36E-04	Regional PEC in sediment (total)

Appendix A17 Indirect exposure via the environment (TGD, Chapter 2)

Name MMA CAS - No.:80-62-6

Input

chemical properties

octanol-water partitioning coefficient [-]	$logK_{OW} := 1.38$ $K_{OW} := 10^{logK_{OW}}$
Henry - partitioning coefficient [Pa*m ^{3}*mol $^{-1}$]	$HENRY := 26.3 \cdot Pa \cdot m^3 \cdot mol^{-1}$
air-water partitioning coefficient [-]	$K_{air\_water} := 0.011$
fraction of the chemical associated with aerosol particles [-]	$F_{ass\_aer} := 2.4 \cdot 10^{-8}$
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 $_{water}$ $^{-1}$]	$PEClocal_{water\_ann} := 1.48 \cdot mg \cdot l^{-1}$
annual average local PEC in air (total) [mg $_{chem}$ * m $_{air}$ $^{-3}$]	$PEClocal_{air\_ann} := 0.381 \cdot mg \cdot m^{-3}$
local PEC in grassland (total), averaged over 180 days [mg $_{chem}$ * kg $_{soil}$ $^{-1}$]	$PEClocal_{grassland} := 0.058 \cdot mg \cdot kg^{-1}$
local PEC in porewater of agriculture soil [mg $_{chem}$ * l $_{porewater}$ $^{-1}$]	$PEClocal_{agr\_soil\_porew} := 0.041 \cdot mg \cdot l^{-1}$
local PEC in porewater of grassland [mg $_{chem}$ * l $_{porewater}$ $^{-1}$]	$PEClocal_{grassland\_porew} := 0.058 \cdot mg \cdot l^{-1}$
local PEC in groundwater under agriculture soil [mg $_{chem}$ * l $_{water}$ $^{-1}$]	$PEClocal_{grw} := 0.041 \cdot mg \cdot l^{-1}$
regional PEC in surface water (dissolved) [mg $_{chem}$ * l $_{water}$ $^{-1}$]	$PECregional_{water} := 1.44 \cdot 10^{-4} \cdot mg \cdot l^{-1}$
regional PEC in air (total) [mg $_{chem}$ * m $_{air}$ $^{-3}$]	$PECregional_{air} := 5.49 \cdot 10^{-5} \cdot mg \cdot m^{-3}$
regional PEC in agriculture soil (total) [mg $_{chem}$ *kg $_{soil}$ $^{-1}$	$PECregional_{agr\_soil} := 1.03 \cdot 10^{-5} \cdot mg \cdot kg^{-1}$
regional PEC in porewater of agriculture soils [mg $_{chem}$ *l $_{water}$ $^{-1}$	$PECregional_{agr\_soil\_porew} := 1.03 \cdot 10^{-5} \cdot mg \cdot l^{-1}$

Results of calculation

$DOSE_{tot_{local}} = 0.132 \cdot \frac{mg}{kg_{bw} \cdot d}$

$DOSE_{tot_{regional}} = 1.676 \cdot 10^{-5} \cdot \frac{mg}{kg_{bw} \cdot d}$

$RDOSE_{drw_{local}} = 31.995 \cdot \%$

$RDOSE_{drw_{regional}} = 24.553 \cdot \%$

$RDOSE_{air_{local}} = 61.77 \cdot \%$

$RDOSE_{air_{regional}} = 70.207 \cdot \%$

$RDOSE_{stem_{local}} = 0.551 \cdot \%$

$RDOSE_{stem_{regional}} = 0.626 \cdot \%$

$RDOSE_{root_{local}} = 0.208 \cdot \%$

$RDOSE_{root_{regional}} = 0.412 \cdot \%$

$RDOSE_{meat_{local}} = 3.38 \cdot 10^{-4} \cdot \%$

$RDOSE_{meat_{regional}} = 3.065 \cdot 10^{-4} \cdot \%$

$RDOSE_{milk_{local}} = 0.006 \cdot \%$

$RDOSE_{milk_{regional}} = 0.006 \cdot \%$

$RDOSE_{fish_{local}} = 5.467 \cdot \%$

$RDOSE_{fish_{regional}} = 4.195 \cdot \%$

European Commission

EUR 19832 EN **European Union Risk Assessment Report methyl methacrylate, Volume 22**

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

Luxembourg: Office for Official Publications of the European Communities

2002 – VIII pp., 184 pp. – 17.0 x 24.0 cm

Environment and quality of life series

ISBN 92-894-1253-4

Price (excluding VAT) in Luxembourg: EUR 29.50

The report provides the comprehensive risk assessment of the substance methyl methacrylate. 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 risk assessment for methyl methacrylate concludes that there is at present concern for the environment and for human health. There is a need for specific risk reduction measures beyond those, which are being applied already.

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LB-NA-19832-EN-C

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

European Union Risk Assessment Report

methyl methacrylate

CAS No: 80-62-6 EINECS No: 201-297-1

Series: 1st Priority List Volume: 22

Price (excluding VAT) in Luxembourg: EUR 29.50

OFFICE FOR OFFICIAL PUBLICATIONS
OF THE EUROPEAN COMMUNITIES
L – 2985 Luxembourg

ISBN 92-894-1253-4