European Chemicals Bureau

Institute for Health and Consumer Protection

European Chemicals Bureau

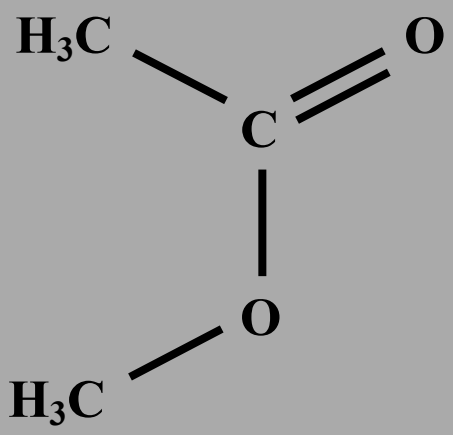
Existing Substances

# European Union Risk Assessment Report

CAS No: 79-20-9

EINECS No: 201-185-2

## methyl acetate




European Union Risk Assessment Report
methyl acetate
CAS: 79-20-9
EC: 201-185-2
PL-1
34

1st Priority List

Volume: 34

EUROPEAN COMMISSION
JOINT RESEARCH CENTRE

EUR 20783 EN

# European Union Risk Assessment Report

## METHYL ACETATE

CAS No: 79-20-9

EINECS No: 201-185-2

## RISK ASSESSMENT

Cataloguing data can be found at the end of this publication
Luxembourg: Office for Official Publications of the European Communities, 2003


*Printed in Italy*

# METHYL ACETATE

CAS No: 79-20-9

EINECS No: 201-185-2

# RISK ASSESSMENT

*Final Report, 2003*

Germany

The risk assessment of methyl acetate has been prepared by Germany on behalf of the European Union.

Contact point:

Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA)
Anmeldestelle Chemikaliengesetz
Friedrich-Henkel-Weg 1-25
44149 Dortmund

Fax: +49 (231) 9071 679
e-mail: chemg@baua.bund.de

| | |
|---|---|
| **Date of Last Literature Search:** | **2002** |
| **Review of report by MS Technical Experts finalised:** | **2001** |
| **Final report:** | **2003** |

## Foreword

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

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

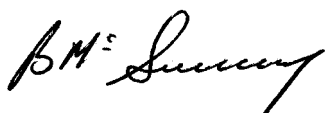
There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each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

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

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

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

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



**Barry Mc Sweeney**
Director-General
DG Joint Research Centre

**Catherine Day**
Director-General
DG Environment

---

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

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

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

# 0 OVERALL RESULTS OF THE RISK ASSESSMENT

CAS-No.: 79-20-0
EINECS-No.: 201-185-2
IUPAC name: methyl acetate

## 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.

Based on the currently available data, methyl acetate represents no risk to the environment for the area of production, processing, formulation and use.

## Human health

Human health (toxicity)

*Workers*

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

This conclusion applies because of:

- Irritation after inhalation in the following scenario:
  - Flooring works, building trade;
- Local effects after repeated inhalation in the following scenarios:
  - Manufacture and further processing as a chemical intermediate (companies that did not submit measurement data);
  - Production of formulations (paints, lacquers, adhesives, cleanser);
  - Metal treatment, electro-engineering, wood treatment;
  - Pulp and paper production (paints and adhesives);
  - Flooring works, building trade;
  - Use of cosmetics.
- Systemic effects after repeated inhalation in the following scenarios:
  - Production of formulations (paints, lacquers, adhesives, cleanser);
  - Metal treatment, electro-engineering, wood treatment;
  - Pulp and paper production (paints and adhesives);
  - Flooring works, building trade.
- Developmental toxicity after inhalation in the following scenario:
  - Flooring works, building trade.

*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.

Human health (risks from physicochemical 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

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

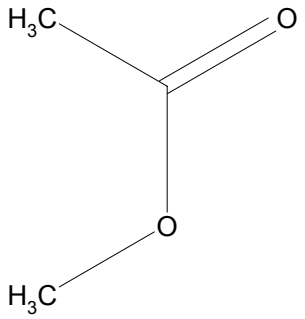
# TABLES

# 1 GENERAL SUBSTANCE INFORMATION

## 1.1 IDENTIFICATION OF THE SUBSTANCE

CAS-No.: 79-20-9
EINECS-No.: 201-185-2
IUPAC name: Methyl acetate
Synonyms: Acetic acid methyl ester
Molecular weight: 74.08 $g \cdot mol^{-1}$
Molecular formula: $C_3H_6O_2$
Structural formula:

Structural formula:




## 1.2 PURITY/IMPURITIES, ADDITIVES

Purity: > 99%
Impurities: acetaldehyde
methanol
water
acetic acid
acetaldehydedimethylacetale
methylformiate
acetone
ethylacetate
vinylacetate
(Wacker-Chemie, 1994; Hoechst AG, 1994)

Dependent on the production process, in addition to the pure substance, a solvent mixture of methyl acetate is formed containing approx. 15 up to 30% acetone, < 8% methanol, 0.5 up to 1.5% water and < 0.05% acetic acid (Hoechst AG, 1992).

## 1.3 PHYSICO-CHEMICAL PROPERTIES

**Table 1.1** Physico-chemical properties

| | | |
|---|---|---|
| Physical state | liquid at 20°C | |
| Melting point | - 98.1°C | CRC Handbook (1991/92) |
| Boiling point | 57°C at 1,013 hPa | CRC Handbook (1991/92) |
| Relative density | 0.928 at 20°C | Römpp (1995) |
| Vapour pressure | 133 hPa at 9.4°C<br>533 hPa at 40°C<br>217 hPa at 20°C | CRC Handbook (1991/92)<br>CRC Handbook (1991/92)<br>Hoechst AG (1994d) |
| Surface tension | 37.3 mN/m at 20°C<br>(conc. 148.2 g/l in water) | Hoechst AG (1994d) |
| Water solubility | 250-295 g/l at 20°C | Hoechst AG (1994d)<br>Wacker-Chemie GmbH (1994a) |
| Partition coefficient<br>log Pow | 0.14 (calculated)<br>0.18 at 20°C | Hoechst AG (1994c)<br>Collander (1951) |
| Flash point | -10°C | CHEMSAFE |
| Auto flammability | 475°C | CHEMSAFE |
| Flammability | highly flammable | Test A.12 and A.13 not conducted because of structural reasons |
| Explosive properties | not explosive | no test because of structural reasons |
| Oxidizing properties | no oxidising properties | no test because of structural reasons |

The data given in the table are related to the pure substance (> 99% purity)
Vapour pressure:

- the value at 20°C can also be interpolated from the literature data and results in 221 hPa which is in good agreement with the given value of 217 Pa in the safety data sheet of the Hoechst AG;
- the value of 217 hPa was used for all further calculations.

## 1.4 CLASSIFICATION

Classification

| | |
|---|---|
| F; R11 | Highly flammable |
| Xi; R36 | Irritating to eyes |
| R66 | Repeated exposure may cause skin dryness or cracking |
| R67 | Vapour may cause drowsiness and dizziness |

Labelling

F; Xi
R: 11-36-66-67
S: (2-)16-26-29-33

According to the data presented below and the criteria of Directive 93/21/EEC, methyl acetate has not to be classified as dangerous for the environment.

Methyl acetate is classified according to water-hazard class 1 (slightly hazardous to water).

In the general administrative provisions relating to the (German) federal law on the prevention of immissions - technical regulations on air pollution control (technical regulations on air pollution control of 27.02.1986) - methyl acetate is named in Annex E and classified according to class II (at a mass flow of 2 kg/h or more, the mass concentration must not exceed 0.1 $g/m^3$).

# 2 GENERAL INFORMATION ON EXPOSURE

## 2.1 PRODUCTION

According to the information from the currently available IUCLID data sets there are four production sites of methyl acetate in the EU. No information is available on possible imports.

The production quantity is given as 30,000 t/a for 1993.

Dependent on the production process, approximately 99.5% pure methyl acetate or a solvent mixture containing 60 to 75% methyl acetate results in the production of methyl acetate. In addition to methyl acetate, the solvent mixture which occurs contains approximately 15 to 30% acetone, <8% methanol, 0.5 to 1.5% water and <0.05% acetic acid (Hoechst AG, 1992).

## 2.2 USES

In Germany, approximately 70% of the methyl acetate which is produced is used as a solvent (e.g. in adhesives, paint systems, in cosmetic agents and cleaning products). A further quantity (approx. 10%) of the substance is used as an intermediate in the manufacture of plant protection products and vitamins. The remainder (20%) is exported and used as an intermediate for the production of sweeteners. The destination is unknown (Hoechst AG, 1994a). Further information on the use of the substance is not available for the EU.

It can be assumed that the use pattern of methyl acetate in Germany is also applicable to the EU. The special conditions which relate to Germany will be considered in the exposure consideration for the area concerning the use of the substance. However, attention must be drawn to the fact that comparable local exposures to methyl acetate during use of the substance are also to be expected in the other EU member states.

The use of methyl acetate as a solvent in adhesives and paint systems is described in the Danish Product Register of January 1995. 6 products with a content of 0 to 1%, 8 products with a content of 1 to 10% and 14 products with a content of 10 to 80% are known. The quantity of the substance used in the products is around 3 t/a (Danish Product Register, 1995).

The substance is also listed in the Swedish Product Register for 1993. Approximately 4 to 6 t/a methyl acetate are used as a solvent and in adhesives (Swedish Product Register, 1993). Methyl acetate is not included in the Norwegian Product Register for 1994. (Norwegian Product Register, 1994).

Products containing methyl acetate are used by consumers.

**Table 2.1** shows the main, industrial and use categories and the mass balance of methyl acetate for the German market.

**Table 2.1** Main, industrial, use categories and mass balance of methyl acetate for the German market

| Main category (MC) | Industrial category (IC) | Use category (UC) | Mass balance [in % of use] |
|---|---|---|---|
| Non-dispersive use (1) | Chemical industry (3) | Intermediate (33) | 30 |
| Wide dispersive use (4) | Personal/domestic (5) | Solvent (48) | 70 |
| Wide dispersive use (4) | Paint, laquers and varnishes industry (14) | Solvent (48) | |

# 3 ENVIRONMENT

## 3.1 ENVIRONMENTAL EXPOSURE

### 3.1.1 Evironmental release

During production, use as an intermediate and use, methyl acetate is expected to enter the environment via the wastewater and the exhaust air.

### 3.1.2 Environmental fate

#### 3.1.2.1 Degradation

Biodegradation

The substance can be classified as "readily biodegradable" on the basis of an available study according to OECD-guideline 301 D (Hoechst AG, 1995b). This closed bottle test indicates 74% biodegradation after 14 days, 75% after 19 days and 70% after 28 days. There is no information on possible intermediates before ultimate degradation of methyl acetate. Probably methanol and acetic acid could be intermediates of the biodegradation. The degradation of the possible intermediates is included in the results of the biodegradation test.

There are no results from simulation tests for biodegradation in wastewater treatment plants, in the aquatic compartment and in soil. Consequently, taking account of the above-mentioned study, the following rate constants may be considered for biodegradation in accordance with the Technical Guideline Document (TGD) (EC, 1996).

**Table 3.1** Degradation constants

| Compartment | Degradation constant |
|---|---|
| Wastewater treatment plant | $kbio_{WWTP}$ = 1 $h^{-1}$ |
| Aquatic environment | $Kbio_{surface\ water}$ = 0.047 $d^{-1}$ |
| Sediment | $kbio_{sed}$ = 0.002 $d^{-1}$ |
| Soil | $kbio_{soil}$ = 0.023 $d^{-1}$ |

See Appendix A1 for calculation

Photodegradation

Direct photolysis of methyl acetate in the atmosphere is not to be expected. However, in the atmosphere gaseous methyl acetate reacts with hydroxyl radicals which have been formed photochemically. On the basis of an atmospheric concentration of the OH-radicals amounting to $5 \cdot 10^5$ OH/$cm^3$ and the rate constant ($kdeg_{air}$) of $0.3182 \cdot 10^{-12}$ $cm^3 \cdot molecule^{-1} \cdot s^{-1}$, a half-life of 50.4 days is calculated for the photochemical degradation in the atmosphere. A half-life of

94 days was determined on the basis of laboratory investigations into photochemical degradation (Atkinson, 1986).

Hydrolysis

The hydrolysis of methyl acetate was examined in an older investigation from 1935. In this, a hydrolysis half-life of approximately 53 days at a temperature of 23.2 to 25.4°C was determined for methyl acetate (148.6 g/l). No information was provided on the pH value of the solution (Handorf and Washburn, 1935).

Hydrolysis half-lives of between approximately 63 days (pH = 8) and approximately 627 days (pH = 7) were calculated for the substance using QSAR calculations. Hydrolysis should therefore not represent a significant elimination process for methyl acetate in the environment.

### 3.1.2.2 Distribution

On account of the vapour pressure of 217 hPa, methyl acetate is expected to evaporate quickly from surfaces.

A Henry constant of 6.43 Pa $m^3$/mol at 20°C is calculated from the data on the vapour pressure and water solubility of methyl acetate given in Section 1. Consequently, the substance is moderately volatile from an aqueous solution. (see Appendix A1 for the calculation).

No bioaccumulation potential is to be expected due to the measured log Pow value for methyl acetate of 0.18. On the basis of this value the Koc is calculated as 12.99 l/kg and the partition coefficients can be calculated according to the organic carbon content in the individual environmental compartments.

**Table 3.2** Partition coefficients

| Compartment | Partition coefficient |
|---|---|
| Soil-water | $Kp_{soil}$ = 0.26 l/kg |
| Sediment-water | $Kp_{sed}$ = 0.649 l/kg |
| Suspended matter-water | $Kp_{susp}$ = 1.299 l/kg |
| Sewage sludge-water | $Kp_{sludge}$ = 4.806 l/kg |

See Appendix A1 for the calculation

The following theoretical distribution in the environment results for methyl acetate using the distribution model according to Mackay (Level 1).

**Table 3.3** Theoretical distribution in the environment

| Compartment | Percentage |
|---|---|
| Air | 69.3 |
| Water | 30.7 |
| Soil | 0.0 |
| Sediment | 0.0 |

Consequently, the atmosphere and the hydrosphere are the target compartments for methyl acetate in the environment.

Elimination in wastewater treatment plants

On the basis of the physico-chemical properties of methyl acetate and in consideration of the rate constant for biodegradation of 1 $h^{-1}$, the elimination in wastewater treatment plants can be determined using the SIMPLETREAT model in accordance with the TGD as follows:

**Table 3.4** Elimination in wastewater treatment plants

| | |
|---|---|
| Evaporation to air (%) | 2.3 |
| Release (dissolved) to water (%) | 12 |
| Adsorpion to sewage sludge (%) | 0 |
| Degradation (%) | 85.7 |
| **Total elimination from water (%)** | **88** |

### 3.1.2.3 Accumulation

No investigations on bioaccumulation are available. The measured log Pow of 0.18 does not provide any indication of a relevant bioaccumulation potential.

The calculated Koc value of 12.99 l/kg (see Appendix A1 for the calculation) also does not indicate that a significant geoaccumulation potential is to be expected for methyl acetate. The substance may be washed out from soil to groundwater by rainwater depending on the elimination in soil by degradation and distribution.

## 3.1.3 Aquatic compartment (incl. sediment)

Where known, the current production volume taken from information provided by the companies is considered in the determination of the $Clocal_{water}$. Since, however, in the case of a change in the production quantity within the quantity ranges indicated in the IUCLID data set no notification has to be made to the notification unit, when adopting the generic approach to the calculation of the $Clocal_{water}$ for production and use as an intermediate, the maximum production quantity or production capacity is considered.

Releases into the wastewater occur during production and use as an intermediate. Since the exposure data submitted by the companies for production and further processing can not be verified (only valuations by the management are available), in accordance with the ESD (Emission Scenario Documents, TGD Chapter 7), releases into the wastewater amounting to 0.3% of the production quantity and 0.7% of the processing quantity are considered.

### 3.1.3.1 Determination of the $Clocal_{water}$ / generic approach with regard to production and use as an intermediate

A generic exposure scenario for the entry of intermediates into the wastewater during production and use as an intermediate is described in the TGD. It corresponds to a realistic “worst-case”

scenario. Taking into consideration a maximum production quantity at one site of 10,000 t/a and a maximum on-site processing of 2,500 t/a, a $Clocal_{water}$ of approximately 5 µg/l results for production and use as an intermediate at one production and processing site (see Appendix A2 for the calculation).

### 3.1.3.2 Determination of the $Clocal_{water}$ / site-specific approach with regard to production and use as an intermediate

Using the currently available information on the individual manufacturers, site-specific exposure calculations can be performed (sites A to C).

For a production quantity of 5,000 t/a (production outside of Germany) the use area is not known. For risk assessment it is therefore assumed that this quantity is processed further at the same site (site D).

Site E represent a fictive site within the EU using the total amount of methyl acetate applied within the EU for the production of sweeteners.

$Clocal_{water}$ values ranging from 0.07 to 4.6 µg/l result for the five sites at which methyl acetate is either produced or used as an intermediate.

**Table 3.5** Determination of $Clocal_{water}$ at production and further processing sites

| Site | Release to wastewater (kg/d) | Size of STP ($m^3$/d) | Min.flow of receiv.water ($m^3$/s) | Conc. effluent STP (µg/l) | Conc. receiv.water (µg/l) |
|---|---|---|---|---|---|
| A | 100 [1)] | 71,000 | 70.5 | 169 | 1.95 |
| B | 50 [1)] | | 1,040 | | 0.07 |
| C | 100 [1)] | 20,700 | 30 | 571.4 | 4.6 |
| D | 166.7 [1)] | | 60 [1)] | | 3.9 |
| E | 116.7 [1)] | | 60 [1)] | | 2.7 |

[1)] based on the default value of the TGD (see Chapter 3.1.2)

### 3.1.3.3 Determination of the $Clocal_{water}$ / generic approach: use

Methyl acetate is used as a solvent for cleaning products, adhesives for floor covering and paint systems (Hoechst AG, 1994a). Since no quantitative breakdown of the application areas is available for the exposure assessment an even distribution between the three uses is assumed.

With an amount of ca. 17,500 t/a used as a solvent, 5,800 t/a for each use is taken as a basis for the calculation of the $Clocal_{water}$.

Use as a solvent in cleaning products and household chemicals

If the substance is used as a solvent in cleaning products and household chemicals, exposure is to be expected during the formulation of the products in the relevant companies. In addition, releases are expected during use of the cleaning products and household chemicals.

For the release estimations based on the use of methyl acetate as a solvent in cleaning products and household chemicals a content of 50% of the substance in the products is used for the derivation of the fraction of main source.

In the case of use as a solvent in cleaning products and household chemicals it is assumed that the total quantity used is released either to household wastewater or to the atmosphere as a result of evaporation.

Use as a solvent in adhesives

If the substance is used as a solvent in adhesives for floor covering exposure is to be expected during the formulation of the final products in the relevant companies. In addition, releases are expected during use of the adhesives for floor covering (e.g. parquet).

For the release estimations based on the use of methyl acetate as a solvent in adhesives a content of 50% of the substance in the products are used for the derivation of the fraction of main source.

As a result of use of the substance as a solvent in adhesives for floor covering the substance is primarily released into the air. A relevant release into the wastewater is not to be expected.

Use as a solvent in paints and lacquers

If the substance is used as a solvent in paints and lacquers exposure is to be expected during the formulation of the final products in the relevant companies. In addition, releases are expected during use of the paints and lacquers.

For the release estimations based on the use of methyl acetate as a solvent in paints and lacquers a content of 50% of the substance in the products is used for the derivation of the fraction of main source for the formulation of the products.

Based on the available information of some companies where paints and lacquers are formulated, methyl acetate is only used in solvent-based products specified as quick-drying paints and lacquers.

In Germany there is a large automobile producer, where methyl acetate is used (ca. 3,800 t/a) as a solvent in quick-drying paints and lacquers. This paints and lacquers are not used in the serial varnishing but only for repairing lacquers. The repairing lacquers are not only used in the parent house but in several workshops with an own varnishing word wide. Based on this information the fraction of main source of 0.1 (TGD, Chapter 3, Appendix I, B-Table 3.13) for the processing of paints and lacquers seems not realistic in this case. If methyl acetate is used in many workshops with an own varnishing more than 10 sites in the region (i.e. Germany) have to be assumed. A realistic fraction of main source would be 0.01 (based on 100 sites) for the use of methyl acetate in workshops with an own varnishing and the spread in site size is already covered.

The remaining 2,000 t/a methyl acetate could either be used in the same use category in paint shops or in paints and lacquers classified as "do-it-yourself" in private use.

In the risk assessment the "worst-case" exposure scenarios for both paints for private and industrial use are calculated side by side (based on the used quantity of 5,800 t/a). The results of the calculations of the $Clocal_{water}$ are summarised in **Table 3.6**.

**Table 3.6** Calculations of $Clocal_{water}$ performed according to the TGD

| Types of Use | Household chemicals | Household chemicals | Solvent in paints and lacquers | Solvent in adhesives for floor covering | Use of paints in the private domain | Processing of paints in paint shops |
|---|---|---|---|---|---|---|
| Tonnage (t/a) | 5,800 | 5,800 | 5,800 | 5,800 | 5,800 | 5,800 |
| Main category | non-dispersive use (Ic) | wide-dispersive use | non-dispersive use (Ic) | non-dispersive use (Ic) | wide- dispersive use | non-dispersive use (Ic) |
| Industrial category<br>Use category | 5 (personal/domestic)<br>48 (solvents) | 5 (personal/domestic)<br>48 (solvents) | 14 (paints)<br>48 (solvent) | 14 (paints)<br>48 (solvent) | 14 (paints)<br>48 (solvent) | 14 (paints)<br>48 (solvent) |
| Life cycle step | formulation | private use | formulation | formulation | private use | processing |
| Number of days | 300 (B-table 2.3) | 365 (B-table 4.1) | 300 (B-table 2.3) | 300 (B-table 2.3) | 300 (B-table 4.4) | 300 (B-table 3.13) |
| Release factor to water | 0.003 (A-table 2.1) | 1 (ESD IC 5/6) | 0.003 (A-table 2.1) | 0.003 (A-table 2.1) | 0.04 (A-table 4.5) | 0.02 (A-table 3.15) |
| Fraction of main source | 0.8 (B-table 2.3) | - | 0.8 (B-table 2.3) | 0.8 (B-table 2.3) | 0.002 (B-table 4.4) | 0.01<br>(see Section 3.1.3.3) |
| Size of STP ($m^3$/d) | 2,000 | 2,000 | 2,000 | 2,000 | 2,000 | 2,000 |
| Dilution in receiv. water | 10 | 10 | 10 | 10 | 10 | 10 |
| $Clocal_{effl.}$ (µg/l) | 2,780 | 117.7 | 2,780 | 2,780 | 93.3 | 230 |
| $Clocal_{water}$ (µg/l) | 278 | 11.8 | 278 | 278 | 9.3 | 23 |

See Appendix A2 for the calculation

#### 3.1.3.4 Data on occurrence in the hydrosphere

No measured values relating to the occurrence of methyl acetate in the hydrosphere are available.

#### 3.1.3.5 Sediment

Data on the occurrence in sediment do not exist for methyl acetate. According to the known physico-chemical properties, there is no indication that methyl acetate accumulates in sediment.

### 3.1.4 Atmosphere

In the case of the production of methyl acetate at the German companies, the release into the atmosphere is estimated as being between 0.2 and 16 t/a in 1993 (Hoechst AG, 1995c). No further information is available with regard to the release into the atmosphere during the production and processing or use of the substance. Since the exposure data submitted by the companies for production and processing cannot be verified (only valuations by the management are available), the releases into the atmosphere are calculated in accordance with the TGD (A- and B-tables in Chapter 3, Appendix I).

Using the SIMPLETREAT model, with regard to methyl acetate, release from industrial wastewater treatment plants as a result of evaporation into the air is estimated as approx. 2.3% of the quantity of the substance entering the wastewater treatment plant. Consequently, an additional release into the atmosphere results for the individual production and processing sites. The same release route is also to be expected for use of the substance.

If the substance is used as a solvent in adhesives for floor covering the substance is primarily released into the air. A calculation of a $Clocal_{air}$ is not possible, but for the regional exposure the whole quantity of methyl acetate which remains in Germany (5,800 t/a) is released to the atmosphere.

By taking into consideration the current production and processing quantities, the exposure tables in Chapter 3, Appendix I of the TGD and the SIMPLETREAT model, it is possible to calculate the releases into the atmosphere and the resultant deposition quantities according to the physico-chemical properties of the substance and the quantities of it which are used. The results of the calculations are summarised in **Table 3.7**.

**Table 3.7** Calculations of $Clocal_{air}$ and $DEPtotal_{ann.}$ performed according to the TGD for the production and processing of methyl acetate

| Company | Site A | Site B | Site C | Site D | Site E |
|---|---|---|---|---|---|
| Tonnage | -[1)] | -[1)] | -[1)] | -[1)] | -[1)] |
| Main category | Ic | Ic | Ic | Ib | Ic |
| Industrial category<br>Use category | 3<br>33 | 3<br>33 | 3<br>33 | 3<br>33 | 3<br>33 |
| Life cycle step | prod. | prod. | prod. | prod. / proc. | proc. |
| Number of days | 300<br>(B-table 1.6) | 300<br>(B-table 1.6) | 300<br>(B-table 1.6) | 300<br>(B-table 1.6) | 300<br>(B-table 1.6) |
| Release factor to air | 0.025<br>(A-table 1.2) | 0.025<br>(A-table 1.2) | 0.025<br>(A-table 1.2) | 0.01 (A-table 1.2)<br>0.001 (A-table 3.3) | 0.005<br>(A-table 3.3) |
| Fraction of main source | 1 | 1 | 1 | 1 | 1 |
| Emission to air from STP in % | 2.3 | 2.3 | 2.3 | 2.3 | 2.3 |
| $Clocal_{air}$ ($mg/m^3$) | 0.232 | 0.116 | 0.232 | 0.051 | 0.023 |
| $DEPtotal_{ann.}$ ($mg/m^2 \cdot d$) | 0.275 | 0.137 | 0.275 | 0.061 | 0.028 |

[1)] Confidential information

**Table 3.8** Calculations of $Clocal_{air}$ and $DEPtotal_{ann}$ performed according to the TGD for the use of methyl acetate

| Types of use | Household chemicals | Household chemicals | Solvent in paints and lacquers | Solvent in in adhesives | Use of paints in the private domain | Processing of paints in paint shops |
|---|---|---|---|---|---|---|
| Tonnage (t/a) | 5,800 | 5,800 | 5,800 | 5,800 | 5,800 | 5,800 |
| Main category | non-dispersive use (Ic) | wide-dispersive use | non-dispersive use (Ic) | non-dispersive use (Ic) | wide-dispersive use | non-dispersive use (Ic) |
| Industrial category<br>Use category | 5 (personal/domestic)<br>48 (solvents) | 5 (personal/domestic)<br>48 (solvents) | 14 (paints)<br>48 (solvent) | 14 (paints)<br>48 (solvent) | 14 (paints)<br>48 (solvent) | 14 (paints)<br>48 (solvent) |
| Life cycle step | formulation | private use | formulation | formulation | private use | processing |
| Number of days | 300 (B-table 2.3) | 365 (B-table 4.1) | 300 (B-table 2.3) | 300 (B-table 2.3) | 300 (B-table 4.4) | 300 (B-table 3.13) |
| Release factor to air | 0.01 (A-table 2.1) | 0.175 (A-table 4.1) | 0.01 (A-table 2.1) | 0.01 (A-table 2.1) | 0.95 (A-table 4.5) | 0.9 (A-table 3.15) |
| Fraction of main source | 0.8 (B-table 2.3) | 0.002 (B-table 4.1) | 0.8 (B-table 2.3) | 0.8 (B-table 2.3) | 0.002 (B-table 4.4) | 0.01 (B-table 3.13) |
| Emission to air from STP in % | 2.3 | 2.3 | 2.3 | 2.3 | 2.3 | 2.3 |
| $Clocal_{air}$ ($mg/m^3$) | 0.043 | 0.002 | 0.043 | 0.043 | 0.010 | 0.048 |
| $DEPtotal_{ann.}$<br>($mg/m^2$ d) | 0.051 | 0.002 | 0.051 | 0.051 | 0.012 | 0.057 |

See Appendix A3 for the calculation

### 3.1.5 Terrestrial compartment

Methyl acetate is expected to enter the soil as a result of deposition from the atmosphere. In this regard the point source of the production and the use as an intermediate of the substance involving the highest amount of air pollution are considered (see Section 3.1.4).

The results of the above-mentioned exposure scenarios for the release of the substance into the soil are summarised in **Table 3.9**.

**Table 3.9** Local PECs and concentrations for the terrestrial compartment

| Type of use | Route of exposure | $PEClocal_{soil\text{-}porew}$ in µg/l | $Clocal_{soil}$ in µg/kg |
|---|---|---|---|
| Site - A/C, production | deposition | 59 | 20 |
| Site - D, production and processing | deposition | 13 | 5 |
| Processing of paints and lacquers in paint shops (e.g. car painting) | deposition | 12.2 | 4.2 |
| Formulation of household chemicals | deposition | 11 | 3.8 |

See Appendix A4 for the calculation

Based on the SIMPLETREAT model (see Section 3.1.2) there is no adsorption of methyl acetate at sewage sludge to be expected and the release to soil with sewage sludge application in agriculture is not taking into account in the risk assessment.

### 3.1.6 Secondary poisoning

Since there is no indication of methyl acetate possessing a bioaccumulation potential, a risk characterisation for exposure via the food chain is not necessary.

### 3.1.7 Regional exposure consideration

In the determination of a regional background concentration all releases, from both point and diffuse sources, are considered. 90% of the total exposure quantity is taken into account for the continental model and 10% of it for the defined regional EU standard model (densely populated area of 200 · 200 km with 20 million inhabitants).

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).

Information is available according to which approx. 70% of the quantity produced is used as a solvent in cleaning products and household chemicals and as a solvent in adhesives, paints and lacquers. Releases into the hydrosphere (see Section 3.1.3.3) and the atmosphere (see Section 3.1.4) are to be expected here.

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 85.7% of the substance is biodegraded and 2.3% volatilised, is assumed for this scenario. The remaining 30% of the water is discharged directly into the hydrosphere. In the case of use as a solvent in adhesives, it is assumed that the total quantity (5,800 t/a) enters the atmosphere.

The individual environmental releases are summarised in **Table 3.10**.

**Table 3.10** Regional environmental releases of methyl acetate

| Field of application | Release into the hydrosphere in t/a | | Release into the atmosphere in t/a |
|---|---|---|---|
| | direct | via WWTPs | |
| Production and processing | / | 19.2 | 708.7 |
| Formulation of cleaning products and household chemicals | / | 2.1 | 58.3 |
| Use of cleaning products and household chemicals | 1,435.5 | 402 | 1,092 |
| Formulation of adhesives | / | 2.1 | 58.3 |
| Use of adhesives | / | / | ca. 5,800 |
| Formulation of paints and lacquers | / | 2.1 | 58.3 |
| Use of paints and lacquers in the case of private use | 69.6 | 19.5 | 5,510 |
| Total | ca. 1,505 | ca. 447 | ca. 13,286 |

In the calculation of the continental and regional model the individual releases are as follows:

**Table 3.11** Continental and regional releases

| | Continental model | Regional model |
|---|---|---|
| Air | 11,958 t/a | 1,328 t/a |
| Soil | / | / |
| Water - direct | 1,355 t/a | 150 t/a |
| - via WWTPs | 402 t/a | 45 t/a |

The input data for the model calculations are presented in detail in Appendix A5. The following regional environmental concentrations result from the calculations:

$PECregional_{aquatic}$ = 0.85 µg/l

$PECregional_{air}$ = 0.13 $\mu g/m^3$

$PECregional_{agr.-soil}$ = 0.013 µg/kg (wwt)

$PECregional_{natural-soil}$ = 0.022 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 a few effect data are available with regard to the ecotoxicological effect of methyl acetate. The valid ones are given in the following list for each group of organisms.

Vertebrates

*Leuciscus idus* $LC_{50}$ (48 h) = 225 mg/l
(static, open system, determination of concentration: DOC);
(Aman and Steinhäuser, 1986)

*Pimephales promelas* $LC_{50}$ (96 h) = 320 mg/l
(flow through, determination of concentration: GC);
(Brooke et al., 1984)

Invertebrates

*Daphnia magna* $EC_{50}$ (48 h) = 1,027 mg/l
(effect: immobilisation, determination of concentration: DOC, closed system)
(Hoechst AG, 1995a)

Plants

*Scenedesmus subspicatus* NOEC (72 h) = 120 mg/l
$EC_{10}$ (72 h) > 120 mg/l
$EC_{50}$ (72 h) > 120 mg/l
(effect: growth inhibition, limit test (120 mg/l max. proved concentration, determination of concentration: DTC, closed system);
(Hoechst AG, 1994b)

Microorganisms

*Photobacterium phosphoreum* $EC_{10}$ (30 min) = 1,730 mg/l
$EC_{50}$ (30 min) = 6,100 mg/l
(effect: inhibition of bioluminescence, nominal concentration);
(Aman and Steinhäuser, 1986)

*Pseudomonas putida* $EC_{10}$ (16 h) = 1,830 mg/l
$EC_{50}$ (16 h) = 6,000 mg/l
(effect: growth inhibition, nominal concentration);
(Aman and Steinhäuser, 1986)

Determination of the $PNEC_{aqua}$

The $PNEC_{aqua}$ will be based on fish as these tests have the lowest $EC_{50}$ values. Results of the study with *Pimephales promelas* with a 96-hour $LC_{50}$ of 320 mg/l is preferred, because it is conducted under flow through conditions and with analytical control using GC. The test with *Leuciscus idus* is not so well documented, it must be assumed that it is conducted in open system.

Consequently, only acute investigations are available for the aquatic compartment and a safety factor of 1,000 has to be applied. Accordingly the following value results:

$PNEC_{aqua}$ = 320 mg/l/1,000 = 320 µg/l

Determination of the $PNEC_{WWTP}$

For the determination of the $PNEC_{WWTP}$ for municipal WWTPs, the result with *Pseudomonas putida* (16-hour $EC_{10}$ = 1,830 mg/l) can be used. According to the guidance given in the TGD, the test with *Photobacterium phosphoreum* (30-min $EC_{10}$ = 1,730 mg/l) was not used. In the case of methyl acetate there is practically no difference between these two test results. According to the TGD, the value of the assessment factor is to be determined as 1. A PNEC is calculated as follows:

$PNEC_{WWTP}$ = 1,830 mg/l/1 = 1,830 mg/l

Sediment

No risk assessment is required for this compartment since there are no indications of adsorption of the substance to sediments and neither measured concentrations of methyl acetate for sediments nor experimental investigations with sediment organisms are available.

### 3.2.2 Atmosphere

No ecotoxicological data are available for this environmental compartment.

### 3.2.3 Terrestrial compartment

No ecotoxicological data are available for terrestrial organisms. In approximation, the aquatic PNEC can be used for the purpose of a risk assessment for the terrestrial compartment and compared with the concentration determined for the soil pore water:

$PNEC_{soil}$ = 320 µg/l (soil pore water)

### 3.2.4 Secondary poisoning

Since methyl acetate does not possess a bioaccumulation potential and is neither classified as "toxic" nor "harmful", it is not necessary for a relevant PNEC to be derived.

## 3.3 RISK CHARACTERISATION

### 3.3.1 Aquatic compartment (incl. sediment)

Wastewater treatment plants

The highest discharge concentration for wastewater treatment plants was calculated as 2.78 for the formulation of paints, lacquers, adhesives and household chemicals and 0.232 mg/l for the processing of paints in paint shops (e.g. car painting). Generic models are used here for the calculation of the $Clocal_{effl.}$. No specific information is available for this area of use of the substance or for the exposure in the environment. Consequently, standard scenarios had to be used for the calculation of the concentrations in the wastewater treatment plants.

Taking into consideration a $PNEC_{WWTP}$ of 1,830 mg/l, a $Clocal_{effl.}$/PNEC ratio of 0.0015 and 0.00012 results for the formulation of paints, lacquers, adhesives and household chemicals and the processing of paints in paint shops (e.g. car painting). Since the $Clocal_{effl.}$/PNEC ratio < 1, there is no risk to the microorganism population in the WWTP.

Aquatic environments

The PEC/PNEC ratios for all of the areas of production, processing and use are summarised in **Table 3.12** (PNEC 320 µg/l):

**Table 3.12** PEC/PNEC ratios for water

| Company/area of use | PEClocal = $Clocal_{water}$+ PECregional in µg/l | $PEC/PNEC_{aqua}$ |
|---|---|---|
| Production and/or processing:<br>• max. production of 10,000 t/a and processing of 2,500 t/a (generic approach) | 5.0 + 0.85 = 5.85 | 0.018 |
| • Site - A | 1.95 + 0.85 = 2.8 | 0.009 |
| • Site - B | 0.07 + 0.85 = 0.92 | 0.003 |
| • Site - C | 4.6 + 0.85 = 5.45 | 0.017 |
| • Site - D | 3.9 + 0.85 = 4.75 | 0.015 |
| • Site - E | 2.7 + 0.85 = 3.55 | 0.011 |
| Formulation of household chemicals | 278 + 0.85 = 279 | 0.872 |
| Use of household chemicals | 11.8 + 0.85 = 12.65 | 0.040 |
| Formulation of paints and lacquers | 278 + 0.85 = 279 | 0.872 |
| Formulation of adhesives | 278 + 0.85 = 279 | 0.872 |
| Processing of paints and lacquers in paint shops (e.g. car painting) | 23 + 0.85 = 23.85 | 0.075 |
| Use of paints and lacquers in the private domain | 9.3 + 0.85 = 10.15 | 0.032 |

As all PEC/PNEC ratios are < 1, on the basis of the currently available data there is no risk to aquatic organisms. **Conclusion (ii)**.

Sediment

No data on the occurrence in sediment or investigations into the effect on benthic organisms are available in connection with methyl acetate. According to the available physico-chemical properties of the substance, there is no indication that methyl acetate accumulates in sediment. Consequently, there is no need for a risk consideration for this compartment. **Conclusion (ii)**.

### 3.3.2 Atmosphere

Due to the atmospheric half-life ($t_{1/2}$ = 74 to 94 days), abiotic effects on the atmosphere, such as global warming and ozone depletion, are not to be expected in connection with methyl acetate. The highest calculated air concentration is around 232 µg/m$^3$ for the production of methyl acetate. Since no data are available on the ecotoxicological effect of the substance in connection with this environmental compartment, it is not possible to undertake a quantitative assessment of this environmental compartment. On the basis of the available information on the substance, tests are not considered to be necessary. **Conclusion (ii**).

### 3.3.3 Terrestrial compartment

Releases into the terrestrial compartment as a result of deposition from the atmosphere are to be expected. The highest deposition rate is due to the production of methyl acetate, implying soil concentrations amounting to 20 µg/kg (TS) and 59 µg/l soil pore water.

Since no ecotoxicological data are available for terrestrial organisms, in approximation, the aquatic PNEC (320 µg/l) is considered for the purpose of the risk assessment of the terrestrial compartment and compared with the concentration determined for the soil pore water. With these data a PEC/PNEC ratio of 0.18 is calculated. Therefore, there is no indication of a risk to the terrestrial environmental compartment at the present time. **Conclusion (ii).**

### 3.3.4 Secondary poisoning

Since there is no indication that methyl acetate possesses a bioaccumulation potential, a risk characterisation for exposure via the food chain is not necessary.

# 4 HUMAN HEALTH

## 4.1 HUMAN HEALTH (TOXICITY)

### 4.1.1 Exposure assessment

#### 4.1.1.1 General discussion

Methyl acetate is used as a chemical intermediate, e.g. for the production of methanol, acetic acid, vitamins and plant protection products (approximately 10% of the produced methyl acetate). The ester is mainly used as a solvent, e.g. for paints, lacquers and adhesives as well as in cosmetics and cleaning products (approximately 70%). The remaining 20% is exported and used to produce sweeteners. The given percentages refer to the use pattern in Germany.

In the Swedish product register, 5 out of 19 products containing methyl acetate have been labelled as consumer products. In Germany, products containing methyl acetate are also used by consumers. Thus, the consumer may be exposed to methyl acetate; the exposure may take place via the inhalatory, dermal or oral route.

#### 4.1.1.2 Occupational exposure

In the area of production and further processing in the chemical industry, inhalation and dermal exposures of workers to methyl acetate may occur during sampling, filling, mixing processes as well as during cleaning, maintenance and repair work.

The application of formulations, e.g. paints and adhesives, present the opportunity of inhalation and dermal exposure, especially, if the formulations are used in spray applications.

The following occupational exposure limits are established for methyl acetate (ARIEL, 2002):

| | |
|---|---|
| Norway (1996) | 305 mg/m$^3$ |
| Sweden (2000) | 450 mg/m$^3$ |
| Denmark (2000) | 455 mg/m$^3$ |
| US: ACGIH, Italy (2000) | 606 mg/m$^3$ |
| US: OSHA (1993), Austria (2001), France (1999), Finland (1999), Germany (2001), Ireland (1999), Switzerland (2001), The Netherlands (2001) | 610 mg/m$^3$ |
| Belgium (1999) | 615 mg/m$^3$ |
| Spain (2000), UK (2001) | 616 mg/m$^3$ |

and the following short-term exposure limits:

| | |
|---|---|
| US: ACGIH, Italy (2000) | 757 mg/m$^3$ |
| US: OSHA (1993), France (1999), Ireland (1999) | 760 mg/m$^3$ |
| Belgium (1999) | 768 mg/m$^3$ |
| Finland (1999), Spain (2000), UK (2001) | 770 mg/m$^3$ |
| Sweden (2000) | 900 mg/m$^3$ |
| Austria (2001), Switzerland (2001) | 1,220 mg/m$^3$ |

In Germany the short-term exposure limit is 2,440 mg/m$^3$ (4 · MAK, 15-min average).

Relevant occupational exposure scenarios are to be expected in the following areas:

- production and further processing as a chemical intermediate (Section 4.1.1.2.1),
- formulation of preparations (Section 4.1.1.2.2),
- use of formulations (paints, adhesives, cleansers, no spray techniques, Section 4.1.1.2.3),
- use of formulations (spraying paints and adhesives, Section 4.1.1.2.4),
- use of formulations for flooring works (Section 4.1.1.2.5),
- use of formulations (nail polish remover) in the cosmetic sector (Section 4.1.1.2.6).

#### 4.1.1.2.1 Production and further processing as a chemical intermediate

In this section, exposure scenarios regarding the production and further processing in the large scale chemical industry (Scenarios 1, 2) are clustered with uses of the substance in the cosmetics industry (Scenario 3), because in both areas high level of protection and similar exposure scenarios are to be expected.

Methyl acetate occurs as a by-product in the synthesis of large-scale chemicals. Production and further processing in the chemical industry occur continuously in closed plants. After processing by distillation the substance exists either pure or in a mixture with 15-30% acetone and < 8% methanol. According to the information provided by a manufacturer, in-company transportation to the point of dispatch is via closed pipelines with intermediate storage in tanks. In the work area concerned with dispatch, the pure substance is filled into drums, containers, settling tanks and tank trailer lorries using extraction and gas-displacement systems, the solvent mixture being filled into tankers. Daily exposure over the full shift is assumed.

Methyl acetate is used as a solvent in cosmetic products, e.g. nail polish remover (methyl acetate content 15%, see Section 4.1.1.2.6) (Hoechst AG, 1995)). Cosmetic products are produced under sanitary conditions. It is to be assumed that, in view of the very high sanitary requirements, workplaces (e.g. workplaces for filling operations) are equipped with suitable exhaust ventilation systems. Since the production quantities are unknown, it is unclear whether production is mainly continuous or on a batch basis.

The manufacture of cosmetics requires facilities that maintain high standards of quality and cleanliness (good manufacturing practices, Kirk-Othmer, 1993). It is to be assumed, that handling methyl acetate as a starting product comprises mainly filling and dosing activities, which last considerably shorter than shift length. For the daily duration of exposure relevant activities, 2 hours per day are regarded to be probable.

Inhalation exposure

*Workplace measurements*

The shift averages (n = 37, 34 are personal sampling) from the areas production and further processing as a chemical intermediate (here: saponification of methyl acetate) are mainly located below the determination limit of 61 mg/m$^3$ (20 ml/m$^3$, for 0.66 l sampling volume). No information on the sampling time or the kind of calculation of the shift averages was given. Measurement results from one of three producers were obtained.

According to information provided by the producer, for measuring methyl acetate in the working areas the following method was used: Sampling is performed by adsorption on activated carbon following by desorption and analytical determination with gaschromatography. The limit of determination for methyl acetate is 61 mg/m$^3$ for 0.66 l sampling volume.

The limit of determination for methyl acetate amounts to 1 mg/m$^3$ (0.3 ml/m$^3$) for 40 l sampling volume (sampling duration of approx. 2 h) (BGAA, 1999).

*EASE estimation (EASE for windows, Version 2.0, 1995)*

Exposure by inhalation to vapour during production, further processing incl. cosmetics industry with local exhaust ventilation (Scenarios 1, 2, 3):

Input parameters: T = 20°C, closed system, significant breaching, LEV present
Level of exposure: 31-154 mg/m$^3$ (10-50 ml/m$^3$)

For the cosmetics industry a daily duration of 2 hours is assumed, leading to a daily exposure level of 8-39 (2.5-12.5 ml/m³).

*Conclusion on inhalation exposure*

The available measurement results (mainly < 61 mg/m$^3$) agree well with the exposure range estimated according to the EASE model of 31-154 mg/m$^3$ (10-50 ml/m$^3$).

The 8-hour TWA of < 61 mg/m$^3$ (20 ml/m$^3$) should be considered in the assessment of the risks in the case of daily, prolonged exposure to methyl acetate (Scenario 1). Since no measurement related information and no short-term exposure levels are given, it cannot be excluded, that short-term exposures during certain activities, (e.g. filling) are higher than 61 mg/m³.

Since only 1 of three producers provided measurement results, the representativeness of the measurement results cannot be presupposed. Therefore the estimates of the EASE-model (31-154 mg/m$^3$, 10-50 ml/m$^3$) are taken in addition to describe exposure for those producers and importers which did not submit any measurement data (Scenario 2).

For the cosmetic industry, a level of daily inhalation exposure of 8-39 mg/m$^3$ (2.5-12.5 ml/m³) should be taken for assessing the risks (Scenario 3).

Dermal exposure

When producing and further processing methyl acetate dermal exposure could occur during activities like drumming, sampling, cleaning, maintenance and repair work. For the unprotected worker, according to the EASE model, potential dermal exposure is assessed as follows:

Input parameters: Non dispersive use, direct handling, intermittent
Level of exposure: 0.1-1 mg/cm$^2$/day.

Considering an exposed area of 420 cm$^2$ (palms of hands) the model yields an exposure level of 42-420 mg/person/day.

For assessing actual dermal exposure levels, it has to be considered that the substance is manufactured and further processed primarily in closed systems and that the use of PPE (here gloves and eye protection) during exposure relevant activities is highly accepted in the large-scale chemical industry. The extent of protection by PPE (here gloves) depends inter alia on the suitability of the recommended material with regard to the permeation properties of substance.

In the case of methyl acetate, the predominant effect reducing potential dermal exposure is the very high volatility of the substance (vapour pressure 21.7 kPa) which leads to considerable low retention times of the substance on the skin or on the protective gloves. This exposure reducing effect cannot be considered if workers have continuous direct contact with the substance, e.g.

dipping hands into the substance. For the area of production and further processing of methyl acetate, this situation is regarded to be rather non-probable. Furthermore, it is assumed, that non-occlusive exposure is the predominant exposure situation.

For the purpose of determining the evaporation rate of methyl acetate, an equation was used which was derived within the framework of a research project (Weidlich and Gmehling 1986; Gmehling et al., 1989). This project was aimed at calculating airborne concentrations of substances when emitted from liquid mixtures under consideration of the evaporation and the spreading of the substance at the workplace. For calculating the evaporation times of substances, an equation was derived based on the mass transfer at the interface between the liquid and the vapour (two-film-theory). Mass transfer during evaporation occurs until the equilibrium state is achieved. The main influence on evaporation is the transfer through the interface.

For pure substances, the following equation is used:

$$t_{(s)} = \frac{m \cdot R \cdot T}{M \cdot \beta \cdot p \cdot A} \cdot K$$

| | | |
|---|---|---|
| t: | time | [s] |
| m: | mass, EASE estimate | [mg] (per cm²) |
| R: | gas constant: 8.314 | $J \cdot K^{-1} \cdot mol^{-1}$ |
| T: | skin temperature | [K] |
| M: | molar mass | $[g \cdot mol^{-1}]$ |
| $\beta$: | coefficient of mass transfer in the vapour phase | $[m \cdot h^{-1}]$, for calculation: |
| $\beta$ = | 8.7 | m/h, see below |
| p: | vapour pressure of the pure substance | [Pa] |
| A: | area, EASE: 1 | $cm^2$ |
| K: | conversion factor | |

The skin temperature amounts normally to 28-32°C (ambient temperature: 20-22°C). The reduction of the skin temperature and accordingly of the vapour pressure caused by the evaporation process is not considered in the equation. This might be done by choosing a lower mean temperature for the evaporation process.

The coefficient of mass transfer $\beta$ is described based on empirical studies:

$$\beta = (0.0111 \cdot v^{0.96} \cdot D_g^{0.19}) / (\nu^{0.15} \cdot X^{0.04})$$

| | | |
|---|---|---|
| $D_g$: | coefficient of diffusion, gas phase | |
| v: | velocity of air | [m/h] |
| $\nu$: | kinematic viscosity of air | [m²/h] |
| X: | length of the area of evaporation in the direction of the air stream | [m] |

In the above given equation, the main influencing parameter is the velocity of the air (v). At workplaces v is often between 0.3 m/s and 0.6 m/s (a velocity higher than 0.5 m/s is felt as non-

convenient). Since the hands from which a substance evaporates are often in motion, the air velocity might be higher. For a conservative approach, a low value (0.3 m/s) was chosen.

For different organic solvents, Dg is approx. 0.05 $m^2$/h. As a range might serve 0.03-0.06 $m^2$/h, so that $Dg^{0.19}$ ranges between 0.58 and 0.51.

A literature value was taken for the kinematic viscosity of air ($5.4396 \cdot 10^{-2}$ $m^2$/h).

The parameter X, representing the length of the area of evaporation in the direction of the air stream [m] is because of its low exponent (0.04) not very influencing. For the calculation, a length of 10 cm was taken.

Taking into account a rather low velocity of air (0.3 m/s), β is about 8.7 m/h. This value is in good correspondence with experimental values of similar substances: For ethyl acetate β amounts to 8 m/h (air velocity 0.31 m/s) and for butyl acetate, a value of 9.2 m/h (air velocity 0.31) was obtained.

For methylacetate with the EASE estimate of 1 mg/$cm^2$, an evaporation time of 4 seconds (T = 30°C) is calculated. For methylacetate on the gloves, an assumed temperature of 20°C leads to an evaporation time of 6 seconds. These values should be regarded to represent the order of magnitude, since it is not known in how far the interaction of the skin with the substance influences the evaporation time. The error caused by this interaction is regarded to be higher than the one caused by the uncertainty of the calculation of $\beta$. For different substances (7 substances were investigated) $\beta$ differs about ± 15%.

This short-retention time of methyl acetate on the skin leads to much lower dermal exposures than predicted by the EASE model which considers dermal exposure during the whole shift (42-420 mg/person/day). Taking into account the high volatility of the substance, daily dermal exposure during the production and further processing of the substance is assessed as low (<< 42-420 mg/person/day).

It might be assumed, that during occasionally cleaning and maintenance activities, the suitability of the worn gloves cannot be presupposed, because tests of suitability are often performed for the pure substances only. Taking these circumstances into account, occasional dermal exposure might be higher. The estimation according to the EASE-scenario

Input parameter: Non dispersive use, direct handling, intermittent
Level of exposure: 0,1-1 mg/$cm^2$/day

leads to exposure levels of 84-840 mg/person/day, if a skin area of 840 $cm^2$, corresponding to the skin area of two hands, is considered. Taking into account the high volatility of the substance, actual dermal exposure is considerably lower. In addition, this exposure level is regarded to represent an occasional situation on a non-daily basis. The level is therefore not considered in the summary of exposure results in **Table 4.6.**

*Conclusion on dermal exposure*

On account of the very high volatility of methyl acetate, dermal exposure is assessed as being much lower than the EASE estimates (<< 42-420 mg/person/day), independent from the use of gloves.

It can be presupposed that eye protection is regularly worn. Therefore skin-to-eye contacts as well as splashes to the eyes can be excluded.

It is to be assumed, that the same situation and exposure assessment is valid for the cosmetic industry.

#### 4.1.1.2.2 Formulation of adhesives, paints and cleaning products

In the following, the available information on the formulation of adhesives, paints, cleansers and diluents are presented (Scenario 4):

Adhesives: According to information provided by a manufacturer, methyl acetate is used in the production of solvent adhesives according to various recipes. In this, the substance is fed to the relevant starting vessels via closed pipelines. Further raw materials and small quantities (amount is unknown) of methyl acetate are added via a manhole in order to set the viscosity.

Paints, lacquers: In the formulation of paints and lacquers according to a given recipe both closed dispersing devices (e.g. agitating mills) and open devices (e.g. three-roll mills) are used, either in continuous or in batch operation (Harnisch et al., 1982). Fully automatic production lines are only rarely employed in the paint industry (e.g. for white dispersion paint). Due to the wide variety of types, batch production can be assumed for most types of paints (Goldschmidt et al., 1984). No detailed information on the kind of handling methyl acetate is available. The high-processing quantities of the substance permit the conclusion that methyl acetate is frequently used in recipes.

Cleaning products: Methyl acetate is used as a solvent in cleaning products (content 15-20% (Hoechst AG, 1995)), which are assumed to be used predominantly as special cleansers to absolve rests of lacquers and adhesives. There is only little information about the production of cleansers. Since the final products and the production quantities are unknown, it is unclear whether production is mainly continuous or on a batch basis. In a NIOSH walk-through survey (1980) through a plant which was engaged in the packaging of commercial aerosols and lotions, the compounding and packaging of a spot remover is described (Orris and Daniels, 1980). Some of the ingredients were hand charged into mixers, which were closed afterwards. Inhalation exposure and daily dermal contact during weighing, filling, sampling, maintenance and repair work has to be considered. It is to be assumed, that the exposure scenario is similar to the production of paints and adhesives. In addition, dilutens containing up to 95% methyl acetate are produced.

The use of methyl acetate to formulate adhesives, paints and cleaning products is not limited to the large-scale chemical industry but occurs in small and medium-sized chemical companies, too.

For small- and medium-sized formulating companies, in principle, it cannot be excluded that, in addition to the level of technical protection realised in the large-scale industry, open systems without local exhaust ventilation are used (Voullaire and Kliemt, 1995). According to this scenario, higher inhalative and, as a result of the non-regular use of gloves, higher dermal exposures than in the large-scale chemical industry are expected e.g. during filling, sampling, charging, cleaning, maintenance and repair works.

Inhalation exposure

*Workplace measurements*

**Table 4.1** Exposures at workplaces during production of formulations

| Working area | Years of measurement | Number of samples | Range of measurement data [mg/m³] | 50th percentile [mg/m³] | 90th percentile [mg/m³] | Duration and frequency | Source |
|---|---|---|---|---|---|---|---|
| **8-hour time weighted average** | | | | | | | |
| Production of adhesives | 1990-1994 | 19 (p) | < 152 | - | - | - | producer |
| Production of paints | 1990-1994 | 51 (p) | < 61 | - | - | - | producer |
| Production of paints and parquet-flooring adhesives: mixing, filling, weighing 1) | 1990-1995 | 29(p) (without LEV)<br>43 (p) (with LEV) | - | 7<br>10 | 294<br>175 | | BGAA (1999), BIA (1998) |
| Production of paints: mixing, grinding, tirutation, filling, cleaning | 1987-1999 | 10 (p) | < 9 | - | - | - | Auffarth and Häger (1991) |
| **Short-term measurement** | | | | | | | |
| Production of adhesives, cleaning of tube filling machine | 1983-1986 | 1 | | 1,590 | | 20 min, without LEV | Auffarth and Häger (1989) |

(p): person related measurement results
1) Exposure in the range of 90th percentiles were obtained during the production of parquet floor adhesives

Due to the measurement method which was applied and the measurement strategy (TRGS 402, 1986), the currently available measurement results are regarded as valid.

The presented shift averages (cf. **Table 4.1**) differ to a large extent. This may be caused by the different levels of protection realised in the large-scale chemical industry (measurement data provided by the producer) and in small- and medium-sized companies and by different amounts of the substances in use.

The 90th percentiles provided by BGAA (1999) are regarded to be a measure for the reasonable worst case.

According to the information of one producer, 356 workers are exposed in the areas of formulation in one company.

*EASE estimation (EASE for Windows Version 2, 1995)*

Exposure by inhalation to vapour during the formulation of paints, lacquers, adhesives and cleansers with local exhaust ventilation:

Input parameters: T = 20°C, closed system, significant breaching, LEV present
Level of exposure: 31-154 mg/m³ (10-50 ml/m³)

Exposure by inhalation to vapour during the formulation of paints, lacquers, adhesives and cleansers without local exhaust ventilation:

Input parameters: T = 20°C, non dispersive use, direct handling, dilution ventilation present
Level of exposure: 310-615 mg/m$^3$ (100-200 ml/m$^3$)

*Conclusion on inhalation exposure*

The production of paints, lacquers, cleansers, diluents and adhesives are clustered because of the similarity of the exposure scenarios.

At workplaces without local exhaust ventilation the 90th percentile amounts to (n = 29) 294 mg/m$^3$ (95 ml/m$^3$, Scenario 4a). The exposures at workplaces with local exhaust ventilation are, at 175 mg/m$^3$ (64 ml/m$^3$, 90$^{th}$ percentile, n = 43, Scenario 4b) are lower. These 90$^{th}$ percentiles should be considered as the reasonable worst case for daily inhalation exposure during the production of formulations containing methyl acetate.

Measurement results and EASE estimations accord only partly: The measurement results obtained at workplaces without LEV are located within the range of the values estimated using the EASE model of 310- 615 mg/m$^3$ (100-200 ml/m$^3$, without LEV). The 90$^{th}$ percentile of the measurement collective obtained at workplaces with LEV exceeds the predicted exposure range.

However, higher exposures may also occur for short periods during certain activities; during cleaning of tube filling machines during production of adhesives, one short-term exposure level of 1,590 mg/m$^3$ (518 ml/m$^3$, 20 min, without LEV) was measured (Auffarth and Häger, 1989).

Dermal exposure

For the area of further processing of methyl acetate to paints, lacquers, adhesives and cleansers, it is to be assumed, that gloves are not regularly worn. The corresponding dermal exposure is assessed for the unprotected worker in application of the EASE model.

Input parameters: T = 20°C, non dispersive use, direct handling, intermittent
Level of exposure: 0.1-1 mg/cm$^2$/day

Regarding dermal exposure, a level amounting to 0.1-1 mg/cm$^2$/day for the handling (e.g. filling work) of the pure substances should be considered in the assessment of the possible risks as a result of daily dermal exposure, if suitable protective equipment is not worn. Considering an exposed area of 420 cm$^2$ (palms of two hands), this dermal exposure amounts to 42-420 mg/person/day.

On account of the high vapour pressure of the substance and the resultant short retention time of the substance on the skin, lower levels of dermal exposure than the estimated ones are to be expected. The evaporation time of the substance cannot be calculated, because the formation of films on the surface of the splashes on the skin could hinder evaporation to some extent.

It cannot be presupposed that eye protection is regularly used. For assessing the risks, hand-to-eye contacts as well as possible splashes to the eye should be considered.

For the production of formulations in the large-scale chemical industry, dermal exposure might be lower if suitable gloves are worn.

#### 4.1.1.2.3 Use of adhesives, paints, lacquers and cleansers (without formation of aerosols)

In this section the uses of paints, lacquers and adhesives in different industrial and skilled trade sectors are described (Scenarios 5-9); for spray applications see Section 4.1.1.2.4 (Scenario 10). The uses of formulations for flooring works (Scenario 11) and for cosmetics purposes (Scenario 12) are described separately in Sections 4.1.1.2.5 and 4.1.1.2.6, respectively.

Paints, lacquers, adhesives and cleaning products which contain methyl acetate are used in wide areas of industrial production (e.g. vehicle production, electro engineering and treatment and processing of metal and wood, the furniture, paper and leather-processing industries). The use of cleanser for cleaning surfaces (e.g. tools) e.g. absolving residual paints or lacquers is expected in areas of electro engineering, fine mechanics, treatment of metal and wood. Often the use of cleansers occurs corresponding to the use of paints, lacquers and adhesives.

The methyl acetate content in cleansers amounts to 5-20% (Hoechst AG, 1995). Adhesives contain differing percentages of methyl acetate (solvent adhesives up to 50% (Auffarth and Häger, 1989); flooring adhesives up to 15%; priming and undercoating paints up to 40% according to the information from IUCLID). According to information from one producer, solvent adhesives may contain 60% methyl acetate. The concentration in paints amounts up to 40%.

The concentration of methyl acetate in diluents may be higher (up to 95%) than in the different formulations. The diluents are often mixed with paints before application in order to achieve a certain viscosity. It is to be assumed, that inhalation exposure during occasional use is covered by the given measurement data (see below). The same is assumed for measurement data given in Section 4.1.1.2.4.

Inhalation and dermal exposures are expected in particular in the case of activities in which preparations are handled in open systems and the use of ventilation and personal protective measures (exhaust ventilation systems, protective gloves) cannot necessarily be assumed, e.g. in small- and medium-sized companies (Voullaire and Kliemt, 1995). On account of the high quantities of the substances which are processed it is to be assumed that methyl acetate is used in many different recipes.

In the case of the use of special methods of application (spray-painting), exposure to aerosols must be considered. These scenarios are presented separately in Section 4.1.1.2.4.

Inhalation exposure

*Workplace measurements*

Measurements performed by the German Workers' Compensation Funds in the further-processing industry during the data-gathering period 1990 to 1995 have been evaluated in an activity-related manner in consideration of the available ventilation equipment (BGAA, 1999; BIA, 1998).

**Table 4.2** Methyl acetate exposures at workplaces during use of formulations (BGAA, 1999; without spray applications)

| Working area | Activities | Year of measure-ments | Number of measure-ments | Local exhaust ventilation (LEV) | 50th percentile [mg/m³] | 90th percentile [mg/m³] | 95th percentile [mg/m³] |
|---|---|---|---|---|---|---|---|
| **Shift average** | | | | | | | |
| Metal treatment, electro-engineering, wood treatment 1) | Surface cleaning | 1990-1995 | 81 (p)<br>39 (p)<br>36 (p) | in total<br>without LEV<br>with LEV | 6<br>1<br>14 | 140<br>18<br>137 | 184<br>51<br>278 |
| Casting- and printing machines, mainly within the processing of wood and metal | Mechanical surface coating | 1990-1995 | 217 (p)<br>75 (p)<br>140 (p) | in total<br>without LEV<br>with LEV | 2<br>5<br>1 | 63<br>84<br>46 | 118<br>119<br>112 |
| Plastic and plastic foam treatment | Gluing | 1990-1995 | 38 (p)<br>14 (p)<br>22 (p) | in total<br>without LEV<br>with LEV | 4<br>1<br>8 | 24<br>18<br>30 | 42<br>99<br>39 |
| Production of shoes | Gluing | 1990-1995 | 48 (p)<br>15 (p)<br>33 (p) | in total<br>without LEV<br>with LEV | 2<br>11<br>2 | 22<br>17<br>23 | 26<br>22<br>25 |
| Pulp and paper production and processing 2) | Coating | 1981-1993 | 67 (p) | without LEV | 1 | 205 | -- |

1) High exposures (in the region of the 90th percentile) were measured when cleaning was carried out over large areas
2) Source: BGAA (1994)
(p): Person-related measurement results

For the use of formulations, in the case of three scenarios (cf. **Table 4.2**), exposure levels measured at workplaces with LEV are higher than at workplaces without LEV. For a better understanding, it should be kept in mind, that occupational exposure levels at similar workplaces depend on the level of technical protection (here: LEV), on the technique of application, on the concentration of methyl acetate and on the amount of the formulation in use. Often, if the handling of large amounts of a substance is required, workplaces are equipped with LEV, whereas workplaces at which small amounts are handled are possibly not equipped with LEV. On the other side, it might be that during the use of special formulations with other hazardous substances, LEV is installed. This circumstance might lead to the situation, that exposures are higher at workplaces with LEV than at those without LEV.

The duration of exposure at these workplaces may differ between 1 to 8 hours, exposure durations shorter than shift length were converted to 8-hour TWAs. Because of the areas and activities it is assumed that for most of the measurements the duration of exposure may be approximately shift length. Frequency is assumed to be daily.

For the area of surface cleaning, cleansers with 20% methyl acetate are assumed to be used. For gluing and coating activities, a methyl acetate concentration of 60% is expected.

Due to the measurement method which was applied and the measurement strategy (TRGS 402, 1986), the currently available measurement results are regarded as valid. Details regarding duration and frequency of exposure, regarding the description of the use processes and the collective of exposed persons are missing. In general inhalation and dermal exposure is to be assumed during sampling and analysis, weighing, transfer, filling, drumming, gluing and spraying as well as during cleaning, maintenance and repair work.

Measurement results relating to exposure during paper coating and furniture varnishing are available from Finland. They correspond essentially to the data provided in the above. For this area, it is not known, whether spay applications are used.

*EASE estimation (EASE for Windows Version 2, 1995)*

Appropriate EASE scenarios are presented in the following.

Exposure by inhalation to vapour during the use of paints, lacquers, adhesives and cleansers with local exhaust ventilation:

Input parameters: T = 20°C, non dispersive use, LEV present
Exposure level: 31-154 mg/m$^3$ (10-50 ml/m$^3$)

Exposure by inhalation to vapour during the use of paints, lacquers, adhesives and cleansers without local exhaust ventilation:

Input parameters: T = 20°C, non dispersive use, direct handling with dilution ventilation
Exposure level: 310-615 mg/m$^3$ (100-200 ml/m$^3$)

The EASE estimation is performed for the pure substance. Since the compositions of the formulations are not known, the partial vapour pressure cannot be calculated.

*Conclusion on inhalation exposure*

The comparison of EASE estimates and the 90$^{th}$ percentiles reveals, that the model estimates seem to overestimate exposure. This might be caused by the non-consideration of the concentration of methyl acetate in the formulation. In addition, the daily duration of the different activities is not known.

It is assumed, that the given inhalation exposure data cover the occasional use of high concentrated diluents. For this reason, no separate exposure scenario is established.

For assessing the risk of daily inhalation exposure the 90$^{th}$ percentiles of the measurement collectives given in **Table 4.2** should be taken:

| | | |
|---|---|---|
| Scenario 5: Metal treatment, electro engineering, wood treatment (surface cleaning) | 5 a) without LEV<br>5 b) with LEV | 18 mg/m³<br>137 mg/m³ |
| Scenario 6: Casting- and printing machines, mainly within the processing of wood and metal (using paints, lacquers, adhesives) | 6 a) wthout LEV<br>6 b) with LEV | 84 mg/m³<br>46 mg/m³ |
| Scenario 7: Plastic and plastic foam treatment (gluing) | 7 a) without LEV<br>7 b) with LEV | 18 mg/m³<br>30 mg/m³ |
| Scenario 8: Production of shoes (gluing) | 8 a) without LEV<br>8 b) with LEV | 17 mg/m³<br>23 mg/m³ |
| Scenario 9: Pulp and paper production and processing (coating, assumed: use of paints, lacquers or adhesives) | without LEV | 205 mg/m³ |

For assessing the risks, it should be noticed, that exposures could be higher at workplaces with LEV (subscenarios b) than without LEV (subscenarios a). This might be caused by the fact that at workplaces with LEV higher amounts of the substance are used than at workplaces without

LEV. The exposure levels of each subscenario should be taken for assessing the risks in order to make clear, that LEV as a single measure is not appropriate to reduce exposure considerably. Changes of technology, of quantities or of the concentration of methyl acetate can strongly influence exposure levels.

It seems to be not appropriate to cluster all scenarios, because the exposure levels ($90^{th}$ percentile) differ to a large extent and it is to be assumed, that differing amounts of substances are used at the workplaces with different techniques.

Dermal exposure

Taking into consideration that personal protective equipment may not be worn, the estimation of dermal exposure levels according to the EASE-model is used independent of the acceptance of use of gloves.

Scenario 5: Metal treatment, electro engineering, wood treatment (surface cleaning)

Input parameters: T = 20°C, non dispersive use, direct handling, extensive
Exposure level: 1-5 mg/cm$^2$/day

Considering a content of 20% methyl acetate the exposure level amounts to 0.2-1 mg/cm$^2$/day. Taking into consideration an exposed area of skin of 1 300 cm$^2$ (hands and part of the forearms), a daily dermal exposure of 26-260 mg/person/day results.

Scenarios 6 – 9: use of paints, lacquers and adhesives

Input parameters: T = 20°C, non dispersive use, direct handling, intermittent
Exposure level: 0.1-1 mg/cm$^2$/day

Scenarios 6, 7: Casting- and printing machines (use of paints, adhesives), plastic and plastic foam treatment

The estimation is performed for formulations containing up to 60% methyl acetate and an affected area of skin of 420 cm$^2$ (hands) is assumed. The estimated exposure levels amount to 25-250 mg/person/day.

Scenario 8: Shoe production (gluing)

If adhesives containing methyl acetate are used, a concentration of 60% methyl acetate and an affected area of skin of 210 cm$^2$ (fingers) are assumed. The estimated exposure amounts to 13-125 mg/person/day.

Scenario 9: Pulp and paper production and processing

A concentration of 60% methyl acetate is assumed for the purpose of estimating the dermal exposure during paper and board production and further processing since the concentrations used here are not known. For an exposure area of skin of 840 cm$^2$ (hands), the resultant level of dermal exposure amounts to 50-500 mg/person/day.

On account of the high vapour pressure of the substance and the resultant short retention time of the substance on the skin, lower levels of dermal exposure than the estimated ones are to be expected. The evaporation time of the substance cannot be calculated, because the formation of films on the surface of the splashes on the skin could hinder evaporation to some extent.

It cannot be presupposed that eye protection is regularly used. For assessing the risks, hand-to-eye contacts as well as possible splashes to the eye should be considered.

#### 4.1.1.2.4 Use of paints, lacquers and adhesives for spray techniques

In this section, scenarios involving the use of spraying techniques in particular spraying of paints, lacquers and adhesives, are described (Scenario 10). In addition to inhalation exposure caused by the evaporation of the substance, droplets aerosols may be a source of exposure.

Spraying of paints, lacquers and adhesives is performed in many different industrial and skilled trade sectors, e.g. vehicle production and repair, treatment and processing of metal and wood, the furniture industry. Methyl acetate is a component of a few building paints which are sprayed onto surfaces using spray guns. In general, spraying techniques are applied in industrial and skilled trade areas.

Spraying may be performed manually or automatically. The latter is often done in spray cabins. Regarding the measurement results presented below, no detailed information on the processes is available.

Inhalation exposure

*Workplace measurements*

**Table 4.3** Methyl acetate exposures at workplaces during spaying of adhesives and paints

| Working area | Activities | Year of measure-ments | Number of measure-ments | Local exhaust ventilation (LEV) | 50th percentile [mg/m³] | 90th percentile [mg/m³] | 95th percentile [mg/m³] |
|---|---|---|---|---|---|---|---|
| **Shift average** | | | | | | | |
| Processing of metal and plastics, finemechanics (BGAA, 1999) | Spray-painting | 1990-1995 | 179 (p)<br>32 (p)<br>135 (p) | in total<br>without LEV<br>with LEV | 9<br>14<br>7 | 66<br>81<br>56 | 86<br>105<br>81 |
| Processing of wood (BGAA, 1999) | Gluing, spraying of adhesives | 1990-1995 | 33 (p)<br>16 (p)<br>17 (p) | in total<br>without LEV<br>with LEV | 1<br>1<br>1 | 19<br>75<br>18 | 118<br>183<br>29 |
| Treatment and processing of wood (BGAA, 1999) | Spray-painting | 1990-1995 | 173 (p)<br>13 (p)<br>160 (p) | in total<br>without LEV<br>with LEV | 1<br>1<br>1 | 10<br>9<br>10 | 34<br>20<br>33 |
| Building trade (BGAA, 1999) | Spray- painting | 1990-1995 | 31 (p)<br>17 (p)<br>11 (p) | in total<br>without LEV<br>with LEV | 3<br>3<br>2 | 30<br>35<br>21 | 36<br>39<br>24 |

(p) Person-related measurement results

One producer provided measurement data regarding spray painting. 44 shift averages were below 61 mg/m$^3$, 5 below 200 mg/m$^3$. Further information is not available.

Due to the measurement method which was applied and the measurement strategy (TRGS 402, 1986), the currently available measurement results are regarded as valid. Details regarding duration and frequency of exposure, regarding the description of the use processes and the collective of exposed persons are missing.

According to the measurement results, the following statements are given (BGAA, 1999):

Adhesives are frequently applied to large areas. In wood working and processing they are also applied by means of spray technologies. In these cases, exposures in the region of the 90$^{th}$ percentile were determined.

In the wood industry, exhaust ventilation systems are mainly used during spray-painting. Workplaces without exhaust ventilation systems relate to areas in which evaporation and drying takes place.

*EASE estimation (EASE for Windows Version 2, 1995)*

The EASE estimations are based on the assumption, that during spraying all volatile components of the paint / adhesive evaporate independent on their specific vapour pressure.

The estimations are based on a formulation with 40% methyl acetate and a solids content of 50%. According to a rough estimation, the aerosol contains approx. 80% methyl acetate. The prediction of the aerosol concentration is based on an average molar weight of 90 g/mol.

Exposure by inhalation through the formation of aerosols during spray-painting and spraying of adhesives:

- Industrial area with local exhaust ventilation:
  Input parameters: T = 20°C, non dispersive use, LEV present
  Level of exposure: 370-750 mg/m$^3$ (100-200 ml/m$^3$, droplet aerosol)

  Considering a content of 40% methyl acetate in the formulation and 80% in the volatile part of the paint, the exposure level amounts to
  295-590 mg/m$^3$ (95-190 ml/m$^3$)

- Industrial area without local exhaust ventilation (same estimation for skilled trade application with dilution ventilation)
  Input parameters: T = 20°C, non dispersive use/wide dispersive use, direct handling, dilution ventilation present
  Level of exposure: 1,865-3,730 mg/m³ (500-1,000 ml/m$^3$)

  Considering a content of 40% methyl acetate in the formulation and 80% in the volatile part of the paint, the exposure level amounts to:
  1,490-2,980 mg/m³ (480-960 ml/m³)

- Skilled trade area without natural ventilation:
  Input parameters: T = 20°C, wide dispersive use, direct handling, without dilution ventilation
  Level of exposure: > 3,730 mg/m³ (> 1,000 ml/m$^3$)

  Considering a content of 40% methyl acetate in the formulation and 80% in the volatile part of the paint, the exposure level amounts to
  > 2,980 mg/m³ (> 960 ml/m³)

*Conclusion on inhalation exposure*

The measurement results obtained during spraying of paints and adhesives depict the possible wide spread exposure levels caused by different working techniques, different concentrations of methyl acetate in the formulations, different amounts of the formulation in use and different

levels of protection. Based on the available information, it is not possible to allocate circumstances leading to low exposure levels, e.g. special products (containing low amounts of methyl acetate) or the use of only small amounts of a formulation per shift to one of the areas given in **Table 4.3**. Taking this lack of information and the similarity of the applied processes (spraying paints or adhesives) into account, until further information is provided, scenarios regarding the spraying of paints and adhesives are clustered.

For assessing the risks of inhalation exposure during spray application of adhesives and paints, 81 mg/m$^3$ for workplaces with LEV (Scenario 10a) and 56 mg/m$^3$ for workplaces without LEV should be taken (Scenario 10b).

The comparison of model predictions and measurement results indicates, that the EASE model overestimates inhalation exposure for spray applications to a large extent. This holds also true if the solids content in paints and adhesives is not considered.

Dermal exposure

Because in this area personal protective equipment cannot be regarded as a general measure, dermal exposure is assessed for the unprotected worker in application of the EASE model.

Input parameters: T = 20°C, non dispersive use, direct handling, intermittent
Level of exposure: 0.1-1 mg/cm$^2$/day

In consideration of the highest content of methyl acetate in formulations of 60% dermal exposure through direct skin contact during spraying of the formulations is estimated to 0.06-0.6 cm$^2$/day. For spraying, a rather high area of exposed skin of 1,300 cm$^2$ (hands and parts of the forearms) is taken into consideration, so that a daily dermal exposure of 78-780 mg/person/day results (Scenario 10).

On account of the high vapour pressure of the substance and the resultant short retention time of the substance on the skin, lower dermal exposure than estimated is to be assumed. The evaporation time of the substance cannot be calculated, because the formation of films on the surface of the splashes on the skin could hinder evaporation to some extent.

It cannot be presupposed that eye protection is regularly used. For assessing the risks, hand-to-eye contacts as well as possible splashes to the eye should be considered.

#### 4.1.1.2.5 Use of formulations for flooring works

Methyl acetate is a component of the solvent mixture contained in primers and adhesives intended for use for flooring works (Scenario 11). As a rule, primers are applied to the undersurface using a roller. Here, large quantities of the material are processed within a short time. During the gluing of flooring materials - apart from parquet - the adhesive is distributed over several square metres. The flooring material is subsequently fixed in position. In the case of parquet-gluing work, less adhesive is applied in each case. The finished products contain differing percentages of methyl acetate (solvent adhesives up to 50% (Auffarth and Häger, 1989); flooring adhesives up to 15%; priming and undercoating paints up to 40% according to the information from IUCLID, flooring precoatings up to 50% (BGAA, 1999).

Information provided by the federal monitoring authorities shows that these works are done campaign wise, with rests of approximately 14 days. Experiences in the Netherlands show that highly specialised companies perform flooring works on a daily scale.

Inhalation and dermal exposures are expected here in connection with activities in which the preparations are applied manually over a large area and for which the use of technical and personal protective measures (local exhaust ventilation, protective gloves) cannot necessarily be assumed. On account of the high quantities of the substance which are used, it is to be assumed that methyl acetate is employed in many different recipes. In the case of the use of special application methods (spray-painting), exposure to aerosols must be considered.

Inhalation exposure

*Workplace measurements*

**Table 4.4** Methyl acetate exposures during flooring works

| Working area | Year of measure-ments | Number of measure-ments | 50th percentile [mg/m³] | 90th percentile [mg/m³] | 95th percentile [mg/m³] | Duration | Source |
|---|---|---|---|---|---|---|---|
| **Shift average** | | | | | | | |
| Flooring works | 1990-1995 | 189(p) | 49 | 768 | 1,094 | - | BGAA (1999) |
| Flooring works (short term) | 1990-1995 | 74(p) | 69 | 2,830 | 3,271 | < 1 h | |
| **Working area** | **Year of measure-ments** | **Number of measure-ments** | **Minimum [mg/m³]** | **50th - percentile [mg/m³]** | **Maximum [mg/m³]** | **Duration** | **Source** |
| **Measurement result** | | | | | | | |
| Parquet laying | | | | | | | |
| Precoating | - | 3 | 7,079 | 7,261 | 10,087 | 20 min | Lüdersdorf et al. (1985) |
| Glueing | - | 9 | 266 | 412 | 780 | 1 – 4 h | |
| Trowel application (2 times/day) | - | 26 | < 2 | 19 | 156 | 20–60 min | |
| Priming (2 different primers) | - | 13<br>7 | 158<br>64 | 360<br>192 | 813<br>775 | 10–30 min | |

Solvent exposures during the laying and varnishing of parquet are given in Lüdersdorf et al. (1985) (cf. **Table 4.4**). Methyl acetate is a component of parquet adhesives, thinners and of fillers. It is stated that during parquet laying the given activities are performed subsequently. Based on the given data, a shift average of approx. 750 mg/m$^3$ can be derived.

Exposure data not presented in **Table 4.4** were given in Diehl (1988) for the laying of parquet: The occupational exposure limit for the air which applies in Germany (610 mg/m$^3$ (200 ml/m$^3$)) is exceeded fourfold (3,050 mg/m$^3$) during priming the undersurface.

The BGAA (1999) provided measurement data which are not subdivided according to the different working steps. It is to be assumed, that the data cover all steps.

Based on the available data, the 90$^{th}$ percentile provided by BGAA is regarded to be a good measure of the reasonable worst case.

*EASE estimation (EASE for Windows Version 2, 1995)*

Exposure by inhalation to vapour during use of paints, lacquers, adhesives and cleansers in the skilled trade area with natural ventilation:

Input parameters: T = 20°C, wide dispersive use, direct handling with dilution ventilation
Level of exposure: 1,540-3,070 mg/m$^3$ (500-1,000 ml/m$^3$)

Exposure by inhalation to vapour during use of paints, lacquers, adhesives and cleansers in the skilled trade area without natural ventilation:

Input parameters: T = 20°C, wide dispersive use, direct handling without dilution ventilation
Level of exposure: > 3,070 mg/m$^3$ (< 1,000 ml/m$^3$)

The EASE estimation is performed for the pure substance. Since the composition of the formulations is not known, the partial vapour pressure cannot be calculated.

*Conclusion on inhalation exposure*

The EASE estimates matches the short-term exposure given in **Table 4.4**. The model overestimates exposure levels in comparison with the shift averages. This might be caused by the non-consideration of the percentage of methyl acetate in the formulations.

For assessing the risks of daily inhalation exposure during flooring works, the 90$^{th}$ percentile of a measurement collective of 768 mg/m$^3$ (247 ml/m$^3$, 8-hour TWA) should be taken (Scenario 11).

In addition, a short-term value of 2,830 mg/m$^3$ (1,065 ml/m$^3$, 90$^{th}$ percentile, duration < 1 h) should be considered for activities such as gluing, priming and laying. The highest short-term values are given in Lüdersdorf et al. (see **Table 4.3**). During precoating 10,087 mg/m³ were reached. These results are not taken for assessing the risks, because the number of measurement results is by far lower than the number given in BGAA (1999). The latter are regarded to be more representative.

Dermal exposure

For works in the area of building trade, the category ”wide dispersive use” is regarded to be appropriate for describing the exposure situation

Input parameters: T = 20°C, wide dispersive use, direct handling, intermittent
Level of exposure: 1-5 mg/cm$^2$/day

Considering a content of 50% methyl acetate the exposure level amounts to 0.5-2.5 mg/cm$^2$/day. Taking into consideration an exposed area of skin of 840 cm$^2$ (hands), a daily dermal exposure of 420-2,100 mg/person/day results.

On account of the high vapour pressure of the substance and the resultant short retention time of the substance on the skin, lower levels of dermal exposure than the estimated ones are to be expected. The evaporation time of the substance cannot be calculated, because the formation of films on the surface of the splashes on the skin could hinder evaporation to some extent.

It cannot be presupposed that eye protection is regularly used. For assessing the risks, hand-to-eye contacts as well as possible splashes to the eye should be considered.

#### 4.1.1.2.6 Use of cosmetic products

Exposures of workers by inhalation and dermal contact are to be expected when products containing methyl acetate, e.g. nail polish remover (methyl acetate content 15%), are handled in the manicure and pedicure trade during the manual application of the finished products (Scenario 12). An inhalation exposure is assumed here which, while occurring on a daily basis, is for short periods only.

Nail polish remover contain different volatile components, inter alia acetone, being as volatile as methyl acetate. Beside solvents, low volatile components like oil and waxes are also ingredients.

Inhalation exposure

*Workplace measurements*

No workplace measurements exist. There is no information on the duration and frequency of exposure or on the collective of exposed persons.

*EASE estimation (EASE for Windows Version 2, 1995)*

Input parameters: T = 20°C, wide dispersive use, direct handling with dilution ventilation
Level of exposure 615-1,540 mg/m$^3$ (200-500 ml/m$^3$)

The EASE estimation is performed for the pure substance. Since the composition of the formulations is not known, the partial vapour pressure cannot be calculated.

Based on the available information on the composition of nail polish removers, it might be, that methyl acetate is enriched in the air compared with the percentage in the liquid formulation. But as other volatile components are also present, it can be assumed for a rough estimation, that this enrichment may be not higher than 2-fold. Therefore, the concentration of methyl acetate in the air might be 30% (15% in the liquid). This leads to exposure levels of

205-510 mg/m$^3$ (66-166 ml/m$^3$)

*Conclusion on inhalation exposure*

Since no measurement results are available, the EASE estimates are taken as a basis to assess exposure. The predicted inhalation exposure level amounts to 205-510 mg/m$^3$ (66-166 ml/m$^3$). Taking into consideration a daily duration of exposure of 2 h, a daily inhalation exposure of 50-130 mg/m$^3$ results (Scenario 12).

Dermal exposure

For the purpose of describing dermal exposure during the use of cosmetic products containing methyl acetate, predictions in application of the EASE model are used:

Input parameters: T = 20°C, wide dispersive use, direct handling, extensive
Level of exposure: 5-15 mg/cm$^2$/day

Considering a content of 15% methyl acetate the exposure level amounts to 0.75-2.25 mg/cm$^2$/day. The consideration of an exposed skin area of 210 cm² leads to daily dermal exposure levels of 160-470 mg/person/day.

On account of the high vapour pressure of the substance and the resultant short retention time of the substance on the skin, a lower dermal exposure than the estimated one is to be assumed. The evaporation time of the substance cannot be calculated, because the formation of films on the surface of the splashes on the skin could hinder evaporation to some extent.

It cannot be presupposed that eye protection is regularly used. Taking into account the rather small amounts of formulations in use, for assessing the risks, hand-to-eye contacts as well as possible splashes can be excluded to a large extent.

#### 4.1.1.2.7 Summary of occupational exposure

Methyl acetate is used as a chemical intermediate and as a solvent in different formulations. About 10% of the produced methyl acetate in Germany is further processed as a chemical intermediate to methanol, acetic acid, vitamins and plant protection products, 70% are used as solvents in paints, adhesives, cleansers etc. and about 20% are exported.

Relevant inhalation and dermal exposure levels are given in **Tables 4.5 and 4.6**, respectively.

For the large-scale chemical industry, it is assumed that the production and further processing of methyl acetate is mainly performed in closed systems. Exposure occurs during certain activities in the manufacturing and further processing (Scenario 1, **Tables 4.5 and 4.6**). Similar exposure situations are assumed for the cosmetic industry (Scenario 3). Taking into account the high level of protection and the very high vapour pressure of 21.7 kPa, dermal exposure is assessed as low. For companies which did not submit any data in default of workplace measurements, inhalation exposure is assessed in application of the EASE model (Scenario 2). Taking into account the high level of protection and the very high vapour pressure of 21.7 kPa, dermal exposure is assessed as low. Dermal exposure is assessed on the basis of the EASE model, too. But taking into account the very high volatility of the substance, dermal exposure is assessed to be much lower than the EASE estimates of 42-420 mg/person/day. Formulation of the substance to paints, lacquers, adhesives and cleansers may occur in the large-scale chemical industry as well as in small- and medium-sized companies, where possibly lower levels of protection than the large-scale chemical industry are realised. The exposure levels given in **Tables 4.5 and 4.6** (Scenario 4) are regarded to be appropriate for the small- and medium-sized companies.

Based on the available information, formulations containing methyl acetate are used as adhesives paints, lacquers and cleanser in different industrial and skilled trade areas. The formulations are inter alia used in spraying and coating techniques. The provided measurement data originate from different branches (Scenario 5 – 9). For the corresponding scenarios, higher 8-hour TWA were measured at workplaces with LEV than at workplaces without LEV. For a better understanding, it should be kept in mind, that occupational exposure levels at similar workplaces depend inter alia on the level of technical protection (here: LEV), the technique of application, the concentration of methyl acetate and on the amount of the substance in use. Often, if the handling of large amounts of a substance is required, workplaces are equipped with LEV, whereas workplaces at which small amounts are handled are possibly not equipped with LEV. This circumstance might lead to the situation, that exposure is higher at workplaces with LEV than at those without LEV. The corresponding exposure scenarios are devided into subscenarios in order to make clear that LEV as a single measure is not appropriate to reduce exposure considerably. Changes of technology, of quantities or of concentration have to be considered additionally.

Spraying of adhesives and paints in different industrial and skilled trade areas is summarised in Scenario 10. The highest inhalation exposure levels were obtained during flooring works (Scenario 11). Methyl acetate may be a component of cosmetic products. The corresponding exposure levels are considered in Scenario 12.

Dermal exposure for Scenario 4-12 is limited because of the very high vapour pressure of 21.7 kPa.

**Table 4.5** Summary of inhalation exposure data of methyl acetate which are relevant for occupational risk assessment

| Inhalation exposure | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Scenario number, area of production and use** | **Form of exposure** | **Activity** | **Duration [h/day]** | **Frequency [days/year]** | **Shift average [mg/m³]** | **Method** | **Short-term exposure [mg/m³] (duration)** | **Method** |
| **Production and further processing** | | | | | | | | |
| 1.Manufacture and further processing as a chemical intermediate | vapour (liquid) | filling, sampling cleaning, maintenance, repair | shift length | daily | < 61 | workplace measurements (detection limit) | -- | -- |
| 2.Manufacture and further processing as a chemical intermediate | vapour (liquid) | see Scenario 1 | shift length | daily | 31-154 | EASE[1)] | -- | -- |
| 3.Production of cosmetics | vapour (liquid) | see Scenario 1 | 2 h (assumed) | daily | 8-39 | EASE, with LEV | -- | -- |
| 4.Production of formulations (paints, lacquers, adhesives, cleanser) | vapour (liquid) | filling, sampling, cleaning, maintenance, repair | not known[2)] | daily | 4a) 294<br>4b) 175 | 90th percentiles without LEV<br>with LEV | 1,590 (20 min) | measurement result |
| **Use of formulations (paints, adhesives, cleansers, no spray techniques)** | | | | | | | | |
| 5.Metal treatment, electro-engineering, wood treatment, 20% methyl acetate in diluted cleansers | vapour (liquid) | cleaning of surfaces | shift length (assumed) | daily | 5a) 18<br>5b) 137 | 90th percentiles without LEV<br>with LEV | -- | -- |

Table 4.5 continued overleaf

**Table 4.5 continued** Summary of inhalation exposure data of methyl acetate relevant for occupational risk assessment

| Inhalation exposure | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Scenario number, area of production and use** | **Form of exposure** | **Activity** | **Duration [h/day]** | **Frequency [days/year]** | **Shift average [mg/m³]** | **Method** | **Short-term exposure [mg/m³] (duration)** | **Method** |
| 6.Casting machine, printing machine, mainly within the treatment of wood and metals, assumption: 60% methyl acetate | vapour (liquid) | filling, sampling, cleaning, maintenance, repair | shift length (assumed) | daily | 6a) 84<br>6b) 46 | 90th percentiles without LEV with LEV | -- | -- |
| 7.Plastic and plastic foam treatment, 60% methyl acetate | vapour (liquid) | gluing | shift length (assumed) | daily | 7a) 18<br>7b) 30 | 90th percentiles without LEV with LEV | -- | -- |
| 8.Production of shoes, 60% methyl acetate | vapour (liquid) | gluing | shift length (assumed) | daily | 8a) 17<br>8b) 23 | 90th percentiles without LEV with LEV | -- | -- |
| 9.Pulp and paper production (paints, adhesives, assumed: 60% methyl acetate) | vapour (liquid) | coating | shift length (assumed) | daily | 205 | 90th percentile | -- | - |
| **Use of formulations (paints, adhesives, cleansers, spray techniques)** | | | | | | | | |
| 10.Spraying of paints, lacquers, adhesives, (assumed 40% methyl acetate) | vapour (liquid, aerosol) | spraying | shift length (assumed) | daily | 10a) 81<br>10b) 56 | 90th percentiles without LEV with LEV | -- | -- |
| **Other uses** | | | | | | | | |
| 11.Flooring works, building trade, 50% methyl acetate | vapour (liquid) | precoating, priming, gluing | shift length (assumed) | daily | 768 | 90th percentiles without LEV | 2,830 without LEV (< 1 hour) | 90th percentile |
| 12.Use of cosmetics (nail lacquer remover, 15% methyl acetate) | vapour (liquid) | application | 2h (assumed) | daily | 50-130 | EASE exp. judg. | -- | -- |

1) EASE estimation for those companies which did not submit any measurement data
2) Daily duration of exposure depends on the production volume

**Table 4.6** Summary of dermal exposure data of methyl acetate relevant for occupational risk assessment

| Dermal exposure | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Scenario number, area of production and use** | **Form of exposure** | **Activity** | **Frequency [days/year]** | **Contact level (according to EASE model)** | **Level of exposure [mg/cm²/day]** | **Exposed area [cm²]** | **Shift average [mg/person/day]** | **Method (use of gloves)** |
| **Production and further processing** | | | | | | | | |
| 1.Manufacture and further processing as a chemical intermediate | liquid | filling, sampling, cleaning, repair maintenance, | daily | intermittent | 0.1-1 with shortened duration of dermal exposure 1) | 420 (palms of hands) | 42-420 with shortened duration of dermal exposure 1) | EASE/ exp. judg. |
| 2.Manufacture and further processing as a chemical intermediate | liquid | See above | daily | intermittent | 0.1-1 with shortened duration of dermal exposure 1) | 420 (palms of hands) | 42-420 with shortened duration of dermal exposure 1) | EASE/ exp. judg. |
| 3.Production of cosmetics | liquid | filling, sampling, cleaning, repair maintenance, | daily | intermittent | 0.1-1 with shortened duration of dermal exposure 1) | 420 (palms of hands) | 42-420 with shortened duration of dermal exposure 1) | EASE/ exp. judg. |
| 4.Production of formulations (paints, lacquers, adhesives, cleanser) | liquid | filling, sampling, cleaning, repair maintenance, | daily | intermittent | 0.1-1 with shortened duration of dermal exposure 2) | 420 (palms of hands) | 42-420 with shortened duration of dermal exposure 2) | EASE (without gloves) |
| **Use of formulations (paint, adhesives cleansers, no spray techniques)** | | | | | | | | |
| 5.Metal treatment, electro-engineering, wood treatment, 20% methyl acetate in diluted cleansers | liquid | cleaning of surfaces | daily | intermittent | 0.02–0.2 with shortened duration of dermal exposure2) | 840 (hands) | 26-260 with shortened duration of dermal exposure2) | EASE (without gloves) |
| 6.Casting machine, printing machine, mainly within the treatment of wood and metals, assumption: 60% methyl acetate | liquid | filling, sampling, cleaning, maintenance, repair | daily | intermittent | 0.06-0.6 with shortened duration of dermal exposure2) | 840 (hands) | 25-250 with shortened duration of dermal exposure 2) | EASE (without gloves) |

Table 4.6 continued overleaf

**Table 4.6 continued** Summary of dermal exposure data of methyl acetate which are relevant for occupational risk assessment

| Dermal exposure | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Scenario number, area of production and use** | **Form of exposure** | **Activity** | **Frequency [days/year]** | **Contact level (according to EASE model)** | **Level of exposure [mg/cm²/day]** | **Exposed area [cm²]** | **Shift average [mg/person/day]** | **Method (use of gloves)** |
| 7.Plastic and plastic foam treatment, 60% methyl acetate | liquid | gluing | daily | intermittent | 0.06-0.6 shortened duration of dermal exposure 2) | 840 (hands) | 25-250 with shortened duration of dermal exposure 2) | EASE (without gloves) |
| 8.Production of shoes, 60% methyl acetate | liquid | gluing | daily | intermittent | 0.06- 0.6 with shortened duration of dermal exposure 2) | 210 (fingers) | 13-125 with shortened duration of dermal exposure 2) | EASE (without gloves) |
| 9.Pulp and paper production (assumed: 60% methyl acetate) | liquid | coating | daily | intermittent | 0.06-0.6 with shortened duration of dermal exposure 2) | 840 (hands) | 50-500 with shortened duration of dermal exposure 2) | EASE (without gloves) |
| **Use of formulations (paint, adhesives cleansers, spray techniques** | | | | | | | | |
| 10.Spraying of paints, lacquers, adhesives (assumed 40% methyl acetate) | liquid, (aerosol) | spraying | daily | intermittent | 0.06-0.6 with shortened duration of dermal exposure 2) | 1,300 (hands and parts of forearms) | 78-780 with shortened duration of dermal exposure 2) | EASE (without gloves) |
| **Other uses** | | | | | | | | |
| 11.Flooring works, building trade, 50% methyl acetate | liquid | precoating, priming, gluing | daily | intermittent | 0.5-2,5 with shortened duration of dermal exposure 2) | 840 (hands) | 420-2,100 with shortened duration of dermal exposure 2) | EASE (without gloves) |
| 12.Use of cosmetics (nail lacquer remover) 15% methyl acetate | liquid | application | daily | extensive | 0.75-2.25 with shortened duration of dermal exposure 2) | 210 (fingers) | 160-470 with shortened duration of dermal exposure 2) | EASE (without gloves) |

1) The EASE estimate is largely reduced because of the short duration time of dermal exposure. The retention time of pure methyl acetate is calculated to 6 seconds (order of magnitude) independent on the use of gloves (non-occlusive exposure).

2) Gloves are not regularly worn. Due to the high vapour pressure of the substance, shortened retention times on the skin are to be expected leading to condsiderable lower dermal exposure levels than estimated with the EASE model. For methyl acetate in mixture the retention time cannot be calculated because of the complex composition of the mixtures and their specific drying behavior.

#### 4.1.1.3 Consumer exposure

The manufacturer describes exposure of the consumer from the use of methyl acetate as a solvent.

According to the Swedish product register, products containing methyl acetate are used as adhesive and paste or glue in the textile industry, for leather, and in households in Sweden. Furthermore, they are offered for public use in repair shops for cars and motorcycles.

In Germany, methyl acetate is known to be used as a component of all-purpose adhesives (content of methyl acetate 50%), of carpet adhesives (content of methyl acetate up to 20%) and of parquet adhesives (content of methyl acetate up to 13%), as a diluent for adhesives (content of methyl acetate 40%), and in addition as a component of nail varnish removers (content of methyl acetate 15%).

In the case reports of the Swiss toxicological information centre, methyl acetate has been listed as a component of nail varnish removers and of adhesives for the household area (Velvart, 1993).

For the assessment of consumer exposure, preferably standard assumptions are used which occur in typical cases of use; in situations where this is not possible, assumptions will rather be arbitrary. The amounts to be used per application are based on the data given by the manufacturer. In adults the weight of 60 kg bw will be considered as the weight of a standard consumer.

On account of the variability of the exposure conditions, individual exposure cannot be defined exactly. Therefore, it would be more appropriate to indicate fields of possible exposure. These have been divided by log ranges (lower range: 1-10, middle range: 10-100, upper range 100-1,000).

##### 4.1.1.3.1 Inhalation exposure

For the assessment of the inhalatory exposure of the consumer, a computer simulation with the aid of the US EPA model SCIES was used estimating consumer exposure under different conditions with house/room air exchange rates ranging from 0.1 to 0.5 times per hour. In the following assessment, the figures used are indicated describing most reasonable scenarios in terms of consumer impairment.

Exposure from all-purpose adhesives

Under conditions of use **(**10 g all-purpose adhesive in a room of 60 $m^3$, content of methyl acetate 50%, 5 times per week for 1 hour each**)**, an exposure of the consumer to methyl acetate will result within the lower mg/kg bw/day range (1.06 mg/kg bw/d; 0.2 room air exchanges/hour).

If a child of 20 kg bw uses this adhesive under the conditions indicated above, exposure will also be within the lower mg/kg bw/day range (0.2 room air exchanges/hour) (reasonable worst case).

Furthermore, as a second reasonable worst-case scenario, it is assumed that a batch of 50 g will be used once a week under the conditions indicated above. Exposure of the consumer will then also be within the lower mg/kg bw/day range (0.2 room air exchanges/hour).

Under conditions of use of all-purpose adhesives containing methyl acetate, the inhalation exposure of the consumer per event was calculated to reach a peak concentration up to 39 mg/m$^3$ assuming a room ventilation rate of 0.2 air exchanges per hour (average concentration during use: 26 mg/m$^3$).

See Appendix A7: copy of the calculation with the US EPA computer model SCIES.

Exposure from adhesives for floor coverings

According to the Swedish product register, methyl acetate is used as a component of adhesives in the textile industry. Information is available about the use of methyl acetate as a component of carpet and parquet adhesives. However, although these adhesives are not primarily meant for consumer use it cannot be excluded that they will be sold to and used by consumers.

*Carpet adhesives*

Under conditions of use of 750 g/m$^2$ carpet adhesive content of methyl acetate 20% in a room with a floor area of 25 m$^2$ and a volume of 60 m$^3$, a single application per year for 2 hours each, the consumer will be exposed to an average concentration of 11,000 mg/m³ per event assuming a room ventilation rate of 0.5 air exchanges per hour. A peak concentration up to 15,000 mg/m$^3$ is calculated. A dose rate of 1.14 mg/kg bw/d would result as yearly average from this exposure.

See Appendix A8: copy of the calculation using the US EPA computer model SCIES.

*Parquet adhesives*

Under conditions of use of 1 kg/m$^2$ parquet adhesive in a room of 25 m$^2$ floor area and a volume of 60 m$^3$ (content of methyl acetate 13%), a single application per year for 4 hours each, the consumer will be exposed to an average concentration of about 6,040 mg/m$^3$ per event assuming a room ventilation rate of 0.5 air exchanges per hour. A peak concentration of 7,860 mg/m$^3$ is calculated. A dose rate of 0.94 mg/kg bw/d would result as yearly average from this exposure.

See Appendix A9: copy of the calculation using the US EPA computer model SCIES.

*Nail varnish removers*

For an assessment of the inhalation exposure of the consumer to methyl acetate when using nail varnish remover, a computer simulation with the aid of the SCIES model is performed. For the reasonable worst case, the following conditions are assumed: daily use of 0.25 ml of a nail varnish remover (containing 15% methyl acetate. An amount of 37.5 mg methyl acetate will then be applied to the nails. For an estimation of the maximal exposure the peak concentration of methyl acetate after use has been taken which is 0.039 mg/m³. It is assmued that the user will stay in the room of use. According to SCIES calculations, the exposure amounts to 0.5 mg per day which would result in a dose rate of 0.008 mg/kg bw/d.

See Appendix 10: copy of the calculation using the US EPA computer model SCIES.

Total inhalation exposure of the consumer

The cumulative inhalation exposure of the consumer by methyl acetate calculated for all kinds of use would be in lower milligram/kg bw and day range (< 3 mg/kg bw/d) when the products are used as intended.

#### 4.1.1.3.2 Dermal exposure

Exposure from glues

According to the product data provided by industry, methyl acetate is used in adhesives and glues that are recommended for hobby and household use.

Dermal exposure may occur during use of the product. It is assumed that the amounts used are in a range of less that 10 g, normally a few drops. It is possible, that these drops can come into contact with skin, e.g. by distributing the glue on surface that is intended to be glued. For this scenario, an exposure can be estimated due to the formula given in the TGD for dermal exposure. Because of the uncertainty of the assumptions, distributions have been estimated instead of point estimates. For estimation of exposure the probabilistic approach taking a Monte-Carlo simulation has been used (software: @RISK).

**Table 4.7** Dermal exposure from glues

| | | | |
|---|---|---|---|
| Amount of glue | Min:<br>Most probable<br>Max: | 0.5<br>1<br>10 | The amount of the used product varies between 0.5 and 10 g with a most probable amount of 1 g (= triangular distribution) |
| Amount of methyl acetate in glues | Min:<br>Max: | 40%<br>60% | = uniform distribution |
| Frequency of use | Daily | | |
| Surface area in contact | Min:<br>Max: | 1 cm²<br>3 cm³ | = 1 bis 3 fingertips |
| Thickness of layer | | 0.1 cm | |

According to these assumptions, the daily exposure by the dermal route by using methyl acetate containing glues would result in 0.4 (minimum) to 5.9 (maximum) mg/kg, with a most probable exposure (median) of 1.4 mg/kg and day. It should be considered, that this amount is valid only for a few minutes because of drying of the glue. In fact, the dermal exposure would be much lower.

Exposure from nail varnish removers

The reasonable worst case is based on a daily use of 0.25 ml of nail varnish remover with a content of methyl acetate of 15%. 37.5 mg methyl acetate per day will then be applied to the nails. A time quantitative calculation of the absorbed amount of methyl acetate is not possible.

It has to be considered, that this amount is valid only for a few minutes because of evaporation of the remover, and that absorption through the nails is very low. In fact, the dermal exposure to nail varnish removers should be much lower. Thus, due to the high-vapour pressure of the substance and the resultant short retention time on the nails the resulting dermal exposure of the consumer is considered to be negligible.

#### 4.1.1.3.3 Oral exposure

Within the scope of German foods legislation, methyl acetate could be used as an extraction solvent for caffeine, irritating substances, etc.

According to Annex 2 ELV [Extraktionslösungsmittelverordnung vom 08.01.1991 (Lebensmittelrecht, 1995)] (extraction solvents that can be used to a limited extent only), the residual content of methyl acetate in extracted foods is limited to 20 mg/kg coffee or tea.

Methyl acetate could also be used as solvent for the manufacture of sugar from molasses; the residual content of methyl acetate in sugar is limited to 1 mg/kg sugar.

According to Annex 3 ELV [Extraktionslösungsmittelverordnung vom 08.01.1991 (Lebensmittelrecht, 1995)], methyl acetate is used as an extraction solvent for the manufacture of flavours from natural flavour carriers; the residual content of methyl acetate is limited to 1 mg/kg of flavoured foods ready for consumption (Lebensmittelrecht, 1995).

Within this legal frame, when consuming 50 g coffee per day, the consumer could be orally exposed to methyl acetate within the middle µg/kg bw/day range (10-100 µg/kg bw/d).

When consuming 100 g sugar manufactured from molasses per day, the consumer could be orally exposed to methyl acetate within the lower µg/kg bw/day range (1-10 µg/kg bw/d).

Exposure from foods

Methyl acetate is also present in food as a natural flavouring substance, e.g. in bananas (13 mg/kg) and other fruit (up to 0.5 mg/kg), in butter (0.01 mg/kg), olive oil (0.03 mg/kg) and alcoholic beverages (0.8-3 mg/kg). The following limit values for methyl acetate have been fixed by the Council of Europe: 30 mg/kg for beverages or food ready for consumption (Europarat, 1992). Taking into account an uptake of such amounts the oral exposure is estimated to be in the lower mg/kg bw/day range (1-10 mg/kg bw/d).

#### 4.1.1.4 Humans exposed via the environment

In accordance with the TGD, the indirect exposure of humans to methyl acetate via the environment, e.g. via food, drinking water and air, must be determined. In the form of a worst-case scenario, the most significant point source (in this case the formulation of household chemicals, adhesives and paints and lacquers) is considered for calculation purposes. This result is then compared with a second calculation which is based on the regional background concentrations (see Section 3.1.7).

The results of these calculations with the corresponding input values are summarised in Appendix A6. It is necessary to note, however, that the utilised calculation model is as yet only provisional. It requires revision as soon as further information is available.

The selected input parameters are summarised in **Table 4.8**.

**Table 4.8** Environmental concentrations used as input for indirect exposure calculations

| | PEClocal scenario (greatest point source) | Regional background concentrations |
|---|---|---|
| Concentration in soil | 0.005 mg/kg | $1.3 \cdot 10^{-5}$ mg/kg |
| Concentration in the surface water | 0.23 mg/l | $8.5 \cdot 10^{-4}$ mg/l |
| Concentration in the atmosphere | 0.035 mg/m$^3$ | $1.3 \cdot 10^{-4}$ mg/m$^3$ |
| Concentration in the groundwater | 0.011 mg/l | $3.65 \cdot 10^{-5}$ mg/l |

The resultant daily doses for the substance are as follows:

- DOSEtot = 14.43 µg/kg body weight day (local scenario).
- DOSEtot = 0.0534 µg/kg body weight day (regional background concentrations).

The calculated uptake quantities via the following routes:

**Table 4.9** Routes of uptake

| Uptake route | % of total uptake | |
|---|---|---|
| | local | regional |
| Drinking water | 45.5 | 45.4 |
| Fish | 0.7 | 0.7 |
| Plant shoot | 1.3 | 1.3 |
| Root | 0.4 | 0.4 |
| Meat | < 0.01 | < 0.01 |
| Milk | < 0.01 | < 0.01 |
| Air | 52.0 | 52.1 |

Air and drinking water are the most significant routes of uptake, when taking both a local and regional approach to the calculation of the indirect exposure.

#### 4.1.1.5 Combined exposure

A person who is exposed indirectly to methyl acetate through the environment may also be exposed through different applications via inhalation as well as oral route. The sum of all types of exposure is expected to amount between 1-10 mg/kg bw/d (lower milligram range).

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

#### 4.1.2.1 Toxicokinetics, metabolism and distribution

Relevant inhalation exposure is generally possible due to high-vapour pressure of methyl acetate (220 hPa at 20°C). Water solubility (295 g/l) and partition coefficient (log Pow) of 0.18 indicate bioavailability of the substance at all routes.

For the *in vitro* hydrolysis of methyl acetate in blood of rats and humans, half-lifes of 2-3 h and about 4 h, respectively, were determined indicating a more rapid hydrolysis in the blood of rats than of humans (Filov, 1961). The hydrolysis was according to a reaction of first order.

Ghittori et al. (1984) reported on a slower hydrolysis of methyl acetate in blood at 37ºC (concentration: 2.18 µgl; 7 hours later: 1.96 µg/l) as compared to the data given by Filov (1961). The products were identified as acetic acid and methanol.

In a more recent paper (Mizunuma et al., 1992) hydrolysis of methyl acetate to methanol *in vitro* was detected when methyl acetate was incubated with human blood (27.9 µg/ml) for 2 to 8 hours at 36°C. The velocity of the reaction was so fast that 60% of methyl acetate was converted to methanol in 2 hours, almost all of methyl acetate disappeared in 8 hours (detection limit 0.1 µg/ml). Concentrations were analysed by head-space gas chromatography, the methanol formation was further confirmed by means of gas chromatography-mass spectrometry. The capacity to hydrolyse methyl acetate was evenly distributed in cellular and noncellular fractions of blood.

After incubation of methyl acetate with carboxylic esterases from nasal mucosa of male F344 rats (S9-homogenate) a rate of hydrolysis of 15 $\pm$ 3 nmol/mg S9-protein/min was determined (Dahl et al., 1987).

After oral administration to rabbits, methyl acetate was hydrolysed to methanol and acetic acid (Tambo, 1973; BG Chemie, 1995). The animals received a dosage of 20 ml/kg bw of a 5% aqueous solution (1,000 mg/kg). Methanol concentration was analysed in the blood from 30 minutes after application up to 5 hours. Methyl acetate could not be detected in any sample whereas methanol was found in blood and urine already after 30 min. Peak concentrations of methanol in the blood were measured after 3 hours and amounted to 0.573 mg/ml. Following oral application methyl acetate is hydrolysed in the gut. Therefore, in blood and urine only methanol and acetic acid were found, not methyl acetate. Similarly, after inhalation exposure in blood and urine only the products of hydrolysis were detectable. 30 to 60 min. after application acidosis was noted for 2-3 hours, apparently because of the formation of acetic acid.

Shortly after start of inhalation exposure of tracheotomized rabbits to methyl acetate in a 645 l chamber for up to 3 hours methyl acetate was found in the exhaled air in a concentration of up to 30-50% of the inhaled quantity (up to 20 mg/l). After termination of exposure no methyl acetate was detected in the exhaled air. Although there was retention of methyl acetate during inhalation, methyl acetate could not be found in the blood indicating a rapid hydrolysis (Filov, 1961; BG Chemie, 1995).

A recent study in rats (HMR, 1999a) reported methyl acetate concentration less than 5 ppm (v/v; < 4.6 mg/l) immediately after 6 hours inhalation exposure (2,000 ppm) on the last day of a

subacute study (6 hours daily, 5 days/week) and 30, 60, 120 min. as well as 18 hours later. At each time point two male rats and two female rats were sacrified to collect blood.

Inhalation exposure of 4 rats to a probably saturated atmosphere of methyl acetate (in 25 l bottles) induced narcotic effects in the animals after 10 to 20 min. After decapitation at this time-point concentrations of 70-80 mg methyl acetate/100 ml were found in the blood. Similar experiments with inhalation exposure to methanol showed that the narcotic effects are mainly induced by methyl acetate (Filov, 1964a,b; BG Chemie, 1995).

Repeated inhalation 2h-exposure of each of 2 test persons to about 200 ppm methyl acetate (165 290 ppm; approx. 610 mg/m$^3$) respectively to methanol (160-225 ppm) 2 times per day (2h interval) over 3-4 days resulted in each of the first exposures per day to enhanced methanol concentrations in urine, which reached a maximum after each second exposure per day respectively within 4 h after second exposure (>10 mg methanol/ l urine). At each next morning the values restored to normal (< 5 mg/l) (Tada et al., 1974).

Species specificity of methanol metabolism

Methanol is metabolised to formaldehyde in liver by alcohol dehydrogenase. Formaldehyde is metabolised to formic acid. Formate is considered to be the toxic metabolite of methanol, remarkable species differences are existing in accumulation of formate. Formate metabolism requires tetrahydrofolate. Monkeys and man are more sensitive to methanol compared to rodents because of a lower tetrahydrofolate content in liver resulting in slower metabolism thus leading to an accumulation of formate (Dorman et al., 1994).

Formate is accumulating in primates only at extremely high dose levels where it exceeds the rate of metabolism. It is assumed that at dosages below 600 mg/kg bw/d no interspecies differences between monkeys and rats were observed (Takeda and Katoh, 1988). Therefore interspecies differences in the metabolism have to be taken into consideration at the LD50/LC50 dose levels or when considering acute toxicity.

The results from Andrews et al. (1987) showed no adverse optic effects in monkeys (and rats) from 20 repeated exposures to up to 5,000 ppm (approx. 6,666 mg/m$^3$) methanol vapours. It was assumed that this dosage did not result in the formation of toxic amounts of formic acid and in ocular damage, however blood levels of formic acid were not investigated. Because these studies revealed no central nervous effects in monkeys, it is considered that the rat is also a useful model to indicate subacute or subchronic toxic effects of methyl acetate at relevant dose levels (below sublethal dosages).

Conclusion on toxicokenetics, metabolism and distribution

After oral exposure methyl acetate is partially cleaved in the gastrointestinal tract into methanol and acetic acid by esterases of the gastric mucosa. The ester is furthermore hydrolysed by esterases of the blood. Similarly, after inhalation exposure of rats to a concentration of 2,000 ppm (6,040 mg/m³) blood concentrations less than 4.6 mg/l were determined. Investigations at higher concentrations have not been performed except those at nearly saturation concentrations. Inhalation exposure at saturation conditions results in the occurrence of methyl acetate in blood.

From the limited *in vitro* hydrolysis data it was estimated roughly that the half-life of methyl acetate amounts 2 to 3 hours (rat blood) and about 2 hours (human blood). In the context of ester hydrolysis local activity of carboxylesterases in the respiratory epithelium is of particular

importance. Investigations in human and rat nasal respiratory and olfactory tissue demonstrated that rat nasal respiratory carboxylesterase activity was about 3-fold higher than that of humans. However, carboxylesterase activity in olfactory regions was similar among both species (Bogdanffy et al., 1998).

#### 4.1.2.2 Acute toxicity

Animal data

Acute toxicity by the oral, dermal, and inhalative routes is low as judged by tests with rats: An oral $LD_{50}$ of 6,482 mg/kg (Smyth et al., 1962), an inhalative $LC_{50}$ of >49 mg/l/4h (Smyth et al., 1962) and a dermal $LD_{50}$ of >2,000 mg/kg (Hoechst AG, 1988a) are reported for rats. A $LC_{50}$ value of > 24 mg/l/8h for mice and a $LC_{50}$ of > 30 mg/l/10h for cats demonstrate similar effects in these species (von Oettingen, 1960).

No clinical symptoms were seen after occlusive application of 2,000 mg/kg (no vehicle used) methyl acetate for 24 hours to the skin of each of 5 male and 5 female rats. None of the rats died and necropsy after an observation period of 14 day did not reveal any abnormalities (Hoechst AG, 1988b). After oral application and after inhalation of substance vapours, animals showed narcotic symptoms, spasms, dyspnea and vomiting; inhalation of vapours in addition caused irritation of eyes and upper respiratory tract (von Oettingen, 1960).

Methyl acetate has narcotic properties if inhaled, but the narcotic action is of short duration. The narcotic concentration for mice starts at 34 mg/l (von Oettingen, 1960) and for cats at 56 mg/l (von Oettingen, 1960). But the narcosis is not smooth inasmuch as in the early stages respiratory disturbances, vomiting and convulsions may appear, and deep narcosis is very poorly tolerated.

It appears further that, within limits, short exposure to high concentrations is somewhat better tolerated than long exposure to low concentrations, and that, although recovery from narcosis is rather prompt, it may take several days until the animals have completely overcome the sequelae (von Oettingen, 1960).

Human data

Accidental inhalation of vapours of methyl acetate for 45 minutes caused severe headache and considerable somnolence which lasted over 6 hours (von Oettingen, 1960). No further data are available. A 69-year-old worker with occupational exposure to methyl acetate vapours had suffered occasionally from giddiness, headache, lassitude, vertigo, and unsteady gait. During some of these attacks he had repeatedly suddenly become blind in both eyes, and developed bilateral atrophy of the optic nerve, a large central scotoma in the left eye, and a concentric narrowing of the visual field of the right eye (von Oettingen, 1960).

Conclusion on acute toxicity

Inhalation of methyl acetate causes severe headache and considerable somnolence in humans that need labelling with the EU risk phrase “R 67, Vapours may cause drowsiness and dizziness”. For Classification, See Section 1.4, Acute toxicity data determined in tests with rats demonstrated an oral $LD_{50}$ >5,000 mg/kg body weight and a dermal $LD_{50}$ >2,000 mg/kg. Inhalation $LC_{50}$ values of 24 mg/l/8 hours for mice and of >30 mg/l/10 hours for cats were

detected. Basing on these data, a classification of the acute toxicity of methyl acetate as harmful is not appropriate.

#### 4.1.2.3 Irritation

Animal data

*Skin irritation*

In a Draize skin irritation test according to EU and OECD guidelines with 4 hours semiocclusive exposure to 0.5 ml methyl acetate each (no vehicle used) for a period of 4 hours, three rabbits did not exhibit any oedema but slight erythema grade 1 at the 1-hour observation time which lasted in 2/3 animals till the 24-hour observation. All erythema were reversible within 48 hours. One of the animals exhibited dry and rough skin at the application site (Hoechst AG, 1988b).

*Eye irritation*

An EU and OECD guideline conform Draize eye irritation test with three rabbits (each was treated with 0.1 ml of the undiluted substance) demonstrated strong irritation of cornea (mean scores for observations at 24, 48 and 72 hours of 1/1.7/1.3), iris mean scores 1/1/1, conjunctival redness (mean scores 1.7/1.7/2) and conjunctival oedema (mean scores 2.7/2.3/3) with white discoloration and bleeding of the conjunctivae; these effects were reversible within 7 days (Hoechst AG, 1988c).

*Respiratory irritation*

A RD50 of 829 ppm for mice was reported (Muller and Greff, 1984).

Human data

Application of 2 drops of methyl acetate to human skin caused cooling and desquamation but no irritation (von Oettingen, 1960). No further more data are available. Exposure to the vapours for 5 minutes leads to irritation of the eyes, nose, throat and trachea from approximately 15 mg/l (Reus, 1933, cited by BG Chemie, 1995, no further data available).

Conclusion on irritation

Methyl acetate has proven to cause only weak skin irritation in humans and in rabbits (no oedema, erythema with maximum grade 1 reversible within 48 hours). Eye irritation however, was strong but reversible within 7 days in a Draize eye test with rabbits (with mean scores for observations after 24, 48 and 72 hours of 1/1/1 for iridial irritation and of 2.7/2.3/3 for conjunctival oedema). Exposure to methyl acetate vapours causes irritation to eyes and respiratory tract of humans. Based on these data, the substance has been classified as “Xi (Irritant)” and labeled as “R 36 (Irritating to eyes)”. For classification, see Section 1.4.

#### 4.1.2.4 Corrosivity

Methyl acetate has proven to cause only weak skin irritation in humans and in rabbits (see Section 4.1.2.3). Eye irritation in rabbits was strong but reversible in a Draize eye irritation test (see Section 4.1.2.3). Thus, methyl acetate has no corrosive properties.

#### 4.1.2.5 Sensitisation

Animal data

No data available.

Human data

Relevant human data are not available. In a maximisation test with 25 volunteers no sensitisation was observed after exposure to 10% methyl acetate in petrolatum (Kligman, 1976). Taking into account the long experience with human exposure to the substance, and the absence of any reports on contact allergy in exposed persons (Klaschka and Vossman, 1994), methyl acetate is not expected to exhibit skin sensitizing properties, especially since the substance is hydrolysed in contact with water by non-specific tissue esterases to methanol and acetic acid. For these substances a skin sensitisation potential is either absent (methanol, Fisher, 1986) or restricted to a few cases (acetic acid, Weil and Rogers, 1951).

#### 4.1.2.6 Repeated dose toxicity

Animal data

Methyl acetate was recently tested in a 28-day inhalation study (HMR, 1999a) which was performed according to the B.8 method (OECD 412). Groups of 10 male and 10 female Sprague-Dawley rats received methyl acetate (test substance purity >99.5%) by nose-only inhalation exposure on concentrations of 0, 75,350 or 2,000 ppm (mean analytical concentrations 79,335 and 2,018 ppm, equivalent to 227, 1,057, 6,040 mg/m³) on 6 hours daily, 5 days per weeks. At the high concentration groups, the body weights and food consumptions were decreased in both sexes (males>females) without significant differences in the mean relative food consumption/kg bw/d, the mean values of erythrocyte counts, hemoglobin and hematocrit were increased, while the total counts of leukocytes and lymphocytes were decreased for these groups. Clinical chemistry examinations revealed a dose-related decrease of cholesterol levels gaining significance in both sexes at the high concentrations and in females at all dose groups. Serum calcium concentrations were increased in both sexes at the high concentration. The ALAT activities were slightly, but significantly increased in high concentration females (41 U/L vs. 34 U/L in controls). Females from the high concentration group showed significantly increases in urine volume and decreases in specific weight. Due to the effect on body weights several absolute organ weights were decreased and relative organ weights were increased in high concentration males. Animals from the high concentrations groups had increased adrenal weights in both sexes and decreased thymus weights in females. Slight significant changes of adrenal and thymus weights were also observed in females of the intermediate concentration group. At necropsy, no compound-related macroscopic findings were observed. Histopathologic examinations revealed slight to moderate degeneration and necrosis of the olfactory epithelium (at level 3 out of 4 sections) of mainly all males and females exposed to the high concentration

of methyl acetate. Any other treatment-related abnormality was observed in any other organs and in any other dose group. As degeneration of the olfactory mucosa occurred at 2,000 ppm, the NOAEC for local effect was estimated to be 350 ppm (1,057 mg/m$^3$). The food efficiency was similar in animals from all groups, therefore the reduction of body weights were considered to be related to the reduced food consumption. The toxicological significance of altered adrenal weight and reduced cholesterol levels was considered to be equivocal as no morphological abnormality of the adrenal was observed. It can be interpreted to indicate nonspecific toxic response e.g. due to stress. However a specific response of the adrenal cortex cannot be excluded; data on the serum levels of steroid hormone concentrations were not generated. The red blood changes may indicate hemoconcentration due to treatment-related increased diuresis observed in high concentration females and/or reduced water consumption. This remains uncertain, because of missing data on the water consumption. The increase of ALAT activity in rats is indicative for hepatocellular damage. In absence of any morphological lesion or any other corresponding change this was considered indicative for a minimal dysfunction of liver cells. The weight reduction of thymus and leucocytopenia/lymphopenia should be discussed to give hint on a possible immunosuppressive effect. This assumption seemed to be uncertain in view of the absence of morphological changes in the thymus or any other immune organ. Overall, there is a concern that diureses, minimal liver cell dysfunction, adrenal weight increase, and reduced serum cholesterol concentrations represented minimal adverse effects due to the methyl acetate treatment. Therefore the NOAEC for systemic effects was also derived to be 350 ppm (1,057 mg/m$^3$).

There are no other valid animal studies on subacute, subchronic or chronic effects of methyl acetate.

In a non-reliable study cited by Flury and Wirth (1933) four cats inhaled 19-21 mg/l methyl acetate for eight days (6 hours/day). One animal died with reduced body weight, the others showed eye irritation, salivation, reduced food consumption and progressive moderate depression of the central nervous system. The blood investigation revealed increased hemoglobin, and erythrocyte values and transient leukocytosis. At the end of the study animals appeared fatigued and recovered slowly.

There are no data from studies with other administration route than the inhalation exposure. Local toxic effects of methyl acetate at other sites of application (gastrointestinal tract, skin) before it undergoes hydrolysis are not excluded (see Section 4.1.2.1).

Human data

Information on repeated human exposures to methyl acetate is rare. Quantitative data on exposure and effects were not well investigated or documented. Workers were exposed to other compounds, so that effects cannot be attributed clearly to methyl acetate. Therefore the relevance of the observed effects to evaluate risks to human health is questionable. Despite these limitations some data from literature are cited below:

Eleven workers out of 47 workers from 7 Swedish paint industries exposed to a mixture of solvents were exposed to methyl acetate (exposure range 3-169 mg/m$^3$, median exposure 13 mg/m$^3$) as well as to other solvents. In comparison to a reference group activities of liver enzymes were similar in the group of 47 employees. No correlation of the results to any of the single solvents was recognised (Lundberg and Hakansson, 1985).

Duquenois and Revel (1934) reported that women working in a shoe-factory suffered from eye irritation, visual disorders, CNS symptoms, difficulties of breathing and heart trouble and identified a liquid mixture of methylformate, ethylformate, ethyl acetate and methyl acetate.

*Skin effects*

It is stated in handbooks, occupational health guidelines and chemical safety cards that methyl acetate not only irritates the skin but causes also symptoms of skin dryness and roughness after acute, long-term or repeated exposure (International Chemical Safety Cards, 1993). Application of 2 drops of methyl acetate to human skin caused cooling and desquamation but no irritation (von Oettingen, 1960).

Conclusion on repeated dose toxicity

Overall, reliable experimental animal data on the local and systemic effects after repeated administration of methyl acetate are restricted to the inhalation exposure. After nose-only inhalation during a 28-day treatment period, methyl acetate induced degeneration/necrosis of the rat olfactory mucosa at a concentration of 2,000 ppm on 6 hours/day, 5 days/week (6,040 mg/m³) (HMR, 1999a). There was some concern on minimal effects of systemic toxicity at this concentration diureses, minimal liver cell dysfunction, adrenal weight increase, and reduced serum cholesterol concentrations).

There are no adequate data from human experience on repeated or prolonged exposure.

Based on general experience that acute and long-time or repeated exposure to methyl acetate defats skin and cause dryness and cracking of the skin, the substance has been labelled with "R 66, Repeated exposure may cause skin dryness or cracking". For classification, see Section 4.1.

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

*Inhalation route*

The NOAEC for local effects on the respiratory tract derived from an accurate 28-day inhalation study in rats (HMR, 1999a) was 350 ppm (1,057 mg/$m^3$).

The NOAEC for systemic effects also derived from the 28-day inhalation study (HMR, 1999a) was 350 ppm (1,057 mg/$m^3$).

*Other administration routes*

No adequate experimental data are available to derive a N/LOAEL for other administration routes.

Comment to the derivation of the NOAECs

*Systemic effects*

In the HMR study (1999a), adrenal weight increase and reduction of serum cholesterol concentrations were clearly dose-related effects. It can be assumed that prolongation of treatment would show more clearly the adversity of effects. At the moment, it is speculative whether the cholesterol reduction and adrenal weight increase is associated with increased diuresis (e.g. via effects on aldosterone synthesis) and/or thymic involution and lymphopenia (e.g. via effects on

glucocorticosteroid synthesis). Although there is no doubt that effects were induced by test-substance exposure, the toxicological significance of treatment-related effects at 350 ppm was considered to be very low or even equivocal.

The findings in the HMR study (1999a) show similarities to those induced by stress. However, in contrast to stress related findings, the methyl acetate effects clearly show dose-dependency at all dose groups gaining significance at the mid and high concentrations tested. Thus, they are clearly attributed to the test substance and not primarily to the testing procedure.

Finally, a NOAEC of 350 ppm is kept for systemic effects unless no other data are available.

Methanol data are not further considered for the assessment of inhalation toxicity of methyl acetate, because a valid inhalation study on the methyl acetate is now available. Data from metabolic products or structurally related substances are of high value if data on the test substance itself are missing or less accurate. They may support other data or give concern on potential toxicity of the test substance.

In case of the study by Andrews et al. (1987, cf. Section 4.1.2.1) data from methanol inhalation effects in rats and monkeys are of lower quality than the HMR study (1999a) on methyl acetate. The Andrews study did not include examinations on hematology, clinical chemistry and the number of organs/tissues was limited (nasal turbinates, trachea, lungs, kidneys, esophagus, liver and eye with optic nerve).

*Local effects*

There is a large gap between the high and mid concentration of methyl acetate tested in the HMR study (1999a). Thus, it could be that the NOAEC might be higher if an additional dose would have been tested.

Celanese (2000) argues that the NOAEC from a pre-study on methyl acetate showing no nasal toxicity at 500 ppm after exposure on 5 consecutive days should be taken as the most appropriate one. In general, studies with longer duration are preferred for the assessment of chronic toxic effects unless there are no specific reasons for exceptions. The preliminary study to the HMR study (1999a) was yet sufficiently reported for the rationale of dose selection. Effects seen at day 5 are not predictive for the outcome after 28 days of exposure to the same concentration.

#### 4.1.2.7 Mutagenicity

Bacterial studies

In a well conducted unpublished bacterial mutagenicity study, methyl acetate did not produce an increase in revertants in Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538, and Escherichia coli WP2uvrA, in the absence or presence of Aroclor-induced rat liver S-9 mix. Methyl acetate was tested up to 5,000 μg/plate (Hoechst, 1988d).

Negative results were also obtained in another study using Salmonella typhimurium strains TA 97, TA 98, TA 100, TA 1535 and TA 1538 in the absence of an metabolic activation system and in the presence of rat or hamster liver S-9 mix, when tested up to 10,000 μg/plate. This study employed a 20-minute preincubation period (Zeiger et al., 1992).

Studies on yeast

The potential for induction of aneuploidy was investigated in the yeast strain D 61.M (Zimmermann et al., 1985). Methyl acetate was positive, however, the lowest dose with an observable effect was as high as 3.38% which is equivalent to appr. 33,800 µg/ml or 456 mmol/l. Therefore, this finding is of low relevance for the *in vivo* situation.

*In vivo* studies

Methyl acetate was negative in a rat bone marrow micronucleus test after inhalation exposure for 28 days (HMR, 1999b). Exposure was for 6 hours on 5 days per week; doses of 75,350 and 2,000 ppm were employed. Groups consisted of 5 male and 5 female animals each. Cell sampling was done 24 h after the last treatment; polychromatic (PCE) and normochromatic (NCE) erythrocytes were analysed. There was no local cytotoxicity (PCE/NCE ratio); toxic signs were observed at the highest testsed dose (for details see Section 4.1.2.6).

Other information

*Methanol*

Methanol has been investigated in detail by Campbell et al. (1991). Mice were exposed by inhalation to 800 or 4,000 ppm methanol for 5 days, and cytogenetic effects were analysed in blood erythrocytes and lung cells. Data on toxicity are not given. The results were uniformly negative; no increased frequencies of micronuclei in blood cells, of sister chromatid exchanges, chromosome aberrations or micronuclei in lung cells were found.

*Acetic acid*

Acetic acid was negative in a bacterial gene mutation test (Ames test; von der Hude et al., 1988). In mammalian cell cultures (CHO cells) acetic acid decreases the pH value; after neutralisation no clastogenic effects were observed (Morita et al., 1990).

Conclusion on mutagenicity

Methyl acetate is negative in a bacterial mutation test and a rat bone marrow micronucleus test. Furthermore, the hydrolysis products methanol and acetic acid do not reveal evidence for a mutagenic potential. There is no concern with respect to mutagenicity. Methyl acetate should not be classified as a mutagen.

#### 4.1.2.8 Carcinogenicity

Experimental data on the carcinogenic potential of methyl acetate are not available.

Additional data of concern

*Methanol*

No significant increase of tumor rate was observed in mice of an 18-month inhalation study exposed to 0, 10, 100, and 1,000 ppm methanol. A 24-month inhalation study on rats exposed to the same concentrations of methanol resulted in a dose-dependent increase of papillary lung

adenoma or adenomatosis in males which gained significance at the 1,000 ppm-dose group. (Data are only reported as summary from Takeda and Katoh, 1988).

Another summary report (NEDO, 1987) possibly presents the same data presented in the Japanese study reported by Takeda and Katoh (1988) as the rat (F344/DuCrj) and mice (Crj:B6C3F1) strains, dosages and treatment durations are identical. In the NEDO publication (1987) on the whole body exposure inhalation study, a higher incidence of lung adenomas was reported to be not related to methanol concentrations (1/52, 5/52, 2/52 and 6/52 in control, 10, 100 and 1,000 ppm males only). The occurrence of the adenomas was reported to be within the range of historical data. The numbers of animals having either adenoma or adenomatoid lesions was dose dependently increased but not significant different from control group (5/52, 6/52, 7/52 and 10/52). A higher, but not significantly increased incidence of phaechromocytomas was seen in the 1,000 ppm females (2/50, 3/51, 2/49 and 7/51 in control, 10, 100 and 1,000 ppm groups).

In summary, methanol was reported not to be carcinogenic in inhalation studies of rats and mice.

*Acetic acid*

No animal data are known on carcinogenic potential of acetic acid.

#### 4.1.2.9 Toxicity for reproduction

Animal data

Fertility impairment: no data available.

Developmental toxicity: no data available.

Human data

No data are available.

Other information

From toxicokinetic studies on rabbits (cf. Section 4.1.2.1) methyl acetate is supposed to be hydrolysed rapidly to methanol and acetic acid by nonspecific esterases present in the blood and in tissues. More detailed investigations on actual methyl acetate concentrations in blood had been performed subsequently to a 28-day inhalation study in rats (HMR, 1999a) during which no methyl acetate (< 4.6 µg/ml) could be detected in any of the blood samples which had been taken immediately after cessation of exposure (cf. Section 4.1.2.1). Taken together it appears from these data that there is no relevant systemic availability of the parent compound itself. Therefore, due to the rapid hydrolysis of the substance, the toxicological properties of the immediate metabolites are taken into consideration for evaluation of methyl acetate toxicity with respect to reproduction.

*Acetic acid*

Limited data indicate that acetic acid is not teratogenic *in vivo*. Teratogenic evaluation of apple cider vinegar was made in rabbits. The administration of up to 1.6 g per kg body weight of the test material daily to pregnant rabbits (days 6 through day 18 of gestation) had no clearly discernible effect on nidation or on maternal or fetal survival. The number of abnormalities seen

in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls. Sodium acetate displayed no teratogenicity in the developing chicken embryo at levels up to 200 mg per kg of egg when injected into the air cell or yolk of unincubated eggs, or at levels up to 100 mg per kg egg when injected into the air cell or yolk of eggs after 96 hours of incubation (cited from NTIS, 1977).

*Methanol*

As to methanol a survey on animal studies relevant to reproduction (fertility/development) is given in the **Table 4.10**.

**Table 4.10** Summary of studies relevant to reproduction with methanol

| Species | Protocol | Results |
|---|---|---|
| Rat (inhalation) | 200 ppm/7 days (6 h/d) | no effects on serum testosterone, LH, corticosterone (Cameron et al., 1984) |
| Rat (inhalation) | 200 ppm/6 weeks (8 h/d, 5 d/week); 50,200, 800 ppm/ 13 weeks (20 h/d, 7d/week) | no effects on testosterone synthesis, testis weight up to and including 800 ppm: no effects on testis (Lee et al., 1991) |
| Rat (inhalation) | 5,000 ppm for 1, 3, 6 hours | no significant effects on serum LH, FSH, and testosterone (Cooper et al., 1992) |
| Mice (gavage) | 1,000 mg/kg for 5 days | no effects on sperm morphology (Ward et al., 1984) |
| **Fertility studies** | | |
| 2-generation-study rat (inhalation) | 10,100, 1,000 ppm (continuously) | up to and including 1,000 ppm no effects on reproductive capacity and capability NOAEC (fertility): 1,000 ppm (NEDO, 1987) |
| **Developmental toxicity studies** | | |
| Rat (inhalation) | 200, 1,000, 5,000 ppm g.d. 7-17 (continuously) | NOAEC (mat.tox.): 1,000 ppm NOAEC (dev.tox.): 1,000 ppm (NEDO, 1987) |
| Rat (inhalation) | 5,000, 10,000 ppm g.d. 1-19 (7 h/d); 20,000 ppm g.d. 7-15 (7 h/d) | NOAEC (mat.tox.): 10,000 ppm NOAEC (dev.tox.): 5,000 ppm (Nelson et al., 1985; 1990) |
| Rat (inhalation) | 15,000 ppm g.d. 7-19 (7 h/d) | no significant changes in postnatal neurobehavioral and neurophysiological development (Stanton et al., 1995) |
| Mice (inhalation) | 1,000, 2,000, 5,000, 7,500, 10,000, 15,000 ppm (7 h/d) g.d. 6-15 | NOAEC (mat.tox.): 5,000 ppm NOAEC (dev.tox.): 1,000 ppm (Rogers et al., 1993) |
| Mice (inhalation) | 10,000 ppm g.d. 6-15 (6 h/d) 5,000, 10,000, 15,000 ppm, g.d. 7-9 (6 h/d) 10,000, 15,000 ppm g.d. 9-11 (6h/d) | NOAEC (mat.tox.): 5,000 ppm LOAEC (dev.tox.): 5,000 ppm (Bolon et al., 1993 ; 1994) |
| Rat (gavage) | 1,600, 2,400, 3,200 mg/kg/d g.d. 1-8 | NOAEL (mat. tox.): 2,400 mg/kg/d NOAEL (dev.tox.): 3,200 mg/kg/d (Cummings, 1993) |

Table 4.10 continued overleaf

**Table 4.10 continued** Summary of studies relevant to reproduction with methanol

| Species | Protocol | Results |
|---|---|---|
| Rat<br>(gavage) | 1.3, 2.6, 5.2 ml/kg<br>g.d. 10 | NOAEL (mat tox.): 2.6 ml/kg<br>LOAEL (dev.tox.): 1.3 ml/kg<br>(Youssef et al., 1991) |
| Rat<br>(oral) | 2% in drinking water<br>(≈ 2,500 mg/kg/d)<br>g.d. 15-17 or 17-19 | no effects on the dams and on fetal development and postnatal growth, indications for behavioral abnormalities<br>(Infurna and Weiss, 1986) |
| Mice<br>(gavage) | 2 . 2,000 mg/kg/d<br>g.d. 6-15 | Embryo-/ fetotoxic and teratogenic effects comparable to inhalatory exposure of 10,000 ppm<br>(Rogers et al., 1993) |

*Fertility studies with methanol*

A 2-generation study with Sprague Dawley rats (NEDO, 1987; Takeda and Kato, 1988; both summary reports) had been performed in accordance to a former OECD guideline for testing of chemicals of October 1980. Groups of 30 animals/sex/dose group (F0 generation) were exposed to 1,000, 100, and 10 ppm methanol (whole body/continuously) from 8-week-old through either end of mating period (for males at 16-week-old or thereafter) or through the mating and gestation period to the end of lactation (females). F1 generation males were exposed from birth to the end of mating (at 14-week-old or thereafter) and F1 generation females from birth through mating, gestation, lactation to weaning of their pups (21 days after delivery). F2 generation males and females were exposed from birth to 21-day-old, and in addition, one animal/sex/litter further exposed up to 8 week old. In general, litter sizes were reduced to 8 pups 4 days after birth. At 21 days after birth, 2 animals/sex/litter were selected for use as subsequent breeders, respectively for use in various other examinations. Remaining pups were sacrificed and subjected to a necropsy.

Observation and examination of F0 generation animals: all animals were observed at least once a day for clinical signs and mortality. From 6 to 16-week-old, animals were weighed weekly as was measured food consumption and water intake. During 2 weeks prior to mating, females were examined for sexual cycle by examination of vaginal smear. During gestation all dams were observed at least once a day for clinical signs, mortality and for signs of abortion and premature delivery. Body weight and food and water consumption was measured on days 0, 7, 14, and 20 of gestation. During the lactation period, dams were observed for nursing behavior including lactation, nest building or cannibalism. Body weight and food and water consumption was measured on postnatal days 0, 4, 7, 14, and 21. After termination of mating, all males were necropsied as appropriate. The testes, epididymides, seminal vesicles and prostate glands were removed and preserved. 21 days after delivery, all dams were necropsied and examined for implantation sites. The vagina, uterus and ovary were preserved.

Observation and examination of F1 generation animals: F1 litters were examined on the day of birth for live pups, dead pups, sex and any external abnormalities. Pups were further observed for general appearance and mortality daily until weaning and at least 5 days a week thereafter. Based on the number of surviving pups on days 0, 4 and 21 of birth, the pup survival rate and weaning rate were calculated. Each litter was weighed on days 0 and 4 (before reduction). After culling pups were weighed individually on days 4, 7, 14 and 21. From weaning to week 14 of birth weight determinations were done weekly. All pups were observed for post-natal morphological differentiation indices including pinna unfolding, eruption of incisors, opening of

eyes, descensus testis and day of vaginal opening. As for movement function tests, all pups after culling were tested for righting on a surface, ipsilateral flexor reflex, pinna reflex, auricular startle response, visual recognition response, pain response, corneal reflex and suspension ability on a particular day before weaning. Movement function tests including emotional test (open field test), learning ability test (pole-climbing test), and movement coordination test (rotor rod test) were performed on 10 pups/sex of animals selected for examination at 5-weeks-old or thereafter. After termination of these tests, pups were sacrificed and necropsied. Pups not used for the latter tests were necropsied at 8-weeks-old or thereafter, and principal organs were weighed. Females selected as subsequent breeders were examined for sexual cycle at 12-weeks or thereafter and mated with males of the same group. Male breeders were necropsied after evidence of insemination and female breeders on day 21 after delivery or thereafter, and the principal organs were weighed.

Observation and examination of F2 generation animals: F2 litters were maintained with their respective dams during lactation until 21-days old and subjected to the same procedures and examinations as for F1 litters. Of these, 1 pup/sex/litter was allowed to survive under exposure after weaning. They were necropsied at 8-week-old and principal organs were weighed.

As to the results of this study, it is reported, that for F0 generation and for F1 generation animals none of the fertility indices including sexual cycle, days needed for insemination, insemination rate or pregnancy rate showed a statistically significant difference. No abnormalities were observed in findings on delivery and on nursing behavior or for the necropsy data of the F0 and the F1 breeders Also there were no differences for body weight, food consumption or water consumption during the gestation and lactation period.

As for the results on the observation of postnatal morphological differentiation, it is reported, that there were no abnormal findings with the exception of slightly earlier descensus testis in pups of the high dose group (1,000 ppm) of the F1 and of the F2 generation.

As for the results of movement function tests, emotional test (open field test) and learning ability test (pole-climbing test) and movement coordination test, it is reported, that there were no significant differences in any exposure group in any generation.

As for organ weights, lower values for the brain weight were reported to be observed in high-dose (1,000 ppm) F1 males and F1 females at 8-week-old necropsy, with similar results obtained for F1 males at 16-weeks-old necropsy (after mating) and for F1 females at 24-weeks-old necropsy (after delivery and lactation). In F2 animals also, lower values for the weight of brain, pituitary gland and thymus were reported to be observed in the high-dose (1,000 ppm) exposed males and females at 8-week-old necropsy. Since figures on organ weights were not provided, the extent of weight changes could not be verified. It is reported, that histopathological examination did not reveal any changes suggesting any effect of treatment in any of these organs.

Data on brain weight were provided from an additional experimental trial performed during the course of the 2-generation study, in which rats of the same strain were exposed to 500, 1,000 and 2,000 ppm methanol gas from day 0 of gestation up to and throughout the F1 generation. Not any effect on brain weight could be detected in the animals of the low-dose exposure group (500 ppm) at weaning (3-weeks-old) or at 6- or 8-weeks-old. In the 1,000 ppm exposed groups marginally lower brain weights were observed in males at weaning and at 6- and 8-weeks-old and in females at weaning but not at the later stages. In the 2,000 ppm exposed groups brain weights in animals of both sexes were statistically significantly lower ($p<0.001$) than that of the controls at 3-, 6- and 8-weeks-old. Brain weight reduction in the 2,000 ppm groups amounted to

about 7.7-12% in female offspring and to about 12-14.6% in male offspring. Taking into consideration that morphological (brain histopathology) and functional examinations including learning ability tests at the 1,000 ppm level during the 2-generation test did not reveal any abnormalities, the subtle brain weight changes reported for the 1,000 ppm concentration level appear not to be of specific toxicological significance.

Thus, from the overall results of this study a NOAEC/fertility of 1,000 ppm (1,300 mg/$m^3$) and a NOAEC/developmental toxicity of 1,000 ppm (1,300 mg/$m^3$) can be derived for methanol for continuous inhalatory exposure.

*Developmental toxicity studies with methanol*

An inhalation teratology test with Sprague Dawley rats (NEDO, 1987; Takeda and Kato, 1988; both summary reports) had been performed in accordance to the Guideline for Toxicological Studies of Drugs of 1984 of the Ministry of Health and Welfare of Japan. Pregnant animals were exposed to 5,000, 1,000 and 200 ppm methanol (whole body/continuously) from day 7 to 17 of gestation. The study was designed to investigate in parallel two different experimental sets: from a total of 36 dams assigned to each exposure group 12 dams/exposure group were used for natural delivery and raising pups until weaning (21-days old), while the others (20-24 dams/exposure group) were used for scheduled sacrifice on day 20 of gestation.

During gestation dams were observed once daily for general appearance and mortality. Body weight, food consumption and water consumption were measured on days 0, 7, 14, 17 and 20 of gestation and on 0, 4, 7, and 21 days after delivery. Dams scheduled for cesarean section were necropsied on day 20 of gestation. They were examined for the number of corpora lutea, implantations, resorptions and live and dead fetuses. Pre- and post-implantation loss rates were calculated from the data obtained. Dams that were allowed to deliver naturally were observed during the raising period for general appearance and for nursing behavior including lactation, nesting and cannibalism. After completion of raising, these dams were necropsied and the post-implantation survival rate was calculated from the number of implantations.

Live fetuses delivered from cesarean section were sexed and examined for external abnormalities including the oral cavity and then weighed. One-half of these fetuses each were then further processed for either visceral or skeletal examination. Delivered offspring (F1 pups) were examined for the number of live births and stillbirths, sex and any abnormalities on the day of birth. At day 4, litters were culled to 8 pups. They were observed for clinical signs and mortality daily until weaning, and at least 5 days a week thereafter. The survival rates were calculated for days 0-4 of birth (survival rate of pups) and days 4-21 of birth (weaning rate). At 21 days after birth pups were separated from their mothers. The animals were then further reared by sex and used for further examinations. Body weight was determined for the litter on days 0 and 4 (before culling) and individually on days 4, 7, 14 and 21 after birth, and once weekly after weaning. Pups were evaluated for postnatal morphological differentiation (day of development of auricles, eruption of incisors, opening of eyelids, descensus testis and vaginal opening). As for movement function tests, all pups after culling were tested for righting on a surface, ipsilateral flexor reflex, auricle reflex, corneal reflex, startle reflex, visual recognition response, pain response and suspension response on a particular day before weaning. At 5-weeks-old, the frequency of interval shifting, standing up, washing face, making toilet, defecation and urination in a circular open field during 3 minutes was determined on about half of the pups. At 6-weeks-old, learning ability was evaluated by repeating the pole-climbing test (condition-avoidance reaction test) with 10 trials a day over 5 days. At 7-weeks-old, the pups were tested for gait and frequency of falling down per 3 minutes on a rotary drum. After termination of the tests pups were necropsied.

Animals not used for the movement function tests were necropsied at 8-weeks-old and weight of the principal organs was determined.

Some overt toxic effects were observed in dams of the high-dose group (5,000 ppm) in terms of depression of maternal weight gain (20 g less than that of the controls) and decreased food consumption and water consumption during gestation, prolongation of gestation period (average 0.7 days) and occurrence of death (two animals died on g.d. 18, respectively 19).

Examinations from scheduled sacrifice on g.d. 20 revealed a larger number of late resorptions and a significantly smaller number of live fetuses/litter (12.9 $\pm$ 4.0) in comparison to the controls (15.0 $\pm$ 1.6) ($P < 0.05$) or to the other groups at the high-dose exposure level (5,000 ppm). In this group the per litter rate of late resorptions to implantations was significantly higher: 10.4% as compared to 0.6% for the control group, and also live fetal body weights were significantly decreased ($P < 0.05$).

Examinations from natural delivery revealed a significantly smaller number of live pups/litter (12.6 $\pm$ 2.5) for the high-dose exposure group (5,000 ppm) in comparison to that of the controls (15.2 $\pm$ 1.6) and a significantly lower post-implantation embryo survival rate per litter (86%) in comparison to the control group (96%).

Examination of fetuses revealed visceral and skeletal abnormalities in the high-dose exposed groups (5,000 ppm), e.g., ventricular septal defects (mean incidence per litter 48%; 16 out of 20 litters affected), cervical ribs (mean incidence per litter 65%; 19 out of 20 litters affected), atresia of cervical arch foramen costotransversarium (mean incidence per litter 45%; all 20 litters affected), bifurcated vertebral centers (mean incidence per litter 15%; 11 out of 20 litters affected, and a delay for almost all ossification parameters.

Evaluation of pups after natural delivery showed significant postnatal mortality for those of the high-dose (5,000 ppm) exposed group, with a survival rate of 82% in comparison to 97-99% in the control and the lower exposed groups. After litter size adjustment (on day 4), there were no more cases of death in any group. Postnatal morphological development of the pups did not reveal any significant changes. Reflex reaction, emotional tests, learning ability and movement coordination did not show any treatment-related changes. Macroscopic evaluations at necropsy at the age of 8-weeks revealed a rather high incidence of 16.5% of unilateral thyroid atrophy in the offspring of the high-dose exposed group. These unilateral defects of the thyroid occurred exclusively in litters of the 5,000 ppm group, with 8 out of 12 litters affected. Organ weight determinations at 8-weeks-old revealed various changes in several organs of the descendants of the high-dose exposed group, however not any organ weight differences, including brain weight, could be revealed in the offspring of the 1,000 ppm exposed group.

Thus, from the overall results of this study, a NOAEC/maternal toxicity of 1,000 ppm (1,300 mg/m$^3$) and a NOAEC/developmental toxicity of 1,000 ppm (1,300 mg/m$^3$) can be derived for methanol for continuous inhalatory exposure.

In a further study with Sprague-Dawley rats which were exposed to 20,000, 10,000, and 5,000 ppm methanol by inhalation from day 7 to 15 of gestation (7 hours/day) and sacrificed on day 20 of gestation. Signs of maternal toxicity (slightly unsteady gait after the initial days of exposure) were reported to have occurred only at the high concentration (20,000 ppm) exposed dams. The exposure of the pregnant rats had no effect on the numbers of corpora lutea or implantations or the percentage of dead or resorbed fetuses. For the fetuses significantly reduced body weights were observed at 10,000 ppm as well as a significant increase in the incidence of visceral (urinary system) and skeletal (vertebral defects, cervical ribs) malformations and of

exencephaly and encephalocelae at 20,000 ppm. For developmental effects a NOAEC of 5,000 ppm (6,500 mg/m$^3$) was derived from this study, with the corresponding blood concentrations (determined for nonpregnant females) reported to range from 0.8 to 2.4 mg methanol/ml during the period of exposure (Nelson et al., 1985, 1990).

In a study with CD-1 mice dams were exposed to 15,000, 10,000, 7,500, 5,000, 2,000, and 1,000 ppm methanol by inhalation from day 6 to 15 of gestation (7 hours/day). There were no visible signs of intoxication of dams following exposure to any level of methanol in this study. One dam died in each of the 7,500, 10,000, and 15,000 ppm methanol exposure groups, but no dose-response relationship was evident for maternal death. No other effects were seen in the dams up to and including concentrations of 5,000 ppm. The authors reported that methanol exposure did not result in effects on maternal weight, since maternal weight gain of the methanol-exposed groups was similar to that of the sham-exposed control throughout pregnancy (no detailled data provided). Evaluation of the pups revealed a dose-related increase of fetuses per litter with extra cervical ribs (33.6, 49.6, 74.4, and 60.0 percent extra cervical ribs/litter at 1,000, 2,000, 5,000, and 15,000 ppm in comparison to 28.0 percent extra cervical ribs/litter in the sham-exposed controls), which was statistically significant at 2,000 ppm and the higher concentrations. Also dose-related increases in the incidences of cleft palate (0.65, 0.17, 8.8, 46.6, 52.7, and 48.3 percent cleft palates/litter at 1,000, 2,000, 5,000, 7,500, 10,000, and 15,000 ppm in comparison to 0.21 percent/litter in sham-exposed controls) and of exencephaly (0, 0.88, 6.9, 6.8, 27.4, and 43.3 percent exencephalies/litter at 1,000, 2,000, 5,000, 7,500, 10,000, and 15,000 ppm in comparison to 0 percent/litter in sham-exposed controls) were observed, which were statistically significant at 5,000 ppm and the higher concentrations). Postimplantation mortality was dose-related increased at concentrations of 7,500 ppm and above. Fetal body weight was not affected below 10,000 ppm. A NOAEC of 1,000 ppm (1,300 mg/m$^3$) for developmental effects was derived from this study, corresponding to blood methanol concentrations of 0.06 to 0.13 mg/ml in the dams (Rogers et al., 1993).

With focus on the investigation of methanol-induced neural tube defects CD-1 mice were exposed to 10,000 ppm methanol by inhalation (6 hours/day) from day 6 to 15 or to 1,500, 10,000, and 5,000 ppm methanol during the most vulnerable period of days 7 to 9 of gestation or to 15,000 and 10,000 ppm methanol during day 9 to 11 of gestation. Maternal toxicity in terms of neurologic effects was observed in approximately 20, 10, and 5% of dams on the first, second, and third day of exposure, respectively, when methanol was administered at 15,000 ppm methanol. Signs included ataxia, circling, tilted heads, or depressed motor activity. Dams recovered within 12 hours after exposure ended. Clinical signs were not apparent in mice exposed to 5,000 or 10,000 ppm. Maternal body weights were equivalent in all groups prior to methanol inhalation. Maternal body weights on gestation day 17 were decreased by exposure to either 10,000 ppm during gestation days 6-15 (41.7 + 1.9 g in treated dams versus 45.4 + 4.3 g in the controls) or to 15,000 ppm on gestation day 7 (45.3 + 2.0 g), gestation days 7-8 (46.1 + 1.8 g), or gestation days 7-9 (45.9 + 1.8 g) in comparison to 51.2 + 0.9 g in controls (gestation days 7-9). Repeated exposure to methanol increased the number of resorptions in litters of dams exposed to 10,000 ppm during gestation days 6-15 (32.2% resorptions/litter in treated dams versus 4.4% in controls) or gestation days 7-9 (13.4% resorptions/litter in treated dams versus 1.1% in controls), or exposed to 15,000 ppm during gestation day 7 (38.6%), gestation days 7-8 (41.9%) or gestation days 7-9 (46.2%) in comparison to 2.7% resorptions/litter in the controls (gestation days 7-9). Fetal body weights on gestation day 17 were reduced in offspring from mice that had inhaled 10,000 ppm during gestation days 6-15 (0.81 + 0.03 g in treated groups versus 0.93 + 0.02 g in the controls) or 15,000 ppm during gestation days 7-8 (0.81 + 0.02 g) or gestation days 7-9 (0.82 + 0.02 g) in comparison to 0.92 + 0.05 g in the controls (gestation

days 7-9). Evaluation of the pups revealed visceral (renal pelvic dilatation) as well as skeletal malformations (cleft palate, tail anomalies) that were induced at exposure to methanol concentrations of > 10,000 ppm. Renal pelvic cavitation was already induced at the lowest concentration of 5,000 ppm (100, 90, and 75% litters affected after exposure to 5,000, 10,000, and 15,000 ppm during gestation days 7-9 in comparison to 41% in the controls; 49.5, 31.2, and 44.9% fetuses affected after exposure to 5,000, 10,000, and 15,000 ppm during gestation days 7-9 in comparison to 4.3% in the controls). Neural tube defects (e.g. exencephaly) were induced at concentrations of 10,000 ppm (0, 30, and 65% litters affected after exposure to 5,000, 10,000, and 15,000 ppm during gestation days 7-9 in comparison to 0% in the controls; 0, 3.6, and 14.7% fetuses affected after exposure to 5,000, 10,000, and 15,000 ppm during gestation days 7-9 in comparison to 0% in the controls). Thus, for developmental effects a LOAEC of 5,000 ppm (6,500 mg/m3) could be derived from this study (Bolon et al., 1993).

In a study in rats treated by gavage on gestation days 1-8 during several independent trials, no effects on embryonic or fetal development or on survival of pubs were revealed with dosages of up to and including 3,200 mg/kg, when evaluated on gestation day 9, 11, or 20. For the dams a significant reduction in body weight gain was revealed for the highest dose group only when evaluated on gestation day 9, whereas no significant changes in body weight gain in any of the dose groups was observed when evaluated on gestation day 20. It is reported that there were no other clinical signs of toxicity noted (Cummings, 1993).

After application of single oral doses of 1.3, 2.6, and 5.2 ml methanol/kg bw to rats on gestation day 10 maternal toxic effects (>10% maternal weight loss) were observed at a dose of 5.2 ml/kg, whereas reduced fetal body weight (11-21%) and a dose-related increase (incidences of 0.6, 4.8, and 6.7% at doses of 1.3, 2.6, and 5.2 ml methanol/kg bw) in anomalies (undescended testes, eye anomalies) were reported also with lower doses (Youssef et al., 1991, abstract only).

With doses of about 2,500 mg/kg applied on gestation days 15-17 or 17 -19 to rats via drinking water (2% solution) no effects on fetal development and postnatal growth were observed. However, treated pups required longer than controls to begin suckling on postnatal day 1 and more time to locate nesting material from their home cages on postnatal day 10 (Infurna and Weiss, 1986).

Investigations in mice treated with 4,000 mg methanol/kg bw on gestation days 6-15 by gavage (methanol was administered in distilled water [12%, w/v] in twice daily doses of 2 g/kg bw each, at a rate of 16 ml/kg/dose, at 8:00 and 15:00 hr) revealed embryo- and fetotoxic as well as teratogenic effects (cleft palate: 43.5 percent/litter in the treated group in comparison to 0 percent/litter in the control group, exencephaly: 28.8 percent/litter in the treated group in comparison to 0 percent/litter in the control group) and impairment of maternal body weight (dam weights in the treated group on gestation days 6, 8, 10, 12, 15, and 17 amounted to 26.5, 29.9, 31.8, 35,3, 37.3, and 38.1 g, respectively, whereas corresponding dam weights in the controls amounted to 26.4, 29.8, 32.1, 36.1, 43.6, and 48.6 g, respectively). The corresponding blood methanol concentrations of about 4 mg/ml were comparable to those after inhalatory exposure to 10,000 ppm methanol, where similar severe effects had been observed (Rogers et al., 1993).

Summary of reproduction studies in rats and mice exposed to methanol

In various investigations in rats and mice methanol did not produce significant effects on different parameters of male fertility.

In a two-generation-study in rats, which were continuously exposed to 10,100, and 1,000 ppm methanol, no effects had been observed on parameters of reproductive capacity and capability of

the first and the second generation. During F1 and F2 progeny postnatal development, subtle weight changes (brain) had been reported for the 1,000 ppm exposed groups, however, without any relevance for postnatal morphological and/or functional development. A NOAEC/fertility of 1,000 ppm (1,300 mg/m$^3$) for methanol was derived from the 2-generation study for continuous inhalatory exposure.

In the developmental toxicity studies, after continuous inhalatory exposure of rats, impaired development of the offspring (reduced numbers of live fetuses, resp. of live pups per litter, increased number of late resorptions, reduced fetal body weight, fetal visceral and skeletal abnormalities, postnatal mortality) was observed at concentrations of 5,000 ppm together with signs of maternal toxicity (reduced body weight gain), whereas at the next lower exposure level (1,000 ppm) such effects were no longer demonstrated. After intermittent inhalatory exposure of rats (7 hours/day) developmental effects (fetal visceral and skeletal abnormalities, reduced fetal body weight) were induced at concentrations of 10,000 ppm, but not at exposure levels of 5,000 ppm. A NOAEC/developmental toxicity of 1,000 ppm (1,300 mg/m$^3$) for methanol was derived from the study with rats for continuous inhalatory exposure. This value is further supported from the studies with mice, during which developmental impairment - in terms of fetal skeletal abnormalities (cervical ribs) - at exposure levels without signs of maternal toxicity was induced already at concentrations of 2,000 ppm (7 hours/day), but not at 1,000 ppm.

For the inhalatory route of exposure, rats during the gestational period appeared to respond more sensitive to a whole-day continuous exposure test design than to daily intermittent (7 hours/day) inhalation exposure of methanol. According to this, the embryo-/fetotoxic effects as observed at 5,000 ppm in the study of NEDO (1987) were accompanied by clearly impaired maternal conditions. At daily intermittent exposure of rats during gestation, fetal visceral and skeletal abnormalities as well as exencephaly and encephalocelia had been revealed for concentration levels of 10,000 and 20,000 ppm, at which feed intake, water consumption and body weights of their dams had not been significantly affected, thus indicating a substance-specific potential for the induction of structural abnormalities. This is further supported by the findings from mice experiments, for which data are only available from intermittent exposure during gestation. As to mice, indications for maternal toxicity in terms of lower maternal weight, clinical signs and occasional maternal deaths were reported for concentration levels of 7,500 ppm and higher. However, as in rats, fetal structural abnormalities were already observed at lower concentration levels of 2,000 and 5,000 ppm.

In the developmental studies in mice and rats methanol was revealed to induce structural abnormalities at exposure levels with, resp. without signs of maternal toxicity. As indicated above (see Section 4.1.2.1), there are species-specific differences in methanol metabolism between primates and rodents. Since there is no accumulation of formate in blood after exposure to methanol in rodents (Kavet and Nauss, 1990), it thus appears that methanol itself represents the developmental toxicant in rodents.

As to the methanol-induced fetotoxic and teratogenic effects observed in the experiments with rodents, these were reported from external exposures during the gestational period leading to methanol concentrations in blood of the dams of about 500 µg/ml in mice (Rogers et al., 1993) and of about 2,000 µg/ml in rats (Nelson et al., 1985) with intermittent inhalatory exposure. No such effects were seen at external exposures leading to blood methanol concentrations in dams of about 63-130 µg/ml in mice (Rogers et al., 1993) with intermittent inhalatory exposure during the gestational period and of 53 and 99 µg/ml in male and female rat offspring (at 9-weeks-old) with continuous inhalatory exposure (NEDO, 1987) during the pre-and postnatal developmental period. Compared to these data from animal experiments, in humans blood methanol

concentrations of about 7-8 µg/ml had been determined after external inhalation exposure to 200 ppm methanol (MAK value) for 6 hours (Lee et al., 1992). In addition, from a PBPK model of inhaled methanol in humans (Perkins et al., 1995) it is obvious that methanol blood concentrations after 8-hour exposure to methanol vapours differ for humans and for laboratory animals, e.g. rats and mice. For instance, predictions from this model indicate about 3.5 to 7 fold lower methanol blood concentrations for humans after 8-hour exposure to 1,000 ppm methanol vapours as compared to blood concentrations in mice.

Conclusion on toxicity for reproduction

There are no data on reproductive toxicity of methyl acetate. However, due to the rapid hydrolysis of this compound it is justified to base hazard assessment with respect to reproduction on the toxicological properties of the immediate metabolites. Concerning the metabolites of methyl acetate, acetic acid appears to be of less significance, since there are no indications of a fetotoxic or teratogenic potential, whereas for methanol some embryo-/fetotoxic and teratogenic effects were demonstrated in rodents, however at relatively high concentrations, respectively maternal toxic concentrations only. A NOEC/fertility for methanol of 1,000 ppm (1,300 mg methanol/$m^3$) was derived from a 2-generation inhalation study in rats (NEDO, 1987). With the assumption that methyl acetate is immediately degraded to methanol at a molar ratio of 1, this value can be converted to NOAEC/fertility of about 3,000 mg methyl acetate/$m^3$. A NOAEC/developmental toxicity for methanol of 1,000 ppm (1,300 mg methanol/$m^3$) was derived from two studies in mice (Rogers et al., 1993) and rats (NEDO, 1987) from intermittent as well as from continuous inhalatory exposure, which can be converted to a NOAEC/developmental toxicity of about 3,000 mg methyl acetate/$m^3$.

## 4.1.3 Risk characterisation

### 4.1.3.1 General aspects

Methyl acetate is a water soluble substance with high volatility. The substance has narcotic properties if inhaled at concentrations of 34 mg/l (mice) and 56 mg/l (cats) with a short duration of the narcotic action after cessation of exposure.

Methyl acetate is absorbed via the lungs in animals and humans, absorption via the oral route is demonstrated. After absorption the substance undergoes hydrolysis to methanol and acetic acid. From the available *in vitro* data it may be anticipated that the half-life of methyl acetate in blood ranges between 2 and 4 hours. Immediately after stopping a 6-hour inhalation exposure to rats (2,000 ppm (6,040 mg/m$^3$)) blood concentrations below the limit of quantification (less than 4.6 mg/l) were determined indicating rapid hydrolysis and high clearance of the substance. It appears from these data that the systemic availability of methyl acetate is low.

The main metabolite is methanol which itself is metabolised to formic acid. Formate is introduced into C1-metabolism after activation by reacting with tetrahydrofolate. Humans as well as monkeys are more sensitive to methanol poisoning compared with rats because of a lower tetrahydrofolate content in liver. Therefore interspecies differences in the metabolism were considered mainly of concern at dose levels leading to acute toxicity. Thus rat is a useful model to indicate subacute/subchronic toxic effects below sublethal dosages.

Assessment of the available animal toxicology data indicates that methyl acetate is of low acute toxicity (rats $LD_{50}$ oral: 6,482 mg/kg bw, dermal: >2,000 mg/kg bw, $LC_{50}$ inhalative >49 mg/l/4h). After oral application and after inhalation of substance vapours, animals showed narcotic symptoms, spasms, dyspnea and vomiting; inhalation of vapours in addition caused irritation of eyes and upper respiratory tract. The narcotic concentration for mice starts at 34 mg/l and for cats with 56 mg/l inhaled.

In humans, accidental inhalation of vapours of methyl acetate caused severe headache and considerable somnolence.

Methyl acetate has proven to cause only weak skin irritation in humans and in rabbits (no oedema, erythema with maximum grade 1 reversible within 48 hours). Eye irritation however, was strong but reversible within 7 days in a Draize eye test with rabbits. Exposure to methyl acetate vapours causes irritation to eyes and respiratory tract of humans.

Taking into account the long experience with human exposure to the substance, methyl acetate is not supposed to exhibit skin sensitising properties although no relevant human or animal date are available.

A valid 28-day inhalation study in rats revealed degeneration/necrosis of the olfactory mucosa (nose) at methyl acetate concentration of 2,000 ppm (6,040 mg/m³) (6 hours/day, 5 days/week). At this concentration, diureses, minimal liver cell dysfunction, adrenal weight increase, and reduces serum cholesterol concentrations indicated effects of methyl acetate. Since no adverse effect was identified at 350 ppm (1,057 mg/m), this concentration was considered to be the NOAEC both for local and systemic effects. At the moment, no repeated dose studies on methyl acetate are available for the oral and dermal route. In a nonvalid study in cats, inhalation exposure for 5 days to 19-21 mg/l methyl acetate resulted in increased hemoglobin and erythrocyte levels, transient leukocytosis, eye irritation and moderate CNS depression.

There are no adequate data from human experience on repeated or prolonged exposure.

Methyl acetate is negative in a bacterial mutation test and a rat bone marrow micronucleus test. Furthermore, the hydrolysis products methanol and acetic acid do not reveal evidence for a mutagenic potential. There is no concern with respect to mutagenicity.

At present no data are known which give relevant concern on cancerogenicity following methyl acetate exposure, although in methanol studies on rats and mice, an increased incidence of lung adenoma/adenomatosis was seen in high dose male rats only.

There are no data available on the reproductive toxicity of methyl acetate itself. However, due to the rapid hydrolysis of the compound it is justified to base hazard assessment with respect to reproduction on the toxicological properties of the immediate metabolites. Concerning the metabolites of methyl acetate, for acetic acid there are no indications of a fetotoxic or teratogenic potential, whereas for methanol embryo-/fetotoxic and teratogenic effects were demonstrated in rodents at relatively high concentrations, maternal toxic concentrations. A NOEC/fertility for methanol of 1,000 ppm (1,300 mg methanol/$m^3$) was derived from a 2-generation inhalation study with rats with continuous exposure. With the assumption that methyl acetate is immediately degraded to methanol at a molar ratio of 1, this value can be converted to NOAEC/fertility of about 3,000 mg methyl acetate/$m^3$. A NOAEC/developmental toxicity for methanol of 1,000 ppm (1,300 mg methanol/$m^3$) was derived from two studies with mice and with rats from intermittent as well as from continuous inhalation exposure, which can be converted to a NOAEC/developmental toxicity of about 3,000 mg methyl acetate/$m^3$.

In Germany, methyl acetate as well as methanol are assigned to the MAK-pregnancy category "C" denoting that no risk for adverse developmental effects has to be expected for female workers in compliance with the respective MAK values of 200 ppm.

#### 4.1.3.2 Workers

##### 4.1.3.2.1 Considerations on evaporation and skin absorption

Methyl acetate is a liquid with a high vapour pressure of 217 hPa at 20°C. In Section 4.1.1.2 it is reported that neat methyl acetate (1 mg/$cm^2$) would evaporate within 4-6 seconds from skin (T: 20-30°C) under usual working conditions of non-occlusive exposure. It is assumed that methyl acetate could be well absorbed as long as it is available for absorption, but quantitative data on skin absorption rates (e.g. flux value) is not known. As a worst-case assumption the highest flux value (human skin *in vivo*) for neat liquids (33 mg/$cm^2$/h; ethyl benzene) of a summary report (Leung and Paustenbach, 1994) is used for a model calculation to estimate skin absorption.

| | |
|---|---|
| Applied dose: | 1 mg/$cm^2$/d |
| Maximal flux: | 33 mg/$cm^2$/h (= 0.0092 mg/ $cm^2$/sec) |
| Time of skin contact: | 6 seconds |

A maximal skin absorption of 0.06 mg/d (= 6% of the applied dose) is calculated for the above conditions. The calculation is uncertain due to its theoretical nature and the general caution as to dermal absorption studies and the applicability of flux values (DEN, 1999; de Heer, 1999), but overall it is expected, that the major part of neat methyl acetate will evaporate before absorption. However, the assessment of preparations (e.g. lacquers, adhesives) should regard that

evaporation might be reduced by a covering film of hardened lacquer at the lacquer/air interphase, that might result in a kind of semi-occlusive exposure.

#### 4.1.3.2.2 Acute toxicity

Inhalation

$LC_{50}$ values of >49,000 mg/m$^3$/4 hours (ca. >16,000 ppm) in rats, >24,000 mg/m$^3$/8 hours (ca. >8,000 ppm) in mice and >30,000 mg/m$^3$/10 hours (ca. >10,000 ppm) in cats are reported. Concentrations of 34,000 mg/m$^3$ (ca. 11,000 ppm) in mice and 56,000 mg/m$^3$ (ca. 19,000 ppm) in cats are described to lead to a short-lasting narcosis. The duration of exposure is unknown. A single case of neurotoxicity (atrophy of the optic nerve, blindness) after inhalation of methyl acetate at work is described. Additionally clinical effects like headache, somnolence and vertigo are reported. A specific human sensitivity towards the metabolite methanol due to kinetic differences in rodents and humans is known. This difference that can lead to neurotoxicity in human is only of importance for the assessment of acute toxicity (see Section 4.1.2.1). Quantitative human data on methyl acetate or methanol are not reported in Section 4.1.2.2. Thus the animal data represent the only quantitative basis for an assessment of acute toxicity.

Comparing the lowest $LC_{50}$ value of >24,000 mg/m$^3$/8 hours in mice and the narcotic concentration of 34,000 mg/m$^3$ in mice with the highest short-term exposure of 2,830 mg/m$^3$ (Scenario 11: flooring works, building trade; without LEV; <1 h) and the highest shift average value of 768 mg/m$^3$ (Scenario 11: flooring works, building trade; without LEV), there is no concern regarding risks of lethality or narcosis on the basis of the available animal data. **Conclusion (ii)**.

Dermal

The occlusive application of 2,000 mg/kg (24 hours) led to no lethality or other effects in rats. Without a specific species extrapolation a dose of 140,000 mg/person (body weight: 70 kg) can be calculated.

Comparing this value with the highest dermal exposure estimate of 420-2,100 mg/person (Scenario 11: flooring works) and having the volatility in mind, there is no concern regarding a risk of lethality or other effects on the basis of the available animal data. **Conclusion (ii)**.

#### 4.1.3.2.3 Irritation/Corrosivity

Inhalation

Irritation of the respiratory tract and the eyes among workers exposed to high concentrations over short periods (ca. 5,000 ppm, 15,000 mg/m$^3$) is described in a study of limited validity. The $RD_{50}$ value in mice is reported to be ca. 2,500 mg/m$^3$ (829 ppm). Clinical signs that might be indicative of a sensory irritation were however not observed in the valid subacute inhalation study in rats up to the highest tested concentration of 6,040 mg/m$^3$ (2,000 ppm). Thus the $RD_{50}$ value is considered to be of minor importance. As to the local effects in the respiratory tract a NOAEC of 1,057 mg/m$^3$ (350 ppm) and a LOAEC of 6,040 mg/m$^3$ (2,000 ppm) with slight to moderate effects in the olfactory epithelium was determined. In addition short information is given in Section 4.1.2.6 on a 5-day inhalation study with a NOAEC of 1,510 mg/m$^3$ (500 ppm)

for nasal effects. Based on the above data methyl acetate can be considered as a respiratory tract irritant. There are no data to describe the threshold for local effects after a single exposure, but another short chain ester of acetic acid, vinyl acetate, can be taken into account for the assessment. The exposure of rats to vinyl acetate for 1, 5 and 20 days led to the same NOAEC (Bogdanffy et al., 1997). Comparing the information on vinyl acetate with the data on methyl acetate (subacute NOAEC of 1,057 mg/m$^3$ and meager information on a 5-day NOAEC of 1,510 mg/m$^3$) it is assumed, that the NAEC for acute exposures of methyl acetate is in the range of 1,000-1,500 mg/m$^3$ taking the lower value as starting point.

Consequently the calculation of the direct MOS of repeated dose toxicity (see below; column (a) of **Table 4.11**) can also be applied for the assessment of acute exposures. As a direct MOS below 3 is considered to be of concern, **conclusion (iii)** applies for Scenario 11, Flooring works, building trade (direct MOS: 1.4).

Dermal

Skin irritation testing showed only slight effects in rabbits after semi-occlusive exposure. Methyl acetate is not classified as irritating to the skin.

Single dermal contact at workplaces is therefore not anticipated to result in relevant local damage. **Conclusion (ii)**.

Eyes

Liquid methyl acetate is irritating to the eyes of rabbits. For risk assessment purposes (according to the general rules of the preparations directive) a concentration of >20% methyl acetate is considered as irritating. Specific concentration limits cannot be deduced from the studies included in the report.

The handling of irritating methyl acetate preparations is assumed in all scenarios of **Table 4.5**, except Scenario 12 (use of cosmetics, 15% methyl acetate). For Scenarios 1, 2 and 3 it is supposed that eye protection is regularly worn; thus a risk of eye irritation is not expected. For all other scenarios it is supposed, that eye protection is not regularly worn. For these scenarios (4-11) splashes to the eye as well as hand-to-eye contact are considered to represent incidents which do not only occur accidentally, but may occur in most exposure situations.

**Conclusion (ii)** is proposed on the grounds that control measures exist which can minimise exposure and risk of irritation, thereby reducing concern. However, these must be implemented and complied with to reduce the risk of damage to eyes.

#### 4.1.3.2.4 Sensitisation

Dermal

Animal data on skin sensitisation are not available. Based on human data and considerations on metabolism methyl acetate is not expected to exhibit skin sensitising properties (see Section 4.1.2.5). Dermal exposure of workers is therefore not anticipated to result in skin sensitisation. **Conclusion (ii)**.

Inhalation

Respiratory sensitisation has not been reported in humans. Methyl acetate is not suspected to be a respiratory sensitiser in human according to the fact that during all the years of use no notice of case reports has been given. There is no concern. **Conclusion (ii)**.

#### 4.1.3.2.5 Repeated dose toxicity

Inhalation (local effects)

Valid human data on repeated inhalation are not available. Short information is given in Section 4.1.2.6 on a 5-day inhalation study that is described as a pre-study of a subacute inhalation study. The dose-response relationship and the study design are not described in detail. A detailed description is available of a subacute inhalation study in rats with concentrations of 0, 227, 1,057, 6,040 mg/m³ (ca. 0, 75, 350 or 2,000 ppm). The NOAEC for local effects was determined at 1,057 mg/m³ (ca. 350 ppm). At the LOAEC of 6,040 mg/m³ (ca. 2,000 ppm) slight to moderate degeneration and necrosis of the olfactory epithelium was observed.

For risk assessment purposes an adjustment of the animal data to human chronic exposure conditions is performed. A duration adjustment from subacute to chronic is based on data from the structurally-related compound vinyl acetate (Bogdanffy et al., 1994; 1997; Owen, 1988) that also represents a short-chain ester from acetic acid. The mechanism of toxicity is assumed to be similar. Inhalation studies in male Sprague Dawley rats (five per dose) for 1, 5 and 20 days (5 days/week, 6 hours/day) showed a NOAEC of 200 ppm and a LOAEC of 600 ppm with histopathological effects in the olfactory epithelium. A 2-year inhalation study in Sprague Dawley rats (5 days/week, 6 hours/day) revealed a NOAEC of 50 ppm and a LOAEC of 200 ppm with the same target organ in both sexes and high incidences up to 51/59 in males. Due to these high incidences the absence of effects in the short-term study at 200 ppm is not considered as a consequence of the reduced animal number. Based on the LOAECs a decrease by a factor of 3 can be deduced from subacute to chronic exposure. Vinyl acetate showed a small decrease of the NOAEC with time and an adjustment factor of 1/3 (subacute/chronic) is considered to be appropriate. Starting with the NOAEC of 1,057 mg/m³ (ca. 350 ppm) for methyl acetate a chronic NAEC in rats of 350 mg/m³ (ca. 110 ppm) is calculated.

The main problem 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 substances in the upper respiratory tract. A further important point is the hydrolysis of the ester. Release of acetic acid in the olfactory epithelium is presumed to be an important cause of site-specific effects and the carboxylesterase activity, responsible for the cleavage might be different in rats and humans. However it is not known whether these species differences lead finally to marked sensitivity differences of rats and humans. For that reason a species extrapolation factor of 1 is used.

Overall a NAEC (human, chronic, local) of 350 mg/m$^3$ (ca. 110 ppm) is estimated. Slight to moderate effects in the olfactory epithelium are expected at a LAEC of 2,010 mg/m$^3$ (ca. 670 ppm). The extrapolated NAEC is 3-fold lower than the experimental NOAEC.

In **Table 4.11** the NOAEC of the experimental study and the adjusted NAEC are compared with the information on long-term inhalation exposure with a daily exposure as described in **Table 4.5** Column (a) refers to the direct MOS based on the experimental NOAEC while column (b) lists the adjusted MOS that is calculated with the adjusted NAEC.

**Table 4.11** MOS values for repeated dose toxicity (inhalation; local and systemic) of methyl acetate

| Area of production and use | Activity | Shift average value ($mg/m^3$) | (a) Direct MOS: (based on a NOAEC of 1,057 $mg/m^3$) | (b) Adjusted MOS: (based on a NAEC of 350 $mg/m^3$) | Conclusion |
|---|---|---|---|---|---|
| **Production and further processing** | | | | | |
| 1) Manufacture and further processing as a chemical intermediate | Filling, sampling cleaning, maintenance, repair | <61 [1)] | >17 | >5.7 | ii |
| 2) Manufacture and further processing as a chemical intermediate | See above | 31-154 [3)] | 6.9-34 | 2.3-11 | **iii (local)** |
| 3) Production of cosmetics | Filling, sampling, cleaning, maintenance, repair | 8-39 [2)] (with LEV) | 27-130 | 9.0-44 | ii |
| 4) Production of formulations (paints, lacquers, adhesives, cleanser) | Filling, sampling, cleaning, maintenance, repair | 4a) 294 [1)] (without LEV) | 3.6 | 1.2 | **iii (local, systemic)** |
| | | 4b) 175 [1)] (with LEV) | 6.0 | 2 | **iii (local, systemic)** |
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** | | | | | |
| 5) Metal treatment, electro-engineering, wood treatment (20% methyl acetate in diluted cleaners) | Cleaning of surfaces | 5a) 18 [1)] (without LEV) | 59 | 19 | **iii** [4)] **(local, systemic)** |
| | | 5b) 137 [1)] (with LEV) | 7.7 | 2.6 | |
| 6) Casting machine, printing machine, mainly within the treatment of wood and metals (assumption: 60% methyl acetate) | Filling, sampling, cleaning, maintenance, repair | 6a) 84 [1)] (without LEV) | 13 | 4.2 | ii |
| | | 6b) 46 [1)] (with LEV) | 23 | 7.6 | ii |
| 7) Plastic and plastic foam treatment (60% methyl acetate) | Gluing | 7a) 18 [1)] (without LEV) | 59 | 19 | ii |
| | | 7b) 30 [1)] (with LEV) | 35 | 12 | ii |
| 8) Production of shoes (60% methyl acetate) | Gluing | 8a) 17 [1)] (without LEV) | 62 | 21 | ii |
| | | 8b) 23 [1)] (with LEV) | 46 | 15 | ii |
| 9) Pulp and paper production (paints, adhesives) (assumption: 60% methyl acetate) | Coating | 205 [1)] | 5.2 | 1.7 | **iii (local, systemic)** |

Table 4.11 continued overleaf

**Table 4.11 continued** MOS values for repeated dose toxicity (inhalation; local and systemic) of methyl acetate

| Area of production and use | Activity | Shift average value (mg/m³) | (a) Direct MOS: (based on a NOAEC of 1,057 mg/m³) | (b) Adjusted MOS: (based on a NAEC of 350 mg/m³) | Conclusion |
|---|---|---|---|---|---|
| **Use of formulations (paints, adhesives, cleaners, spray techniques)** | | | | | |
| 10) Spraying of paints, lacquers, adhesives (assumption: 40% methyl acetate) | Spraying | 10a) 81 [1)] (without LEV) | 13 | 4.3 | ii |
| | | 10b) 56 [1)] (with LEV) | 19 | 6.3 | ii |
| **Other uses** | | | | | |
| 11) Flooring works, building trade, (50% methyl acetate) | Precoating, priming, gluing | 768 [1)] | 1.4 | 0.5 | **iii (local, systemic)** |
| 12) Use of cosmetics (nail lacquer remover) (15% methyl acetate) | Application | 50-130[(2)] | 8.1-21 | 2.7-7.0 | **iii (local)** |

1) Measurements
2) EASE
3) EASE estimation for those companies which did not submit any measurement data
4) The measured concentrations were higher at workplaces with LEV compared to those without LEV (for further explanation see Section 4.1.1.2.3); concern is generally expressed for this scenario

An adjusted MOS of 3 is considered to be high enough because of the nature and severity of effect (minimal to moderate effects in the upper respiratory tract) and the large dose gap of six between the LOAEC and the NOAEC. Intraspecies variability within the human population is regarded as well as the increased respiratory volume of workers due to physical activity. There is concern for the following scenarios (**conclusion (iii)**):

2) Manufacture and further processing as a chemical intermediate (companies which did not submit any measurement data)
4 a/b) Production of formulations (paints, lacquers, adhesives, cleanser)
5 a/b) Metal treatment, electro-engineering, wood treatment
9) Pulp and paper production (paints, adhesives)
11) Flooring works, building trade
12) Use of cosmetics (nail lacquer remover)

Inhalation (systemic effects)

Based on the above mentioned inhalation study a systemic NOAEC of 1,057 mg/m³ (ca. 350 ppm) was determined. The effects at the LOAEC of 6,040 mg/m³ (ca. 2,000 ppm) were interpreted to be of some concern on minimal effects of systemic toxicity (diuresis, minimal liver cell dysfunction, adrenal weight increase and reduced serum cholesterol concentrations). Compound related macroscopic findings or histopathologic effects of systemic toxicity were not observed.

For risk assessment purposes an adjustment of the animal data to human chronic exposure conditions is performed. Data on vinyl acetate are not taken into account, because they are only

considered to be relevant for the assessment of local effects. As to a duration adjustment from subacute to chronic exposure the observed minimal systemic effect without histopathological manifestation is not expected to cause a considerable decrease of the NAEC with time. According to Section 4.1.2.6 it is more expected that prolongation of treatment would show more clearly the adversity of effects. The default value for a duration adjustment from subacute to chronic exposure of 1/6 (BAU, 1994) is assumed to be too high and a reduced value of 1/3 is taken. Thus local and systemic effects are adjusted with the same factor.

The next adjustment step, an interspecies extrapolation of systemic effects is performed with a factor of 1 and does not change the value.

Overall a NAEC (human, chronic, systemic) in the region of 350 mg/m$^3$ (ca. 110 ppm) is estimated. Systemic effects are expected at a LAEC of 2,010 mg/m$^3$ (ca. 670 ppm). The extrapolated NAEC is 3-fold lower than the experimental NOAEC.

In **Table 4.11** the NOAEC of the experimental study and the adjusted NAEC are compared with the information on long-term inhalation exposure with a daily exposure as described in **Table 4.5** Column (a) refers to the direct MOS based on the experimental NOAEC while column (b) lists the adjusted MOS that is calculated with the adjusted NAEC.

An adjusted MOS of 2 is considered to be high enough because of the nature and severity of effect (diuresis, minimal liver cell dysfunction, adrenal weight increase and reduced serum cholesterol concentrations) and the large dose gap of six between the LOAEC and the NOAEC. In addition the member states agreed to raise concern for Scenario 5 (metal treatment, electro-engineering, wood treatment; MOS: 2.6). The high measured exposure of 137 mg/m$^3$ (with LEV) and the limited information on workplace protection in the field of the further use support this decision. There is concern for the following scenarios (**conclusion (iii)**):

4a/b) Production of formulations (paints, lacquers, adhesives, cleanser)
5a/b) Metal treatment, electro-engineering, wood treatment
9) Pulp and paper production (paints, adhesives)
11) Flooring works, building trade

Dermal (local effects)

Dermal studies with repeated application are not available. Based on the defatting solvent character of methyl acetate repeated contact can lead to skin dryness or cracking of skin (R 66).

Chronic dermal exposure is assumed for the Scenarios 4-12 of **Table 4.6**. In that case damage to the skin cannot be excluded. **Conclusion (ii)** is proposed on the grounds that control measures exist which can minimise exposure and risk of skin damage, thereby reducing concern. However, these must be implemented and complied with to reduce the risk of skin damage.

Dermal (systemic effects)

Dermal studies with repeated application are not available. Thus the inhalation study with repeated application is taken into account.

For risk assessment purposes an adjustment of the animal data to human chronic exposure conditions is performed. A duration and an interspecies adjustment was already performed in the chapter “Inhalation (systemic)”.

In the following a route-to-route extrapolation is added. Data on absorption rates via inhalation and the dermal route is not available. A comparison of $LD_{50}$ and $LC_{50}$ values to estimate systemic toxicity via different routes is not possible since precise values are not available. Since toxicological data are not available to perform a substance specific route-to-route extrapolation the default assumption of an equivalent systemic availability via different routes is used for the calculation. But this is probable only in the case of an extensive occlusive skin contact. Under non-occlusive conditions the high vapour pressure of 217 hPa (20 C) leads to evaporation that reduces the amount available for skin penetration. In case of a non-occlusive exposure systemic dermal toxicity will be overestimated by this approach.

Starting with the adjusted inhalatory NAEC (human, chronic, systemic) of 350 mg/m$^3$ (ca. 110 ppm) and assuming a breathing volume of 10 m$^3$ per shift a dose of >3,500 mg/person/d is calculated, that is considered as the dermal NAEL (human, chronic, systemic) for the calculation of an adjusted MOS. Systemic effects are expected at a LAEL of >20,100 mg/person/day. For the calculation of a direct MOS a 3-fold higher value is to be taken.

In **Table 4.12,** the direct and the adjusted NAEL are compared with the information on long-term and daily dermal exposure as described in **Table 4.6**. Column (a) refers to the direct MOS based on a NAEL that was calculated without duration adjustment while column (b) lists the adjusted MOS that is calculated with the adjusted NAEL.

**Table 4.12** MOS values for repeated dose toxicity (dermal; systemic) of methyl acetate

| Area of production and use | Activity | Shift average value (mg/p/day)[(1)] | (a) Direct MOS: (based on a NAEL of >10,500 mg/p/d) | (b) Adjusted MOS: (based on a NAEL of >3,500 mg/p/d) | Conclusion |
|---|---|---|---|---|---|
| **Production and further processing** | | | | | |
| 1 & 2) Manufacture and further processing as a chemical intermediate | Filling, sampling cleaning, maintenance, repair | 42-420 | >25 | >8.3 | ii |
| 3) Production of cosmetics | Filling, sampling, cleaning, maintenance, repair | 42-420 | >25 | >8.3 | ii |
| 4) Production of formulations (paints, lacquers, adhesives, cleanser) | Filling, sampling, cleaning, maintenance, repair | 42-420 | >25 | >8.3 | ii |
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** | | | | | |
| 5) Metal treatment, electro-engineering, wood treatment (20% methyl acetate in diluted cleaners) | Cleaning of surfaces | 26-260 | >40 | >13 | ii |
| 6) Casting machine, printing machine, mainly within the treatment of wood and metals (assumption: 60% methyl acetate) | Filling, sampling, cleaning, maintenance, repair | 25-250 | >42 | >14 | ii |

Table 4.12 continued overleaf

**Table 4.12 continued** MOS values for repeated dose toxicity (dermal; systemic) of methyl acetate

| Area of production and use | Activity | Shift average value (mg/p/day)[1] | (a) Direct MOS: (based on a NAEL of >10,500 mg/p/d) | (b) Adjusted MOS: (based on a NAEL of >3,500 mg/p/d) | Conclusion |
|---|---|---|---|---|---|
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** continued | | | | | |
| 7) Plastic and plastic foam treatment (60% methyl acetate) | Gluing | 25-250 | >42 | >14 | ii |
| 8) Production of shoes (60% methyl acetate) | Gluing | 13-125 | >84 | >28 | ii |
| 9) Pulp and paper production (paints, adhesives) assumption: 60% methyl acetate) | Coating | 50-500 | >21 | >7 | ii |
| **Use of formulations (paints, adhesives, cleaners, spray techniques)** | | | | | |
| 10) Spraying of paints, lacquers, adhesives (assumption: 40% methyl acetate) | Spraying | 78-780 | >13 | >4.5 | ii |
| **Other uses** | | | | | |
| 11) Flooring works, building trade, (50%methyl acetate) | Precoating, priming, gluing | 420-2,100 | >5 | >1.7 | ii |
| 12) Use of cosmetics (nail lacquer remover) (15% methyl acetate) | Application | 160-470 | >22 | >7.4 | ii |

1) EASE

An adjusted MOS of higher than 2 is considered to be out of concern because of the nature and severity of effect (diuresis, minimal liver cell dysfunction, adrenal weight increase and reduced serum cholesterol concentrations) and the large dose gap of six between the LOAEC and the NOAEC. For the assessment of Scenario 11 (adjusted MOS of >1.7) the expected evaporation should be regarded. There is no concern. **Conclusion (ii)**.

Combined exposure (systemic effects)

Systemic health effects due to combined exposure (inhalation and dermal contact) are to be assessed in addition to route-specific considerations. The MOS values listed in **Table 4.13** for combined exposure are calculated according to the formula:

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

**Table 4.13** MOS values for repeated dose toxicity (combined exposure) of methyl acetate

| Area of production and use | Activity | (a) Combined direct MOS | (b) Combined adjusted MOS | Conclusion |
|---|---|---|---|---|
| **Production and further processing** | | | | |
| 1) Manufacture and further processing as a chemical intermediate | Filling, sampling, cleaning, maintenance, repair | >10 - >17 | >3.4 - >5.7 | ii |
| 2) Manufacture and further processing as a chemical intermediate | See above | >5.4 - 6.9 | >1.8 – 2.3 | ii |
| 3) Production of cosmetics | Filling, sampling, cleaning, maintenance, repair | >13 - 27 | >4.3 - 9.0 | ii |
| 4) Production of formulations (paints, lacquers, adhesives, cleanser) | Filling, sampling, cleaning, maintenance, repair | 4a) >3.1 – 3.6 (without LEV)<br>4b) >4.8 – 6.0 (with LEV) | >1.0 – 1.2 (without LEV)<br>>1.6 – 2.0 (with LEV) | ii<br>ii |
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** | | | | |
| 5) Metal treatment, electro-engineering, wood treatment (20% methyl acetate in diluted cleaners) | Cleaning of surfaces | 5a) >24 – 59 (without LEV)<br>5b) >6.5 – 7.7 (with LEV) | >7.7 - 19 (without LEV)<br>>2.2 – 2.6 (with LEV) | ii [1)] |
| 6) Casting machine, printing machine, mainly within the treatment of wood and metals (assumption: 60% methyl acetate) | Filling, sampling, cleaning, maintenance, repair | 6a) >9.9 - 13 (without LEV)<br>6b) >15 - 23 (with LEV) | >3.2 – 4.2 (without LEV)<br>>4.9 – 7.6 (with LEV) | ii<br>ii |
| 7) Plastic and plastic foam treatment (60% methyl acetate) | Gluing | 7a) >25 - 59 (without LEV)<br>7b) >19 - 35 (with LEV) | >8 - 19 (without LEV)<br>>6.5 - 12 (with LEV) | ii<br>ii |
| 8) Production of shoes, (60% methyl acetate) | Gluing | 8a) >36 - 62 (without LEV)<br>8b) >30 - 46 (with LEV) | >12 - 21 (without LEV)<br>>9.8 - 15 (with LEV) | ii<br>ii |
| 9) Pulp and paper production (paints, adhesives) (assumption: 60% methyl acetate) | Coating | >4.2 – 5.2 | >1.4 – 1.7 | ii |

Table 4.13 continued overleaf

**Table 4.13 continued** MOS values for repeated dose toxicity (combined exposure) of methyl acetate

| Area of production and use | Activity | (a) Combined direct MOS | (b) Combined adjusted MOS | Conclusion |
|---|---|---|---|---|
| **Use of formulations (paints, adhesives, cleaners, spray techniques)** | | | | |
| 10) Spraying of paints, lacquers, adhesives (assumption: 40% methyl acetate) | Spraying | 10a) >6.5 – 13 (without LEV)<br><br>10b) >7.7 – 19 (with LEV) | >2.2 – 4.3 (without LEV)<br><br>>2.6 – 6.3 (with LEV) | ii<br><br>ii |
| **Other uses** | | | | |
| 11) Flooring works, building trade, (50%methyl acetate) | Precoating, priming, gluing | >1.1 – 1.4 | >0.4 – 0.5 | ii |
| 12) Use of cosmetics (nail lacquer remover) (15% methyl acetate) | Application | >5.9 – 8.1 | >2.0 – 2.7 | ii |

1) The assessment of the scenario is not separated as to the application of LEV (see Table 4.11)

As to the MOS values of combined exposure it is tried to describe the uncertain contribution of the dermal route by ranges. The upper fixed value of the ranges is the MOS value of the inhalatory route assuming no relevant influence of the dermal route due to evaporation while the lower end reflects the maximal additional influence of the dermal route.

An adjusted MOS of 2 is considered to be high enough because of the nature and severity of effect (diuresis, minimal liver cell dysfunction, adrenal weight increase and reduced serum cholesterol concentrations) and the large dose gap of six between the LOAEC and the NOAEC. As to Scenario 2 (MOS: >1.8-2.3) concern is not derived, because the quick evaporation of the neat compound questions the relevance of the lower value (>1.8). Concern for the scenarios 4, 5, 9 and 11 is already derived above under Inhalation (systemic effects). There is no additional scenario, for which concern is raised only due to combined exposure. **Conclusion (ii)**.

#### 4.1.3.2.6 Mutagenicity

Methyl acetate is negative in a bacterial mutation test and a rat bone marrow micronucleus test. Furthermore, the hydrolysis products methanol and acetic acid do not reveal evidence for a mutagenic potential. There is no concern with respect to mutagenicity. **Conclusion (ii)**.

#### 4.1.3.2.7 Carcinogenicity

There are no carcinogenicity studies on methyl acetate. The cleaving product methanol was reported not to be carcinogenic in inhalation studies of rats and mice. There is no indication for a mutagenic potential. Based on this information, methyl acetate is not suspected to be carcinogenic. **Conclusion (ii)**.

#### 4.1.3.2.8 Toxicity for reproduction

Fertility impairment

*Inhalation*

A fertility study or further studies with methyl acetate that can be used to assess fertility impairment are not described in Section 4.1.2.9. As an additional information it should be added that in the subacute inhalation study in rats no effects in the reproductive organs were observed up to the highest tested concentration of 6,040 mg/m$^3$ (ca. 2,000 ppm). The investigations on the kinetics of hydrolysis revealed that methyl acetate was not detectable in blood. Thus the assessment of methyl acetate is considered in Section 4.1.2.9 to be possible on the basis of the cleaving product methanol. A 2-generation-study in rats with continuous exposure showed no effect on reproduction up to the highest tested concentration of 1,000 ppm. This concentration is equivalent to a methyl acetate concentration of 1,000 ppm (ca. 3,000 mg/m³). Further adjustment steps to human exposure conditions at workplaces are not applied. The human NAEC for fertility impairment is considered to be 3,000 mg/m³ (1,000 ppm). The direct and the adjusted MOS can be calculated with the same value. In **Table 4.14** the NAEC is compared with the information on inhalation exposure as described in **Table 4.5**.

**Table 4.14** MOS values for fertility impairment and developmental toxicity of methyl acetate via inhalation

| Area of production and use | Activity | Shift average value (mg/m³) | Fertility impairment/ developmental toxicity MOS (direct and adjusted): based on a NAEC of 3,000 mg/m³ | Conclusion |
|---|---|---|---|---|
| **Production and further processing** | | | | |
| 1) Manufacture and further processing as a chemical intermediate | Filling, sampling cleaning, maintenance, repair | < 61 [1)] | >49 | ii |
| 2) Manufacture and further processing as a chemical intermediate | See above | 31-154 [3)] | 19-97 | ii |
| 3) Production of cosmetics | Filling, sampling, cleaning, maintenance, repair | 8-39 [2)] (LEV) | 77-375 | ii |
| 4) Production of formulations (paints, lacquers, adhesives, cleanser) | Filling, sampling, cleaning, maintenance, repair | 4a) 294 [1)] (without LEV) | 10 | ii |
| | | 4b) 175 [1)] (with LEV) | 17 | ii |
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** | | | | |
| 5) Metal treatment, electro-engineering, wood treatment (20% methyl acetate in diluted cleaners) | Cleaning of surfaces | 5a) 18 [1)] (without LEV) | 170 | ii |
| | | 5b) 137 [1)] (with LEV) | 22 | ii |

Table 4.14 continued overleaf

**Table 4.14 continued** MOS values for fertility impairment and developmental toxicity of methyl acetate via inhalation

| Area of production and use | Activity | Shift average value ($mg/m^3$) | Fertility impairment/ developmental toxicity MOS (direct and adjusted): based on a NAEC of 3,000 $mg/m^3$ | Conclusion |
|---|---|---|---|---|
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** continued | | | | |
| 6) Casting machine, printing machine, mainly within the treatment of wood and metals assumption: (60% methyl acetate) | Filling, sampling, cleaning, maintenance, repair | 6a) 84 [1] (without LEV)<br>6b) 46 [1] (with LEV) | 36<br>65 | ii<br>ii |
| 7) Plastic and plastic foam treatment (60% methyl acetate) | Gluing | 7a) 18 [1] (without LEV)<br>7b) 30 [1] (with LEV) | 167<br>100 | ii<br>ii |
| 8) Production of shoes, (60% methyl acetate) | Gluing | 8a) 17 [1] (without LEV)<br>8b) 23 [1] (with LEV) | 180<br>130 | ii<br>ii |
| 9) Pulp and paper production (paints, adhesives) (assumption: 60% methyl acetate) | Coating | 205(1) | 15 | ii |
| **Use of formulations (paints, adhesives, cleaners, spray techniques)** | | | | |
| 10) Spraying of paints, lacquers, adhesives (assumption: 40% methyl acetate) | Spraying | 10a) 81 [1] (without LEV)<br>10b) 56 [1] (with LEV) | 37<br>54 | ii<br>ii |
| **Other uses** | | | | |
| 11) Flooring works, building trade (50% methyl acetate) | Precoating, priming, gluing | 768 [1] | 3.9 | **iii (develop. toxicity)** |
| 12) Use of cosmetics (nail lacquer remover) (15% methyl acetate) | Application | 50-130 [2] | 23-60 | ii |

1) Measurements
2) EASE
3) EASE estimation for those companies which did not submit any measurement data

It should be regarded that an effect was not detected up to the highest tested concentration. In addition the fundamental study had a continuous instead of an intermittent exposure and the body burden was about 4-fold higher compared to a 6 hours/day study. A specific effect on fertility is not expected. It is not considered to be appropriate to derive concern. **Conclusion (ii)**.

*Dermal*

Dermal studies for the assessment of fertility impairment are not available. Thus the inhalation study of the preceding chapter is taken into account.

For risk assessment purposes an adjustment of the animal data to human chronic exposure conditions is performed as described under "Repeated dose toxicity/dermal". A dermal NAEL (human, fertility impairment) of >30,000 mg/person/d is calculated.

In **Table 4.15** the estimated NAEL is compared with the information on dermal exposure as described in **Table 4.6.**

**Table 4.15** MOS values for fertility impairment and developmental toxicity of methyl acetate via the dermal route

| Area of production and use | Activity | Shift average value (mg/p/day) [1)] | Fertility impairment/ developmental toxicity MOS (direct and adjusted): based on a NAEL of > 30,000 mg/person/d | Conclusion |
|---|---|---|---|---|
| **Production and further processing** | | | | |
| 1 and 2) Manufacture and further processing as a chemical intermediate | Filling, sampling cleaning, maintenance, repair | 42-420 | >71 | ii |
| 3) Production of cosmetics | Filling, sampling, cleaning, maintenance, repair | 42-420 | >71 | ii |
| 4) Production of formulations (paints, lacquers, adhesives, cleanser) | Filling, sampling, cleaning, maintenance, repair | 42-420 | >71 | ii |
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** | | | | |
| 5) Metal treatment, electro-engineering, wood treatment (20% methyl acetate in diluted cleaners) | Cleaning of surfaces | 26-260 | >120 | ii |
| 6) Casting machine, printing machine, mainly within the treatment of wood and metals (assumption: 60% methyl acetate) | Filling, sampling, cleaning, maintenance, repair | 25-250 | >120 | ii |
| 7) Plastic and plastic foam treatment (60% methyl acetate) | Gluing | 25-250 | >120 | ii |
| 8) Production of shoes, (60% methyl acetate) | Gluing | 13-125 | >240 | ii |
| 9) Pulp and paper production (paints, adhesives) (assumption: 60% methyl acetate) | Coating | 50-500 | >60 | ii |
| **Use of formulations (paints, adhesives, cleaners, spray techniques)** | | | | |
| 10) Spraying of paints, lacquers, adhesives (assumption: 40% methyl acetate) | Spraying | 78-780 | >38 | ii |

Table 4.15 continued overleaf

**Table 4.15 continued** MOS values for fertility impairment and developmental toxicity of methyl acetate via the dermal route

| Area of production and use | Activity | Shift average value (mg/p/day) [1)] | Fertility impairment/ developmental toxicity MOS (direct and adjusted): based on a NAEL of > 30,000 mg/person/d | Conclusion |
|---|---|---|---|---|
| **Other uses** | | | | |
| 11) Flooring works, building trade (50% methyl acetate) | Precoating, priming, gluing | 420-2,100 | >14 | ii |
| 12) Use of cosmetics (nail lacquer remover) (15% methyl acetate) | Application | 160-470 | >64 | ii |

1) EASE

It should be regarded that an effect was not detected up to the highest tested concentration. In addition the fundamental study had a continuous instead of an intermittent exposure and the body burden was about 4-fold higher compared to a 6 hours/day study. A specific effect on fertility is not expected. It is not considered to be appropriate to derive concern. **Conclusion (ii)**.

*Combined exposure*

Fertility impairment due to combined exposure (inhalation and dermal contact) is to be assessed in addition to route-specific considerations. The procedure is described under "Repeated dose toxicity"; the combined MOS values are listed in **Table 4.16.**

**Table 4.16** MOS values for fertility impairment and developmental toxicity of methyl acetate for combined exposure

| Area of production and use | Activity | Fertility impairment/ developmental toxicity combined MOS (direct and adjusted) | Conclusion |
|---|---|---|---|
| **Production and further processing** | | | |
| 1) Manufacture and further processing as a chemical intermediate | Filling, sampling, cleaning, maintenance, repair | >29 - >49 | ii |
| 2) Manufacture and further processing as a chemical intermediate | See above | >15 - 19 | ii |
| 3) Production of cosmetics | Filling, sampling, cleaning, maintenance, repair | >37 - 77 | ii |
| 4) Production of formulations (paints, lacquers, adhesives, cleanser) | Filling, sampling, cleaning, maintenance, repair | 4a) >8.7 - 10 (without LEV)<br>4b) >14 - 17 (with LEV) | ii<br>ii |
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** | | | |
| 5) Metal treatment, electro-engineering, wood treatment (20% methyl acetate in diluted cleaners) | Cleaning of surfaces | 5a) >70 - 170 (without LEV)<br>5b) >19 - 22 (with LEV) | ii<br>ii |

Table 4.16 continued overleaf

**Table 4.16 continued** MOS values for fertility impairment and developmental toxicity of methyl acetate for combined exposure

| Area of production and use | Activity | Fertility impairment/ developmental toxicity combined MOS (direct and adjusted) | Conclusion |
|---|---|---|---|
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** continued | | | |
| 6) Casting machine, printing machine, mainly within the treatment of wood and metals<br>assumption: 60% methyl acetate) | Filling, sampling, cleaning, maintenance, repair | 6a) >28 - 36 (without LEV)<br>6b) >42 - 65 (with LEV) | ii<br>ii |
| 7) Plastic and plastic foam treatment (60% methyl acetate) | Gluing | 7a) >70 - 167 (without LEV)<br>7b) >55 - 100 (with LEV) | ii<br>ii |
| 8) Production of shoes (60% methyl acetate) | Gluing | 8a) >100- 180 (without LEV)<br>8b) >84- 130 (with LEV) | ii<br>ii |
| 9) Pulp and paper production (paints, adhesives) (assumption: 60% methyl acetate) | Coating | >12 - 15 | ii |
| **Use of formulations (paints, adhesives, cleaners, spray techniques)** | | | |
| 10) Spraying of paints, lacquers, adhesives (assumption: 40% methyl acetate) | Spraying | 10a) >19 - 37 (without LEV)<br>10b) >22 - 54 (with LEV) | ii<br>ii |
| **Other uses** | | | |
| 11) Flooring works, building trade (50% methyl acetate) | Precoating, priming, gluing | >3.5 - 3.9 | **iii (developmental toxicity)** |
| 12) Use of cosmetics (nail lacquer remover) (15% methyl acetate) | Application | >17 – 23 | ii |

As to the MOS values of combined exposure it is tried to describe the uncertain contribution of the dermal route by ranges. The upper fixed value of the ranges is the MOS value of the inhalation route assuming no relevant influence of the dermal route due to evaporation while the lower end reflects the maximal additional influence of the dermal route.

The lowest MOS value of Scenario 11 is quite low (>3.5-3.9), but according to the reasoning given under the single routes of exposure it is not considered to be appropriate to derive concern. **Conclusion (ii)**.

Developmental toxicity

*Inhalation*

There are no developmental studies with methyl acetate. As mentioned above it is considered to be justified to perform an assessment based on the cleaning products (Section 4.1.2.9).

Concerning acetic acid it is stated that there are no indications for a fetotoxic or teratogenic potential. A NOAEC is not available. As to methanol a NOAEC of 1,000 ppm was derived from two developmental studies in mice and rats with intermittent (7 hours) as well as continuous (24 hours) exposure by inhalation. Since an intermittent exposure is more appropriate to assess a workplace exposure profile, the study from Rogers et al. (1993) in mice (gestation day 6-15) with concentrations of 0, 1,000, 2,000, 5,000, 7,500, 10,000, 15,000 ppm is used for a quantitative assessment. The NOAEC for fetotoxicity was 1,000 ppm, the value for maternal toxicity was 5,000 ppm. Pubs revealed extra cervical ribs at 2,000 ppm and above and an increased incidence of cleft palate and exencephaly at 5,000 ppm and above. The respective NAECs of methyl acetate would be ca. 3,000 mg/m³ (1,000 ppm) for developmental toxicity and ca. 15,000 mg/m$^3$ (5,000 ppm) for maternal toxicity. Further adjustment steps to human exposure conditions at workplaces are not applied. The human NAEC for developmental toxicity is considered to be 3,000 mg/m$^3$ (1,000 ppm). The direct and the adjusted MOS can be calculated with the same value. In **Table 4.14** the NAEC is compared with the information on inhalation exposure as described in **Table 4.5.**

Methanol appears to be the developmental toxicant in rodents. So information on methanol blood levels in rodents and humans should be regarded (Section 4.1.2.9). Developmental toxicity in rodents was detected only at considerably increased methanol blood levels. Human exposure to methanol (200 ppm; equivalent to 200 ppm/600 mg/m$^3$ methyl acetate) for 6 hours led to methanol blood levels that were clearly below those of the developmental LOAECs and the NOAECs in rodent studies. Human blood levels at higher concentrations have been estimated in a shortly mentioned PK-modeling approach of unclear reliability. Thus uncertainties remain concerning the assessment of developmental toxicity at higher concentrations.

Concern is derived for Scenario 11 (flooring works, building trade) with the highest exposure of 768 mg/m$^3$ and a MOS of 3.9. **Conclusion (iii)**.

Scenario 4 (production of formulations without LEV (paints, lacquers, adhesives, cleanser)) with a MOS of 10 and all other scenarios with higher MOS values are not considered to be of concern because of the information on methanol blood levels in humans. **Conclusion (ii)**.

*Dermal*

Dermal studies for the assessment of developmental toxicity are not available. Thus the inhalation study of the preceding chapter is taken into account.

For risk assessment purposes an adjustment of the animal data to human chronic exposure conditions is performed as described under “Repeated dose toxicity/dermal”. A dermal NAEL (human, developmental toxicity) of >30,000 mg/person/d is calculated.

In **Table 4.15** the estimated NAEL is compared with the information on dermal exposure. The adjusted MOS (>14) are considered to be high enough. No concern is derived. **Conclusion (ii)**.

*Combined exposure*

Developmental toxicity due to combined exposure (inhalation and dermal contact) is to be assessed in addition to route-specific considerations. The procedure is described under “Repeated dose toxicity”; the MOS values, that are the same as those for fertility impairment are listed in **Table 4.16**. Below the table is an explanation of the values added.

Concern for Scenario 11 is already derived above under Inhalation (developmental toxicity). There is no additional scenario, for which concern is raised only due to combined exposure. **Conclusion (ii)**.

#### 4.1.3.2.9 Conclusions of the occupational risk assessment

The conclusions of the occupational risk assessment are summarised in **Table 4.17**. In addition the occupational exposure limits could be reevaluated in the light of the subacute inhalation study, that was performed as a consequence of the risk assessment process.

**Table 4.17** Conclusions of the occupational risk assessment

| Area of production and use | Activity | Irritation Inhalation | Repeated dose toxicity | | Developmental toxicity |
|---|---|---|---|---|---|
| | | | Inhalation, local | Inhalation, systemic | Inhalation |
| **Production and further processing** | | | | | |
| 2) Manufacture and further processing as a chemical intermediate [2)] | Filling, sampling, cleaning, maintenance, repair | ii | **iii** | ii | ii |
| 4a/b) Production of formulations (paints, lacquers, adhesives, cleanser) | Filling, sampling, cleaning, maintenance, repair | ii | **iii** | **iii** | ii |
| **Use of formulations (paints, adhesives, cleaners, no spray techniques)** | | | | | |
| 5a/b) Metal treatment, electro-engineering, wood treatment | Cleaning of surfaces | ii | **iii** | **iii** | ii |
| **Use of formulations (paints, adhesives, cleaners, spray techniques)** | | | | | |
| 9) Pulp and paper production (paints, adhesives) | Coating | ii | **iii** | **iii** | ii |
| **Other uses** | | | | | |
| 11) Flooring works, building trade | Precoating, priming, gluing | **iii** | **iii** | **iii** | **iii** |
| 12) Use of cosmetics (nail lacquer remover) | Application | ii | **iii** | ii | ii |

[1)] Scenarios of concern are listed in bold
[2)] Companies which did not submit measurement results

### 4.1.3.3 Consumers

#### 4.1.3.3.1 Acute toxicity

Following the exposure assessment, consumers are not expected to be exposed to methyl acetate at $LD_{50}$ doses (oral: 6,482 mg/kg bw, dermal: >2,000 mg/kg bw). Therefore, the substance is of no concern for the consumer in relation to acute oral or dermal toxicity.

However, the inhalation route of exposure may be of concern, because in rats methyl acetate has demonstrated an inhalation $LC_{50}$ of >49,000mg/m³/4 hours. There are no data available on the no-effect concentration in rats. Narcotic actions of methyl acetate are observed in mice and cats with concentrations higher than 34,000 mg/m³ and 56,000 mg/m³, respectively. When using carpet and parquet adhesives peak concentrations up to 15,000 mg/m³ have been estimated applying to the SCIES model. However, estimated peak concentrations are at least fourfold higher than measurements at workplace which resulted in exposures up to 3,200 mg/m³ under working conditions (see Section 4.1.1.2.3).

Taking into account the high vapour pressure, the frequency and duration of application of carpet and parquet adhesives by the consumer and all assumptions being applied in the exposure estimation scenarios, methyl acetate should be considered of no concern for the consumer. **Conclusion (ii)**.

#### 4.1.3.3.2 Irritation

Methyl acetate has proven to cause only weak skin irritation in humans and in rabbits. Eye irritation however, was strong but reversible within 7 days in a Draize eye test with rabbits. Exposure to methyl acetate vapours causes irritation to eyes and respiratory tract of humans.

Based on these data, the substance has been classified as “Xi (Irritant)” and labelled as “R 36 (Irritating to eyes)”.

**Conclusion (ii).**

#### 4.1.3.3.3 Sensitisation

In a maximisation test with 25 volunteers no skin sensitisation was observed. There are no further data including the results of animal tests. Methyl acetate is not supposed to have skin sensitising properties. In addition, the substance is hydrolysed by non-specific esterases to methanol and acetic acid. There is no concern. **Conclusion (ii)**.

#### 4.1.3.3.4 Repeated dose toxicity

Using a standard “worst-case” scenario for adhesives consumers may be exposed to an average concentration of 26 mg/m$^3$ during use (assuming an application time of 60 min) and to a peak concentration of 39 mg/m$^3$.

Considering the inhalation exposure resulting from other applications (carpet and parquet adhesives) considerable higher concentrations have been calculated. However, in view of the

infrequent use of these adhesives (once per year) these scenarios have not been forwarded for a repeated dose risk characterisation.

Reliable experimental animal data on the local and systemic effects after repeated administration of methyl acetate are restricted to inhalation exposure.

After nose-only inhalation during a 28-day treatment period, methyl acetate induced degeneration/necrosis of the rat olfactory mucosa at a concentration of 2,000 ppm (6,040 mg/m³). Minimal effects without pathophysiological meaning at this concentration were observed (diureses, minimal liver cell dysfunction, adrenal weight increase, and reduced serum cholesterol concentrations). A NOAEC of 350 ppm (1,057 mg/m$^3$) was derived for local effects at the respiratory tract as well as for systemic effects.

For the decision on the appropriateness of MOS, the following aspects have been considered and taken into account:

Overall confidence in the database

The data taken into account for performing the risk characterisation have been evaluated with regard to their reliability, relevance and completeness according to Section 3.2 of the TGD. The data were submitted to the Competent Authority as a private report. The report was adequately detailed and in accordance with internationally recognised guidelines and to GLP (see Section 4.1.2.6).

The findings of the study are not contradictory to other data from nonvalid animal investigations so that the judgment can be based on the database.

There are no reasons to assume limited confidence on the data being the basis of the risk characterisation.

Uncertainty arising from the variability in the experimental data

The study cited above allows to conclude on treatment-related changes of the rat olfactory mucosa.

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

Intra- and interspecies variation

Data on kinetics of the substance and its metabolites do not allow to calculate the intraspecies and interspecies variability by applying modern approaches. However, it is well known that the content of tetrahydrofolate differs among species.

Research on human and rat nasal respiratory and olfactory tissue with whole turbinates *in vitro* using vinyl acetate as substrate has shown that rat nasal respiratory carboxylesterase activity was about 3-fold higher than that of humans. However, the olfactory carboxylesterase activity was similar between both species.

Species differences in tetrahydrofolate and, hence, the capacity for formate metabolism has to be considered.

Nature and severity of the effect

The main effect considered as "critical effect" is the degeneration/necrosis of the olfactory mucosa (irreversible, serious health effect).

There are no reasons to assume that the effects shown in the animal experiments are limited to the species tested, thus being not of relevance for humans. Therefore there is no reason to assume concern which would have to be expressed in an increased MOS.

Dose response relationship

In rats no steep dose-response-relationship is observed for the effects at the olfactorium. At the LOAEC (6,040 mg/m$^3$, 2,000 ppm) the changes in the olfactory epithelium were observed.

Therefore there is no reason to assume concern which would have 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 methyl acetate via inhalation for a short time period, whereas oral and dermal exposures are assumed of minor importance. The NOAEC used for the discussion of the MOS regarding this exposure route is derived from a 28-day inhalation study on rats (exposure time 6 hours/day).

There are no reasons to assume that special concern can be derived from this procedure or from the available toxicokinetic information.

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

Following the inhalation exposure scenario 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 – Local effects*

During application of all-purpose adhesives the consumer may be exposed to a concentration of 26 mg/m$^3$ methyl acetate (for 60 min) with a peak value of 39 mg/m$^3$.

Therefore, the margin of safety for local effects between the

calculated exposure level of 26 mg/m$^3$

and the

NOAEC for local effects of 1,057 mg/m$^3$

is judged to be sufficient because a worst-case exposure scenario was taken into account (with an application time of 1 hour) and the mentioned effects were observed at a high concentration of 2,000 ppm (no steep dose-response-relationship). There is a large distance between the high and the mid concentration of methyl acetate used in the HMR study. It could be that the NOAEC might be higher if an additional dose would have been tested. **Conclusion (ii)**.

*MOS for inhalation exposure scenario – Systemic effects*

During application of all-purpose adhesives the consumer may be exposed to a concentration of 26 mg/m$^3$ methyl acetate (for 60 min) which results in a daily dose of about 1 mg/kg bw/d.

In the repeated dose toxicity study on rats (28-day inhalation) the NOAEC for systemic effects was 350 ppm (1,057 mg/l). The derived concentration in air is converted as follows to the inhaled amount of the substance using the respiratory minute volume 0.8 l/min/kg and exposure duration of 360 min/day:

$$1{,}057 \text{ mg/l} \cdot 0.8 \text{ l/min/kg} \cdot 360 \text{ min/day} = 304 \text{ mg/kg bw/d.}$$

No further adjustment of the animal data to the human exposure has been performed for this risk assessment.

The margin of safety for systemic effects between the
exposure level of 1 mg/kg bw/d
and the
converted NOAEL of 304 mg/kg bw/d

is judged to be sufficient even taking into account some uncertainty in the derivation of the NOAEC from the 28-day study. **Conclusion (ii)**.

#### 4.1.3.3.5 Mutagenicity

Methyl acetate is negative in a bacterial mutation test and a rat bone marrow micronucleus assay. Furthermore, the hydrolysis products methanol and acetic acid do not reveal evidence for a mutagenic potential. There is no concern with respect to mutagenicity. **Conclusion (ii)**.

#### 4.1.3.3.6 Carcinogenicity

At present data which cause for relevant concern on carcinogenicity of methyl acetate are not known. In methanol studies on rats and mice, an increased incidence of lung adenoma/adenomatosis was seen in high dose male rats only. **Conclusion (ii)**.

#### 4.1.3.3.7 Toxicity for reproduction

There are no data available on the reprotoxic potential of methyl acetate itself. However, due to the rapid hydrolysis of the substance (cf. Section 4.1.2.1) the effect assessment with respect to reproduction is based on the toxicological properties of the immediate metabolites.

For acetic acid there are no indications of a fetotoxic or teratogenic potential, whereas for methanol embryo-/fetotoxic and teratogenic effects were demonstrated in rodents at relatively high concentrations, respectively maternal toxic concentrations. With methanol 1,300 mg/m$^3$ was derived for the NOEC/fertility as well as for the NOAEC/developmental toxicity. Under the assumption that methyl acetate is immediately degraded to methanol at a molar ratio of 1, this value can be converted to NOAEC/fertility as well as NOAEC/developmental toxicity of about 3,000 mg methyl acetate/m$^3$.

*MOS for inhalation exposure scenario – Fertility and developmental toxicity*

During application of all-purpose adhesives the consumer may be exposed to a concentration of 26 mg/m$^3$ methyl acetate (for 60 min).

NOAEC values of about 3,000 mg/m$^3$ methyl acetate for fertility as well as developmental toxicity were obtained by conversion from methanol data.

The margin of safety between the
calculated exposure level of 26 mg/m$^3$
and the
methanol-converted NOAEC of 3,000 mg/m$^3$

is judged to be sufficient. Species differences in the metabolism of formate due to a lower tetrahydrofolate content in the liver of primates have to be taken into account, however, at the low exposure conditions there should be no concern. **Conclusion (ii)**.

#### 4.1.3.4 Humans exposed via the environment

Indirect exposure to methyl acetate via the environment occurs mainly by air and drinking water. $PECs_{air}$ of 0.035 mg/m$^3$ and of 0.00013 mg/m$^3$ have been calculated for the local (at a point source) and the regional scenario, respectively (cf. **Table 4.9**). Following the local scenario data (at a point source) an intake of a total daily dose of 0.0144 mg/kg bw/d is calculated (as a worst case). For the regional scenario, the respective figure is smaller (0.0534 µg/kg bw/d).

Repeated dose toxicity

*Local effects*

In a repeated dose toxicity study on rats (28-day inhalation) the NOAEC for local effects was 350 ppm (1,057 mg/m$^3$).

Comparison air exposure - Local scenario/NOAEC

$$\frac{\text{Indirect air exposure}}{\text{NOAEC}} = \frac{0.035 \text{ mg/m}^3}{1{,}057 \text{ mg/m}^3}$$

The margin of safety for local effects between the calculated exposure and the NOAEC is judged to be sufficient for the local scenario. Thus, the substance is of no concern in relation to indirect exposure via the air.

Comparison air exposure - Regional scenario/NOAEC

$$\frac{\text{Indirect air exposure}}{\text{NOAEC}} = \frac{0.00014 \text{ mg/m}^3}{1{,}057 \text{ mg/m}^3}$$

The margin of safety for local effects between the calculated exposure and the NOAEC is judged to be sufficient for the local as well as the regional scenario. Thus, the substance is of no concern in relation to indirect exposure via the air. **Conclusion (ii)**.

*Systemic effects*

In a repeated dose toxicity study on rats (28-day inhalation) the NOAEC for systemic effects was 350 ppm (1.057 mg/l). Minimal effects of systemic toxicity were observed at 2,000 ppm. The derived concentration in air is converted as follows to the inhaled amount of the substance using the respiratory minute volume 0.8 l/min/kg and exposure duration of 360 min/day:

$$1{,}057 \text{ mg/l} \cdot 0.8 \text{ l/min/kg} \cdot 360 \text{ min/day} = 304 \text{ mg/kg bw/d.}$$

No further adjustment of the animal data to the human exposure via the environment has been performed for this risk assessment.

Comparison indirect exposure - Local scenario/NOAEL

$$\frac{\text{Indirect exposure}}{\text{NOAEL}} = \frac{0.0144 \text{ mg/kg bw/d}}{304 \text{ mg/kg bw/d}}$$

The margin of safety for systemic effects between the calculated exposure and the converted NOAEC is judged to be sufficient for the local scenario even taking into account some uncertainty in the NOAEL (cf Section 4.1.2.6). Thus, the substance is of no concern in relation to indirect exposure via the environment. **Conclusion (ii)**.

Comparison indirect exposure - Regional scenario/NOAEL

$$\frac{\text{Indirect exposure}}{\text{NOAEL}} = \frac{0.000053 \text{ mg/kg bw/d}}{304 \text{ mg/kg bw/d}}$$

The margin of safety for systemic effects between the calculated exposure (regional background concentration) and the NOAEL is judged to be sufficient for the regional scenario even taking into account some uncertainty in the NOAEL (cf. Section 4.1.2.6). Thus, the substance is of no concern in relation to indirect exposure via the environment. **Conclusion (ii)**.

Toxicity for reproduction

There are no data available on the reprotoxic potential of methyl acetate itself. However, due to the rapid hydrolysis of the substance (cf. Section 4.1.2.1) the effect assessment with respect to reproduction is based on the toxicological properties of the immediate metabolites acetic acid and methanol. Due to the even lower exposure via the environment as compared to the direct exposure there is no concern (cf. Section 4.1.1.3). Thus, the margin of safety is considered to be sufficient. **Conclusion (ii)**.

#### 4.1.3.5 Combined exposure

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

Comparison combined exposure / NOAEL

$$\frac{\text{Combined exposure}}{\text{NOAEL}} = \frac{<10 \text{ mg/kg bw/d}}{304 \text{ mg/kg bw/d}}$$

The margin of safety between the estimated combined exposure and the NOAEL is judged to be sufficient. Thus, the substance is considered of no concern in relation to combined exposure. **Conclusion (ii)**.

## 4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

Explosive properties and oxidising properties of methyl acetate are not considered to form a hazard. Since methyl acetate is highly flammable, adequate worker protection measures must be observed. Risk reduction measures beyond those which are being applied already are not considered necessary. **Conclusion (ii)**.

# 5 RESULTS

## 5.1 ENVIRONMENT

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

Based on the currently available data, methyl acetate represents no risk to the environment for the area of production, processing, formulation and use.

Although the exposure routes requiring regulation were determined in consideration of the site-specific information on the use quantity and the use structure in Germany, it can, however, be assumed that the use structure of methyl acetate in Germany is also applicable to the EU. Attention is drawn to the fact that comparable local exposures to methyl acetate are also to be expected in the other EU member states.

## 5.2 HUMAN HEALTH

### 5.2.1 Human health (toxicity)

#### 5.2.1.1 Workers

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

This conclusion applies because of:

- Irritation after inhalation in the following scenario:
  - Flooring works, building trade;
- Local effects after repeated inhalation in the following scenarios:
  - Manufacture and further processing as a chemical intermediate (companies that did not submit measurement data);
  - Production of formulations (paints, lacquers, adhesives, cleanser);
  - Metal treatment, electro-engineering, wood treatment;
  - Pulp and paper production (paints and adhesives);
  - Flooring works, building trade;
  - Use of cosmetics.
- Systemic effects after repeated inhalation in the following scenarios:
  - Production of formulations (paints, lacquers, adhesives, cleanser);
  - Metal treatment, electro-engineering, wood treatment;
  - Pulp and paper production (paints and adhesives);
  - Flooring works, building trade.
- Developmental toxicity after inhalation in the following scenario:
  - Flooring works, building trade.

#### 5.2.1.2 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.

#### 5.2.1.3 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.

### 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.

# 6 REFERENCES


Aman W, Steinhäuser KG (1986). Bewertung wassergefährdender Stoffe. Bayrisches Landesamt für Wasserwirtschaft (Umweltbundesamt), Zusammenfassender Zwischenbericht zum Forschungsvorhaben Nr. 82-102 05 308.

Andrews LS, Clary JJ, Terrill JB, Bolte HF (1987). Subchronic inhalation toxicity of methanol. J. Tox. Environ. Health **20,** 117-124.

ARIEL (2002). ARIEL Insight 2.0 database. For survival in a world of expanding chemical regulations. March 2002.

Atkinson R (1986). Chem. Rev. Vol. 86, S. 69, 140, 197.

Auffarth J, Häger J (1989). Exposition beim Umgang mit lösemittelhaltigen Zubereitungen - Herstellung von Lösemittelklebstoffen. Schriftenreihe der Bundesanstalt für Arbeitsschutz, GA 30, Wirtschaftsverlag NW.

Auffarth J, Häger J (1991). Lösemittelbelastungen in der Lackindustrie. Projekt Nr. 664.3, Bundesanstalt für Arbeitsschutz (BAU).

BAU (1994). Neue Stoffe am Arbeitsplatz. Ein Bewertungskonzept, Amtliche Mitteilungen der Bundesanstalt für Arbeitsschutz, Sonderdruck März 1994, Dortmund.

BG Chemie (1995). Essigsäure-methylester. Toxikologische Bewertung Ausgabe 02/95, Berufsgenossenschaft der chemischen Industrie (BG Chemie) Heidelberg.

BGAA (1994). BIA-Dokumentation-MEGA, Auswertung vom 09.11.1994.

BGAA (1996). Expositionsbeschreibung für Methylacetat. Written communication from 05.02.1996, Berufsgenossenschaftlicher Arbeitskreis “Altstoffe“ (BGAA).

BGAA (1999). Altstoffe-Expositionen am Arbeitsplatz. Berufsgenossenschaftlicher Arbeitskreis “Altstoffe”, Hauptverband der gewerblichen Berufsgenossenschaften, BGAA-Report 1/99, St. Augustin.

BIA (1998). Written communication from 23.04.98.

BIA-Dokumentation-MEGA (1994). Auswertung vom 09.11.1994.

Bogdanffy MS, Dreef-van der Meulen HC, Beems RB, Feron VJ, Cascieri TC, Tyler TR, Vinegar MB, Rickard RW (1994). Chronic toxicity and oncogenicity inhalation study with vinyl acetate in the rat and mouse. Fund. Appl. Toxicol. **23**, 215-229.

Bogdanffy MS, Gladnick NL, Kegelman T, Frame SR (1997). Four-week inhalation cell proliferation study of the effects of vinyl acetate on rat nasal epithelium. Inhalation Toxicology **9**, 331-350.

Bogdanffy, MS, Sarangapani, R, Kimbell JS, Frame SR, Plowchalk DR (1998). Analysis of vinyl acetate metabolism in rat and human nasal tissues by an *in vitro* gas uptake technique. Toxicol. Sci. **46**, 235-246.

Bolon B, Dorman DC, Janszen D, Welsch F (1993). Phase-specific developmental toxicity in mice following maternal methanol inhalation. Fundam. Appl. Toxicol. **21**, 508-516.

Brooke LT, Call DJ, Geiger DL and Northcott CE (1984). Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas), Vol. I, University of Wisconsin-Superior, 57-58.

Cameron AM, Nilsen OG, Haug E, Eik-Nes KB (1984). Circulating concentrations of testosterone, luteinizing hormone and follicle stimulating hormone in male rats after inhalation of methanol. Arch. Toxicol. Suppl. **7**, 441-443.

Campbell JA, Howard DR, Backer LC, Allen JW (1991). Evidence that methanol inhalation does not induce chromosome damage in mice. Mutation Research **260**, 257-264.

Celanese (2000). Letter by Celanese Europe Chemicals GmbH, 02.03.2000.

CHEMSAFE, national data base for safety data of the Physikalisch-Technischen Bundesanstalt, Braunschweig, established by expert judgement.

Collander R (1951). The partition of organic compounds between higher alcoholsand water. Acta Chemica Scandinavia **5**, 774-780.

Cooper RL, Mole ML, Rehnberg GL, Goldman JM, McElroy WK, Hein J, Stoker TE (1992). Effect of inhaled methanol on pituitary and testicular hormones in chamber acclimated and non-acclimated rats. Toxicology **71**, 69-81.

CRC Handbook (1991). Handbook of Chemistry and Physics; CRC Press, Inc., 72nd ed.

Cummings AM (1993). Evaluation of the effects of methanol during early pregnancy in the rat. Toxicology **79**, 205-214.

Dahl AR, Miller SC, Petridou-Fischer J (1987). Carboxylesterases in the respiratory tract of rabbits, rats and Syrian hamsters. Toxicol. Lett. **36**, 129-136.

Danish Product Register of January (1995).

de Heer et al. (1999). Principles for Study Protocols addressing the Dermal Absorption of Pesticides. Organisation for Applied Scientific Research (TNO), TNO Nutrition and Food Research Institute, TNO Report V98.356, Zeist, The Netherlands.

DEN (1999). Dermal exposure network: Issues relating to the risk assessment of dermal exposures; An output of the EU dermal exposure network, compiled on behalf of the network by J. Jackson (1999).

Diehl B (1988). "Gefahrstoffbelastung bei Fußbodenlegearbeiten - Lösemittelproblem", Humane Produktion **10**, 30-35.

Dorman DC, Moss OR, Farris GM, Janszen D, Bond JA, Medinsky MA (1994). Pharmacokinetics of inhaled $^{14}$C-methanol and methanol-derived $^{14}$C-formate in normal and folate-deficient cynomolgus monkeys.Toxicol. Appl. Pharmacol. **128**, 229-238.

Duquenois MM, Revel PP (1934). Intoxications professionelles par vapeurs de quelques esters employés comme solvants. J. Pharm. Chem. **19**, 590-601.

EC (1996). Technical Guidance Document in support of the Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances. Parts 1-4. Office for Official Publications of the EC, Luxembourg.

Europarat (1992). Flavouring substances and natural sources of flavourings. **4,** Auflage, Band 1.

Fassett DW (1963). Patty's Industrial Hygiene and Toxicology, 2nd rev. ed., Vol. II, Fassett et al., Inc., New York, 1847-1934.

Filov VA (1961). Retention und Umwandlung von niedermolekularen Estern im Organismus. Gig. Tr. Prof. Zabol **5**, 14-19 (in Russian).

Filov VA (1964a). Über den Vergleich der Intensität der narkotischen Wirkung von Methyl- und Ethylacetat, sowie ihrer Metabolismusprodukte. Farmakol. Toksikol. **27,** 492-493 (in Russian).

Filov VA (1964b). Kinetics of accumulation of substances in biological systems characterized by free penetration and subsequent breakdown. Doklady Akademii Nauk SSSR **157**, 1006-1009.

Fisher AA (1986). Contact Dermatitis. 3rd edition. Lea & Febiger, Philadelphia 1986, p. 853 and 886.

Flury F, Wirth W. (1933). Zur Toxikologie der Lösungsmittel, (Verschiedene Ester, Aceton, Methylalkohol). Arch. Gewerbepathol. Gewerbehyg. **5**, 1-90.

Frederick LJ, Schulte PA, Apol A (1984). Investigation and control of occupational hazards associated with the use of spirit duplicators. Am. Ind. Hyg. Assoc. J. **45**, 51.

Ghittori S, Imbriani M, Borlini F, Pezzagno G, Zadra P (1984). Studio sulla stabilita degli esteri nel sangue *in vitro*. Boll. Soc. Ital. Biol. Sper. **60**(11), 2207-2213.

Gmehling J, Weidlich U, Lehmann E, Fröhlich N (1989). Verfahren zur Berechnung von Luftkonzentrationen bei Freisetzung von Stoffen aus flüssigen Produktgemischen, Teil 1 und 2, Staub – Reinhaltung der Luft, **49**, 227-230, 295-299.

Goldschmidt A, Hantschke B, Knappe E, Vock GF (1984). Glasurit-Handbuch; Farben und Lacke der BASF Farben und Fasern AG, 11. Aufl. S. 154.

Handorf and Washburn (1935). Am. Soc. **57**, 1201-1203.

Harnisch H, Steiner R, Winnacker K (eds.),(1982). "Chemische Technologie", Bd.6, "Organische Technologie II", 4. Aufl.

HMR Deutschland GmbH Pro Tox (1999a). Methyl Acetate 28-days Inhalation Toxicity Study in Rats. HMR Deutschland GmbH. ProTox. Report-Nr 99.0011 v. 16th April 1999.

HMR Deutschland GmbH Pro Tox (1999b). Mammalian Erythrocyte Micronucleus Test after 20 Exposures within 28 days, 6 hours/day of a Rat Subacute Inhalation Toxicity Study. Report No. 99.0004; April 28th, 1999.

Hoechst AG (1988a). Pharma Forschung Toxikologie und Pathologie: Methylacetat. Prüfung der akuten dermalen Toxizität an der Wistar Ratte. Unpublished report No. 88.0181, 17.02.1988.

Hoechst AG (1988b). Pharma Forschung Toxikologie und Pathologie: Methylacetat. Prüfung auf Hautreizung am Kaninchen. Unpublished report No. 88.0125, 08.02.1988.

Hoechst AG (1988c). Pharma Forschung Toxikologie und Pathologie: Methylacetat. Prüfung auf Augenreizung am Kaninchen. Unpublished report No. 88.0168, 16.02.1988.

Hoechst AG (1988d). Methyl acetate: Study of the mutagenic potential in strains of S. typhimurium (Ames test) and E. coli. Unpublished report No. 88.0406, 1988.

Hoechst AG (1992). Mitteilung der Hoechst AG zur Standard - Lieferspezifikation vom 01.07.1992.

Hoechst AG (1994). GB Chemikalien, Qualitätsmanagement, Prüflaboratorium E 529, analytical report on purity/impuriteis, 05.08.1994.

Hoechst AG (1994a). Mitteilung der Hoechst AG vom 21.11.1994.

Hoechst AG (1994b). Prüfung der Schadwirkung gegenüber Algen (Algentoxizität) von Methylacetat vom 28.10.1994.

Hoechst AG (1994c). Data print; calculation of the log Pow-value, 20.05.1994.

Hoechst AG (1994d). Safety data sheet, 05.01.1994.

Hoechst AG (1995). Written communication from 03.07.95.

Hoechst AG (1995a). Prüfung der toxischen Wirkung von Methylacetat auf Kleinkrebse (Daphnia magna) vom 10.01.1995.

Hoechst AG (1995b). Prüfung zum biologischen Abbau von Methylacetat vom 18.01.1995.

Hoechst AG (1995c). Mitteilung der Hoechst AG vom 22.02.1995.

Infurna R, Weiss B (1986). Neonatal behavioral toxicity in rats following prenatal exposure to methanol. Teratology **33**, 259-265.

International Chemical Safety Cards (1993). Commission of the European Communities, Directorate General Employment, Industrial Relations and Social Affairs, Industrial Health and Safety EUR 1261/8 EN.

Kavet R, Nauss KM (1990). The toxicity of inhaled methanol vapors. Crit. Rev. Toxicol. **21**, 21-50.

Kirk-Othmer (1993). Cosmetics in Encyclopedia of Chemical Technology, 4th ed., Vol.**7** p. 578.

Klaschka F, Vossmann D (1994). Kontaktallergene: Chemische, klinische und experimentelle Daten (Allergen-Liste). Erich Schmidt Verlag, Berlin 1994.

Kligman AM (1976). Report to RIFM (18.05.1976). Cited in: Opdyke (1979), Food Cosmet. Toxicol. **17**, 859-861.

Lebensmittelrecht (1995). Textsammlung, Becksche Textausgabe, Vol. **1**, November 1995.

Lee EW, Brady AN, Brabec MJ, Fabel T (1991). Effects of methanol vapors on testosterone production and testis morphology in rats. Toxicol. Ind. Health **7**, 261-275.

Lee EW, Terzo TS, D`Arcy JB, Gross KB, Schreck RM (1992). Lack of blood formate accumulation in humans following exposure to methanol vapor at the current permissible exposure limit.of 200 ppm. Am. Ind. Hyg. Assoc. J. **53**, 99-104.

Leung HW and Paustenbach DJ (1994). Techniques for estimating the percutaneous absorption of chemicals due to occupational and environmental exposure. Appl. Occup. Environ. Hyg. **9**, 187-197.

Lüdersdorf R, Fuchs A, Fuchs GHP, Schäcke G (1985). "Lösemittelbelastung beim Verlegen und Lackieren von Parkettböden'', Zbl. Arbeitsmed. **35**, 273-278.

Lundberg I, Hakansson M (1985). Normal serum activities of liver enzymes in Swedish paint industry workers with heavy exposure to organic solvents. Brit. J. Ind. Med. **42**, 596-600.

Medinsky MA und Dorman DC (1994). Assessing risks of low-level methanol exposure, CIIT Activities **14**,1-8.

Mercedes Benz AG (1993). Announcement from 25.01.1993.

Merck (1989). The Merck Index 11, 5933. Merck & Co., Inc. Rahway, N.J. USA.

Mizunuma K, Kawai T, Yasugi T, Horiguchi S, Iwami O, Ikeda M (1992). *In vitro* hydrolysis of methyl acetate, a limitation in application of head-space gaschromatography in biological monitoring of exposure. Toxicol. Lett. **62**, 247-253.

Morita T, Takeda K, Okumura K (1990). Evaluation of clastogenicity of formic acid, acetic acid and lactic acid on cultured mammalian cells. Mutation Research **240**, 195-202.

Muller J, Greff G (1984). Recherche de relations entre toxicité de molécules d'intérêt industriel et propriétés physico-chimiques: Test d'irritation des voies aeriennes supérieures appliqué à quatre familles chimiques. Fd. Chem. Toxicol. **22**, 661-664.

NEDO (1987). Toxicological Research of methanol as a fuel for Power Station, Summary Report on Tests with Monkeys, Rats and Mice. New Energy Development Organization. Tokyo, Japan.

Nelson BK, Brightwell WS, Krieg Jr. EF (1990). Developmental toxicology of industrial alcohols: A summary of 13 alcohols administered by inhalation to rats. Toxicol. Ind. Health **6**, 373-387.

Nelson BK, Brightwell WS, MacKenzie DR, Khan A, Burg JR, Weigel WW, Goad PT (1985). Teratological assessment of methanol and ethanol at high inhalation levels in rats. Fundam. App. Toxicol. **5**, 727-736.

Norwegian Product Register for 1994.

NTIS (1977). No. PB-274670, FDA/BF-78/16. **In**: Life Sci. Res. Office, Fed. Am. Soc. Exp. Biol., Bethesda, MD.

Orris P, Daniels WJ (1980). Hazard Evaluation and Technical Assistance Branch, Division of Surveillance, Hazard Evaluation, and Field Studies, NIOSH, Cincinnati, Ohio, 1-3.

Owen PE (1988). Vinyl Acetate: 104-Week Inhalation Combined Chronic Toxicity and Carcinogenicity Study in the Rat and Mouse. Report-No. 5547-51/15. Hazleton, UK.

Perkins RA, Ward KW, Pollack GM (1995). A Pharmacokinetic model of inhaled methanol in humans and comparison to methanol disposition in mice and rats. Environmental Health Perspectives **103**, 726-733.

Rogers JM, Mole ML, Chernoff N, Barbee BD, Turner C, Logson TR, Kavlock RJ (1993). The developmental toxicity of inhaled methanol in the CD-1 mouse, with quantitative dose-response modeling for estimation of benchmark doses. Teratology **47**, 175-188.

Römpp CD Chemie Lexikon (1995). Version 1.0, Stuttgart/New York-Georg Thieme Verlag.

Smyth HF, Carpenter CP, Weil CS, Pozzani UC, Striegel JA (1962). Range-finding toxicity data: List VI. Am. Ind. Hyg. Assoc. J. **23**, 95-107.

Stanton ME, Crofton KM, Gray LE, Gordon CJ, Boyes WK, Mole ML, Peele DB, Bushnell PJ (1995). Assessment of offspring development and behavior following gestational exposure to inhaled methanol in the rat. Fundam. Appl. Toxicol. **28**, 100-110.

Swedish Product Register for 1993.

Tada O, Nakaaki K, Fukabori S (1974). Verfahren zur Beurteilung der Methanol- und Methylacetat-Exposition (deutsche Übersetzung aus dem Japanischen) J. Sci. Lab. **50**, 239-248.

Takeda K, Katoh M (1988). Long-term Effects of Methanol Vapor at Low Concentration. Proc. of the 8th Int. Symp. Alcohol Fuels, Tokyo, Japan.

Tambo S (1973). Toxicity hazard of paint thinners with particular emphasis on the metabolism and toxicity of acetate esters. Nichidai Igaku Zasshi **32**, 349-360.

Toxicity Research Laboratory (1986). Cited in: Environmental Protection Agency (EPA) (1989). Health and Environmental Effects Profile for Methylacetate. Govt. Reports Announcements and Index (GRA&I), Issue 04, 1989, NTIS/PB89-11856, 46 p.

TRGS 402 (1986). Technische Regeln für Gefahrstoffe, Ermittlung und Beurteilung der Konzentration gefährlicher Stoffe in der Luft in Arbeitsbereichen, BArbBl **11**, S. 92 - 96, 1986 mit Änderungen und Ergänzungen: BArbBl. **10**, 1988 und **9**,1993 und **3**,1997.

Velvart J (1993). Toxikologie der Haushaltsprodukte, 3. Auflage, Verlag Hans Huber, Bern.

von der Hude W, Behm C, Gürtler R, Basler A (1988). Evaluation of the SOS chromo-test. Mutation Research **203**, 181-194.

von Oettingen WF (1960). The aliphatic acids and their esters: Toxicity and potential dangers. The saturated monobasic aliphatic acids and their esters. Arch. Ind. Health **21**, 28-65.

Voullaire E, Kliemt G (1995). Gefahrstoffe in Klein- und Mittelbetrieben: Neue Wege überbetrieblicher Unterstützung. Schriftenreihe der Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Forschungsbericht 703, Wirtschaftsverlag, NW, Bremerhaven.

Wacker Chemie GmbH (1994). Analytical report.

Wacker Chemie GmbH (1994a). Safety data sheet, 22.11.1994.

Wacker Chemie GmbH (1995). Announcement from Dr. Engel dated 07.08.1995.

Wacker Chemie GmbH (1995). Mitteilung der Wacker Chemie GmbH vom 14.02.1995.

Ward JB, Hokanson JA, Smith ER, Chang LW, Pereira MA, Whorton EB, Legator MS (1984). Sperm count, morphology and fluorescent body frequency in autopsy service workers exposed to formaldehyde. Mutation Research **130**, 417-424.

Weidlich U, Gmehling J (1986). Expositionsabschätzung. Eine Methode mit Hinweisen für die praktische Anwendung. Schriftenreihe der Bundeanstalt für Arbeitsschutz und Arbeitsmedizin, Forschungsbericht **488**, Verlag NW, Bremerhaven.

Weil AJ, Rogers HE (1951). Allergenic reactivity to simple aliphatic acids in man. J. Invest. Dermatol. **17**, 227-231.

Youssef AF, Baggs RB, Weiss B, Miller RK (1991). Methanol teratogenicity in pregnant long Evans Rats. Teratology **43**, 467.

Zeiger E, Anderson B, Haworth S, Lawlor T, Mortelmans K (1992). Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals. Environ. Mol. Mutagen. 19, Suppl. **21**, 2-141.

Zimmermann FK, Mayer VW, Scheel I, Resnick MA (1985). Acetone, methyl ethyl ketone, ethyl acetate, acetonitrile and other polar aprotic solvents are strong inducers of aneuploidy in Saccharomyces cerevisiae. Mutation Research **149**, 339-351.

# 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 |
| BOD | Biochemical Oxygen Demand |
| 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 90 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) |
| OC | Organic Carbon content |
| 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 |
| ThOD | Theoritical Oxygen Demand |

| | |
|---|---|
| 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

melting point: $MP := 175 \cdot K$

vapour pressure: $VP := 21700 \cdot Pa$

water solubility: $SOL := 250000 \cdot mg \cdot l^{-1}$

part. coefficient octanol/water: $LOGP_{OW} := 0.18$

moleculare weight: $MOLW := 0.0741 \cdot kg \cdot mol^{-1}$

gas constant: $R := 8.3143 \cdot J \cdot mol^{-1} \cdot K^{-1}$

temperature: $T := 293 \cdot K$

conc. of suspended matter in the river: $SUSP_{water} := 15 \cdot mg \cdot l^{-1}$

density of the solid phase: $RHO_{solid} := 2500 \cdot kg \cdot m^{-3}$

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**

$$HENRY := \frac{VP \cdot MOLW}{SOL} \qquad HENRY = 6.432 \cdot Pa \cdot m^3 \cdot mol^{-1}$$

$$\log\left(\frac{HENRY}{Pa \cdot m^3 \cdot mol^{-1}}\right) = 0.808$$

$$K_{air\_water} := \frac{HENRY}{R \cdot T} \qquad K_{air\_water} = 0.003$$

**solid/water-partition ceefficient $Kp_{comp}$ and total compartment/water-partition coefficient $K_{comp\_water}$**

$a := 0.52$ (a,b from chapter 4.3, table 1)

$b := 1.02$

$K_{OC} := 10^{a \cdot LOGP_{OW} + b} \cdot l \cdot kg^{-1}$ $K_{OC} = 12.99 \cdot l \cdot kg^{-1}$

Suspended matter

$Kp_{susp} := 0.1 \cdot K_{OC}$ $Kp_{susp} = 1.299 \cdot l \cdot kg^{-1}$

$K_{susp\_water} := Fwater_{susp} + Fsolid_{susp} \cdot Kp_{susp} \cdot RHO_{solid}$ $K_{susp\_water} = 1.225$

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

$factor := 1 + Kp_{susp} \cdot SUSP_{water}$ $factor = 1$

Sediment

$Kp_{sed} := 0.05 \cdot K_{OC}$ $Kp_{sed} = 0.649 \cdot l \cdot kg^{-1}$

$K_{sed\_water} := Fwater_{sed} + Fsolid_{sed} \cdot Kp_{sed} \cdot RHO_{solid}$ $K_{sed\_water} = 1.125$

Soil

$Kp_{soil} := 0.02 \cdot K_{OC}$ $Kp_{soil} = 0.26 \cdot l \cdot kg^{-1}$

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

$K_{soil\_water} = 0.59$

Sludge

$K_{p\_sludge} := 0.37 \cdot K_{OC}$ $K_{p\_sludge} = 4.806 \cdot l \cdot kg^{-1}$

**Elimination in STPs**

rate constant in STP: k =1 $h^{-1}$ elimination P = f ( k, logpow, logH) =88 %

fraction directed to surface water $Fstp_{water}$=12 %

**biodegradation in different compartments**

surface water

$kbio_{water} := 4.7 \cdot 10^{-2} \cdot d^{-1}$ (cTGD, table 5)

soil

$DT50bio_{soil} := 30 \cdot d$ (cTGD, table 6)

$kbio_{soil} := \frac{\ln(2)}{DT50bio_{soil}}$ $kbio_{soil} = 0.023 \cdot d^{-1}$

sediment

$kbio_{sed} := \frac{\ln(2)}{DT50bio_{soil}} \cdot Faer_{sed}$ $kbio_{sed} = 0.002 \cdot d^{-1}$

**degradation in surface waters**

$khydr_{water} := 1.1 \cdot 10^{-3} \cdot d^{-1}$

$kphoto_{water} := 1 \cdot 10^{-99} \cdot d^{-1}$

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

$kdeg_{water} = 0.048 \cdot d^{-1}$

**Atmosphere**

calculation of CONjunge * SURFaer for the OPS-model

$VPL := \frac{VP}{\exp\left[6.79 \cdot \left(1 - \frac{MP}{285 \cdot K}\right)\right]}$ $VP := wenn(MP > 285 \cdot K, VPL, VP)$ $VP = 2.17 \cdot 10^{4} \cdot Pa$

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

$Fass_{aer} = 4.608 \cdot 10^{-9}$

degradation in the atmosphere

$kdeg_{air}$ =1,375*$10^{-2}$ $d^{-1}$ (see AOP-calculation)

# Appendix A2 Calculation of $Clocal_{water}$

Calculation of $Clocal_{water}$ for aquatic compartment during production and processing of chemicals at one site

**status: TGD, ESD, IC-3**

$d := 86400 \cdot s$

**chemical: Methylacetate CAS-Nr.: 79-20-9 generic model**

$a := 365 \cdot d$

$\mu g := 10^{-9} \cdot kg$

Production volume: $T_1 := 10000 \cdot t \cdot a^{-1}$

Processing volume: $T_2 := 2500 \cdot t \cdot a^{-1}$

Emissionsfactor for production (TGD, IC-3)): $f_1 := 0.3 \cdot \%$

Emissionsfaktor for processing (TGD, IC-3) $f_2 := 0.7 \cdot \%$

Duration of emission forproduction (TGD, tab. B1.6) $Temission_1 := 300 \cdot d \cdot a^{-1}$

Duration of emission for processing(TGD, tab. B3.2) $Temission_2 := 150 \cdot d \cdot a^{-1}$

Fraction of emission directed to water:
(SimpleTreat, k:1h-1; logH:0.81 ; $\log K_{ow}$:0.18 ) $Fstp_{water} := 12 \cdot \%$

River flow rate (TGD , IC-3): $V := 60 \cdot m^3 \cdot s^{-1}$

Factor (1 + $K_p$ * SUSPwater): $FACTOR := 1$

***Emission per day:***

$$Elocal_{water} := \frac{T_1 \cdot f_1}{Temission_1} + \frac{T_2 \cdot f_2}{Temission_2} \qquad Elocal_{water} = 216.67 \cdot kg \cdot d^{-1}$$

**Concentration in surface water:**

$$Clocal_{water} := \frac{Elocal_{water} \cdot Fstp_{water}}{V \cdot FACTOR} \qquad Clocal_{water} = 5.02 \cdot \mu g \cdot l^{-1}$$

***Release to hydrosphere:***

$$RELEASE_{sw} := \left(T_1 \cdot f_1 + T_2 \cdot f_2\right) \cdot Fstp_{water} \qquad RELEASE_{sw} = 5.7 \cdot t \cdot a^{-1}$$

Estimation of $Clocal_{water}$ at formulation of household chemicals

Status: TGD, IC:5,6 UC:48

$d := 86400 \cdot s$

$a := 365 \cdot d$

**chemical: Methylacetate CAS-Nr.: 79-20-9**

| | |
|---|---|
| Total annual tonnage of chemical: | $TONNAGE := 5800 \cdot t \cdot a^{-1}$ |
| Release factor (TGD,table A-2.1): | $f_{emission} := 0.003$ |
| Fraction of main source (B-table:2.3): | $Fmainsource := 0.8$ |
| Waste water flow of wwtp: | $EFFLUENT_{stp} := 2000 \cdot m^3 \cdot d^{-1}$ |
| Duration of emission (B-table:2.3): | $Temission := 300 \cdot d \cdot a^{-1}$ |
| Fraction of emission directed to water (SimpleTreat; k:1h$^{-1}$; logPow:0,18 ; logH:0,81) | $Fstp_{water} := 12 \cdot \%$ |
| Dilution factor (TGD): | $DILUTION := 10$ |
| Factor (1+Kp * SUSPwater): | $FACTOR := 1$ |

***Emission per day:***

$$Elocal_{water} := \frac{TONNAGE \cdot Fmainsource \cdot f_{emission}}{Temission} \qquad Elocal_{water} = 46.4 \cdot kg \cdot d^{-1}$$

***Influent concentration:***

$$Clocal_{inf} := \frac{Elocal_{water}}{EFFLUENT_{stp}} \qquad Clocal_{inf} = 23.2 \cdot mg \cdot l^{-1}$$

***Effluent concentration:***

$$Clocal_{eff} := Clocal_{inf} \cdot Fstp_{water} \qquad Clocal_{eff} = 2.78 \cdot mg \cdot l^{-1}$$

**Concentration in surface water:**

$$Clocal_{water} := \frac{Clocal_{eff}}{FACTOR \cdot DILUTION} \qquad Clocal_{water} = 278.4 \cdot \mu g \cdot l^{-1}$$

***Total release for the regional model ( without elimination in STPs ):***

$$RELEASE := TONNAGE \cdot f_{emission} \qquad RELEASE = 17.4 \cdot t \cdot a^{-1}$$

***Annual average local concentration in water:***

$$Clocal_{water\_ann} := Clocal_{water} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}} \qquad Clocal_{water\_ann} = 0.23 \cdot mg \cdot l^{-1}$$

Calculation of $Clocal_{water}$ for aquatic compartment through use of HPV-household chemicals (>1000 t/year)

Status: TGD, ESD, modified IC-5, IC-6

$a := 365 \cdot d$

$\mu g := 10^{-9} \cdot kg$

$Temission = 365 \cdot d \cdot a^{-1}$

| | |
|---|---|
| Quantity of detergent chemical | $X := 5800000 \cdot kg \cdot a^{-1}$ |
| Population of area or number of people consuming detergent chemical (D): | $Y := 81000000$ |
| Amount of waste water per inhabitant: | $WASTEW_{inhab} := 200 \cdot l \cdot d^{-1}$ |
| Inhabitants per wwtp: | $CAPACITY_{stp} := 10000$ |
| Fraction of emission directed to water: (k:1 h-1; logH:0.81; logKow:0.18 ) | $Fstp_{water} := 12 \cdot \%$ |
| Waste water flow of wwtp: | $EFFLUENT_{stp} := 2000 \cdot m^3 \cdot d^{-1}$ |
| Dilution factor (TGD): | $DILUTION := 10$ |
| Factor ($1+K_p$ * SUSPwater): | $FACTOR := 1$ |

***Emission per day:***

$Elocal_{water} := X \cdot Y^{-1} \cdot CAPACITY_{stp}$ $\quad Elocal_{water} = 1.962 \cdot kg \cdot d^{-1}$

***Influent concentration:***

$$Clocal_{inf} := \frac{Elocal_{water}}{EFFLUENT_{stp}} \qquad Clocal_{inf} = 980.89 \cdot \mu g \cdot l^{-1}$$

***Effluent concentration:***

$Clocal_{eff} := Clocal_{inf} Fstp_{water}$ $\quad Clocal_{eff} = 117.71 \cdot \mu g \cdot l^{-1}$

**Concentration in receiving water:**

$$Clocal_{water} := \frac{Clocal_{eff}}{DILUTION \cdot FACTOR} \qquad Clocal_{water} = 11.77 \cdot \mu g \cdot l^{-1}$$

***Emission for $PEC_{regional}$ (without wwtp):***

$RELEASE := X$ $\quad RELEASE = 5.8 \cdot 10^3 \cdot t \cdot a^{-1}$

***annual average local concentration in surface water:***

$Clocal_{water\_ann} := Clocal_{water}$ $\quad Clocal_{water\_ann} = 11.77 \cdot \mu g \cdot l^{-1}$

Estimation of $Clocal_{water}$ at formulation of chemicals for paints, laques and varnishes or adhesives (used as a solvent)

Status: TGD, A + B Tables, IC-14

$a := 365 \cdot d$

Total annual tonnage of chemical: $TONNAGE := 5800 \cdot t \cdot a^{-1}$

Release factor (A 2.1 ): $f_{emission} := 0.003$

Fraction of main source (B 2.3): $Fmainsource := 0.8$

Waste water flow of wwtp: $EFFLUENT_{stp} := 2000 \cdot m^3 \cdot d^{-1}$

Duration of emission (B 2.3): $Temission := 300 \cdot d \cdot a^{-1}$

Fraction of emission directed to water (SimpleTreat; k:1h$^{-1}$; logPow:0,18 ; logH:0,81) $Fstp_{water} := 12 \cdot \%$

Dilution factor (TGD): $DILUTION := 10$

Factor (1+Kp * SUSPwater): $FACTOR := 1$

***Emission per day***

$$Elocal_{water} := \frac{TONNAGE \cdot Fmainsource \cdot f_{emission}}{Temission} \qquad Elocal_{water} = 46.4 \cdot kg \cdot d^{-1}$$

***Influent concentration:***

$$Clocal_{inf} := \frac{Elocal_{water}}{EFFLUENT_{stp}} \qquad Clocal_{inf} = 23.2 \cdot mg \cdot l^{-1}$$

***Effluent concentration:***

$$Clocal_{eff} := Clocal_{inf} \cdot Fstp_{water} \qquad Clocal_{eff} = 2.78 \cdot mg \cdot l^{-1}$$

**Concentration in surface water:**

$$Clocal_{water} := \frac{Clocal_{eff}}{FACTOR \cdot DILUTION} \qquad Clocal_{water} = 0.28 \cdot mg \cdot l^{-1}$$

***Total release for the regional model ( without elimination in STPs ):***

$$RELEASE := TONNAGE \cdot f_{emission} \qquad RELEASE = 17.4 \cdot t \cdot a^{-1}$$

***Annual average local concentration in water:***

$$Clocal_{water\_ann} := Clocal_{water} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}} \qquad Clocal_{water\_ann} = 0.23 \cdot mg \cdot l^{-1}$$

Estimation of $Clocal_{water}$ of chemicals for paints, laques and varnishes (private use)

Status: TGD, A + B Tables, IC-14

| | |
|---|---|
| Total annual tonnage of chemical: | $TONNAGE := 5800 \cdot t \cdot a^{-1}$ |
| Release factor (A 4.5, solvent based): | $f_{emission} := 0.04$ |
| Fraction of main source (B 4.5): | $Fmainsource := 0.002$ |
| Waste water flow of wwtp: | $EFFLUENT_{stp} := 2000 \cdot m^3 \cdot d^{-1}$ |
| Duration of emission (B 4.5): | $Temission := 300 \cdot d \cdot a^{-1}$ |
| Fraction of emission directed to water: (SimpleTreat; k:1h$^{-1}$; logPow:0,18 ; logH:0,81) | $Fstp_{water} := 12 \cdot \%$ |
| Dilution factor (TGD): | $DILUTION := 10$ |
| Factor (1+Kp * SUSPwater): | $FACTOR := 1$ |

***Emission per day***:

$$Elocal_{water} := \frac{TONNAGE \cdot Fmainsource \cdot f_{emission}}{Temission} \qquad Elocal_{water} = 1.55 \cdot kg \cdot d^{-1}$$

***Influent concentration:***

$$Clocal_{inf} := \frac{Elocal_{water}}{EFFLUENT_{stp}} \qquad Clocal_{inf} = 0.77 \cdot mg \cdot l^{-1}$$

***Effluent concentration:***

$$Clocal_{eff} := Clocal_{inf} \cdot Fstp_{water} \qquad Clocal_{eff} = 92.8 \cdot \cdot l^{-1}$$

**Concentration in surface water:**

$$Clocal_{water} := \frac{Clocal_{eff}}{FACTOR \cdot DILUTION} \qquad Clocal_{water} = 9.28 \cdot \cdot l^{-1}$$

***Total release for the regional model ( without elimination in STPs ):***

$$RELEASE := TONNAGE \cdot f_{emission} \qquad RELEASE = 232 \cdot t \cdot a^{-1}$$

***Annual average local concentration in water:***

$$Clocal_{water\_ann} := Clocal_{water} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}} \qquad Clocal_{water\_ann} = 7.627 \cdot 10^{-3} \cdot mg \cdot l^{-1}$$

Estimation of $Clocal_{water}$ of chemicals for paints, laques and varnishes at processing

Status: TGD, A + B Tables, IC-14

| | |
|---|---|
| Total annual tonnage of chemical: | $TONNAGE := 5800 \cdot t \cdot a^{-1}$ |
| Release factor (A 3.15, solvent based): | $f_{emission} := 0.02$ |
| Fraction of main source (RAR): | $Fmainsource := 0.01$ |
| Waste water flow of wwtp: | $EFFLUENT_{stp} := 2000 \cdot m^3 \cdot d^{-1}$ |
| Duration of emission (B 3.13): | $Temission := 300 \cdot d \cdot a^{-1}$ |
| Fraction of emission directed to water: (SimpleTreat; k:1h$^{-1}$; logPow:0,18 ; logH:0,81) | $Fstp_{water} := 12 \cdot \%$ |
| Dilution factor (TGD): | $DILUTION := 10$ |
| Factor (1+Kp * SUSPwater): | $FACTOR := 1$ |

***Emission per day***:

$$Elocal_{water} := \frac{TONNAGE \cdot Fmainsource \cdot f_{emission}}{Temission} \qquad Elocal_{water} = 3.87 \cdot kg \cdot d^{-1}$$

***Influent concentration:***

$$Clocal_{inf} := \frac{Elocal_{water}}{EFFLUENT_{stp}} \qquad Clocal_{inf} = 1.93 \cdot mg \cdot l^{-1}$$

***Effluent concentration:***

$$Clocal_{eff} := Clocal_{inf} \cdot Fstp_{water} \qquad Clocal_{eff} = 0.23 \cdot mg \cdot l^{-1}$$

**Concentration in surface water:**

$$Clocal_{water} := \frac{Clocal_{eff}}{FACTOR \cdot DILUTION} \qquad Clocal_{water} = 0.02 \cdot mg \cdot l^{-1}$$

***Total release for the regional model ( without elimination in STPs ):***

$$RELEASE := TONNAGE \cdot f_{emission} \qquad RELEASE = 116 \cdot t \cdot a^{-1}$$

***Annual average local concentration in water:***

$$Clocal_{water\_ann} := Clocal_{water} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}} \qquad Clocal_{water\_ann} = 0.019 \cdot mg \cdot l^{-1}$$

# Appendix A3 Atmosphere (OPS model) - Calculation of $Clocal_{air}$ and $PEClocal_{air}$

**stage of life cycle:formulation household chemical**
**IC:5,6 UC:48 MC:Ic**

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

tonnage for specific scenario:

$TONNAGE := 5800 \cdot t \cdot a^{-1}$

release factor (table A-2.1):

$f_{emission} := 0.01$

fraction of main source (table B-2.3):

$Fmainsource := 0.8$

days of use per year(table B-2.3):

$Temission := 300 \cdot d \cdot a^{-1}$

release during life cycle to air:

$RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 58 \cdot t \cdot a^{-1}$

local emission during episode to air:

$$Elocal_{air} := \frac{Fmainsource RELEASE}{Temission}$$

$Elocal_{air} = 154.667 \cdot kg \cdot d^{-1}$

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 (App.II)

$Fstp_{air} := 2.3 \cdot \%$

local emission rate to water during emission episode

$Elocal_{water} := 46.4 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode

$Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 1.067 \cdot kg \cdot d^{-1}$

local concentation in air during emission episode:

$Clocal_{air} := wenn(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air})$

$Clocal_{air} = 0.043 \cdot mg \cdot m^{-3}$

annual average concentration in air, 100m from point source

$$Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$$

$Clocal_{air\_ann} = 0.035 \cdot mg \cdot m^{-3}$

regional concentration in air

$PECregional_{air} := 1.3 \cdot 10^{-4} \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air

$PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.035 \cdot mg \cdot m^{-3}$

## 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)

$Fass_{aer} := 4.608 \cdot 10^{-9}$

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

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

$$DEPtotal = 0.062 \cdot mg \cdot m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.051 \cdot mg \cdot m^{-2} \cdot d^{-1}$$

**stage of life cycle:privat use of household chemicals**

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

tonnage for specific scenario:

$TONNAGE := 5800 \cdot t \cdot a^{-1}$

release factor (table A 4.1):

$f_{emission} := 0.175$

fraction of main source (table B 4.1):

$Fmainsource := 0.002$

days of use per year:

$Temission := 365 \cdot d \cdot a^{-1}$

release during life cycle to air:

$RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 1.015 \cdot 10^{3} \cdot t \cdot a^{-1}$

local emission during episode to air:

$Elocal_{air} := \frac{Fmainsource RELEASE}{Temission}$

$Elocal_{air} = 5.562 \cdot kg \cdot d^{-1}$

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 (App.II)

$Fstp_{air} := 2.3 \cdot \%$

local emission rate to water during emission episode

$Elocal_{water} := 1.962 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode

$Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 0.045 \cdot kg \cdot d^{-1}$

local concentation in air during emission episode:

$Clocal_{air} := wenn\left(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air}\right)$

$Clocal_{air} = 0.002 \cdot mg \cdot m^{-3}$

annual average concentration in air, 100m from point source

$Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$

$Clocal_{air\_ann} = 0.002 \cdot mg \cdot m^{-3}$

regional concentration in air

$PECregional_{air} := 1.3 \cdot 10^{-4} \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air

$PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.002 \cdot mg \cdot m^{-3}$

## Calculation of the deposition rate

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

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

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

$$Fass_{aer} := 4.608 \cdot 10^{-9}$$

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$^{-1}$ |

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

total deposition flux during emission episode

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

$$DEPtotal = 0.002 \cdot mg\,m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.002 \cdot mg\,m^{-2} \cdot d^{-1}$$

**stage of life cycle:formulation of paints or adhesives**
**IC:5,6 UC:48 MC:Ic**

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

tonnage for specific scenario:

$TONNAGE := 5800 \cdot t \cdot a^{-1}$

release factor (Ic, A 2.1):

$f_{emission} := 0.01$

fraction of main source (table B 2.3):

$Fmainsource := 0.8$

days of use per year(table B 2.3):

$Temission := 300 \cdot d \cdot a^{-1}$

release during life cycle to air:

$RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 58 \cdot t \cdot a^{-1}$

local emission during episode to air:

$Elocal_{air} := \frac{Fmainsource RELEASE}{Temission}$

$Elocal_{air} = 154.667 \cdot kg \cdot d^{-1}$

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 (App.II)

$Fstp_{air} := 2.3 \cdot \%$

local emission rate to water during emission episode

$Elocal_{water} := 46.4 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode

$Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 1.067 \cdot kg \cdot d^{-1}$

local concentation in air during emission episode:

$Clocal_{air} := wenn\left(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air}\right)$

$Clocal_{air} = 0.043 \cdot mg \cdot m^{-3}$

annual average concentration in air, 100m from point source

$Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$

$Clocal_{air\_ann} = 0.035 \cdot mg \cdot m^{-3}$

regional concentration in air

$PECregional_{air} := 1.3 \cdot 10^{-4} \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air

$PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.035 \cdot mg \cdot m^{-3}$

## Calculation of the deposition rate

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

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

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

$Fass_{aer} := 4.608 \cdot 10^{-9}$

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$^{-1}$ |

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

total deposition flux during emission episode

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

$$DEPtotal = 0.062 \cdot mg\,m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.051 \cdot mg\,m^{-2} \cdot d^{-1}$$

**stage of life cycle:privat use of paints**

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

tonnage for specific scenario: $TONNAGE := 5800 \cdot t \cdot a^{-1}$

release factor (table A 4.5, solvent based): $f_{emission} := 0.95$

fraction of main source (table B 4.5): $Fmainsource := 0.002$

days of use per year: $Temission := 300 \cdot d \cdot a^{-1}$

release during life cycle to air: $RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 5.51 \cdot 10^{3} \cdot t \cdot a^{-1}$

local emission during episode to air: $Elocal_{air} := \frac{Fmainsource \cdot RELEASE}{Temission}$

$Elocal_{air} = 36.733 \cdot kg \cdot d^{-1}$

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 (App.II) $Fstp_{air} := 2.3 \cdot \%$

local emission rate to water during emission episode $Elocal_{water} := 1.55 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode $Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 0.036 \cdot kg \cdot d^{-1}$

local concentation in air during emission episode: $Clocal_{air} := wenn\left(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air}\right)$

$Clocal_{air} = 0.01 \cdot mg \cdot m^{-3}$

annual average concentration in air, 100m from point source $Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$

$Clocal_{air\_ann} = 0.008 \cdot mg \cdot m^{-3}$

regional concentration in air $PECregional_{air} := 1.3 \cdot 10^{-4} \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air $PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.009 \cdot mg \cdot m^{-3}$

## 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)

$$Fass_{aer} := 4.608 \cdot 10^{-9}$$

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

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

$$DEPtotal = 0.015 \bullet mg \cdot m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.012 \bullet mg \cdot m^{-2} \cdot d^{-1}$$

**stage of life cycle:processing of paints**

$a := 365 \cdot d$

$mg := 1 \cdot 10^{-6} \cdot kg$

tonnage for specific scenario: $TONNAGE := 5800 \cdot t \cdot a^{-1}$

release factor (table A 3.15, solvent based): $f_{emission} := 0.9$

fraction of main source (RAR): $Fmainsource := 0.01$

days of use per year: $Temission := 300 \cdot d \cdot a^{-1}$

release during life cycle to air: $RELEASE := TONNAGE \cdot f_{emission}$

$RELEASE = 5.22 \cdot 10^{3} \cdot t \cdot a^{-1}$

local emission during episode to air: $Elocal_{air} := \frac{Fmainsource \cdot RELEASE}{Temission}$

$Elocal_{air} = 174 \cdot kg \cdot d^{-1}$

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 (App.II) $Fstp_{air} := 2.3 \cdot \%$

local emission rate to water during emission episode $Elocal_{water} := 3.87 \cdot kg \cdot d^{-1}$

local emission to air from STP during emission episode $Estp_{air} := Fstp_{air} \cdot Elocal_{water}$

$Estp_{air} = 0.089 \cdot kg \cdot d^{-1}$

local concentation in air during emission episode: $Clocal_{air} := wenn\left(Elocal_{air} > Estp_{air}, Elocal_{air} \cdot Cstd_{air}, Estp_{air} \cdot Cstd_{air}\right)$

$Clocal_{air} = 0.048 \cdot mg \cdot m^{-3}$

annual average concentration in air, 100m from point source $Clocal_{air\_ann} := Clocal_{air} \cdot \frac{Temission}{365 \cdot d \cdot a^{-1}}$

$Clocal_{air\_ann} = 0.04 \cdot mg \cdot m^{-3}$

regional concentration in air $PECregional_{air} := 1.3 \cdot 10^{-4} \cdot mg \cdot m^{-3}$

annual average predicted environmental concentration in air $PEClocal_{air\_ann} := Clocal_{air\_ann} + PECregional_{air}$

$PEClocal_{air\_ann} = 0.04 \cdot mg \cdot m^{-3}$

## 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)

$$Fass_{aer} := 4.608 \cdot 10^{-9}$$

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

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

$$DEPtotal = 0.07 \bullet mg \cdot m^{-2} \cdot d^{-1}$$

annual average total depostion flux

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

$$DEPtotal_{ann} = 0.057 \bullet mg \cdot m^{-2} \cdot d^{-1}$$

# Appendix A4 Exposure of soil

**processing of paints**

$i := 1..3$

annual average total deposition flux: $DEPtotal_{ann} := 0.057 \cdot mg \cdot m^{-2} \cdot d^{-1}$

soil-water partitioning coefficient: $K_{soil\_water} := 0.59$

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

air-water partitioning coefficient: $K_{air\_water} := 0.003$

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

PECregional: $PECregional_{natural\_soil} := 2.19 \cdot 10^{-5} \cdot mg \cdot kg^{-1}$

**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:

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

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

| | $\frac{Clocal_{soil_i}}{ppm}$ | | $\frac{PEClocal_{soil_i}}{ppm}$ |
|---|---|---|---|
| $Clocal_{soil}$ = | $4.231 \cdot 10^{-3}$ | $PEClocal_{soil}$ = | $4.253 \cdot 10^{-3}$ |
| $Clocal_{agr.soil}$ = | $4.231 \cdot 10^{-3}$ | $PEClocal_{agr.soil}$ = | $4.253 \cdot 10^{-3}$ |
| $Clocal_{grassland}$ = | $5.961 \cdot 10^{-3}$ | $PEClocal_{grassland}$ = | $5.982 \cdot 10^{-3}$ |

**Indicating persistency of the substance in soil**

initial concentration after 10 years:

| $\frac{C_{soil\_10_i}}{ppm}$ |
|---|
| $4.231 \cdot 10^{-3}$ |
| $4.231 \cdot 10^{-3}$ |
| $5.961 \cdot 10^{-3}$ |

initial concentration in steady-state situation:

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

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

| $\frac{C_{soil\_ss_i}}{ppm}$ |
|---|
| $4.231 \cdot 10^{-3}$ |
| $4.231 \cdot 10^{-3}$ |
| $5.961 \cdot 10^{-3}$ |

fraction of steady-state in soil achieved:

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

| $Fst\_st_i$ |
|---|
| 1 |
| 1 |
| 1 |

**concentration in pore water**

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

$Clocal_{soil\_porew_i}$ in $mg \cdot l^{-1}$

| | | |
|---|---|---|
| $Clocal_{soil\_porew}$ | = | 0.01219 |
| $Clocal_{agr.soil\_porew}$ | = | 0.01219 |
| $Clocal_{grassland\_porew}$ | = | 0.01717 |

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

$PEClocal_{soil\_porew_i}$ in $mg \cdot l^{-1}$

| | | |
|---|---|---|
| $PEClocal_{soil\_porew}$ | = | 0.01225 |
| $PEClocal_{agr.soil\_porew}$ | = | 0.01225 |
| $PEClocal_{grassland\_porew}$ | = | 0.01724 |

**concentration in ground water**

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

**formulation of household chemicals**

$i := 1..3$

annual average total deposition flux: $DEPtotal_{ann} := 0.051 \cdot mg \cdot m^{-2} \cdot d^{-1}$

soil-water partitioning coefficient: $K_{soil\_water} := 0.59$

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

air-water partitioning coefficient: $K_{air\_water} := 0.003$

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

PECregional: $PECregional_{natural\_soil} := 2.19 \cdot 10^{-5} \cdot mg \cdot kg^{-1}$

**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:

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

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

| | $\frac{Clocal_{soil_i}}{ppm}$ |
|---|---|
| $Clocal_{soil}$ = | $3.785 \cdot 10^{-3}$ |
| $Clocal_{agr.soil}$ = | $3.785 \cdot 10^{-3}$ |
| $Clocal_{grassland}$ = | $5.333 \cdot 10^{-3}$ |

| | $\frac{PEClocal_{soil_i}}{ppm}$ |
|---|---|
| $PEClocal_{soil}$ = | $3.807 \cdot 10^{-3}$ |
| $PEClocal_{agr.soil}$ = | $3.807 \cdot 10^{-3}$ |
| $PEClocal_{grassland}$ = | $5.355 \cdot 10^{-3}$ |

**Indicating persistency of the substance in soil**

initial concentration after 10 years:

| $\frac{C_{soil\_10_i}}{ppm}$ |
|---|
| $3.785 \cdot 10^{-3}$ |
| $3.785 \cdot 10^{-3}$ |
| $5.333 \cdot 10^{-3}$ |

initial concentration in steady-state situation:

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

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

| $\frac{C_{soil\_ss_i}}{ppm}$ |
|---|
| $3.785 \cdot 10^{-3}$ |
| $3.785 \cdot 10^{-3}$ |
| $5.333 \cdot 10^{-3}$ |

fraction of steady-state in soil achieved:

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

| $Fst\_st_i$ |
|---|
| 1 |
| 1 |
| 1 |

**concentration in pore water**

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

$Clocal_{soil\_porew_i}$ in $mg \cdot l^{-1}$

| | | |
|---|---|---|
| $Clocal_{soil\_porew}$ | = | 0.01091 |
| $Clocal_{agr.soil\_porew}$ | = | 0.01091 |
| $Clocal_{grassland\_porew}$ | = | 0.01537 |

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

$PEClocal_{soil\_porew_i}$ in $mg \cdot l^{-1}$

| | | |
|---|---|---|
| $PEClocal_{soil\_porew}$ | = | 0.01097 |
| $PEClocal_{agr.soil\_porew}$ | = | 0.01097 |
| $PEClocal_{grassland\_porew}$ | = | 0.01543 |

**concentration in ground water**

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

# Appendix A5 Euses and SimpleBox2.0a calculations

Euses Report

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

**SimpleBox2.0a - calculation of continental and regional PEC's**

- adaptation to TGD (1996)

| INPUT - Methylacetate | | | |
|---|---|---|---|
| Parameter names acc. SimpleBox20 | Unit | Input | Parameter names according Euses |
| **Physicochemical properties** | | | |
| COMPOUND NAME | [-] | Methylacetate | Substance |
| MOL WEIGHT | [g.mol$^{-1}$] | 74,08 | Molecular weight |
| MELTING POINT | [° C] | -98,1 | Melting Point |
| VAPOR PRESSURE(25) | [Pa] | 21700 | Vapour pressure at 25°C |
| log Kow | [log10] | 0,18 | Octanol-water partition coefficient |
| SOLUBILITY(25) | [mg.l$^{-1}$] | 295000 | Water solubility |
| **Distribution - Partition coefficients** | | | |
| **- Solids water partitioning (derived from Koc)** | | | |
| Kp(soil) | [l.kg$_d^{-1}$] | 0,26 | Solids-water partitioning in soil |
| Kp(sed) | [l.kg$_d^{-1}$] | 0,649 | Solids-water partitioning in sediment |
| Kp(susp) | [l.kg$_d^{-1}$] | 1,299 | Solids-water partitioning in sudpended matter |
| **- Biota-water** | | | |
| BCF(fish) | [l.kg$_w^{-1}$] | 0 | Biocentration factor for aquatic biota |
| **Degradation and Transfromation rates** | | | |
| **- Characterisation and STP** | | | |
| PASSreadytest | [y / n] | y | Characterization of biodegradability |
| **- Environmental Total Degradation** | | | |
| kdeg(air) | [d$^{-1}$] | 7,37E-03 | Rate constant for degradation in air |
| kdeg(water) | [d$^{-1}$] | 4,70E-02 | Rate constant for degradation in bulk surface water |
| kdeg(soil) | [d$^{-1}$] | 2,30E-02 | Rate constant for degradation in bulk soil |
| kdeg(sed) | [d$^{-1}$] | 2,30E-03 | Rate constant for degradation in bulk sediment |
| **Sewage treatment (e.g. calculated by SimpleTreat)** | | | |
| **- Continental** | | | |
| FR(volatstp) [C] | [-] | 2,30E-02 | Fraction of emission directed to air (STPcont) |
| FR(effstp) [C] | [-] | 1,20E-01 | Fraction of emission directed to water (STPcont) |
| FR(sludgestp) [C] | [-] | 0,00E+00 | Fraction of emission directed to sludge (STPcont) |
| **- Regional** | | | |
| FR(volatstp) [R] | [-] | 2,30E-02 | Fraction of emission directed to air (STPreg) |
| FR(effstp) [R] | [-] | 1,20E-01 | Fraction of emission directed to water (STPreg) |
| FR(sludgestp) [R] | [-] | 0,00E+00 | Fraction of emission directed to sludge (STPreg) |
| **Release estimation** | | | |
| **- Continental** | | | |
| Edirect(air) [C] | [t.y$^{-1}$] | 11958 | Total continental emission to air |

| | | | |
|---|---|---|---|
| STPload [C] | [$t.y^{-1}$] | 402 | Total continental emission to wastewater |
| Edirect(water1) [C] | [$t.y^{-1}$] | 1355 | Total continental emission to surface water |
| Edirect(soil3) [C] | [$t.y^{-1}$] | 0 | Total continental emission to industrial soil |
| Edirect(soil2) [C] | [$t.y^{-1}$] | 0 | Total continental emission to agricultural soil |

**- Regional**

| | | | |
|---|---|---|---|
| Edirect(air) [R] | [$t.y^{-1}$] | 1328 | Total continental emission to air |
| STPload [R] | [$t.y^{-1}$] | 45 | Total continental emission to wastewater |
| Edirect(water1) [R] | [$t.y^{-1}$] | 150 | Total continental emission to surface water |
| Edirect(soil3) [R] | [$t.y^{-1}$] | 0 | Total continental emission to industrial soil |
| Edirect(soil2) [R] | [$t.y^{-1}$] | 0 | Total continental emission to agricultural soil |

## OUTPUT - Methylacetate

| Parameter names acc. SimpleBox20 | Unit | Output | Parameter names according Euses |
|---|---|---|---|
| **Physicochemical properties** | | | |
| COMPOUND NAME | [-] | Methylacetate | Substance |
| **Output** | | | |
| **- Continental** | | | |
| PECsurfacewater (total) | [$mg.l^{-1}$] | 1,13E-04 | Continental PEC in surface water (total) |
| PECsurfacewater (dissolved) | [$mg.l^{-1}$] | 1,13E-04 | Continental PEC in surface water (dissolved) |
| PECair | [$mg.m^{-3}$] | 6,68E-05 | Continental PEC in air (total) |
| PECagr.soil | [$mg.kg_{wwt}^{-1}$] | 6,41E-06 | Continental PEC in agricultural soil (total) |
| PECporewater agr.soil | [$mg.l^{-1}$] | 1,85E-05 | Continental PEC in pore water of agricultural soils |
| PECnat.soil | [$mg.kg_{wwt}^{-1}$] | 1,11E-05 | Continental PEC in natural soil (total) |
| PECind.soil | [$mg.kg_{wwt}^{-1}$] | 1,11E-05 | Continental PEC in industrial soil (total) |
| PECsediment | [$mg.kg_{wwt}^{-1}$] | 9,27E-05 | Continental PEC in sediment (total) |
| **- Regional** | | | |
| PECsurfacewater (total) | [$mg.l^{-1}$] | 8,51E-04 | Regional PEC in surface water (total) |
| PECsurfacewater (dissolved) | [$mg.l^{-1}$] | 8,51E-04 | Regional PEC in surface water (dissolved) |
| PECair | [$mg.m^{-3}$] | 1,32E-04 | Regional PEC in air (total) |
| PECagr.soil | [$mg.kg_{wwt}^{-1}$] | 1,27E-05 | Regional PEC in agricultural soil (total) |
| PECporewater agr.soil | [$mg.l^{-1}$] | 3,65E-05 | Regional PEC in pore water of agricultural soils |
| PECnat.soil | [$mg.kg_{wwt}^{-1}$] | 2,19E-05 | Regional PEC in natural soil (total) |
| PECind.soil | [$mg.kg_{wwt}^{-1}$] | 2,19E-05 | Regional PEC in industrial soil (total) |
| PECsediment | [$mg.kg_{wwt}^{-1}$] | 7,03E-04 | Regional PEC in sediment (total) |

# Appendix A6 Humans exposed via the environment

**( TGD On New and Existing Chemicals, chapter 2 )**

| *Parameter [Unit]* | *Symbol* |
|---|---|
| **Definitions ( for the use in this document )** | |
| definition of the unit 'kg$_{bw}$' for body weight | $kg_{bw} := 1 \cdot kg$ |
| definition of the unit 'd' for day | $d := 1 \cdot Tag$ |
| | $scenario := 1..2$ |
| | $local := 1$<br>$regional := 2$ |
| **Constants** | |
| gas - constant R | $R := 8.314 J \cdot K^{-1} \cdot mol^{-1}$ |
| **Defaults** | |
| volumefraction air in plant tissue<br>[-] | $Fair_{plant} := 0.3$ |
| volumefraction water in planttissue<br>[-] | $Fwater_{plant} := 0.65$ |
| volumefraction lipids in plant tissue<br>[-] | $Flipid_{plant} := 0.01$ |
| bulk density of plant tissue<br>[$kg_{wet\ plant} * m_{plant}^{-3}$] | $RHO_{plant} := 700 \cdot kg \cdot m^{-3}$ |
| leaf surface area<br>[$m^2$] | $AREA_{plant} := 5 \cdot m^2$ |
| conductance (0.001 m*s$^{-1}$)<br>[m*d$^{-1}$] | $g_{plant} := 0.001 \cdot m \cdot s^{-1}$ |
| shoot volume<br>[$m^3$] | $V_{leaf} := 0.002 \cdot m^3$ |
| transpiration stream<br>[$m^3$*d$^{-1}$] | $Q_{transp} := 1 \cdot 10^{-3} \cdot m^3 \cdot d^{-1}$ |
| correction exponent for differences between plant lipids and octanol<br>[-] | $b := 0.95$ |
| growth rate constant for dilution by growth<br>[d$^{-1}$] | $kgrowth_{plant} := 0.035 \cdot d^{-1}$ |
| pseudo-first order rate constant for metabolism in plants<br>[d$^{-1}$] | $kmetab_{plant} := 0 \cdot d^{-1}$ |
| pseudo-first order rate constant for photolysis in plants<br>[d$^{-1}$] | $kphoto_{plant} := 0 \cdot d^{-1}$ |

concentration in meat and milk

| | |
|---|---|
| daily intake of grass [$kg_{wet\ grass}*d^{-1}$] | $IC_{grass} := 67.6 \cdot kg \cdot d^{-1}$ |
| daily intake of soil [$kg_{wet\ soil}*d^{-1}$] | $IC_{soil} := 0.46 \cdot kg \cdot d^{-1}$ |
| daily intake of air [$m_{air}^3*d^{-1}$] | $IC_{air} := 122 \cdot m^3 \cdot d^{-1}$ |
| daily intake of drinkingwater [$l*d^{-1}$] | $IC_{drw} := 55 \cdot l \cdot d^{-1}$ |

*daily intake for human*

| | |
|---|---|
| daily intake for the several pathways [$kg_{chem}*d^{-1}$] or [$m^3*d^{-1}$] | $IH_{drw} := 2 \cdot l \cdot d^{-1}$ |
| | $IH_{fish} := 0.115 \cdot kg \cdot d^{-1}$ |
| | $IH_{stem} := 1.2 \cdot kg \cdot d^{-1}$ |
| | $IH_{root} := 0.384 \cdot kg \cdot d^{-1}$ |
| | $IH_{meat} := 0.301 \cdot kg \cdot d^{-1}$ |
| | $IH_{milk} := 0.561 \cdot kg \cdot d^{-1}$ |
| | $IH_{air} := 20 \cdot m^3 \cdot d^{-1}$ |
| bioavailability through route of intake [-] | $BIO_{inh} := 0.75$ |
| | $BIO_{oral} := 1.0$ |
| average body weight of human [kg] | $BW := 70 \cdot kg_{bw}$ |

## Input

### *chemical properties*

| | |
|---|---|
| octanol-water partitioning coefficient [-] | $\log K_{OW} := 0.18$ <br> $K_{OW} := 10^{\log K_{OW}}$ |
| Henry - partitioning coefficient [Pa*m$^3$*mol$^{-1}$] | $HENRY := 6.52 \cdot Pa \cdot m^3 \cdot mol^{-1}$ |
| air-water partitioning coefficient [-] | $K_{air\_water} := 0.003$ |
| fraction of the chemical associated with aerosol particles [-] | $F_{ass\_aer} := 4.545 \cdot 10^{-9}$ |
| half-life for biodegration in surface water [d] | $DT_{50\_bio\_water} := 15 \cdot d$ |

### *environmental concentrations*

| | |
|---|---|
| annual average local PEC in surface water (dissolved) [$mg_{chem}$ * $l_{water}^{-1}$] | $PEClocal_{water\_ann} := 0.23 \cdot mg \cdot l^{-1}$ |
| annual average local PEC in air (total) [$mg_{chem}$ * $m_{air}^{-3}$] | $PEClocal_{air\_ann} := 0.035 \cdot mg \cdot m^{-3}$ |
| local PEC in grassland (total), averaged over 180 days [$mg_{chem}$ * $kg_{soil}^{-1}$] | $PEClocal_{grassland} := 0.0053 \cdot mg \cdot kg^{-1}$ |
| local PEC in porewater of agriculture soil [$mg_{chem}$ * $l_{porewater}^{-1}$] | $PEClocal_{agr\_soil\_porew} := 0.0109 \cdot mg \cdot l^{-1}$ |
| local PEC in porewater of grassland [$mg_{chem}$ * $l_{porewater}^{-1}$] | $PEClocal_{grassland\_porew} := 0.0154 \cdot mg \cdot l^{-1}$ |
| local PEC in groundwater under agriculture soil [$mg_{chem}$ * $l_{water}^{-1}$] | $PEClocal_{grw} := 0.0109 \cdot mg \cdot l^{-1}$ |
| regional PEC in surface water (dissolved) [$mg_{chem}$ * $l_{water}^{-1}$] | $PECregional_{water} := 0.85 \cdot 10^{-3} \cdot mg \cdot l^{-1}$ |
| regional PEC in air (total) [$mg_{chem}$ * $m_{air}^{-3}$] | $PECregional_{air} := 1.3 \cdot 10^{-4} \cdot mg \cdot m^{-3}$ |
| regional PEC in agriculture soil (total) [$mg_{chem}$*$kg_{soil}^{-1}$ | $PECregional_{agr\_soil} := 1.3 \cdot 10^{-5} \cdot mg \cdot kg^{-1}$ |
| regional PEC in porewater of agriculture soils [$mg_{chem}$*$l_{water}^{-1}$ | $PECregional_{agr\_soil\_porew} := 3.65 \cdot 10^{-5} \cdot mg \cdot l^{-1}$ |

Definition of the concentrations used for indirect exposure

$C_{water_{local}} := PEClocal_{water\_ann}$

$C_{air_{local}} := PEClocal_{air\_ann}$

$C_{grassland_{local}} := PEClocal_{grassland}$

$C_{agr\_porew_{local}} := PEClocal_{agr\_soil\_porew}$

$C_{grass\_porew_{local}} := PEClocal_{grassland\_porew}$

$C_{grw_{local}} := PEClocal_{grw}$

$C_{water_{regional}} := PECregional_{water}$

$C_{air_{regional}} := PECregional_{air}$

$C_{grassland_{regional}} := PECregional_{agr\_soil}$

$C_{agr\_porew_{regional}} := PECregional_{agr\_soil\_porew}$

$C_{grass\_porew_{regional}} := PECregional_{agr\_soil\_porew}$

$C_{grw_{regional}} := PECregional_{agr\_soil\_porew}$

bioconcentration in fish

bioconcentration factor for fish
[$m_{water}^{3}*kg_{chem}^{-1}$]

$$BCF_{fish} := 10^{0.85 \cdot \log K_{OW} - 0.7} \cdot l \cdot kg^{-1}$$

modified equation for logKow > 6

$$BCF_{fish} := wenn\left[\log K_{OW} > 6, \left[-0.278 \left(\log K_{OW}\right)^2 + 3.38 \cdot \log K_{OW} - 5.94\right] \cdot l \cdot kg^{-1}, BCF_{fish}\right]$$

$$C_{fish_{scenario}} := BCF_{fish} \cdot C_{water_{scenario}}$$

bioconcentration in plants

$$K_{plant\_water} := Fwater_{plant} + Flipid_{plant} \cdot K_{OW}^{b}$$

$$Croot_{agr\_plant_{scenario}} := \frac{K_{plant\_water} \cdot C_{agr\_porew_{scenario}}}{RHO_{plant}}$$

$$TSCF := 0.784 e^{\frac{-\left(\log K_{OW} - 1.78\right)^2}{2.44}}$$

remark: for $\log K_{OW}$ out of the range from -0.5 to 4.5
the TSCF is limited by the values for $\log K_{OW}$ = -0.5 resp. 4.5

$$TSCF := wenn\left(\log K_{OW} < -0.5, 0.903, TSCF\right)$$

$$TSCF := wenn\left(\log K_{OW} > 4.5, 0.832, TSCF\right)$$

$$K_{leaf\_air} := Fair_{plant} + \frac{K_{plant\_water}}{K_{air\_water}}$$

$$kelim_{plant} := kmetab_{plant} + kphoto_{plant}$$

$$\alpha := \frac{AREA_{plant} \cdot g_{plant}}{K_{leaf\_air} \cdot V_{leaf}} + kelim_{plant} + kgrowth_{plant}$$

$$\beta_{agr\_plant_{scenario}} := C_{agr\_porew_{scenario}} \cdot TSCF \cdot \frac{Q_{transp}}{V_{leaf}} + \left(1 - F_{ass\_aer}\right) \cdot C_{air_{scenario}} \cdot g_{plant} \cdot \frac{AREA_{plant}}{V_{leaf}}$$

$$C_{leaf\_crops_{scenario}} := \frac{\beta_{agr\_plant_{scenario}}}{\alpha \cdot RHO_{plant}}$$

$$\beta_{grass\_plant_{scenario}} := C_{grass\_porew_{scenario}} \cdot TSCF \cdot \frac{Q_{transp}}{V_{leaf}} + \left(1 - F_{ass\_aer}\right) \cdot C_{air_{scenario}} \cdot g_{plant} \cdot \frac{AREA_{plant}}{V_{leaf}}$$

$$C_{leaf\_grass_{scenario}} := \frac{\beta_{grass\_plant_{scenario}}}{\alpha \cdot RHO_{plant}}$$

purification of drinking water

system may defined dependent from the aerobic biodegradation

$$system := wenn\left(DT_{50\_bio\_water} < 10 \cdot d, 0, 1\right)$$

select a column on dependence from log $K_{OW}$

$$FIndex := wenn\left(logK_{OW} < 4, 0, wenn\left(logK_{OW} > 5, 2, 1\right)\right)$$

$$Fpur_{logKow} := \begin{bmatrix} 1 & \frac{1}{4} & \frac{1}{16} \\ 1 & \frac{1}{2} & \frac{1}{4} \end{bmatrix}$$

$$Fpur := \frac{Fpur_{logKow_{system, FIndex}}}{wenn\left(HENRY > 100 \cdot Pa \cdot m^3 \cdot mol^{-1}, 2, 1\right)}$$

$$C_{drw_{scenario}} := wenn\left[C_{grw_{scenario}} > \left(C_{water_{scenario}} \cdot Fpur\right), C_{grw_{scenario}}, C_{water_{scenario}} \cdot Fpur\right]$$

Biotransfer to meat and milk

$$BTF_{meat} := 10^{-7.6 + logK_{OW}} \cdot kg^{-1} \cdot d$$

remark: for $logK_{OW}$ out of the range from 1.5 to 6.5

the $BTF_{meat}$ is limited by the values for $logK_{OW}$ = 1.5 resp. 6.5

$$BTF_{meat} := wenn\left(logK_{OW} < 1.5, 7.943 \cdot 10^{-7} \cdot kg^{-1} \cdot d, BTF_{meat}\right)$$

$$BTF_{meat} := wenn\left(logK_{OW} > 6.5, 0.07943 \cdot kg^{-1} \cdot d, BTF_{meat}\right)$$

$$C_{meat_{scenario}} := BTF_{meat} \cdot \left(\begin{array}{l} C_{leaf\_grass_{scenario}} \cdot IC_{grass} + C_{grassland_{scenario}} \cdot IC_{soil} \cdots \\ + C_{air_{scenario}} \cdot IC_{air} + C_{drw_{scenario}} \cdot IC_{drw} \end{array}\right)$$

$$BTF_{milk} := 10^{-8.1 + \log K_{OW}} \cdot kg^{-1} \cdot d$$

remark: for $\log K_{OW}$ out of the range from 3 to 6.5

the $BTF_{milk}$ is limited by the values for $\log K_{OW}$ = 1.5 resp. 6.5

$$BTF_{milk} := wenn\left(\log K_{OW} < 3, 7.943\,10^{-6} \cdot kg^{-1} \cdot d, BTF_{milk}\right)$$

$$BTF_{milk} := wenn\left(\log K_{OW} > 6.5, 0.02512\,kg^{-1} \cdot d, BTF_{milk}\right)$$

$$C_{milk_{scenario}} := BTF_{milk} \left( \begin{array}{l} C_{leaf\_grass_{scenario}} \cdot IC_{grass} + C_{grassland_{scenario}} \cdot IC_{soil} \cdots \\ + C_{air_{scenario}} \cdot IC_{air} + C_{drw_{scenario}} \cdot IC_{drw} \end{array} \right)$$

## total daily intake for human

daily dose through intake of several pathways

[$kg_{chem}*kg_{bw}^{-1}*d^{-1}$]

$$DOSE_{drw_{scenario}} := \frac{C_{drw_{scenario}} \cdot IH_{drw}}{BW}$$

$$DOSE_{air_{scenario}} := \frac{C_{air_{scenario}} \cdot IH_{air} \cdot BIO_{inh}}{BW \cdot BIO_{oral}}$$

$$DOSE_{stem_{scenario}} := \frac{C_{leaf\_crops_{scenario}} \cdot IH_{stem}}{BW}$$

$$DOSE_{root_{scenario}} := \frac{Croot_{agr\_plant_{scenario}} \cdot IH_{root}}{BW}$$

$$DOSE_{meat_{scenario}} := \frac{C_{meat_{scenario}} \cdot IH_{meat}}{BW}$$

$$DOSE_{milk_{scenario}} := \frac{C_{milk_{scenario}} \cdot IH_{milk}}{BW}$$

$$DOSE_{fish_{scenario}} := \frac{C_{fish_{scenario}} \cdot IH_{fish}}{BW}$$

*total daily intake for human*

total daily intake for human as sum of each pathway

[$kg_{chem}*kg_{bw}^{-1}*d^{-1}$]

$$DOSE_{tot_{scenario}} := DOSE_{drw_{scenario}} + DOSE_{fish_{scenario}} + DOSE_{stem_{scenario}} + DOSE_{root_{scenario}} \cdots + DOSE_{meat_{scenario}} + DOSE_{milk_{scenario}} + DOSE_{air_{scenario}}$$

relative doses of specific different pathway (%)

$$RDOSE_{drw_{scenario}} := \frac{DOSE_{drw_{scenario}} \cdot 100\%}{DOSE_{tot_{scenario}}}$$

$$RDOSE_{air_{scenario}} := \frac{DOSE_{air_{scenario}} \cdot 100\%}{DOSE_{tot_{scenario}}}$$

$$RDOSE_{stem_{scenario}} := \frac{DOSE_{stem_{scenario}} \cdot 100\%}{DOSE_{tot_{scenario}}}$$

$$RDOSE_{root_{scenario}} := \frac{DOSE_{root_{scenario}} \cdot 100\%}{DOSE_{tot_{scenario}}}$$

$$RDOSE_{meat_{scenario}} := \frac{DOSE_{meat_{scenario}} \cdot 100\%}{DOSE_{tot_{scenario}}}$$

$$RDOSE_{milk_{scenario}} := \frac{DOSE_{milk_{scenario}} \cdot 100\%}{DOSE_{tot_{scenario}}}$$

$$RDOSE_{fish_{scenario}} := \frac{DOSE_{fish_{scenario}} \cdot 100\%}{DOSE_{tot_{scenario}}}$$

## Results of calculation

$DOSE_{tot_{local}} = 0.014427 \cdot \frac{mg}{kg_{bw} \cdot d}$

$DOSE_{tot_{regional}} = 5.344029 \cdot 10^{-5} \cdot \frac{mg}{kg_{bw} \cdot d}$

$RDOSE_{drw_{local}} = 45.549912 \cdot \%$

$RDOSE_{drw_{regional}} = 45.444577 \cdot \%$

$RDOSE_{air_{local}} = 51.986313 \cdot \%$

$RDOSE_{air_{regional}} = 52.127604 \cdot \%$

$RDOSE_{stem_{local}} = 1.318636 \cdot \%$

$RDOSE_{stem_{regional}} = 1.322194 \cdot \%$

$RDOSE_{root_{local}} = 0.393638 \cdot \%$

$RDOSE_{root_{regional}} = 0.35585 \cdot \%$

$RDOSE_{meat_{local}} = 4.183916 \cdot 10^{-4} \cdot \%$

$RDOSE_{meat_{regional}} = 4.180008 \cdot 10^{-4} \cdot \%$

$RDOSE_{milk_{local}} = 0.007798 \cdot \%$

$RDOSE_{milk_{regional}} = 0.007791 \cdot \%$

$RDOSE_{fish_{local}} = 0.743285 \cdot \%$

$RDOSE_{fish_{regional}} = 0.741566 \cdot \%$

## Appendix A7 All purpose adhesives, SCIES modelling

Substance:
Methylacetat

CAS:
79-20-9

Computer model used:
EPA-model: SCIES
(Screening-Level Consumer Inhalation Exposure Software)

Category of consumer products:
All purpose adhesive

Results:
User potential dose rate from inhalation:

| | | |
|---|---|---|
| | 23157 | Milligramm/yr |
| = | 63.44 | Milligramm/day |
| = | 1.06 | Milligramm/kg b.w. and day |

Peak:
(Concentration in zone of release during period of use)
38.97 $mg/m^3$

Generic Product

| | | | |
|---|---|---|---|
| Annual Frequency of Use: | 260 | Events/Year | |
| Mass of Product: | | 10.000 | grams |
| Duration of Use: | | 1.000 | Hours |
| Zone 1 Volume: | | 60.000 | cubic meters |
| Whole House Volume : | 292.000 | cubic meters | |
| House Air Exchange Rate: | 0.200 | room air exchange/hr | |
| User Inhalation Rate: | 1.300 | cubic meter/hr (during use) | |
| Non-User Inhalation Rate: | | 1.100 | cubic meter/hr (& User after use) |
| Molecular Weight: | | 74.080 | g/mole |
| Vapor Pressure: | | 1.628E+02 | torr |
| Weight Fraction: | | 0.500 | |
| Starting Time: | | 12:00 | NOON |

OUTPUT SUMMARY

Evaporation Time: 0.018 Hours
Release Time: 1.000 Hours (Duration of Exposure)
Duration Following Each Use: 33.000 Hours
Interval Between Uses: 34.000 Hours

User Potential Dose Rate From Inhalation: 23156.918 mg/yr
Non-User Potential Dose Rate From Inhalation: 21806.490 mg/yr

| | Peak ($mg/m^3$) | Average ($mg/m^3$) |
|---|---|---|
| Concentration in zone of release | | |
| During period of use | 25.966 | 38.964 |
| During period after use | 2.602 | 34.087 |
| Concentration in Zone 2 | | |
| During period of use | 3.628 | 8.593 |
| During period after use | 2.274 | 12.151 |
| Concentration to which User and Non-User are exposed | | |
| Person Using Product (user) | 2.243 | 38.964 |
| Person Not Using Procut (non-user) | 2.243 | 38.964 |

HOURLY ACTIVITY PATTERN

User: 1 1 1 1 1 1 2 3 4 5 4 2 4 6 7 4 2 2 7 4 4 4 1 1
Non-User: 1 1 1 1 1 1 1 3 2 4 4 2 4 7 6 4 2 2 6 4 4 4 1 1
Hour: 03 06 09 15 18 21 24

START HOUR

## Appendix A8 Carpet adhesives, SCIES modelling

Substance:
Methylacetat

CAS:
79-20-9

Computer model used:
EPA-model: SCIES
(Screening-Level Consumer Inhalation Exposure Software)

Category of consumer products:
Carpet adhesives

Results:
User potential dose rate from inhalation:

| | | |
|---|---|---|
| | 24978 | Milligramm/yr |
| = | 68.43 | Milligramm/day |
| = | 1.14 | Milligramm/kg b.w. and day |

Peak:
(Concentration in zone of release during period of use)
15034 mg/$m^3$

Generic Product

| | | | |
|---|---|---|---|
| Annual Frequency of Use: | 1 | Events/Year | |
| Mass of Product: | | 18750.000 | grams |
| Duration of Use: | | 2.000 | Hours |
| Zone 1 Volume: | | 60.000 | cubic meters |
| Whole House Volume: | 292.000 | cubic meters | |
| House Air Exchange Rate: | 0.500 | room air exchanges/hr | |
| User Inhalation Rate: | 1.300 | cubic meter/hr (during use) | |
| Non-User Inhalation Rate: | | 1.100 | cubic meter/hr (& User after use) |
| Molecular Weight: | | 74.080 | g/mole |
| Vapor Pressure: | | 1.628E+02 | torr |
| Weight Fraction: | | 0.200 | |
| Starting Time: | 12:00 | NOON | |

OUTPUT SUMMARY

Evaporation Time: 0.018 Hours
Release Time: 2.000 Hours (Duration of Exposure)
Duration Following Each Use: 8758.000 Hours
Interval Between Uses: 8760.000 Hours

User Potential Dose Rate From Inhalation: 24978.261 mg/yr
Non-User Potential Dose Rate From Inhalation: 20587.789 mg/yr

| | Peak ($mg/m^3$) | Average ($mg/m^3$) |
|---|---|---|
| Concentration in zone of release | | |
| During period of use | 10976.142 | 15033.941 |
| During period after use | 2.072 | 12912.809 |
| Concentration in Zone 2 | | |
| During period of use | 3062.350 | 6028.006 |
| During period after use | 1.808 | 6296.382 |
| Concentration to which User and Non-User are exposed | | |
| Person Using Product (user) | 2.137 | 11761.425 |
| Person Not Using Product (non-user) | 2.137 | 11761.425 |

HOURLY ACTIVITY PATTERN

User: 1 1 1 1 1 1 2 3 4 5 4 2 4 6 7 4 2 2 7 4 4 4 1 1
Non-User: 1 1 1 1 1 1 1 3 2 4 4 2 4 7 6 4 2 2 6 4 4 4 1 1
Hour: 03 06 09 15 18 21 24

START HOUR

## Appendix A9 Parquet adhesives, SCIES modelling

Substance:
Methylacetat

CAS:
79-20-9

Computer model used:
EPA-model: SCIES
(Screening-Level Consumer Inhalation Software)

Category of consumer products:
Parquet adhesives

Results:
User potential dose rate from inhalation:

| | | |
|---|---|---|
| | 20661 | Milligramm/yr |
| = | 56.6 | Milligramm/day |
| = | 0.94 | Milligramm/kg b.w. and day |

Peak:
(Concentration in zone of release during period of use)
7855 mg/$m^3$

Generic Product

| | | | |
|---|---|---|---|
| Annual Frequency of Use: | 1 | Events/Year | |
| Mass of Product: | | 25000.000 | grams |
| Duration of Use: | | 4.000 | Hours |
| Zone 1 Volume: | | 60.000 | cubic meters |
| Whole House Volume: | 292.000 | cubic meters | |
| House Air Exchange Rate: | 0.500 | room air exchanges/hr | |
| User Inhalation Rate: | 1.300 | cubic meter/hr (during use) | |
| Non-User Inhalation Rate: | | 1.100 | cubic meter/hr (& User after use) |
| Molecular Weight: | | 74.080 | g/mole |
| Vapor Pressure: | | 1.628E+02 | torr |
| Weight Fraction: | | 0.130 | |
| Starting Time: | | 12:00 | NOON |

OUTPUT SUMMARY

Evaporation Time: 0.018 Hours
Release Time: 4.000 Hours (Duration of Exposure)
Duration Following Each Use: 8756.000 Hours
Interval Between Uses: 8760.000 Hours

User Potential Dose Rate From Inhalation: 20660.621 mg/yr
Non-User Potential Dose Rate From Inhalation: 15829.959 mg/yr

| | Peak ($mg/m^3$) | Average ($mg/m^3$) |
|---|---|---|
| Concentration in zone of release | | |
| During period of use | 6038.298 | 7857.382 |
| During period after use | 1.211 | 6885.083 |
| Concentration in Zone 2 | | |
| During period of use | 2366.215 | 3935.666 |
| During period after use | 1.092 | 3967.880 |
| Concentration to which User and Non-User are exposed | | |
| Person Using Product (user) | 1.643 | 5096.617 |
| Person Not Using Prodcut (non-user) | 1.643 | 5096.617 |

HOURLY ACTIVITY PATTERN

User: 1 1 1 1 1 1 2 3 4 5 4 2 4 6 7 4 2 2 7 4 4 4 1 1
Non-User: 1 1 1 1 1 1 1 3 2 4 4 2 4 7 6 4 2 2 6 4 4 4 1 1
Hour: 03 06 09 15 18 21 24

START HOUR

# Appendix A10 Nail varnish removers

```
Substance: Methyl acetate
Use: General Product

Computer model used: EPA-SCIES

Category of consumer products:
Nail varnish remover

Results:
User potential dose rate:       200 mg/yr
=       0.5 mg/day
=       0.008 mg/kg/day

Peak
Concentration in zone of release after period of use:        0.029 mg/m3


Annual Frequency of Use :         365 Events/Year
Mass of Product                 0.250 grams
Duration of Use                 0.250 Hours
Zone 1 Volume                  15.000 cubic meters
Whole House Volume            292.000 cubic meters
House Air Exchange Rate :       0.200 room air exchanges/hr
User Inhalation Rate            1.300 cubic meter/hr (during use)
Non-User Inhalation Rate:       1.100 cubic meter/hr (& User after use)
Molecular Weight               74.080 g/mole
Vapor Pressure              1.600E-02 torr
Weight Fraction                 0.150
Starting Time                   12:00 NOON


OUTPUT SUMMARY
Evaporation Time:            123.205 Hours
Release Time:                     24 Hours (Use Interval)
Duration Following Each Use:  23.750 Hours
Interval Between Uses:        24.000 Hours

  User Potential Dose Rate From Inhalation:              200.264 mg/yr
  Non-User Potential Dose Rate From Inhalation  :        200.094 mg/yr
-------------------------------------------------------------------------
                                          Average (mg/m3)   Peak (mg/m3)
                                                            --------------
----------
  Concentration in zone of release
         During period of use                   0.009           0.012
         During period after use                0.034           0.039

  Concentration in Zone 2
         During period of use                   0.000           0.001
         During period after use                0.021           0.026

  Concentration to which User and Non-User are exposed
         Person Using Product (user)            0.021           0.039
         Person Not Using Product (non-user)    0.021           0.039
```

European Commission

**EUR 20783 EN** **European Union Risk Assessment Report methyl acetate, Volume 34**

*Editors: S.J. Munn, R. Allanou, K. Aschberger, F. Berthault, J. de Bruijn, C. Musset, S. O'Connor, S. Pakalin, G. Pellegrini, S. Scheer, S. Vegro.*

Luxembourg: Office for Official Publications of the European Communities

2003 –VIII pp., 158 pp. – 17.0 x 24.0 cm

Environment and quality of life series

The report provides the comprehensive risk assessment of the substance methyl acetate. 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 humans and the environment, laid down in Commission Regulation (EC) No. 1488/94.

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

The human health risk assessment for methyl acetate concludes that there is concern for workers. For consumers and humans exposed via the environment the risk assessment concludes that risks are not expected.

The environmental risk assessment for methyl acetate concludes that there is at present no concern for the atmosphere, the aquatic ecosystem, the terrestrial ecosystem or for microorganisms in the sewage treatment plant.

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

The mission of the JRC is to provide customer-driven scientific and technical support for the conception, development, implementation and monitoring of EU policies. As a service of the European Commission, the JRC functions as a reference centre of science and technology for the Union. Close to the policy-making process, it serves the common interest of the Member States, while being independent of special interests, private or national.

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

European Union Risk Assessment Report

**methyl acetate**

CAS No: 79-20-9 EINECS No: 201-185-2

Series: 1st Priority List Volume: 34