Institute for Health and Consumer Protection

European Chemicals Bureau

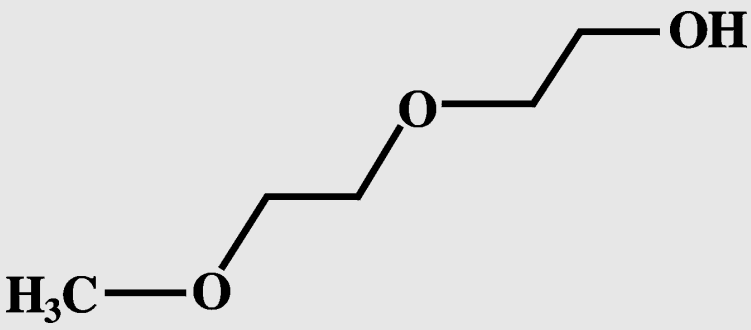
Existing Substances

European Union Risk Assessment Report

CAS No.: 111-77-3

EINECS No.: 203-906-6

2-(2-methoxyethoxy)ethanol



1st Priority List

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RISK ASSESSMENT

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RISK ASSESSMENT

Final report, July 1999

The Netherlands

Rapporteur for the risk evaluation of 2-(2-methoxyethoxy)ethanol is the Ministry of Housing, Spatial Planning and the Environment (VROM) in consultation with the Ministry of Social Affairs and Employment (SZW) and the Ministry of Public Health, Welfare and Sport (VWS). Responsible for the risk evaluation and subsequently for the contents of this report is the rapporteur.

The scientific work on this report has been prepared by the Netherlands Organisation for Applied Scientific Research (TNO) and the National Institute of Public Health and Environment (RIVM), by order of the rapporteur.

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Review of report by MS Technical Experts finalised:	**September, 1997**
Final Report:	**July, 1999**

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.

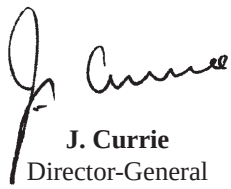
The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[2], which is supported by a technical guidance document[3]. Normally, the "Rapporteur" and individual companies producing, importing and/or using the chemicals work closely 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 risks from exposure to chemicals overall.

H.J. Allgeier
Director-General
Joint Research Centre



J. Currie
Director-General
Environment, Nuclear Safety and Civil Protection

[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. 111-77-3
EINECS-No. 203-906-6
IUPAC name 2-(2-methoxyethoxy)ethanol

Environment

( ) i) There is need for further information and/or testing
(X) ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied
( ) iii) There is a need for limiting the risks: risk reduction measures which are already being applied shall be taken into account

Consumers

( ) i) There is need for further information and/or testing
( ) ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied
(X) iii) There is a need for limiting the risks: risk reduction measures which are already being applied shall be taken into account

Conclusion (iii) is reached because:
- the risk assessment indicates a possible concern for consumers through the uses of paint or paint stripper containing the substance.

Workers

( ) i) There is need for further information and/or testing
( ) ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied
(X) iii) There is a need for limiting the risks: risk reduction measures which are already being applied shall be taken into account

Conclusion (iii) is reached because:
- based on the information available with respect to anticipated effects after occupational dermal exposure (repeated dose studies) risk reducing measures should be taken for occupational exposure scenarios 1, 2 and 4.
- based on the information available with respect to anticipated effects after occupational dermal exposure (developmental effects) risk reducing measures should be taken for occupational exposure scenario 2 (production of products containing DEGME) and 4 (manual application of products containing DEGME).

It might be possible that in some industrial premises these worker protection measures are already applied.

In relation to all other potential adverse effects and the worker population it is concluded that based on the available information at present no further information/testing on the substance is needed.

CONTENTS

EUSES calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.ei.jrc.it.

IUCLID Data Sheet can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.ei.jrc.it.

1 GENERAL SUBSTANCE INFORMATION

Identification of the substance

CAS-No.:	111-77-3
EINECS-No.:	203-906-6
IUPAC name:	2-(2-methoxyethoxy)ethanol
Synonyms:	DEGME diethylene glycol methyl ether diglycol monomethyl ether 3,6-Dioxa-1-heptanol Dowanol DM ethanol, 2,2'oxybis-, monomethyl ether ethanol, 2-(2-methoxyethoxy)- (6CI, 8CI, 9CI) Emkanol MDG ethylene diglycol monomethyl ether 1-hydroxy-3,6-dioxaheptan beta-Methoxy-beta'-hydroxydiethyl ether methoxydiglycol methyl carbitol methyldiethoxol methyldiglykol methyl diglycol ether methyl dioxitol Poly-Solv DM
Molecular formula:	$C_5 H_{12} O_3$
Structural formula:	CH_3-O-CH_2-CH_2-O-CH_2-CH_2-OH
Molecular weight:	120.2

Purity/impurities, additives

Purity:	99-100%
Impurity:	ethane-1,2-diol (0-0.5%); water (0-0.1%); 2-methoxyethanol (0-0.4%); 2(2-(2-methoxyethoxy)ethoxy)ethanol (0-0.2%)
Additives:	2,6-di-tert-butyl-p-cresol or butylated hydroxytoluene as anti-oxidant (50-150 ppm)(added only to FSII grades)

Physico-chemical properties

Physical state:	liquid
Melting point:	-65 °C
Boiling point:	190-196 °C
Relative density:	1.018-1.022 g/cm^3
Vapour pressure:	≤ 0.3 (20 °C); 0.24 (25 °C) hPa
Surface tension:	34.8 mN/m at 25 °C
Water solubility:	miscible
Partition coefficient n-octanol/water:	-0.682 (log value)
Granulometry:	not relevant

Conversion factors	
(101 kPa, 20 °C):	1 ppm = 5.01 mg/m^3; 1 mg/m^3 = 0.20 ppm
Flammability:	none, based on flashpoint (88-91 °C), autoflammability temperature (215 °C) and structural formula and thermodynamic properties
Explosive propert.:	none, based on structural formula and thermodynamic properties
Oxidising propert.:	none, based on structural formula and thermodynamic properties

These data were taken from Hoechst AG 1992, Hoechst AG 1993, Windholz 1982, Windholz 1982, Hansch and Leo (1979), BASF AG 1994, ICI Product Safety Data Sheet 1994, BASF Unpublished Report and John Wiley and Sons (1983).

Classification

Classification and labelling according to the 25th ATP of Directive 67/548/EEC:
Classification: Repr. Cat 3; R 63
Labelling: Xn R63 S(2-)36/37

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

The substance 2-(2-methoxyethoxy)ethanol (hereafter referred to as DEGME) belongs to the group of glycol ethers, which are mainly used as co-solvents. During 1990-1993 the annual production of DEGME in Europe was 20,000 tonnes. The annual tonnage put on the European market was about 9000 tonnes. The remaining 11,000 tonnes is exported outside the EU. No data on import are given. The EU production larger than 1,000 tonnes per year was located at six different sites (see **Table 2.1**). DEGME is produced by the reaction of ethylene oxide and methanol with an alkalic katalysator.

Table 2.1 Production sites of DEGME (1990-1993).

Company	Location
ICI Chemicals & Polymers Ltd.[1]	Wilton (Cleveland), United Kingdom
DOW Benelux N.V.[2]	Terneuzen, The Netherlands
Hoechst AG	Frankfurt/Main, Germany
BASF AG	Ludwigshafen, Germany
Enichem	Priolo (Sicily), Italy
ICI C&P France SA[3]	Choques, France

[1] since 1-2-1995 Union Carbide acquired ICI's production unit for glycolethers.
[2] DOW Benelux N.V. has stopped production and import of DEGME since 1992.
[3] since 1-2-1995 contract manufacturer for Union Carbide

2.2 USE PATTERN

Table 2.2 shows the industrial and use categories of DEGME for the European market.

Table 2.2 Industrial and use categories of DEGME.

Industrial category	IC no.	Use category	UC no.
- Fuel industry	9	Fuel additive (jet fuel anti-icing agent)	28
		Fuel additives (e.g. diluent for hydraulic brake fluids)	28
- Chemical industry: chemicals used in synthesis	3	Intermediates	33
- Chemical industry: basic chemicals	2	Solvents (e.g. processing solvent for manufacturing of pharmaceuticals)	48
- Paints, lacquers and varnishes industry	14	Solvents (e.g. diluent for metal salt dryers added to oil based paints)	48
- Others	15	Cleaning/washing agents and disinfectants (e.g.solvent in aqueous floor polish)	9

The main use of DEGME is as an anti-icing agent in jet fuel. DEGME is further used as chemical intermediate, basic chemical (processing solvent) and solvent in paints or floor polish. Paragraph 4.1.1.0 contains more detailed information on the usages of DEGME. Quantitative estimates indicate that around 75% is used as anti-icing agent in jet fuel, 15% is divided over various use categories and the remaining 10% is used as chemical intermediate (Andries 1996). More detailed figures on other categories than the anti-icing agent and chemical intermediate are currently not available.

3 ENVIRONMENT

3.1 EXPOSURE ASSESSMENT

3.1.0 General

DEGME may be released into the environment during its production and other life cycle steps. Emission to water is expected to be the most important entry route of DEGME. General characteristics of DEGME which are relevant for the exposure assessment are discussed below:

a) Degradation

Hydrolysis
No experimental data are available on hydrolysis. However, DEGME is not expected to hydrolyse based on the absence of hydrolysable groups (Lyman *et al.* 1990).

Photodegradation
If DEGME is present in ambient air it is expected to exist almost entirely in the vapour phase, based on a vapour pressure of 0.24 hPa at 25 °C, where vapour phase reactions with photochemically produced hydroxyl radicals may be important. A QSAR-method (Atkinson 1985) is applied for a first estimation for primary transformation rates. The overall OH rate constant for DEGME has been estimated to be $2.44 \cdot 10^{-11}$ cm^3/molecule·second at 25 °C (74). The estimated value corresponds to an atmospheric half-life of about 16 hours at an atmospheric concentration of $5 \cdot 10^5$ hydroxyl radicals molecule/cm^3 (74).
Since DEGME does not adsorb ultraviolet radiaton within the solar spectrum, direct photolysis in the atmosphere is not expected to occur (Kligman 1972).

Biodegradation
The available aerobic biodegradation test results for DEGME are summarised in **Table 3.1**.
Although most tests were carried out according to (international) standard test guidelines, sometimes important information about test conditions and results is lacking (summarised data only). Nevertheless, the total set of information available is regarded as being sufficient to draw a conclusion on the degradation potential of DEGME.

Ready biodegradability tests

a) BOD5-tests
The test results of three BOD5-tests were not consistent with each other. In the first test, DEGME was shown to be biodegradable (BOD5/COD > 0.5). However, no information was available on the concentration of inoculum and whether this inoculum was adapted or non-adapted. For that reason no conclusion could be drawn from this test on the readily biodegradibility of DEGME. In the second and third BOD5-test with non-adapted inoculum no readily biodegradation of DEGME was observed.
From the available data of the BOD5 tests it is concluded that DEGME is not readily biodegradable.

b) Closed bottle and Modified Sturm test
In the Closed Bottle test 68% of DEGME was biodegraded after 28 days. DEGME failed, however, to meet the 14-day window criterium of 60%.

Table 3.1 Biodegradation test results for DEGME.

No.	Type of test	Detection	Result	Day	Method	Conc. of TS	Conc. of inoculum	Ref.
1	BOD5-test	O_2 uptake	86 %[3] 71 % 60 %	5 5 5	Other	1 mg/l 2.5 mg/l 5 mg/l	Unknown[a]	Hoechst AG 1976
2	BOD5-test	O_2 uptake	7 %[1] 33 %[2]	5	APHA No. 219, 1971	Unknown	10 ml[d]	Bridie *et al.* 1979
3	BOD5-test	O_2 uptake	0 %[2]	5	Vaishnav & Babeu, 1986	Unknown	Unknown[b]	Niemi *et al.* 1987
4	Ready test: Closed Bottle test	O_2 uptake	10 %[1] 29 % 48 % 68 %	8 15 20 28	OECD301D	3 mg/l	≤ 5 effluent ml/ltest[b]	Shell Research Limited 1982
5	Ready test: Modified Sturm test	CO2-evolution	10,17 %[1*] 45,70 % 60,80 % 77,89 %	7 15 20 28	OECD301B	20 mg/l	≤ 30 SS mg/l[c]	Shell Research Limited 1982
6	Inherent biodegr.test	O_2 uptake	69 %[3] 22 %	20 10	APHA, 1971	Unknown	Unknown[b]	DOW Unpublished Report, 1975
7	Inherent biodegr.test	COD-determ.	100 %[1] 41 %	7 4	Other	650 mg/l	Unknown[c]	Hoechst AG 1976
8	Inherent biodegr.test Zahn-Wellens	DOC die away	97 %[1] 40 %	14 11	OECD302B	400 mg DOC/l	1000 mg/l[c]	BASF Unpublished Report

[a]: polyvalent inoculum diluted with natural water
[b]: (domestic) sewage
[c]: activated sludge from (industrial) STP
[d]: effluent from STP
[ss]: suspended solids

[1]: non-adapted inoculum
[2]: adapted inoculum
[3]: no information on adaptation or non-adaptation of inoculum available
*: duplicates

Two test results (duplicates) of the Modified Sturm test showed more than 75% biodegradation after 28 days. Only one of the duplicates, however, reached the 10-day window criterium of 70%.
The test results of tests no. 4 and 5 indicate that DEGME seems to be readily biodegradable. However, two out of three results failed to meet the time-window criteria. Therefore, DEGME can not be considered unequivocally as ready biodegradable.

Inherent biodegradability tests
In test no. 6 it was unclear whether it concerned a test on ready or inherent biodegradability, because no information on both concentration of test substance and inoculum was given. As a worst case approach the test was therefore regarded as an inherent biodegradability test. The results of the three inherent tests are consistent with each other. In all three tests DEGME showed more than 70% biodegradation. In tests no. 7 and 8 DEGME was completely biodegraded within 10 days. DEGME was ultimately and inherently biodegradable in these tests.

Conclusion
It can be concluded that DEGME seems to be readily degradable. However, as not all biodegradation pass levels are reached within the 10/14 time windows, DEGME is considered as ready biodegradable, but failing the 10 days window in the further risk assessment process.

b) Distribution
The Henry's Law constant of $2.9 \cdot 10^{-3}$ Pa.m^3/mol 20 °C (EUSES: see http://ecb.ei.jrc.it) indicates that volatilisation of DEGME from surface waters is not expected to be an important fate process.
The estimated K_{oc} of 0.353 l/kg indicates that DEGME will be highly mobile in soil (K_p soil of 0.007 l/kg; EUSES: see http://ecb.ei.jrc.it).
Owing to the complete miscibility of DEGME in water, physical removal may occur from air by precipitation and dissolution in clouds. However, its short atmospheric residence time suggests that wet deposition is of limited importance.

c) Accumulation
Bioaccumulation
No experimental data on bioaccumulation was available. Therefore BCF-values for fish and worm were calculated using the log K_{ow}. The estimated BCF-values amount to 1.4 (l/kg) and 3.3 (kg/kg) for, respectively, fish and worm (EUSES: see http://ecb.ei.jrc.it). Although it is realised that the relationship between BCF and log K_{ow} may not be valid at such low log K_{ow}-values it can be concluded that in view of these BCFs, DEGME is expected to have a low bioaccumulating potential in the environment.

3.1.1 Emission scenarios

3.1.1.0 General

For the environmental exposure assessment of DEGME both site-specific and generic emission scenarios are used for calculating the PEC-values in the various compartments. Site-specific scenarios are based on actual data from industry on emission patterns etc., whereas generic scenarios are primarily based on model calculations. Generic scenarios are used if no data were obtained from either industry or other bodies. An overview of the emission scenarios for DEGME is given in **Table 3.2**. For the releases of DEGME during production, two site-specific (A and B) and two generic scenarios (C and D) are used. Releases during processing and formulation are calculated using one generic scenario (E). The latter is subdivided in three subscenarios (E1, E2

Table 3.2 General overview of site-specific and generic emission scenarios for production (I) and use (II).

I
Production
Specific scenario A
Specific scenario B
Generic scenario C
Generic scenario D

II
Use: formulation/processing
Generic scenario E1: anti-icing agent in jet fuel
Generic scenario E2: basic chemical
Generic scenario E3: chemical intermediate

and E3). E1 is related to the major use category of DEGME, i.e. an anti-icing agent in jet-fuel, whereas E3 focusses on the use category of chemical intermediates. As the actual distribution of DEGME within the three remaining use categories is not clear, it is assumed ("worst case") in scenario E2 that all is used as "basic chemical", i.e. the category with the highest releases to the environment.
The exposure assessment is based on the EU-Technical Guidance Document (TGD 1996) applying the European Union System for the Evaluation of Substances (EC 1996). The input parameters and results of the EUSES calculations are shown in http://ecb.ei.jrc.it.

3.1.1.1 Local releases from production

The local releases of DEGME from production for the site-specific and generic scenarios are presented in **Table 3.3**. Specific scenario A represents a site that only produces DEGME. The plant in specific scenario B is known to both produce and process DEGME. So it has to be noted that this scenario includes releases from both production and processing for different industry- and use categories. The release amount for scenarios A and B are provided by industry. In generic scenario C a production per site of 5,000 tonnes was chosen, which is the upper limit of the IUCLID production range. Scenario C differs from generic scenario D as for the latter the actual annual production tonnage (2,500 tonnes) and also the actual main production category (1b) were provided by industry. Scenario D can thus be regarded as more realistic and site-specific (intermediate between site-specific and generic scenario).

3.1.1.2 Local releases from formulation and processing

The local release estimates for formulation and processing of DEGME for the three generic scenarios are given in **Table 3.4**. Use volumes are calculated with the percentages given in paragraphs 2.2 and 3.1.1.0 (75% for anti-icing agent in jet fuel, 15% for basic chemicals and 10%

Table 3.3 Local releases from production.

	Site-specific scenario A	Site-specific scenario B	Generic scenario C	Generic scenario D
Annual production tonnage	no data	no data	5,000	2,500
Main category	no data	no data	batch process with multi-purpose equipment (III, default)	continuous production (1b)
Number of production days	2-25	300	300 (Table B1.1)[2]	300 (Table B1.1)[2]*
Release estimates (%) air water	 no data no data	 no data no data	 0.1 (Table A1.1)[2] 0.3	 0.001 (Table A1.1)[2] 0.3
Amount released (kg/d) air water	 0.2 35	 2.7 670[1]	 17 50	 0.08 25

[1] includes releases from production and processing: 0.1 kg/d (waste water) for production and 670 kg/d (water) for processing (industry - and use categories: 9/5 (anti-icing agent), 2/48 (Basic chemicals-solvent), 3/33 (Chemical intermediate), 14/48 (Solvent in paints), 15/48 (Solvent in other products).

[2] A and B tables refer to TGD.

Table 3.4 Local releases of DEGME from formulation and processing.

	Generic scenario E1	**Generic scenario E2**	**Generic scenario E3**
Tonnage	9000 · 0.75 = 6750	9000 · 0.15 = 1350	9000 · 0.10 = 900
Main category	multi-purpose equipment (III)	non-dispersive use (III)	multi-purpose equipment (III)
Industrial category Use category	9 (Fuel industry) 5 (Anti-icing agent)	2 (Basic chemicals) 48 (Solvent)	3 (Chemicals used in synthesis) 33 (Intermediates)
Life cycle step	formulation	processing	processing
Number of days Fraction of main source	300 (Table B2.2)[1] 0.1	135 (Table B3.2)[1] 0.4	90 (Table B3.2)[1] 0.4
Release estimates (%) air water	 0.5 (Table A2.1)[1] 0.3	 5 (Table A3.2)[1] 85	 0.1 (Table A3.3)[1,2] 2
Amount released (kg/d) air water	 11.3 6.8	 200 3400	 4 80

[1] A and B tables refer to TGD. Fractions of the chemical in formulation is set at 1 (worst case).

[2] According to emmission scenario document IC-3 Chemical industry: Chemicals used in synthesis lower release factors could be used for estimating the aquatic releases, but the document does not yet give an estimate for atmospheric releases. The generic table in the TGD is chosen as a worst case approach for the current risk assessment of DEGME.

for chemical intermediate). For the local and regional calculations a tonnage of 9,000 tonnes/a, i.e. the fraction of the total annual EU production that is actually processed in the EU, is used as the basic tonnage. This approach is a deviation from the TGD where it is mentioned that only 10% of the European consumption is assumed to take place within the region. However, as there is no information from industry to support this assumption, it is felt that the figure of 9,000 tonnes is to be used as a (realistic) worst case starting-point.

The fraction of main source of 0.1 for the generic scenario E1 formulation of DEGME as anti-icing agent in jet fuel is a deviation from the TGD where a figure of 1 is mentioned. Information from industry indicated that DEGME is used as anti-icing agent mainly in army jets, as these are not supplied with a heating equipment for the fuel tanks. Therefore the main customers are different armies in- and outside Europe. Inside these armies the product is delivered to different depots where it is formulated locally. One company already stated that “their” DEGME is distributed to around 80 air bases throughout the EU. From this it is concluded that the TGD fraction of main source of 1 is unrealistically high. A fraction of main source of 0.1 is considered a better (still conservative) estimate.

3.1.1.3 Summary of local release estimates

The local release estimates for production and processing are summarised in **Table 3.5**. In all scenarios the environmental releases of DEGME to waste water are much higher than those to the atmosphere. Only in scenario E1, the formulation of DEGME in jet fuel, the emission to air is estimated to be higher than that to water. The basic chemical scenario (E2) gives the highest releases to both water and air.

Table 3.5 Summary of local release estimates.

Scenario	Amount released (kg/d)	
Specific scenario A - production	air water	0.2 35
Specific scenario B - production/processing	air water	2.7 670
Generic scenario C - production	air water	17 50
Generic scenario D - production	air water	0.08 25
Generic scenario E1 (Anti-icing agent) - formulation	air water	11.3 6.8
Generic scenario E2 (Basic chemicals) - processing	air water	200 3400
Generic scenario E3 (Chemical intermediate) - processing	air water	4 80

3.1.1.4 Regional and continental releases

The regional release includes all relevant life cycle stages of DEGME. For production it is assumed that there is only one production site in the region. The production scenario with the highest environmental releases, i.e. scenario C, is used as input for the life cycle stage production. (Note: the aquatic release of scenario B (670 kg/d) is mainly attributed to processing and therefore not used as "the highest producer"; see footnote **Table 3.3)**. The regional releases are estimated to be **294 kg/d** to air, **2300 kg/d** to waste water and **987 kg/d** directly to surface water.
Concentrations in air and water are also estimated at a continental scale (Europe) to provide inflow concentrations for the regional environment. These concentrations are not used as endpoints for exposure. The continental releases are estimated to be **41 kg/d** to air, **86 kg/d** to waste water and **37 kg/d** directly to surface water. It has to be borne in mind that in EUSES a nested version of the multi-media fate model SimpleBox is implemented and this implies that for calculating continental concentrations both regional and continental release data are taken into account.

3.1.2 Local Predicted Environmental Concentrations

3.1.2.1 Aquatic compartment

For the generic scenarios it is assumed that the amounts released to water will enter a sewage treatment plant (STP). According to the STP elimination rate tables in the TGD (Appendix II) no volatilisation or sorption to sludge occurs during sewage treatment of DEGME. During sewage treatment around 67% (DT50=0.096 days) of DEGME is expected to be removed by biodegradation.

Table 3.6 Characteristics for the PEC calculations in the aquatic environment. Site-specific information is given in bold.

	specific scenario A	**specific scenario B**	**Generic scenario E2**	**Generic scenario C, D, E1 and E3**
Biodegradation STP	no data	67%	67%	67%
Size STP (m^3/day)	**240**	**$4 \cdot 10^5$**	2000 (default)	2000 (default)
Dilution factor	**50**	**150**[1]	**50**	10 (default)

[1] based on 10-percentile flow rate of river.

The effluent concentration leaving the STP is divided by a dilution factor, resulting in the PEC_{local} in surface water. Relevant general data for the PEC calculations in the aquatic compartment are presented in **Table 3.6**. It is known that the production of DEGME and its usage as processing solvent often take place at the same site. For two production sites dilution factors of 50 and 150 were reported and the two remaining ones are known to discharge their effluent water into either sea or estuary (most probably high dilution factor, although 10 is used in currenrt RAR). Therefore for generic scenario E2 a dilution factor of 50 is considered a more realistic estimate instead of a default factor of 10.
Industry indicated that in site-specific scenario A no STP, but only a drainage system with a flow of 240 m^3/day is present.

Sewage treatment plant
The predicted environmental concentrations of DEGME in the effluent of the sewage treatment plant during emission periods are given in **Table 3.7**. For calculating this concentration the daily amount released to water is multiplied by 0.33 (percentage that is not removed from STP) and then divided by the volume of the STP.

Table 3.7 PECs in the effluent of an STP.

Scenario	**PEC (mg/l) in STP**
Specific scenario A - production	146[1]
Specific scenario B - production/processing	0.5
Generic scenario C - production	8
Generic scenario D - production	4
Generic scenario E1 (Anti-icing agent) - formulation	1
Generic scenario E2 (Basic chemicals) - processing	554
Generic scenario E3 (Chemical intermediate) - processing	13

[1] concentration in drainage system, no biodegradation was assumed (information from industry)

Table 3.8 Local PECs in surface water.

Scenario	PEC_{local} (mg/l) surface water
Specific scenario A - production	2.9
Specific scenario B - production/processing	0.02
Generic scenario C - production	0.8
Generic scenario D - production	0.4
Generic scenario E1 (Anti-icing agent) - formulation	0.1
Generic scenario E2 (Basic chemicals) - processing	11
Generic scenario E3 (Chemical intermediate) - processing	1.3

Surface water

The local PECs in surface water, i.e. the average dissolved water concentrations during emission periods are presented in **Table 3.8**. For this calculation the effluent concentrations are divided by the dilution factor.

Table 3.9 Local PECs in soil.

Scenario	PEC_{local} (mg/kg) terrestrial
Specific scenario A - production	0.0004
Specific scenario B - production/processing	0.0007
Generic scenario C - production	0.004
Generic scenario D - production	0.002
Generic scenario E1 (Anti-icing agent) - formulation	0.001
Generic scenario E2 (Basic chemicals) - processing	0.2
Generic scenario E3 (Chemical intermediate) - processing	0.004

3.1.2.2 Terrestrial compartment

The EUSES model takes into account both the application of STP sludge on agricultural soil and the deposition from air for the calculation of DEGME concentrations in the terrestrial compartment. **Table 3.9** gives the terrestrial PECs at a local scale (i.e. the concentration measured 30 days after sludge application).

3.1.2.3 Atmosphere

The calculated annual average DEGME concentrations in air (100 m from point source) are presented in **Table 3.10**.

Table 3.10 Local PECs in air.

Scenario	PEC_{local} (mg/m^3)
Specific scenario A - production	$4.8 \cdot 10^{-5}$
Specific scenario B - production/processing	$6.2 \cdot 10^{-4}$
Generic scenario C - production	$3.8 \cdot 10^{-3}$
Generic scenario D - production	$2.1 \cdot 10^{-5}$
Generic scenario E1 (Anti-icing agent) - formulation	0.003
Generic scenario E2 (Basic chemicals) - processing	0.02
Generic scenario E3 (Chemical intermediate) - processing	$2.7 \cdot 10^{-4}$

3.1.2.4 Non compartment specific exposure relevant to the food chain

Concentrations of DEGME in fish and worm (local and regional combined) are given in **Table 3.11**.

Table 3.11 PECs in fish and worm.

Scenario	PEC worm (mg/kg)	PEC fish (mg/kg)
Specific scenario A - production	0.001	1.7
Specific scenario B - production/processing	0.001	0.02
Generic scenario C - production	0.004	0.5
Generic scenario D - production	0.002	0.3
Generic scenario E1 Anti-icing agent) - formulation	0.002	0.08
Generic scenario E2 (Basic chemicals) - processing	0.1	2.9
Generic scenario E3 (Chemical intermediate) - processing	0.004	0.2

3.1.3 Regional Predicted Environmental Concentrations

Table 3.12 shows the calculated regional PECs for air, water and soil at the regional scale.

Table 3.12 Regional PECs in air, water and soil.

compartment	PEC regional
air	$2 \cdot 10^{-6}$ (mg/m^3)
water	0.01 (mg/l)
soil	$3 \cdot 10^{-4}$ (mg/kg)

3.2 EFFECTS ASSESSMENT

3.2.1 Aquatic compartment

3.2.1.1 Short-term toxicity to fish

The DEGME short-term toxicity studies for fish are summarised in **Table 3.13**.

Table 3.13 Short-term fish toxicity data of DEGME.

No.	Species	Duration (h)	LC50 (mg/l) 95% C.I.	Method	References
1	Pimephales promelas	96	5700 (5600-5900)	EPA,1975	DOW Unpublished Report 1979
2	Pimephales promelas	96	> 500	Other	DOW Unpublished Report
3	Lepomis macrochirus	96	7500	Other	Dawson GW, Jennings AL, Drozdowski D, Rider E 1977
4	Oncorhynchus mykiss	96	> 1000	EPA, 1975	TSCATS 1983
5	Carassius auratus	24	> 5000	APHA,1971	19 Bridie AL, Wolff CJM, Winter M 1979

The short-term toxicity tests were conducted according to (international) standard tests. Only nominal test concentrations were given.
In test no. 2 with P. promelas essential information is lacking. In the test with C. auratus the exposure time of 24 hours is relatively short. Therefore, the results of these tests will only be used as supportive information.

In three out of five tests no effect was found at the highest concentration tested. The other two tests (test 1 and 3) resulted in LC50-values of 5700 and 7500 mg/l, respectively. A slight increase of toxicity in time was found in the test with P. promelas: the LC50-values for 24 hours exposure is 6400 mg/l.

The lowest fixed LC50, i.e. 5700 mg/l, will be taken into consideration with the results from other taxonomic groups for the derivation of the PNEC for the aquatic compartment.

3.2.1.2 Short-term toxicity to daphnids

Table 3.14 shows the DEGME short-term toxicity studies for daphnids.

Table 3.14 Short-term daphnid toxicity data of DEGME.

No.	Species	Duration (h)	EC50 (mg/l) 95% C.I.	Method	References
1	Daphnia magna	48	1192 (1100-1300)	EPA,1975	DOW Unpublished Report 1979
2	Daphnia magna	48	> 1000	EPA,1975	TSCATS 1983
3	Daphnia magna	48	> 500	EPA,1975	BASF AG 1992

All short-term D.magna toxicity tests with DEGME were conducted according to (international) standard test guidelines. Only nominal test concentrations were given.

No effect was shown at the highest concentration tested in tests no. 2 and 3. The EC50 of 1192 mg/l will be taken into consideration with the results from other taxonomic groups for the derivation of the PNEC for the aquatic compartment.

3.2.1.3 Toxicity to algae

There are two DEGME toxicity studies available for algae (see **Table 3.15**).

Table 3.15 Algae toxicity data of DEGME.

Species	Duration (h)	EC50, biomass (mg/l)	Method	References
Selenastrum capricornutum	96	> 1000	Other	TSCATS 1983
Scenedesmus subspicatus	72	> 500	DIN 38412 Part 9	BASF AG 1992

Both algae biomass studies were conducted according to (international) standard test guidelines. Only nominal test concentrations are given. In the Selenastrum test the cell concentration was determined after 96 hours and in the Scenedesmus test chlorophyll A fluoresence was measured for establishing biomass changes.
No $EC50_{biomass}$ for algae could be established at concentration levels up to 1000 mg/l.
The algae test results will be taken into consideration with the results from other aquatic toxicity studies when deriving the PNEC for the aquatic ecosystem.

3.2.1.4 Toxicity to micro-organisms

The DEGME microbial toxicity studies are shown in **Table 3.16**.

Table 3.16 Micro-organism toxicity data of DEGME.

Species	Duration (h)	EC50 (mg/l)	Method	References
Activated sludge	0.5	> 1995	No data	BASF Unpublished Report
Pseudomonas putida	17	> 10,000	DIN 38412 Part 8	BASF AG 1992

Information about the method used in the activated sludge test is scarce. Three test concentrations ranging from 15-1995 mg/l were used and inhibition of the respiration rate was measured. The test with P. putida was carried out according to a standard (national) method. Growth inhibition (optical density measurements) was determined at eight nominal test concentrations.
In the activated sludge test no inhibition of the respiration rate was found at concentrations up to 1995 mg/l (only 10% inhibition at 15 mg/l). Contrary, a stimulus of the respiration rate was found at DEGME concentrations of 150 and 1995 mg/l (55 and 85%, respectively). The EC50 and EC90 (17 hours) in the test with P. putida were found to be higher than 10,000 mg/l.
Both test results with micro-organisms are in line with the results of the biodegradation studies with DEGME (see paragraph 3.1.0). From the available data it can be concluded that DEGME causes no acute adverse effects to micro-organisms.

3.2.1.5 PNEC for the aquatic compartment

The PNEC for the aquatic compartment is extrapolated from the EC50 for Daphnia (1192 mg/l).
Strictly speaking and following the TGD, the absence of long-term toxicity data for DEGME leads to the use of a factor 1,000. This would result in a PNEC of 1.2 mg/l.
It is felt, however, that in the case of DEGME there are a number of reasons to deviate from this rule and use an extrapolation factor of 100:
a) on top of the base set (fish, daphnids and algae) data from a fourth trophic level, i.e. micro-organisms, is available (test with P. putida)
b) data for several fish species are available
c) DEGME has shown a low short-term toxicity to water organisms (all reported L(E)C50-values are > 500 mg/l) and in several tests no effects were observed even at the highest test concentration. This means that the "real" L(E)C50 is probably higher.
d) DEGME can be classified as a compound which acts by non-polar narcosis. This can be concluded from the observation that there is no significant difference between the L(E)C50 values for fish, Daphnia, algae and bacteria (factor < 10), which is typical for this category of substances.
This conclusion is further supported by Verhaar *et al.* (1993). (Bol *et al.* 1993), who classified linear ethers on structural grounds as "class 1 type compounds", i.e. compounds showing narcosis or baseline toxicity. Using the equations for non-polar narcotics given in Appendix II of Chapter 4 of the TGD, ecotoxicity QSAR data can be estimated (**Table 3.17**). These data (esp. fish) are reasonably consistent with the experimental data.

Table 3.17 QSAR ecotoxicity data for DEGME.

Species	Endpoint	Value (mg/l)
Pimephales promelas	96 h LC_{50}	18,600
Brachydanio rerio/P. promelas	28-32 d NOEC	2,500
Daphnia magna	48 h EC_{50}	25,500
Daphnia magna	16 d NOEC	8,800
Selenastrum capricornutum	72-97 h EC_{50}	34,000

The extrapolation with a factor 100 leads to a PNEC for the aquatic environment of 12 mg/l.

$PNEC_{aquatic}$ = 12 mg/l

3.2.1.6 $PNEC_{micro\text{-}organisms}$

In principal, no $PNEC_{micro\text{-}organisms}$ can be determined because of the lack of fixed IC50 or NOEC data in both available tests. As in the activated sludge test a stimulus was found at 1995 mg/l this result is considered less appropriate than the P. putida test for estimating a $PNEC_{micro\text{-}organisms}$. As a worst case approach the value of 10,000 mg/l will be used as the EC_{50}. Using an extrapolation factor of 10, this results in a $PNEC_{micro\text{-}organisms}$ of 1000 mg/l.

$PNEC_{micro\text{-}organisms}$ = 1000 mg/l

3.2.2 Terrestrial compartment

The utilisation of DEGME by four different micro-organisms which were isolated from soil was investigated. DEGME was the only carbon source of in the media. No growth of the four strains of micro-organisms was measured. As this test is not suitable for deriving a PNEC and no other information is available on the terrestrial environment, no PNEC for terrestrial organisms can be derived directly.

3.2.2.1 PNEC for terrestrial compartment

As stated in 3.2.2, there are no data available for directly deriving a PNEC for the terrestrial compartment. Therefore the PNEC-terrestrial was estimated from the PNEC for aquatic organisms using the equilibrium partitioning approach. This results in a $PNEC_{terrestrial}$ of 1.4 mg/kg (EUSES).

$PNEC_{terrestrial}$ = 1.4 mg/kg

3.2.3 Atmosphere

No data available.

3.2.4 Non compartment specific effects relevant to the food chain

No specific data available.

3.3 RISK CHARACTERISATION

3.3.1 Aquatic compartment (local)

Table 3.18 PEC/PNEC ratios for micro-organisms.

Scenario	$PEC/PNEC_{micro\text{-}organisms}$
Specific scenario A - production	not applicable
Specific scenario B - production/processing	0.0005
Generic scenario C - production	0.008
Generic scenario D - production	0.004
Generic scenario E1 (Anti-icing agent) - formulation	0.001
Generic scenario E2 (Basic chemicals) - processing	0.6
Generic scenario E3 (Chemical intermediate) - processing	0.01

Micro-organisms

The PECs of DEGME in the effluent of a sewage treatment plant for the various emission scenarios are presented in paragraph 3.1.2 (**Table 3.7**). The PNEC for micro-organisms is 1000 mg/l (paragraph 3.2.1.6). **Table 3.18** shows the PEC/PNEC ratios for micro-organisms. No ratio is given for site-specific scenario A, because in that situation no sewage treatment plant, but only a drainage system, is present.

In all exposure scenarios the PECs do not exceed the PNEC for micro-organisms (**conclusion ii**).

Table 3.19 PEC/PNEC ratios for aquatic organisms.

Scenario	ratio $PEC/PNEC_{aquatic}$
Specific scenario A - production	0.2
Specific scenario B - production/processing	0.001
Generic scenario C - production	0.07
Generic scenario D - production	0.04
Generic scenario E1 (Anti-icing agent) - formulation	0.01
Generic scenario E2 (Basic chemicals) - processing	0.9
Generic scenario E3 (Chemical intermediate) - processing	0.1

Aquatic organisms

The local PECs in water for the various emission scenarios are presented in paragraph 3.1.2 (**Table 3.8**). The PNEC for aquatic organisms is 12 mg/l. **Table 3.19** gives the PEC/PNEC ratios for aquatic organisms.

In all emission scenarios the PECs do not exceed the PNEC for aquatic organisms (**conclusion ii**).

Sediment
As neither monitoring data on levels of DEGME in sediment nor ecotoxicity data for benthic organisms are available, no risk characterisation is conducted for sediment.

3.3.2 Terrestrial compartment (local)

In none of the emission scenarios the PEC soil exceeds the PNEC for the terrestrial compartment (**conclusion ii**). All PEC/PNEC ratios are < 0.2.

3.3.3 Atmosphere (local)

No environmental risk characterisation can be carried out for the air compartment, since there are no specific effect data.

3.3.4 Non compartment specific exposure relevant to the food chain

In all scenarios the ratio of the PEC in fish/worm and the PNEC for predators is < 1 (**conclusion ii**). For the selected PNEC for predators (90 mg/kg): see conclusion of paragraph 4.1.2.6.

3.3.5 Regional risk characterisation

All PECs calculated for the regional scale (**Table 3.12**) do not exceed the corresponding PNECs (**conclusion ii**). No regional environmental risk characterisation could be carried for air, since there are no specific effect data.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.0 General discussion

The human population may be exposed to DEGME 1) at the workplace, 2) from use of consumer products and 3) indirectly via the environment.
An overview of the use of DEGME (industrial and use categories) is given in **Table 2.2**.

More specified uses of DEGME are (Kligman 1972):
- as coupling agent for preparing miscible organic aqueous systems
- as solvent for dyes, nitrocellulose and resins; metal solvent for mineral oil-soap and mineral oil-sulfonated oil mixtures, solvent for setting the twist and conditioning yarns and cloth.
- in cleaning solutions, dye baths
- as stabililiser of emulsions
- as solubiliser and blending aid in the varnish industry
- as component of printing pastes, stamping inks, ball-point pastes
- in hydraulic fluids
- as raw material for plasticisers

The human population can be exposure to DEGME containing products by inhalation as well as by dermal contact and ingestion.

In Switzerland, Norway, Germany, Sweden and Denmark DEGME has been found in more than 50 products, several of which are available to consumers (e.g. paints and varnishes) (KEMI 1995; Danish product register 1995).

Consumer exposure data are scarce. Drinking water supplies in the USA have been shown to contain the DEGME, but concentrations were not given. No specific data are available for Europe.

The concentration of DEGME in indoor air is estimated at 1-20 µg/m^3, with a peak concentration of 8000 µg/m^3. In similarity with data available for DEGBE (2-(2-butoxyethoxy)ethanol) it is expected that peak concentrations will occur while painting (Lanting *et al.* 1991). However, measured data are not available.

4.1.1.1 Occupational exposure

Occupational exposure is possible due to production of DEGME, due to formulation of products containing DEGME and due to the use of products containing DEGME.
Workers in the following industries may be exposed:

- basic chemicals (production);
- chemical products (e.g. paints, cleaning agents);
- transport and retail of fuels (fuels);

- painters (lacquers, wood stain, cleaning agents);
- wood industry (lacquers, wood stain);
- metal product industries (lacquers, cleaning agents, hydraulic fluids);
- leather industry (leather dyes);
- textile industry (textile dyes);
- cleaners (cleaning agents);
- printing presses (probably as a cleaner);
- users of oils, fats and waxes in several industries.

The professional use of ink pads and ball points is considered not to be relevant for risk assessment of DEGME, because of the very small amounts used compared to the other uses. Based on the available information it is assumed that DEGME is not used in printing inks.

The use of products may include:

- transfer of liquids by means of a transfer line and pumping: transfer of lacquers, inks or dyes into application equipment, transfer of hydraulic fluid, transfer of fuels;
- manual transfer of liquids or pastes: lacquers, inks, dyes, hydraulic fluids, cleaning agents:
- manual cleaning or degreasing: cleaning agents used by cleaners and in the metal products industry;
- manual painting using a brush, a roll or spray painting equipment: lacquers and wood stains applied by painters, in parts of the wood industry and the metal products industry;
- automated painting or coating using a lacquer curtain, automated spray painting or dipping in the wood industry, the metal products industry, the leather industry and the textile industry.

The routes of exposure are exposure by inhalation of vapours and/or aerosols (spraying of lacquers) and by skin contact.

Relevant populations potentially exposed are workers in the above mentioned industries, specifically those workers that may have more or less direct contact with the substance, being:

- workers in production facilities of DEGME or of products containing DEGME, e.g. drumming the (pure) substance products containing the substance or transferring the substance or products to other systems in the chemical industries (drumming, connecting a transfer line);
- workers cleaning production facilities and equipment for the production of DEGME and products containing DEGME;
- workers using products containing DEGME in the above mentioned industries.

The following data (if available) are used for occupational exposure assessment:

- physico-chemical data of DEGME and products containing the substance: physical appearance, vapour pressure at room temperature, percentage of DEGME in products;
- data regarding methods of use and use pattern of the substance and products potentially containing DEGME and exposure control pattern in the relevant industries (from the HEDSET or other sources);
- exposure data for DEGME from the HEDSET and other sources (literature, exposure databases);
- exposure data for other glycol ethers with similar use patterns (analogues) from literature and exposure databases;
- results from exposure models (EASE model (inhalation and dermal exposure assessment), EPA transfer model).

The exposure is assessed using the available information on substance, processes and work tasks. More detailed information on these parameters may lead to a more accurate exposure assessment.

In this part of the assessment, external (potential) exposure is assessed using relevant models and other available methods in accordance with the Technical Guidance Documents and agreements made at official Meetings of Competent Authorities. Internal dose depends on external exposure and the percentage of the substance that is absorbed (either through the skin or through the respiratory system).

The exposure is assessed without taking account of the possible influence of personal protective equipment (PPE). If the assessment as based on potential exposure indicates that risks are to be expected, the use of personal protective equipment may be one of the methods to decrease actual risks, although other methods (technical and organisational) are to be preferred. This is in fact obligatory following harmonised European legislation.
Knowledge of effectivity of PPE in practical situations is very limited. Furthermore, the effectivity is largely dependent on site-specific aspects of management, procedures and training of workers. A reasonably effective use of proper PPE for skin exposure is tentatively assumed to reduce the external exposure with 85%. For respiratory protection the efficiency depends largely on the type of protection used. Without specific information, a reduction efficiency of 90% will be used, equivalent to the assigned protection factors for supplied-air respirators with a half mask in negative pressure mode (NIOSH, 1987). Better protection devices will lead to higher protection. Imperfect use of the respiratory protection will lower the practical protection factor compared to the assigned factor. These estimations of reduction are not generally applicable “reasonable worst case” estimations, but indicative values based on very limited data. Furthermore, this reduction of external exposure does not necessarily reflect the reduction of absorbed dose. It has to be noted, that the use of PPE can result in a relatively increased absorption through the skin (effect of occlusion), even if the skin exposure is decreased. This effect is very substance-specific. Therefore, in risk assessment it is not possible to use default factors for reduction of exposure as a result of the use of PPE.
In some specific situations a preliminary assessment of the possible influence of PPE exposure will be made. This regards situations in which the failure to use adequate protective equipment properly will often lead to acute adverse effects on the worker. Examples of such situations are manual handling of very corrosive substances and handling materials with high temperatures.

There is a large number of industries in which DEGME is produced and/or used. In many cases, the processes and activities that may lead to emission of DEGME into the workplace and hence to exposure of workers are however similar. The combinations of industries and products can be clustered in “similar occupational exposure scenarios” based upon the type of process and activity and the possibilities for exposure that relate to that process and activities.
The following occupational exposure scenarios will be considered:

1 - production of DEGME, including quality control sampling and drumming, cleaning of production equipment; handling pure DEGME;
2 - production of products containing DEGME, including transferal, mixing, quality control sampling and drumming, cleaning of mixing equipment;
3 - transferal of products containing DEGME to application equipment (automated or manual) and automated application of products containing DEGME, including printing (automated application);

4 - manual application of products containing DEGME, such as spray application, brushing, rolling, cleaning (including manual transferal and mixing of such products).

Some of the scenarios may have different exposure levels for different subgroups of workers. However, available (exposure) data often does not allow distinguishing the subgroups and therefore these scenarios will not be subdivided.

Hardly any measured levels of occupational exposure to DEGME were found in a limited literature search or in the occupational exposure databases searched (NIOSH 1987; AMI 1995; INRS 1995; NEDB 1995). Confidential data was received from one producer containing concentrations in production and drumming departments. No information on sampling duration and control measures in use is presented in these data (Company B 1995).

Assessment approaches used in this exposure assessment are:
- measured data (limited);
- expert judgement;
- analogy approach;
- EPA transfer model;
- EASE model (inhalation and dermal exposure assessment)

In this report for each occupational exposure scenario the general description of exposure will be followed by measured data (if available), and results from similar substances in comparable exposure scenarios. This will be followed by suitable inhalation models. The several methods of estimation for inhalation exposure will be compared using expert judgement and a choice for the best applicable estimators will be made.
Dermal exposure will be described and assessed by means of EASE.

The following parameters of exposure are assessed for each (sub)scenario:
- *full shift reasonable worst case inhalation exposure level:* the inhalation exposure level considered representative for a high percentile (90 to 95 percentile) of the distribution of full shift exposure levels;
- *full shift typical inhalation exposure level:* the inhalation exposure level considered representative for the central tendency of the distribution of full shift exposure levels;
- *short term inhalation exposure level:* the inhalation exposure level considered representative for a high percentile (90 to 95 percentile) of the distribution of short term exposure levels; short term exposure is for this purpose considered to be exposure for up to one hour, with typical durations of approximately 15 minutes;
- *dermal exposure level:* the dermal exposure level considered representative for a high percentile (90 to 95 percentile) of the full shift dermal exposure levels.

In Annex 3 data from measurements on analogues for manual application are presented. The annex contains data for scenarios comparable to the ones mentioned above. In Annex 4 assumptions and results of relevant calculations using the EPA transfer model are presented.

Scenario 1: production of DEGME

Production of DEGME may lead to some emission into the air. Production is in closed systems, except for activities such as sampling and drumming. Drumming of DEGME at the production facilities is usually done using adequate local exhaust ventilation (LEV). The use pattern is either "closed system" (for the production system itself) or "non-dispersive use" (for sampling and drumming). Drumming (in tank trucks, tank cars or drums) is probably highly automated and apart from effective local exhaust ventilation, also separation may be used as a means of lowering exposure levels.

Duration and frequency of exposure may be up to 8 hours per day on all working days (depending on the amount produced and the organisation of work). Tank filling probably takes up to one hour per tank.

Measured data

Relevant data for other glycol ethers and glycol ether acetates show long-term exposure levels that are generally well below 10 mg/m^3, although outliers at or above 20 mg/m^3 occasionally occur (Clapp *et al.* 1984; Piacitelli *et al.* 1989A; Piacitelli *et al.* 1990; Company B 1994; Company B 1996; ECETOC 1994).

Some use of local exhaust ventilation, enclosures, automation, etc. was made in the bulk loading area of the facility in reference (Piacitelli *et al.* 1990), for other references data on control measures are not available at this moment.

Short-term exposure levels reported are below 10 mg/m^3 (Piacitelli *et al.* 1989A; Piacitelli *et al.* 1990).

The substances mentioned in most of the references have a considerable higher vapour pressure than DEGME, but are still "low volatility compounds" in the EASE model.

Models

Concentrations calculated by the EPA transfer model (typical and worst case room averaged concentrations, not calculating the influence of LEV) are given in **Table 4.1**.

Table 4.1 Typical and worst case room average concentrations for drumming of DEGME: EPA transfer model.

Type of container	Concentrations (mg/m^3)	
	Typical	Worst case
Rail car	0.05	0.30
Tank truck	0.02	0.47
Drums (200 L)	1.16	104.49

Very good local exhaust ventilation during drumming in drums may capture more than 95% of all vapours emitted (PEI Associates 1988), lowering the exposure levels in a worst case situation for drums to 5.2 mg/m^3.

The estimate of exposure levels of a substance of low volatility, used in non-dispersive use with adequate local exhaust ventilation by the EASE model is 0.5-3 ppm (≈ 2.5-15 mg/m^3). For non-dispersive use and other patterns of control the following exposure levels are calculated:

- segregation: 3-10 ppm (≈ 15-50 mg/m^3);
- direct handling with dilution ventilation: 10-50 ppm (≈ 50-250 mg/m^3);
- direct handling without dilution ventilation: 50-100 ppm (≈ 250-500 mg/m^3).

Inhalation exposure; conclusions

The comparison between model results and measured data should be made based on similarity of situations. However, the similarity is difficult to assess, because the control pattern in the measured data is often not presented with the results. Generally, either "closed system" or "closed system breached = non dispersive use" is the use pattern in the basic chemicals industries. Local exhaust ventilation is common. The combinations between these use patterns and control patterns are expected to be the relevant ones for the measured data as well. In general the results from EASE are expected to be relatively high, since they are applicable for substances with vapour pressures up to 1500 Pa, while DEGME has a vapour pressure of only 30 Pa. Considering this, the measured exposure or concentration levels from one producer (63 measurements in 5 years, concentrations up to 1.6 ppm ≈ 8.0 mg/m^3) (Company B 1995) and the data from analogues compare reasonably well with the results from EASE for non-dispersive use and adequate local exhaust ventilation.
The results from the EPA transfer model do not appear to be excessive, considering that the model does not take into account LEV, although the model results are somewhat higher than the measured data. This may be due to a difference in level of containment or due to automation and segregation between workers and source, that is not accounted for in the EPA transfer model.

Considering the use of highly automated filling lines, proper local exhaust ventilation and separation for drumming, for this scenario the results for "worst case" of the EPA transfer model, corrected for an efficient removal of vapours by local exhaust ventilation, will be used as (reasonable) worst case estimates of exposure levels. Typical exposure levels are expected to be half the worst case level (expert judgement). Short-term values will only be slightly higher, since the long-term values are derived from modelling drumming. It is estimated that these may be two times the long-term values (expert judgement).

Dermal exposure

Due to the automated procedures during drumming, only limited skin exposure is possible in drumming. Drumming into rail cars and tank trucks will be done using transfer lines, while drumming into drums may lead to contact with contaminated drums if drums overflow, or fill spouts are not fitted correctly. The latter source of exposure is considered to be accidental, since leaking drums are expected to be rare.
Dermal exposure is assessed by EASE.
Based on EASE the estimates of dermal exposure levels of DEGME are for tank filling activity the following.

- Non-dispersive use with direct handling and intermittent contact: 0.1-1mg/cm^2/day. Because filling probes with handholds, that will not be very contaminated, are common, an exposure level of 0.05-0.5 mg/cm^2/day will be used in the reasonable worst case exposure assessment.

It is assumed that during these activities half of two hands will be exposed. This corresponds with an exposed area of 420 cm^2, which results in a reasonable worst case estimate of 21-210 mg/day. Accidental contact with contaminated drums will lead to a higher area of the skin exposed, but will be incidental exposure. The possibility of dermal exposure cannot be excluded based upon available data.

The estimates made by EASE are used for the dermal exposure assessment. The reasonable worst case exposure becomes 210 mg/day (**Table 4.3**).

Conclusions scenario 1

The following exposure levels will be used for further risk assessment for scenario 1.

- Inhalation exposure; reasonable worst case, full shift: ≈ 5.2 mg/m^3;
- Inhalation exposure; reasonable worst case, short term: ≈ 10.4 mg/m^3;
- Inhalation exposure; typical, full shift: 2.6 mg/m^3;
- Dermal exposure; reasonable worst case: 210 mg/day.

Scenario 2: production of products containing DEGME

Paints and varnishes are assumed to contain up to 10% DEGME and may be drummed in large drums (200 L). Paint removers may contain up to 35% DEGME, but are proably drummed in cans with a volume up to 10 L. Jet fuel contains much lower percentages of DEGME and is only drummed in tank trucks or rail cars.

Transferal of DEGME to other chemical production systems is expected to be done by connecting transfer lines, leading to substantially lower emission compared to drumming. Inhalation exposure is therefore expected to be clearly below the levels estimated for scenario 1, while short-term levels may be equal.

During mixing of products in paint production, cleaning agent production, etc. volatile substances may evaporate, especially if systems are only partially closed. Liquid products will be drummed, paste-like products will be packed in suitable containers. The packing of non-liquid products is expected to give less emission by evaporation and less possibilities for skin contact. Therefore only mixing and drumming of liquid products will be considered here. Liquids (lacquers, stains, inks, cleaning agents) may be drummed in drums and cans of different size.

In facilities formulating jet fuel, control measures equivalent to those in scenario 1 are expected to be normal, due to the high toxicity compounds in jet fuel. However, in other formulating facilities, e.g. for paints and inks, technical control measures generally are not as extensive and effective as those taken in the production facilities. The use of the presented “use pattern” and “control pattern” in the EASE model is thus justified.

Duration and frequency of exposure may be full shift and daily, although transferal of DEGME at the beginning of the process and drumming may be done only during a part of the day, in which case the duration of skin exposure potential is less than full shift.

Measured data

Exposure levels for other glycol ethers and glycol ether acetates in paint industry and other formulating facilities are presented in several references. Maximum long term exposure levels measured were between < 1 ppm and approximately 24 ppm (< 2 mg/m^3 and ≈ 92 mg/m^3) (Angerer *et al.* 1990; Piacitelli *et al.* 1989B; Piacitelli *et al.* 1990; NEDB 1995; Guirguis *et al.* 1994). Guirguis *et al.* (1994) only present percentages above Threshold Limit Values (TLVs). No results above TLVs of 25, 5 and 25 were found in chemical industries for EGBE, EGEEA[1] and EGPE[2]. Short-term levels (approximately 15 minutes) were up to ≈ 7 ppm (≈ 21 mg/m^3) according to Piacitelli *et al.* (1990) and Piacitelli and Krishnan (1989).

[1] ethylene glycol ethyl ether acetate
[2] ethylene glycol mono-n-propyl ether

Models

The EPA transfer model only calculates concentrations for pure substances. The vapour generation rate for substances from mixtures can only be calculated with a good degree of certainty if the exact composition of the mixture is known. However a reasonable correction for non-pure substances is multiplying the results of the model with the fraction of substance in the mixture, assuming ideal physical behaviour of the mixture.

Using this correction the following concentrations are calculated (**Table 4.2**):

Table 4.2 Typical and worst case room average concentrations for drumming of products containing DEGME: EPA transfer model, correction by fraction of DEGME in product, assuming at maximum 10% DEGME.

Type of container	Concentrations (mg/m^3)	
	Typical	Worst case
Cans (10 L)	< 0.01	0.52
Small cans (1 L)	< 0.01	0.52
Drums (200 L)	0.11	10.45

Very good local exhaust ventilation during drumming in drums may capture more than 95% of all vapours emitted (PEI Associates 1988), lowering the exposure levels in a worst case situation for drums to 0.5 mg/m^3.

Such very good local exhaust ventilation is not considered to represent the reasonable worst case situation.

Drumming of paint remover (35% DEGME) in cans of 10 L leads to worst case calculated concentrations, according to the EPA model, of approximately 2 mg/m^3.

For calculations using the EASE model the same assumptions and input data are used as for scenario 1.

Inhalation exposure; conclusions

The correct use pattern and control pattern for the industries mixing chemical products are either non-dispersive use or wide dispersive use and local exhaust ventilation or dilution ventilation.

The EASE model uses data of substances “that can be considered to be used as pure substances” for estimating resulting exposure levels. The suitability of the EASE model for substances that are small components in mixtures is therefore uncertain. The model may overestimate exposure levels for this type of component, since the vapour pressure to be used in the model should be corrected to account for the possible lower emission of vapour from a mixture.

The lower-end results from the category of “non-dispersive use, direct handling with dilution ventilation” agree very good with the data for EGEEA and EGBE from Angerer *et al.* (1990). Results from the EPA transfer model and the data from analogues appear to agree reasonably well, though the EPA transfer model may even underestimate exposure levels, since it does not take into account any other emission sources than drumming, while mixing is also a source of exposure. Given the low vapour pressure and the small percentage of substance in the total product, the results from the EASE model for direct handling with local exhaust ventilation are considered not to be applicable to DEGME.

The results from the EPA transfer model for "worst case" (drumming of paints into drums) will be used as indicative for typical exposure levels, considering that this model does not take into account other sources than drumming, while reasonable wordst case exposure levels are expected to be twice as high (expert judgement). Short-term levels are expected to be up to twice "reasonable worst case" long-term levels.

Dermal exposure

Skin exposure levels due to transfer of DEGME at the beginning of the process are equal to scenario 1, since the activity and concentration of the substance in the handled product is equal. It is assumed that similar handholds are used on transfer lines as are available in tank filling.

Since the transferal is only performed during a part of the day the exposure assessed by EASE changes. For transferal from tanks only a single transfer per day is considered. Based on EASE the estimate of dermal exposure levels of DEGME is for this activity the following:

- transferal from drums: non-dispersive use with direct handling and intermittent contact: 0.1-1 mg/cm^2/day;
- transferal from tanks: non-dispersive use with direct handling and incidental contact: 0-0.1 mg/day.

Assuming that similar filling probes are used for transferal from tanks as during tank filling in scenario 1, the estimation will be done using a reasonable worst case exposure of 0-0.05 mg/cm^2/day. Since the exposed area during the transferal of the product is about 420 cm^2, the dermal exposure becomes 42-420 mg/day (drums) or 0-21 mg/day (tanks).

The exposure assessed by EASE will be used for the risk assessment (**Table 4.3**).

Conclusions scenario 2

The following exposure levels will be used for further risk assessment for scenario 2.

- Inhalation exposure; reasonable worst case, full shift: ≈ 21 mg/m^3;
- Inhalation exposure; reasonable worst case, short term: ≈ 42 mg/m^3;
- Inhalation exposure; typical, full shift: 11 mg/m^3;
- Dermal exposure; reasonable worst case: 420 mg/day.

Scenario 3: automated application of products containing DEGME

The application of products containing DEGME with automated equipment usually involves preparation of the product (e.g. paint blending to reach a specific colour), transferal of products from containers to the equipment (either automated or manual), the actual application and finishing work (curing of coatings, mounting of parts, cleaning of equipment. Cleaning of equipment is often performed by the same workers that also perform the other tasks, but it is a task that is not performed daily to a large extent.

The application with automated equipment is in the scope of this assessment considered to be a non-dispersive or wide dispersive activity, generally with either the use of adequate LEV or segregation between emission sources and workers, except for the manual loading process. Although the formation of aerosols is in some cases possible (e.g. automated spray coating), it is assumed that this particular type of process will be enclosed with LEV and segregation of sources and workers, leading to exposure levels that are not higher than the levels due to widely dispersed use with segregation between sources and workers.

Duration of inhalation exposure is full shift, possibly with peaks during manual transferal. Skin exposure potential will be limited to the transferal activities. Frequency of exposure is daily.

Measured data

This scenario includes printing, textile finishing and leather finishing. The following exposure levels were reported for other glycol ethers and their acetates in this kind of use. Maximum full-shift exposure levels measured were between < 1 mg/m^3 and 187 mg/m^3, with the highest levels measured in printing facilities (Clapp *et al.* 1984; Norwegian Exposure Database 1995; Piacitelli *et al.* 1990; Veulemans *et al.* 1978; NEDB 1995; Guirguis *et al.* 1994; Vincent *et al.* 1994). Short-term levels reported are in the same range (Norwegian Exposure Database 1995; Piacitelli *et al.* 1990; NEDB 1995).

Models

The applicable results from the EASE model, considering products containing at maximum 10% of DEGME and application at room temperature are:

- non-dispersive; LEV: 0.5-3 ppm (≈ 2.5-15 mg/m^3);
- non-dispersive; segregation: 3-10 ppm (≈ 15-50 mg/m^3);
- wide dispersive; segregation: 10-50 ppm (≈ 50-250 mg/m^3).

Given the low volatility of DEGME, levels at the lower ends of the given ranges are more likely than higher levels.

Inhalation exposure; conclusions

Combining the information from modelling with the data from analogues with higher vapour pressures, the reasonable worst case exposure level for automated application is estimated to be up to the lowest modelled level in this scenario (0.5 ppm = 2.5 mg/m^3), while typical levels are expected to be clearly below this value (< 1 mg/m^3). Short-term levels are expected to be up to five times the reasonable worst case estimate.

Dermal exposure

Skin exposure is to be expected from transferal of products, either by connecting a transfer line or by manual liquid transfer.

Since the activity of transferal is not full shift, EASE assumes the contact level to be intermittent.

The dermal exposure assessments made by EASE are the following (product contains 10% DEGME):

- connecting a transfer line: non-dispersive use with direct handling and incidental contact; 0-0.1 mg/cm^2/day;
  the exposed area is assumed to be 420 cm^2, this results in an exposure of 0-4 mg/day;
- bench scale liquid transfer: non-dispersive use with direct handling and intermittent contact; 0.1-1 mg/cm^2/day;
  the exposed area is assumed to be 420 cm^2, this results in an exposure of 4-42 mg/day.

The highest value from the dermal exposure assessment made by EASE will be used for the risk assessment (**Table 4.3**).

Conclusions scenario 3

The following exposure levels will be used for further risk assessment for scenario 3.

- Inhalation exposure; reasonable worst case, full shift: ≈ 2.5 mg/m^3;
- Inhalation exposure; reasonable worst case, short term: ≈ 12.5 mg/m^3;
- Inhalation exposure; typical, full shift: < 1 mg/m^3;
- Dermal exposure; reasonable worst case: 42 mg/day.

Occupational scenario 4: manual application of products containing DEGME

There is no certainty regarding the possible use of products containing DEGME for spray applications. According to industry, such use is unknown to them. However, DEGME is used as component of solvent based paints - amongst others in the metal products industry, in which spray coating is very usual. Furthermore, many other glycol ethers are common components of lacquers that are sprayed onto surfaces. Therfore, the possible use of DEGME containing products cannot be disregarded (as a reasonable worst case assumption) without further pertinent information to the contrary.

Manual application of products containing DEGME is a type of wide dispersive use, sometimes without the presence of any other exposure control than personal protective equipment (not even dilution ventilation).

Spray application leads to formation of aerosols and hence to relatively high exposure levels by inhalation. It is wide-dispersive use, direct handling, usually with some kind of segregation. For spray application LEV is commonly, though not always, used.

Brushing and rolling are generally assumed to lead to lower inhalation exposure levels than spray application. Segregation between sources and worker is not common in this type of manual application and will not be considered in this scenario.

Duration and frequency of exposure may be full shift and daily.

Measured data

Measured data for DEGME are mentioned in two publications. Norbäck *et al.* (1995) report results of twenty measurements of one hour in which some glycol ethers were studied. The measurements were done indoors during rolling of paint, except one case of spray painting. DEGBE was detected in four samples. The maximum exposure level (1-h TWA) was 8.1 mg/m^3. Indicative exposure values were established for exposure levels of DEGME, analysed by a method without full validation and assuming 100% recovery. The number of detected values is not mentioned. The maximum value presented is 0.02 mg/m^3. No information is presented regarding the percentages of DEGME and DEGBE in the paints. The exposure level of the sums of volatile organic compounds was low for the one sample of spray painting, compared with the highest values for rolling. Hansen *et al.* (117) report measurements of concentrations of several substances in ambient air during and after application of water borne paints. Samples were taken by stationary and personal samplers for 20 minutes in 15 representative workplaces under normal conditions.The number of measurements per working place and the number of paints containing specific substances was not reported. It is assumed that only brushing and rolling was used. Concentrations of DEGME in the work area are reported to be 8-32 mg/m^3. Details on concentrations in one workplace show that after application of sealing waterborne paint containing DEGBE during one day only, the concentration increased to 5 mg/m^3 during application and hardly decreased during the next day (3 measured values: approximately 5, 4 and 3 mg/m^3) consecutively. The third day, after ventilation of the room, the concentrations still reached 2 mg/m^3.

The maximum reported full-shift exposure levels for more volatile glycol ethers and glycol ether acetates in spray application are between < 1 mg/m^3 and 80 mg/m^3 (Clapp *et al.* 1984; Norwegian Exposure Database 1995; Piacitelli *et al.* 1990; Sparer *et al.* 1988; Veulemans *et al.* 1978). Vincent *et al.* (1994) mention an average of ≈ 55 mg/m^3, suggesting a maximum level higher than the ones in the other references. Guirguis *et al.* (1994) report that existing occupational exposure levels were not exceeded. Data regarding short-term exposure levels are mentioned in a number of sources. Maximum levels are between 3 mg/m^3 and ≈ 93 mg/m^3. Maximum short-term levels (duration of measurements 15 to 18 minutes) are roughly five times the maximum full-shift levels for the same activity in the same reference (Norwegian Exposure Database 1995; Piacitelli *et al.* 1990).

Reported maximum exposure levels for glycol ethers and glycol ether acetates for full-shift exposure during other manual application are between < 1 mg/m^3 and 210 mg/m^3 (Clapp *et al.* 1984; Norwegian Exposure Database 1995; Piacitelli *et al.* 1990; Veulemans *et al.* 1978; Zaebst 1984; NEDB 1995; Guirguis *et al.* 1994; Vincent *et al.* 1994). In a specific case, that is not representative for the manual use of glycol ethers, maximum levels for EGBE (vapour pressure ≈ 80 Pa) were around 100 mg/m^3 (Kelly 1993). In this case large amounts were used to dissolve mastic from a floor. The data from Hubner *et al.* (1992) on testing of brakehoses regard another non-representative use of glycol ethers.
In some of the references a clear distinction between automated application and manual application cannot be made. Short-term exposure levels were measured for DEGBE and some other glycol ethers in a limited number of studies. Maximum levels reported were up to 5.2 mg/m^3 for DEGBE (vapour pressure ≈ 2.7 Pa) in cleaning with undiluted cleaner and manual painting (Hansen *et al.* 1987) and were between < 1 mg/m^3 and 60 mg/m^3 for more volatile glycol ethers (Hansen *et al.* 1987; Gibson *et al.* 1991). Full-shift and short-term measurements cannot be compared since only in one reference (with very low exposure levels) both types of measurements were performed simultaneously.

Models
The EASE model is used for the application of paints by correcting the vapour pressure of the substance for the percentage of substance in the mixture (assumed to be 10%) before entering this parameter in the model.

The applicable results for spray application from the EASE model as provided in diskette are independent of the vapour pressure of the substance and are:
- spray application; uncontrolled: > 1000 ppm (> 5000 mg/m^3);
- spray application; dilution ventilation present: 500-1000 ppm (≈ 2500-5000 mg/m^3);
- spray application; segregation: 100-200 ppm (≈ 500-1000 mg/m^3).

This is in contradiction with the explanation in the Technical Guidance Document regarding aerosol formation in EASE in which it is stated that aerosol formation leads to a tendency to be airborne that is one category higher than would be expected without aerosol formation. The software version appears to be faulty. Correct levels would be:
- spray application; uncontrolled: 200-500 ppm (1000-2500 mg/m^3);
- spray application; dilution ventilation present: 100-200 ppm (500-1000 mg/m^3);
- spray application; segregation: 10-50 ppm (50-250 mg/m^3).

The applicable results from the EASE model for other manual applications are:
- no spray application; dilution ventilation present: 100-200 ppm (≈ 500-1000 mg/m^3);
- no spray application; no dilution ventilation: 200-500 ppm (≈ 1000-2500 mg/m^3).

Inhalation exposure: conclusions
Although in the EASE model spray applications and (other) manual applications are considered to be different, the exposure levels from analogues are similar for spray coating and brushing, rolling and cleaning. Probably the use of better control techniques in spray coating or differences in percentage of substance in product or exposure duration compensate the higher emission. For this assessment the two types of application are therefore considered in one scenario.
Only two sources with actual data for DEGME are available. In one of these, a non-validated analytical method is used. The presentation of results is not very detailed in both publications.

Data from Hansen *et al.* (1987) show that manual application of paints with up to 4% DEGME lead to concentrations (20 minutes TWA) of 8-32 mg/m^3. The detailed data for one representative workplace show that concentrations of low volatility substances such as DEGBE do not rapidly drop after painting and may remain relatively high for some days. The concentrations of DEGME are expected to behave rather similarly, although DEGME is slightly more volatile. The short term measurements, that may have included more than one measurement period per day, are therefore more or less indicative of full shift exposure levels. The results of the EASE model appear to be excessively high. This is probably due to the fact that the EASE model is not fully suited for minor components of mixtures and that the "low volatility compounds" category in EASE is very broad (vapour pressures up to 1500 Pa). Long-term exposure levels of up to 20 mg/m^3 and short-term levels of up to 100 mg/m^3 appear to be possible for EGMEA (vapour pressure ≈ 270 Pa), derived from the values in the printing department in reference (Norwegian Exposure Database 1995). Even the values given with the assessment as performed according to the Technical Guidance Document are much higher than values for other substances with (very) low vapour pressure. For substances with very low volatility used in spray coating, data from literature suggests that an exposure level of up to 10.8 mg/m^3 as 8-hr time weighted average is possible, while peaks of up to 180 mg/m^3 (10-20 minutes) are estimated (Rodriguez 1987; Pisaniello and Muriate 1989; Lesage *et al.* 1992; Alexandersson *et al.* 1987; Janko *et al.* 1992). The percentage of these substances in paint (up to 15%) may be somewhat higher than the percentage of DEGME (up to 10%) An exposure level of up to 35 mg/m^3 as 8-hr time weighted average **total mist** concentration appears to be possible during manual spray painting according to one of the references (Rodriguez 1987).

Considering the measured data for DEGME and DEGBE, model estimation with correction of vapour pressure before running the model, the data on other low volatility compounds and the limited number of data from analogues with relatively low vapour pressure (EGBE; vapour pressure ≈ 80 Pa and EGBEA; vapour pressure ≈ 50 Pa), long-term exposure levels of up to 20 mg/m^3 (approximately two-thirds of the highest short term value for DEGME) and short-term levels of up to 100 mg/m^3 (three times the highest reported short term value) appear to be possible. Typical long-term values may be up to the levels for DEGBE (vapour pressure ≈ 2.7 Pa) given by Hansen *et al.* (1987) (5 mg/m^3).

Dermal exposure

Skin contact due to manual transfer of liquids, spray application and brushing, rolling and cleaning is to be expected. In several of the references of Annex 3 the importance of skin exposure is stressed. In spray painting the potential exposure is not only to hands and arms, but to a large part of the body. Actual exposure will often be limited to hands, arms, face and neck.

Based on EASE, the estimates of dermal exposure levels are for the different activities the following (it is assumed that the product contains 5-10% DEGME):

- bench scale liquid transfer with small volumes; non-dispersive use with direct handling and intermittent contact; exposed area = 200 cm^2: 1-20 mg/day;
- limited manual contact; non-dispersive use with direct handling and intermittent contact; exposed area: fingers of one hand (during carefully rolling) = 200 cm^2: 1-20 mg/day;
- spray painting; wide dispersive use with direct handling and intermittent contact; exposed area: two hands, part of the forearms and head = 1300 cm^2: 325-1950 mg/day.

For paint remover (35% DEGME) limited manual contact, non-dispersive use with handling and intermittent contact is expected. Combined with an exposed area of 200 cm^2 the exposure per day is calculated to be 7-70 mg/day.

The highest value given by the dermal exposure assessments made by EASE are used for the risk assessment (**Table 4.3**).

Conclusions scenario 4

The following exposure levels will be used for further risk assessment for scenario 4.

- Inhalation exposure; reasonable worst case, full shift: ≈ 20 mg/m^3;
- Inhalation exposure; reasonable worst case, short term: ≈ 100 mg/m^3;
- Inhalation exposure; typical, full shift: ≈ 5 mg/m^3;
- Dermal exposure; reasonable worst case: 1950 mg/day.

Table 4.3 Conclusions on occupational exposure estimates.

Scenario	Exposure		Estimated inhalation exposure level (mg/m^3)						Estimated skin exposure level (mg/day)[A]
			Full-shift				Short-term		
	Duration (hr/day)	Frequency (day/year)	Typical	Method[B]	Worst-case	Method[B]	Level	Method[B]	
1: production of DEGME	6-8	100-200	2.6	Expert	5.2	EPA-LEV	10.4	Expert	210
2: production of products containing DEGME	6-8 or less	100-200	11	EPA	21	Expert	42	Expert	420
3: automated application of products containing DEGME	6-8 inhal. 0-2 skin	100-200	< 1	Analogues	2.5	EASE	12.5	Analogues	42
4: manual application of products containing DEGME	6-8	100-200	5	Analogues	10	Analogues	100	Analogues	1950

A) Skin exposure levels estimated by EASE model

B) Final result largely derived from measured= measured data from DEGME; Expert = Expert judgement considering other data; EPA-LEV = EPA transfer model considering efficient LEV; EPA = EPA transfer model without LEV; Analogues = measured data from analogues; EASE = EASE model.

4.1.1.2 Consumer exposure

DEGME is used in several products see chapter 4.1.1.0, some of which are available to consumers. In **Table 4.4** the registered uses (including consumer uses) for DEGME are given per country, also tonnage (if stated) are listed.

The identified consumer products are water and solvent based paints and varnishes, paint strippers, cleaning agents, self-shining emulsions, solvents, floor sealants, windscreen washer liquids, skin-cleaning products (soap) and skin-care products. Other specified data are not available. Also in the U.S. DEGME is found in consumer products like stamp pad ink, wood stains, brake fluid, varnish remover and cleaning solution (SIDS 1996).

Table 4.4 Number and tonnage/year of DEGME containing (consumer) products in Europe.

Country	Products	Consumer Products (DEGME conc.)	Tonnage/year (cons.pr.)	Reference
CH	321	≈ 60 (1-10%) 46 (10-100%)	n.s.[1]	Letter Bundesamt für Gesundheitswesen 1996
D	n.s.	≈ 6	n.s.[1]	Letter Bundesanstalt für Arbeitsschutz und Arbeitsmedizin 1996
NO	29	5	95 (BASF AG 1994)	Letter SFT 1996
DK	110	n.s.[1]	72	Danish product register 1995
S	60	9 (0.18-30%)	700	KEMI 1995; Lindquist 1995

[1] n.s. = not stated

With respect to the low vapour pressure as well as the use volumes of DEGME per event, the major sources for consumer exposure could be water base paints and paint strippers. To a minor extent the use of DEGME in cleaning agents is also a potential source for consumer exposure.

Except for the indoor concentration estimates already mentioned (mean: 1-20 µg/m^3; peak: 8000 µg/m^3) exposure data are not available.
The following data (if available) are used for the consumer exposure assessment:
- physical-chemical data of DEGME (molecular weight, log K_{ow}, vapour pressure at room temperature)
- contact parameters (where, how long and how often contact with the consumer products)
- concentration parameters (e.g. percentage of DEGME in consumer products (or for other glycol ethers used in similar products)
- exposure data for DEGME (or for other glycol ethers in similar products)
- results from consumer exposure models (CONSEXPO model, SCIES model, PERMSKIN model).

With respect to indicated principal consumer uses of DEGME and the availability of information especially about the concentration of DEGME in the consumer products three exposure scenario's are considered: paints, paint stripper and windscreen washer liquid.
We used the CONSEXPO model, version 1.04 (Van Veen 1995) for the estimation of the exposure. CONSEXPO contains a number of models for the estimation of exposure and uptake (during use) of substances via the inhalatory, dermal and oral routes. For all scenarios a relative density of 1 g/m^3 was assumed.

Scenario I: Paint
When DEGME is used as an ingredient in paints the main exposure routes are by inhalation and by skin contact. The concentration of DEGME in paints is ranging from 1-10% (KEMI 1995; Lindquist 1995; Danish product register 1995; Letter Bundesamt für Gesundheitswesen 1996). The consumer exposure is estimated with the CONSEXPO model using exposure scenario “evaporation from mixture”. Details of the parameters used and the results of the modelling are presented in Annex 5.1. The outcome of the modelling has been obtained through a reasonable worst case approach.

Results CONSEXPO model:
Assuming the use of paints 1/month for 3 hours with 5 kg/event results in an average inhalatory exposure concentration per event of 4.1 mg/m^3. The dermal exposure from vapours, was estimated to be 55 mg/cm^3. These routes simultaneously result in a total internal dose rate of 0.56 mg/kg b.w./day (yearly average) after inhalation and dermal exposure, assuming 75% and 100% absorption, respectively.

Scenario II: Paint stripper/remover
The use of DEGME as an ingredient in paint stripper was also modelled. In the Swedish product register it is given that the amount of DEGME in paint strippers/removers is usually no more than 30%, however no distinction is made between consumer products and products used for professional use (Lindquist 1995). As a worst case approach the value of 30% is used in the exposure model. The consumer exposure is estimated with the CONSEXPO model using exposure scenario "evaporation from mixture". Details of the parameters used and the results of the modelling are presented in Annex 5.2. The outcome of the modelling has been obtained through a reasonable worst case approach.

Results CONSEXPO model:
Assuming the use of paint stripper for 3 hours with 1 kg/event results in an average inhalatory exposure concentration of 148 mg/m^3. The dermal exposure from vapours, was estimated to be 300 mg/cm^3. These figures may result in an internal dose rate of 0.37 mg/kg b.w./day (yearly average) after inhalatory and dermal exposure, assuming 75% and 100% absorption, respectively.

Scenario III: Windscreen washer liquid
As a specific case of the use of DEGME in cleaning agents its use in windscreen washer liquid is modelled. The windscreen washer liquids are diluted solutions of surfactants. Glycols and isopropylalcohols are used as solvent. The weight fraction for this use of DEGME is ≤ 1% (Lindquist 1995). Weight fractions for other glycol ethers usually do not exceed 10% (Velvart 1993). A value of 1% is used in the exposure model.
The exposure is estimated with the CONSEXPO model using exposure scenario "constant concentration". Details of the parameters used and the outcome of the model is presented in Annex 5.3. The outcome of the modelling has been obtained through a reasonable worst case approach.

Results CONSEXPO model:
Assuming the use of windscreen washer liquid 3/day for 3 min. with 500 mg/event results in an inhalatory exposure concentration of 2.2 mg/m^3. Dermal exposure occurring via air was negligble. This results in a total internal dose rate of 0.02 mg/kg b.w./day (yearly average) assuming 75% absorption for the inhalatory route.

4.1.1.3 Indirect exposure via the environment

DEGME may be released to the environment via effluents at sites where it is produced or is used as an anti-icing agent in jet fuel and as a chemical intermediate or solvent. Those indirect exposure routes via the environment are taken into account in chapter 3.1.1. For the release of DEGME during production two site specific scenarios (A and B) two generic scenarios (C and D) are used and release during processing and formulation are calculated using generic scenario (E). The exposure assessment is based on EU-TGD (1996) applying the European Union System for the

Evaluation of Substances (EC 1996). The input parameters and results of the EUSES calculations are shown in Annex 1.
The local concentration estimates in air for the different scenarios are presented in **Table 4.5**.
The total daily human intake via air, drinking water and food for all emission scenarios at local scale are given in **Table 4.6**.

Table 4.5 Local (100 m from point source) concentration estimates (annual average) in air.

Specific or generic	Concentration air (100 m. from source) (µg/m^3)
Specific scenario A - production	0.086
Specific scenario B - production/processing	0.62
Generic scenario C - production	3.8
Generic scenario D - production	0.021
Generic scenario E1 (Anti-icing agent) - formulation	3
Generic scenario E2 (Basic chemicals) - processing	20
Generic scenario E3 (Chemical intermediate) - processing	0.27

Table 4.6 Total daily intake via air, drinking water and food for all emission scenarios at local scale.

Specific or generic	Total human intake (mg/kg day)
Specific scenario A - production	0.0751
Specific scenario B - production/processing	0.008
Generic scenario C - production	0.068
Generic scenario D - production	0.011
Generic scenario E1 (Anti-icing agent) - formulation	0.349
Generic scenario E2 (Basic chemicals) - processing	0.383
Generic scenario E3 (Chemical intermediate) - processing	0.0138

From all scenarios it can be calculated that the intake via drinking water and via the leaf of crops are the major routes followed by the intake via air and fish.

Table 4.7 shows the calculated regional air concentration and total human intake for the regional scale.

Table 4.7 Regional scale air concentration and total human intake.

All emission scenarios	Regional scale
PEC- air (mg/m^3)	2.01E-6
Total human intake (mg/kg day)	4.39E-4

4.1.1.4 Combined exposure

Although it is possible that humans are exposed to DEGME under different circumstances (e.g. exposure at the workplace and exposure from consumer products or indirectly via the environment) no such cases have been described at this stage of the assessment.

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

4.1.2.1 Toxico-kinetics, metabolism, and distribution

Dermal absorption, *in vitro*
The absorption of DEGME through human skin was investigated *in vitro*. The absorption rate using isolated human abdominal epidermis was 0.206 ± 0.156 mg/cm^2/hr for 98% pure DEGME (receptor liquid: tritiated water) (Dugard *et al.* 1984).

Metabolism, *in vivo*
No studies on the absorption, metabolism or excretion of DEGME are available.
However, a metabolism study was available for the structurally related chemical diethyleneglycol dimethyl ether (DEGDME). When rats were administered a single oral dose of either 0.051 or 5.1 mM ^{14}C-DEGDME approximately 86 to 90% of the radioactivity was recovered in the urine within 96 hours. The principal urinary metabolites were (2-methoxyethoxy)acetic acid (DEGMEA) and methoxyacetic acid accounting for 70% and 6%, respectively, of the administered doses. DEGME was a metabolite as well and was excreted in the urine accounting for 0.3% of the low dose, but less than 0.1% of the high dose (Cheever *et al.* 1988).

Conclusion
DEGME is readily absorbed through the skin. The absorption rate through human skin *in vitro* was 0.21 mg/cm^2/hr.
No metabolism studies are available for DEGME. The administration, however, of a single oral dose of diethyleneglycol dimethyl ether (DEGDME) to rats results in the hydrolysis of the substance into DEGME, probably followed by the biotransformation into (2-methoxyethoxy)acetic acid which was excreted in the urine together with a small amount of DEGME. This study indicates that DEGME will possibly be metabolised. Conclusions about absorption and excretion cannot be drawn.

4.1.2.2 Acute toxicity

Animal studies
Several studies have been carried out with different species and by different routes. They are summarised in the **Table 4.8**.
It can be concluded that DEGME has a low acute oral and dermal toxicity.
After the oral treatment of rats signs of toxicity before death included giddiness, loss of balance and apathy as well as liver and kidney damage. In mice effects on the autonomic nervous system, somnolence and cyanosis were seen.
In dermally treated rabbits sluggishness, unsteady gait and prostration were observed. Erythema was seen at day 1.
In the available inhalation studies with rats no death occurred. Signs of toxicity were narcosis, apathy and lying on the stomach or side. Macroscopic effects were observed in liver and kidneys.

Table 4.8 Summary of acute toxicity studies.

ACUTE TOXICITY		SPECIES	PROTOCOL	RESULTS
4.1.2.2	Oral	Mouse	Unknown	LD50 = 8222 mg/kg (Gig Naselannyh Mest 29 37 1990)
		Rat	Unknown	LD50 = > 5500-9210 mg/kg (Patty's Industrial Hygiene & Toxicology 1982; Smyth *et al.* 1948; Smyth *et al.* 1941)
		Rat	Unknown	LD50 = 6900 mg/kg (Union Carbide Corporation 1984)
		Guinea Pig	Unknown	LD50 = 4160 mg/kg (Smyth *et al.* 1941)
		Rabbit	Unknown	LD50 = > 4080-7190 mg/kg (BASF AG 1961; Patty's Industrial Hygiene & Toxicology 1982)
	Inhalation	Rat	Unknown	1 hr LC50 > 200 mg/L (MB Research Laboraties Inc. 1977)
		Rat	Unknown	No mortality after an 8 hr exposure to a saturated atmosphere of DEGME at 20°C (BASF AG 1960)
		Rat	corr. OECD	No mortality after an 6 hr exposure to a saturated atmosphere of DEGME (Union Carbide Corporation 1984)
	Dermal	Rabbit	Unknown	LD50 = 6540-20400 mg/kg (Ethel Browning's 1965; Union Carbide Data Sheet 1967)
		Rabbit	Unknown	LD50 = 9284 mg/kg b.w. (Union Carbide Corporation 1984)

Human data
There are no human data on acute toxicity.

Conclusion
According to EC criteria the compound does not need to be classified on the basis of its acute toxicity.

4.1.2.3 Irritation

Animal studies
Skin
In several experiments with rabbits (Union Carbide Corporation 1984; BASF AG 1960; DOW Chemical company 1954 and MB Research laboraties Inc. 1977) skin irritation was studied. In an OECD-like test (Union Carbide Corporation 1984) rabbits received 0.5 ml of the test substance on the clipped intact skin under occlusive conditions. No irritation was seen at all observation periods (5 hrs., 1, 2, and 3 days). The remaining studies showing no irritation or very slight irritation were only available as abstract.

Inhalation
There are no irritating effects reported after single short-term exposure by inhalation.

Eyes
In a well performed eye irritation study (Union Carbide Corporation 1984), corresponding to OECD guidelines, 0.1 ml undiluted DEGME was applied to the rabbit eye. Observations were made after

1, 4, 24, 48 or 72 hours. The primary irritation score was 0.53 (scores are given in the IUCLID Data Sheet: http://ecb.ei.jrc.it). The substance was concluded not to be irritating to the eye.
Other reported studies were limited reported or available as abstract and not performed to current guidelines (Union Carbide Data Sheet 1967; BASF AG 1960; Prehled Prumyslove Toxikol Org Latky 628 1986; MB Research laboraties Inc. 1977; Rowe *et al.* 1993).

Human data
There are no human data on irritation.

Conclusion
Based on the available skin and eye irritation studies DEGME should not be classified as an irritant to the skin and eye. In the 90-day dermal study irritation (Hobson *et al.* 1986) was not scored and in the rabbit teratogenicity studies (John *et al.* 1983) no irritation was observed.

4.1.2.4 Corrosivity

DEGME is not corrosive to skin, eyes and respiratory tract (see 4.1.2.3).

4.1.2.5 Sensitisation

Animal studies
In a very limited study no sensitising effects were reported in guinea pigs after the subcutaneous application of 0.08-8mg of DEGME followed 10 days later by an epidermal application for 7 days (Pastushenko *et al.* 1985).
Recently the skin sensitising potential of DEGME was tested by the maximisation test according to OECD and EEC guidelines (Bury 1997). Female Pirbright-white guinea pigs were tested using 99.93% pure DEGME. The control group included 5 animals and the treated group 20 animals, a positive control group was not used. During the induction phase the treatment group received on 2 intradermal injections with 0.1 ml of 5% DEGME in FCA, 0.1 ml of FCA or 0.1 ml of 5% DEGME in isotonic saline. The injection sites were left uncovered. Due to strong irritation reactions of the skin after intradermal injection with FCA 9wit and without DEGME), 10% sodium dodecylsulfate was not applied at day 6. On day 7 the treatment group received the last induction with 0.5 ml undiluted DEGME under an occlusive patch on the shoulder for 48 h. For the challenge on day 21 each animal was dermally administered with 0.5 mml undiluted DEGME under occlusive conditions for 24 h. Observations were made 24 and 48 hours thereafter. 0/10 Animals of the treatment group showed a positive skin response after the challenge.

Human data
In a 48 hour closed patch test a solution of DEGME in 25% petrolatum produced no irritation in 25 human subjects. (Kligman 1972).
DEGME was tested at a concentration of 20% petrolatum in a maximisation test with 25 human volunteers. No sensitisation was observed (Kligman 1972).

Conclusion
DEGME needs not to be classified as a skin sensitiser, based on the results of the well performed maximisation test (Bury 1997).

4.1.2.6 Repeated dose toxicity

Animal data

The results of the repeated dose studies are summarised in **Table 4.9**.

Table 4.9 Summary of repeated dose toxicity studies with DEGME.

REPEATED DOSE TOXICITY		SPECIES	PROTOCOL	RESULTS
4.1.2.6	Oral[1]	Rat	other: dose of 0,125, 250, 500, 1000, 2000, 3000, 4000 mg/kg/d	11 d no effects at 1000 mg/kg bw /d (Yamano *et al.* 1993)
		Rat	other: dose of 500, 1000, 2000 mg/kg/d	20 d no effects at 500 mg/kg bw/d (Kawamoto *et al.* 1990)
		Rat	other: dose of 900, 1800, 3600 mg/kg/d	6 w NOAEL = 900 mg/kg b.w. (Krasavage *et al.* 1982)
	Inhalation	Rat	other: doses of 0, 0.15, 0.49, 1.06 mg/L	90 d NOAEL ≥ 1.06 mg/L (Miller *et al.* 1985)
	Dermal	Guinea pig	other: doses of 0, 40, 200, 1000 mg/kg/d	90 d marginal LOAEL = 40 mg/kg bw/d (Hobson *et al.* 1986)

[1] Both the 11d and 20 d oral studies were not considered suitable for deriving a NOAEL.

Oral studies

In a preliminary dose-finding study groups of 5 female Wistar rats were treated by gavage with 0, 125, 250, 500, 1000, 2000, 3000 or 4000 mg DEGME/kg/day for 11 days. Body weight gain and food consumption were decreased at dose levels ≥ 3000 mg/kg b.w. A reduction in white and red blood cell count, haemoglobin and haematocrit levels was observed at the highest dose; Haematocrit levels were also decreased at 3000 mg/kg b.w. A dose related decrease in relative thymus and pituitary weight was observed ≥ 2000 mg/kg b.w. significantly at 4000 mg/kg b.w.

Kidney weight was increased at 4000 mg/kg b.w. No effects were observed at 1000 mg/kg b.w./day (Yamano *et al.* 1993).

A decrease in thymus weight was also observed in a dose-response study with male rats dosed 500, 1000 or 2000 mg DEGME/kg b.w. by gavage for 20 days. The highest dose was also administered in a time course study for 1, 2, 5 or 20 days. At the highest dose body weight as well as liver and testes weight were decreased. Light microscopy revealed lymphocyte depletion in the thymus cortex at 2000 mg/kg b.w. after 5 days of treatment. No effects were observed at the lowest dose of 500 mg/kg b.w./day (Kawamoto *et al.* 1990).

In a gavage study male rats were administered 0, 900, 1800 or 3600 mg DEGME/kg b.w. for 6 weeks. The mid and high dose level caused decreased body weight accompanied by decreased food consumption. At 3600 mg/kg b.w. relative liver, heart and kidney weight were increased and absolute and relative testis weight were decreased. Testis athrophy was observed in 50% of the high dose rats accompanied by evidence of degenerated spermatozoa in the epididymus and hypospermia. In one rat at 3600 mg/kg b.w. hyperkeratosis of the stomach was observed and at the same dose proteinaceous casts were seen in 90% of the rats. The NOAEL in this study is 900 mg/kg b.w. (Krasavage *et al.* 1982).

In a range finding study rats were given DEGME in the drinking water at dose levels ranging from 190 to 1830 mg/kg b.w.days for 30 days. Loss of appetite and reduced growth were observed at dose levels ≥ 790 and ≥ 1440 mg/kg b.w./day, respectively. Histopathological investigations performed on liver, kidney, spleen and testes revealed unspecified micropathological changes at all dose levels (Harada *et al.* 1975). Since only summarised data were available and with respect to the range finding character of the experiment, this study was considered not to be of relevance for the derivation of an overall NOAEL and/or LOAEL.

Effects on enzymes in serum and in liver tissue
Male Wistar rats (4/group) were administered by gavage 0, 500, 1000 or 2000 mg DEGME/kg b.w. for 1, 2, 5 or 20 days. After 5 and 20 days relative liver weight was decreased and hepatic microsomal protein was increased and cytochrome P-450 was induced at the highest dose level. Cytochrome B5 and NADPH-cytochrome C-reductase were not affected. No change in cytosolic ADH activity was observed. Considering the extent of the observed changes, the effect parameters used are not sufficiently indicative for effects on biotransformation activity (Kawamoto *et al.* 1990).
In a study according to a similar protocol (see Kawamoto *et al.* 1990) the activities of γGT, ALAT, ASAT and ALP in serum were measured as well as γGT activitities in various tissues. The enzyme activities were not altered. γGT activity in brain was significantly increased compared to control values. DEGME did not cause a significant increase of hepatic microsomal γGT activity, except for the rats which were administered 2000 mg/kg b.w./day for 4 weeks (5 days/week) (Kawamoto *et al.* 1992).

Effects on immune response
Groups of male Fisher 344 rats were immunised with trinitrophenyllipopolysaccharide (TNP-LPS) 4 or 28 hours prior to the first exposure to 100, 200, 400 or 800 mg DEGME/kg b.w./d for 2 days. Three days following immunisation the plaque-forming cell (PFC) response to TNP-LPS was determined. No alteration in the immune respons to TNP-LPS was observed (Smialowicz *et al.* 1992).

Conclusion
The available data set for oral toxicity is sufficient to derive an overall NOAEL.
DEGME caused effect in liver, kidney, heart and testis. The NOAEL is established at 900 mg/kg b.w.

Inhalation studies
A OECD-like study with Fischer 344 rats (GLP) is available with 10 rats/sex/group.
The rats were exposed in Rochester-type inhalation chambers (whole body exposure) to 0, 20, 100 or 216 ppm DEGME vapours (equal to 0, 150, 490 or 1060 mg/m^3) 6 hour/day, 5 days/week for 90 days. The highest exposure level was the maximum practically attainable concentration and was more than 60% of the theoretical maximum vapour concentration at 25 °C and 1 atm pressure. At 1060 mg/m^3 no treatment related effects on body weights, haematology, clinical chemistry, urinalysis organ weights, macroscopy and histopathology were observed. The NOAEL is ≥ 1060 mg/m^3 (Miller *et al.* 1985).

Conclusion
In the only available inhalation study no effects were observed in rats at the highest practically attainable concentration of 1060 mg/m^3 for 6 hour/day, 5 days/week for 90 days.

Dermal studies

In a 13 week study groups of 6 male Hartley guinea pigs were dermally exposed to 40, 200 or 1000 mg DEGME kg/b.w./d for 6 hour/day, 5 days/week for 90 days. The substance was applied neat to 2·2 gauze patches which were affixed to the shaven backs under occlusive conditions. A control group of 7 guinea pigs was kept.

No irritation was observed. A dose related increase in serum LDH was observed ≥ 200 mg/kg/day, significant at 1000 mg/kg b.w./d. MCH concentrations were increased at the highest dose. In all dose groups elevated urinary calcium levels were observed however, without any evidence of renal mineralisation or renal damage. Decreased spleen weight was observed in mid and high dose groups. No organ weight changes were seen (data on thymus weight were not available). At histopathology the occurrence of mild periportal hepatocellular fatty changes was increased at all dose levels (0/7, 2/6, 6/6 and 6/6 at 0, 40, 200 or 1000 mg/kg/day, respectively). Focal coagulation necrosis of the liver was observed in all groups (including control) but the observed incidences showed no dose relationship. Histopathological changes in the testes were not observed. The LOEL in this study is 40 mg/kg b.w.

The evaluation of the relevance of the observed increased incidence of fatty changes is rather difficult, especially at the low dose level [2/6 (n.s.)]. Changes which could be related to the observed fatty changes, e.g. increased liver weight were not observed. In addition 90-day tests in guinea pigs are quite unusual and background data on fatty vacuolisation in untreated guinea pigs are not available. Since it cannot be excluded that the observed fatty changes in the liver are an adverse effect and taking these consideration into account, the rapporteur considered, as a worst case approach, the low dose of 40 mg/kg b.w. as a marginal effect level. For risk assessment the choice of the assessment factors and the size of the MOS should be judged in the light of the considerations given above.

Conclusion

One dermal study was available with guinea pigs. DEGME caused decreased spleen weight ≥ 200 mg/kg b.w. and slight histopathological changes in the liver and elevated urinary calcium levels ≥ 40 mg/kg b.w./d. A marginal LOAEL of 40 mg/kg b.w. is established. In the dermal reprotoxicity study performed with rabbits (see **Table 4.11**) maternal toxicity was observed at 750 mg/kg b.w., but not at 250 mg/kg b.w.

Human data

There are no human data on repeated toxicity

Conclusion repeated dose studies

A number of oral tests with DEGME were available. An overall NOAEL of 900 mg/kg b.w./d is established and used for modelling.

In a 90-day inhalation study with rats no effects were observed at the highest dose of 1060 mg/m^3 (duration corrected value: 189 mg/m^3).

Guinea pigs exposed dermally to DEGME showed decreased spleen weight ≥ 200 mg/kg b.w. and slight histopathological changes in the liver and elevated urinary calcium levels at doses ≥ 40 mg/kg b.w./day. A marginal effect level of 40 mg/kg b.w. is established in this study.

Based on these data the substance need not to be classified according to EC guidelines.

4.1.2.7 Mutagenicity

All available mutagenicity assays are summarised in **Table 4.10**.

Table 4.10 Summary of mutagenicity assays with DEGME.

GENETIC TOXICITY		SPECIES	PROTOCOL	RESULTS
4.1.2.7	Bacterial Test (Gene mutation)	S.typhimurium (5 strains)	other: Ames *et al.* 1975	negative with and without S9 (ICI PLC 1980)
		S.typhimurium (4 strains)	OECD 471	negative with and without S9 (BASF AG 1989)
	Cytogenetic assay (chromosomal aberrations)	Chinese hamster V79 cells	OECD 473	negative with and without S9 (Müller 1997)

The mutagenic potential of DEGME was tested in 2 Ames assays. No reverse mutations were induced in *Salmonella typhimurium* strains TA 1535, TA1538, TA1537, TA100 or TA98 with and without metabolic activation using the direct plate incorporation method. The results of this assay were only presented in an abstract (ICI PLC 1980). Another Ames test was performed according to OECD guidelines using *Salmonella typhimurium* strains TA1535, TA1537, TA100 or TA98. The DEGME concentrations used were 20 5000 µg/plate. No reverse mutations were induced with and without metabolic activation (BASF AG 1989).
Recently an *in vitro* mammalian chromosome aberration test according to OECD 473 was performed. The test was performed under GLP conditions and carried out in V79 Chinese hamster cells with doses upto 1201.7 µg/ml (= 10 mM) with and without metabolic activation in 2 independent experiments. In both experiments the highest concentration produces a lowering of the mitotic index at 28 h (but not at 20 h) fixation interval. DEGME was not mutagenic in this chromosome aberration test system. The positive controls (EMS and CPA, without and with metabolic activation) yielded positive results (Müller 1997).

Conclusion
DEGME is negative in assays detecting gene mutation in bacteria in all Salmonella typhimurium strains tested with and without metabolic activation. No chromosomal aberrations were observed, in a test according to OECD guidelines, in V79 Chinese hamster cells with and without metabolic activation. The data submitted are acceptable to establish the mutagenic potential of DEGME and are in accordance with respect to the basic requirements as specified in Annex VIIA of Directive 67/548/EC.
It is concluded that DEGME is not mutagenic.

4.1.2.8 Carcinogenicity

There are no carcinogenicity studies with animals nor human data available. This is acceptable according to the basic requirements as specified in Annex VIIA of Directive 67/548/EC. The lack of mutagenic potential and the effects observed in the repeated dose toxicity studies does not give cause for concern for carcinogenicity.

4.1.2.9 Toxicity for reproduction

Animal studies

The fertility studies as well as the developmental/teratogenicity studies are summarised in **Table 4.11**.

Oral fertility studies

The effects of DEGME on the testes of male mice and rats were investigated.

In mice no effects were observed on testicular weight, seminal vesicles and coagulating gland weight and mean WBC count after the administration of 2% DEGME in drinking water for 25 days (Nagano *et al*. 1984). Fifty rats were given 5.1 mmol/kg b.w. by gavage for upto 20 days. Groups of 5 rats were sacrificed intercurrently and their testes were examined histopathologically. No abnormalities were observed (Cheever *et al*. 1988).

Oral and s.c. developmental studies

Chernoff-Kavlok teratogenicity screening assays were performed with mice (oral) and rats (s.c.). In mice 4000 mg/kg b.w., the only dose tested, reduced the number of viable litters significantly in the presence of 10% maternal mortality (Schuler *et al*. 1984). The subcutaneous administration of 250, 500 or 1000 µl/kg DEGME to female rats from day 6 to 20 of gestation showed no maternal

Table 4.11 Summary of studies relevant to reproduction with DEGME.

EFFECTS on FERTILITY & DEVELOPMENTAL TOXICITY		SPECIES	PROTOCOL	RESULTS
4.1.2.9	Fertility studies Oral	Mice	testicular toxicity: 0 or 2% in drinking water	25 d NOAEL ≥ 4000 mg/kg b.w./day (Nagano *et al.* 1984)
		Rat	testicular toxicity: 5.1 mmol/kg b.w. (612 mg/kg b.w.)	20d NOAEL ≥ 612 mg/kg b.w. (Cheever *et al.* 1988)
	Developmental toxicity Oral	Mice	Chernoff-Kavlok: 4000 mg/kg b.w. day 7-14 of gestation	< 4000 mg/kg b.w. (Schuler *et al.* 1984)
		Rat	other: 0, 200, 600 or 1800 mg/kg b.w. day 7-17 of gestation	NOAEL (matern. tox) 600 mg/kg/b.w. (Yamano *et al.* 1993) NOAEL (embryotox.) 200 mg/kg b.w.
		Rat	Other: 0, 720, 2165 mg/kg/ b.w day 7-16 of gestation	NOAEL (matern. tox) 720 mg/kg/b.w. (Hardin *et al.* 1986; Hardin *et al.* 1985) NOAEL (develop.tox) <720 mg/kg b.w.
	Dermal	Rabbit	Other: 0, 50, 250, 750 mg/kg b.w. day 6-18 of gestation	NOAEL (matern. tox) 250 mg/kg b.w. (John *et al.* 1984; Scortichini *et al.* 1986) NOAEL (embryotox.) 50 mg/kg b.w.
	S.C.	Rabbit	Chernoff-Kavlok: ≈ 0, 250 , 500 or 1000 µg/kg day 6-20 of gestation	NOAEL 1000 mg/kg b.w. (Doe 1984; Doe *et al.* 1983, Wickramaratne 1987)

toxicity. At the highest dose the percentage of pups surviving on day 5 was marginally, but not significantly reduced (Doe 1984, Doe *et al.* 1983, Wickramaratne 1987).
In a developmental study 22 rats/group received 0, 200, 600 or 1800 mg/kg DEGME in water by gavage from day 7 to 17 of gestation. On day 20 of gestation 20 dams/group were killed and the remaining 8 dams/group kept for a postnatal study (see also IUCLID data sheet, http://ecb.ei.jrc.it). maternal toxicity as evidenced by decreased body weight gain, food consumption and thymus weight was observed in rats at 1800 mg DEGME/kg. At the same dose the duration of gestation was increased with about 2 days. The number of pups surviving 4 days was decreased at 600 and 1800 mg/kg (58/93 and 2/37, respectively; control: 92/100). High dose fetuses exhibited an increased incidence in the occurence of external malformations like anasarca and anury (14.1%) and dorsum subcutaneous hematomas (13.5%). At 600 and 1800 mg/kg an increase in visceral malformations was observed: 2.4% and 28% respectively, the majority being aortic arch and ventricular septal defects. 25.4% and 100% of the mid and high dose group fetuses had unilateral or bilateral thymnic remnants. Dilated renal pelvis was found in 52.8% of the highest dose group. The degree of ossification was affected at both 600 and 1800 mg/kg b.w. The NOAEL's for maternal toxicity and fetotoxicity are 600 and 200 mg/kg b.w., respectively (Yamano *et al.* 1993).
In another study with rats DEGME was administered at doses of 0, 720 or 2165 mg/kg b.w. from day 7-16 of gestation. Only very slight maternal toxicity was observed at the highest dose of 2165 mg/kg b.w. (decrease in food consumption day 7-12 and slight decrease in body weight on day 21). Fetal weight and litter size were significantly reduced at 2165 mg/kg b.w. and 2/23 litters were completely resorbed. At doses ≥ 720 mg/kg b.w. the incidence of reduced cranial ossification was increased and the ossification of the appendicular skeleton was reduced. At the same doses the incidence of dilated renal pelvis was increased. At 2165 mg/kg b.w. visceral malformations especially of the cardiovascular system (double aortic arch, right aortic arch and ventricular septal defect) were significantly increased. Only very slight maternal toxicity was observed at 2165 mg/kg b.w. The LOAEL for developmental toxicity is 720 mg/kg b.w. (Hardin *et al.* 1986, Hardin *et al.* 1985).

Dermal developmental studies
DEGME was dermally adminstered to groups of pregnant rabbits at doses of 0, 50, 250 or 750 mg/kg b.w. from day 6-18 of gestation. At 750 mg/kg b.w. maternal toxicity as evidenced by a decreased body weight gain during treatment and decreases in RBC and PCV levels was observed. At the highest dose the percentage of resorbed implantations was markedly increased. The fetal alterations included an increased incidence of mild fore limb flexure, dilitation of the renal pelvis, retrocaval ureter, cervical spurs and delayed ossification of the skull and sternebral bones at the highest dose. The incidence of delayed ossification of the hyoid and sternebrae and cervical spur were seen at 250 and 750 mg/kg b.w. No embryo/foetotoxic and teratogenic effects were observed at 50 mg/kg b.w. (John *et al.* 1984; Scortichini *et al.* 1986).

Human data
There are no human data on reproduction toxicity of DEGME.

Conclusion reproduction toxicity
No testicular effects were seen in mice and rats administered 4000 mg/kg b.w in drinking water or ≈ 610 mg/kg b.w. by gavage, respectively. It should be noted that in a 6 weeks repeated dose study with rats the testes weight was decreased and testicular atrophy and altered sperm production was observed at 3600 mg DEGME/kg b.w. (see 4.1.2.6).
In a Chernoff-Kavlok assay with mice the number of viable litters was reduced after the single

oral administration of 4000 mg/kg b.w. from gestation day 7-14. In a similar assay no effects were observed after the s.c. administration of 1000 µl/kg (≈ 1020 mg/kg) to pregnant rats.
Two oral developmental studies are available. In both studies visceral malformations especially of the cardiovascular system were observed at concentrations ≥ 1800 mg/kg b.w. The NOAELs for maternal toxicity and fetotoxicity are 600 and 200 mg/kg b.w., respectively.
The dermal administration of DEGME at doses upto 750 mg/kg b.w. to pregnant rabbits from day 6-18 of gestation caused maternal toxicity at the highest dose. No adverse embryotoxic or fetal effects as well as no teratogenic effects were observed at 50 mg/kg b.w.
The rapporteur proposes labelling with R-phrase 63: Possible risk of harm to the unborn child.

4.1.3 Risk characterisation

4.1.3.0 General aspects

The human population may be exposed to DEGME at the workplace, both from use of consumer products and indirectly via the environment (see 4.1.1.1, 4.1.1.2, 4.1.1.3).

In the data set animal and only one human study (sensitisation) were available. Most of the studies were not performed according to current standards, and were in some cases not suitable for the overall assessment.

The majority of the acute toxicity studies have not been performed to current guidelines. Based on the available data DEGME has a low acute oral and dermal toxicity, LD_{50}'s being ≥ 5500 mg/kg b.w.(rat) and ≥ 6540 mg/kg b.w.(rabbit), respectively. No death occurred in the available inhalation studies with rats.
Based on the available skin and eye irritation studies DEGME need not to be classified as an irritant to the skin and eye. Classification as sensitising agent is not indicated.

With respect to repeated dose toxicity the available data set for oral toxicity revealed an overall NOAEL of 900 mg/kg b.w. In the available inhalation study no effects were observed in rats at the highest administered dose of 1060 mg/m^3 for 6 hour/day, 5 days/week for 90 days. In a dermal study with guinea pigs DEGME related effects were seen at all dose groups. Decreased spleen weight was observed at doses of ≥ 200 mg/kg b.w. and slight histopathological changes in the liver and elevated urinary calcium levels were seen at ≥ 40 mg/kg b.w. day. A marginal effect level of 40 mg/kg b.w. is established, however it should be noted that the size of the margins of safety and assessment factors should be judged in the light of the fact that there is no firm evidence that the observed fatty changes in the liver are an adverse effect.

DEGME is considered to be not mutagenic. Data on carcinogenicity are not available.

In fertility studies with mice and rats DEGME caused no effects in mice and rats at 4000 mg/kg b.w in drinking water or ≈ 610 mg/kg b.w. by gavage, respectively. However, in the 6 week repeated dose study with rats the testes weight was decreased and testicular atrophy and altered sperm production was observed at 3600 mg/kg b.w. (see 4.1.2.6).
In oral developmental studies no embryotoxic or teratogenic effects were observed at a dose of 200 mg/kg bw/d. At high doses (≥ 1800 mg/kg b.w.) visceral malformations especially of the cardiovascular system were observed. In the available dermal developmental study a NOAEL of 50 mg/kg bw/d is established.

4.1.3.1 Workers

Assuming that oral exposure is prevented by personal hygienic measures, the risk characterisation for workers is limited to the dermal and inhalation routes of exposure

Acute toxicity
Given the effects observed in the acute inhalation and dermal studies it is concluded that 2-(2-methoxyethoxy)ethanol is of no concern for workers with regard to acute effects (**conclusion ii**).

Irritation
Given the effects observed in the skin and eye irritation studies, it is concluded that DEGME is of no concern for workers with regard to irritating effects (**conclusion ii**).

Corrosivity
See irritation (**conclusion ii**).

Sensitisation
Given the results from the dermal sensitisation studies it is concluded that DEGME is of no concern for workers with regard to skin sensitisation (**conclusion ii**).
There are neither data from human experience nor other indications for respiratory sensitisation.

Repeated-dose toxicity
Dermal exposure
Starting-points for the risk assessment for workers exposed by skin contact are (a) the estimated dermal exposure levels for the different occupational exposure scenarios (see chapter 4.1.1.1 and **Table 4.2**), and (b) the marginal LOAEL (40 mg/kg bw/d) from the semichronic dermal study in guinea pigs. Given the estimated frequency of exposure (100-200 days/year) chronic exposure is assumed for risk characterisation. The MOSs between the marginal LOAEL and the regarding dermal exposure levels are listed in **Table 4.12**. The MOSs are evaluated by comparison with the minimal MOS (100). In Annex 1 the assessment factors used to establish the minimal MOS are given (**Table A1.1**). There is concern when the MOS is lower than the minimal MOS. The conclusions are given in **Table 4.12**.

Based on the risk assessment for dermal exposure as mentioned in **Table 4.12**, it is concluded that dermal exposure to DEGME introduces a risk for workers in exposure scenarios 1, 2, and 4 when used without risk reduction measures (**conclusion iii**). It might be possible that in some industrial premises worker protection measures are already applied. The study design of the dermal study is limited. It might be possible that a well performed dermal study with rats or rabbits will give relevant information. However, it cannot be predicted whether this will lead to conclusion ii.

Inhalation exposure
Starting-points for the risk assessment for workers exposed by inhalation are (a) the estimated inhalation exposure levels for the different occupational exposure scenarios (see chapter 4.1.1.1 and **Table 4.2**), and (b) the NOAEL from the semichronic inhalation study with rats. In this study the highest dose level tested (1060 mg/m^3, i.e. the highest practically attainable concentration) did not induce adverse effects. Comparing this level expressed in mg/kg bw/day (approx. 305 mg/kg bw/d, assuming an inhalation volume of 240 ml/min and a body weight of 0.3 kg for rats) with the

Table 4.12 Occupational risk assessment of DEGME for repeated dose toxicity.

Occupational scenario/subscenario	Risk assessment for full-shift inhalation exposure[A]			Risk assessment for full-shift dermal exposure		
	Estimated inhalation exposure (mg/m^3) worst case	MOS[B]	Conclusion[C]	estimated dermal exposure (mg/day)	MOS[D]	Conclusion[E]
1: production of DEGME	5.2	204	ii	210	13	iii
2: production of products containing DEGME	21	50	ii	420	7	iii
3: automated application of products containing DEGME	2.5	424	ii	42	66	ii
4: manual application of products containing DEGME	20	53	ii	1950	1	iii

[A] Worst case assuming 8 hrs exposure a workday;

[B] calculation based on a NOAEL of 1060 mg/m^3;

[C] the conclusion is reached by considering the magnitude the MOS, taking into account a number of additional parameters as described in the TGD. An approach to do so is given in Annex 1 (**Table A1.2**) and Annex 2;

[D] calculated based on a LOAEL of 40 mg/kg bw/d and a body weight of the worker of 70 kg;

[E] the conclusion is reached by considering the magnitude the MOS, taking into account a number of additional parameters as described in the TGD. An approach to do so is given in Annex 1 (**Table A1.1**) and Annex 2;

marginal LOAEL of the semichronic dermal study with guinea pigs might indicate a lower toxicity by inhalation than after contact with skin or otherwise that guinea pigs are more susceptible than rats. Given the estimated frequency of exposure (100-200 days/year) chronic exposure is assumed for risk characterisation. The MOS between the NOAEL and the regarding inhalation exposure levels are listed in **Table 4.12**. The MOSs are evaluated by comparison with the minimal MOS (23). In Annex 1 the assessment factors used to establish the minmal MOS are given (**Table A1.2**). There is concern when the MOS is lower than the minimal MOS. The conclusions are given in **Table 4.12**.

Given the risk assessment for full-shift inhalation exposure, as mentioned in **Table 4.12**, it is concluded that, based upon the present information, no health risks due to occupational exposure are to be expected (**conclusion ii**).

Combined exposure

Given the toxicity data available no clear conclusions (qualitative or quantitative) can be drawn on the resemblence of the toxicity of DEGME as consequence of internal exposure after contact with the skin and the toxicity as consequence of the internal exposure after inhalation. Therefore, the assessment of the risk after combined exposure (i.e., the risk due to the internal exposure resulting from both the dermal and the inhalation exposure) can only be made with rough assumptions and by introducing a lot of uncertainties.

Given the conclusionsdrawn for the inhalation and dermal routes separately, it is assumed that internal exposure of the worker as result from uptake via inhalation will not significantly contribute to the risk as estimated for dermal exposure.

Mutagenicity

Given the results from the mutagenicity studies it is concluded that DEGME is of no concern for workers with regard to mutagenicity (**conclusion ii**).

Carcinogenicity

No data on carcinogenicity are available.

Given the results from the mutagenicity studies and the repeated dose studies with 2-(2-methoxyethoxy)ethanol it is concluded that there are no reasons for concern for workers with regard to carcinogenicity (**conclusion ii**).

Reproductive toxicity

Dermal exposure

Starting-points for the risk assessment for workers exposed by skin contact are (a) the NOAEL (50 mg/kg bw/d) from the dermal developmental study in rabbits, and (b) the estimated dermal exposure levels for the different occupational exposure scenarios (see chapter 4.1.1.1 and **Table 4.2**).

The MOS between the NOAEL and the regarding dermal exposure levels are listed in **Table 4.13**.

The MOSs are evaluated by comparison with the minimal MOS (14). In Annex 1 the assessment factors applicable to establish the minimal MOS are given (**Table A1.3**). There is concern when the MOS is lower than the minimal MOS. The conclusions are given in **Table 4.13**.

Based on the risk assessment for dermal exposure as mentioned in **Table 4.13** it is concluded that developmental effects due to occupational skin contact cannot be excluded for scenario 2 (production of products containing DEGME) and scenario 4 (manual application of products containing DEGME (**conclusion iii**).

Inhalation exposure

There are neither reproduction toxicity studies by inhalation available nor sufficient data to perform a quantitative route-to-route extrapolation (e.g. absorption data are lacking).

It is expected that there is no concern for reproduction effects after inhalation exposure (conclusion ii) because (1) reproduction effects most probably occur at higher dose levels than the critical effects as observed in the repeated dose studies (see e.g. HBORV derm/chronic (28 mg/day) and the HBORV derm/repro (243 mg/day)), and (2) there is no concern for adverse effects after chronic inhalation exposure.

The results of the inhalation and dermal toxicity studies indicate that DEGME is more toxic after contact with the skin than by inhalation exposure. However, the results do not allow a conclusion on difference in type of effects. It should be noted that the qualitative route-to-route extrapolation, as described above, is only valid when the type of effects will not be influenced by the route of administration.

It is concluded that there are no reasons for concern for occupational inhalation exposure with regard to reproduction effects (**conclusion ii**).

Table 4.13 Occupational risk assessment of DEGME for reproduction toxicity after dermal exposure.

Occupational scenario/subscenario	Risk assessment for full-shift dermal exposure		
	Estimated dermal exposure (mg/day)	MOS[A]	Conclusion[B]
1: production of DEGME	210	17	ii
2: production of products containing DEGME	420	8	iii
3: automated application of products containing DEGME	42	83	ii
4: manual application of products containing DEGME	1950	2	iii

[A] based on a NOAEL of 50 mg/kg bw/d and a body weight of the worker of 70 kg;

[B] the conclusion is reached by considering the magnitude the MOS, taking into account a number of additional parameters as described in the TGD. An approach to do so is given in Annex 1 (**Table A1.3**) and Annex 2.

Occupational limit values

In a draft report of the Dutch Expert Committee on Occupational Standards (Dutch Expert Committee for Occupational Standards 1995) a HBROEL of 23 mg/m^3 was established for DEGME. This report relies on the same studies as were summarised in the HEDSET. The DECOS limit-value is based on the NOAEL from the dermal developmental toxicity study with rabbits (50 mg/kg bw/d), assuming 50% dermal absorption, 76% retention by inhalation, a respiratory volume of 10 m^3/ working day and a bodyweight of 70 kg. A safety factor of 10 is introduced to extrapolate from rabbits to man and to compensate for the minimal effects observed in the dermal semichronic study at 40 mg/kg bw/d. It is noted, that the value derived is in well agreement with the limit value used for risk characterisation for repeated exposure.
Occupational standards, established by other national and international bodies, are not described.

The toxicity profile of DEGME indicates, that the dermal route of exposure gives more reasons for concern than the respiratory route.

4.1.3.2 Consumers

Starting point for the risk characterisation are the inhalatory LC50-rat (200 mg/l), the marginal effect level (40 mg/kg b.w.) from the semichronic dermal quinea pig study (repeated dose toxicity) and the NOAEL (50 mg/kg b.w.) from the dermal developmental study in rabbits (reproductive toxicity).

Scenario I

For the use of DEGME as solvent in aequous paint an inhalatory exposure concentration per event of 4.1 mg/m^3 has estimated by the CONSEXPO model in an acute scenario. The margin of safety between the 1hr inhalatory $LC_{50\text{-rat}}$ value of 200 mg/l (see 4.1.2.2) and the estimated inhalatory concentration/event has been calculated to be 4.8E+4. Taken into account all data available, this margin of safety is judged to be sufficient (**conclusion ii**).

Repeated dose toxicity

The margin of safety between the marginal LOAEL of 40 mg/kg bw/day (uptake basis assuming the bioavailability via the dermal route is 100%) from the semichronic dermal study in guinea pigs

and the estimated total daily uptake has been calculated to be about 70. Taken into account intra- and inter- species variation and the use of a marginal subchronic marginal effect level, it is indicated that there is concern for consumers (**conclusion iii**).

Reproductive toxicity

The margin of safety between the NOAEL from the dermal developmental study in rabbits (50 mg/kg b.w., uptake basis assuming the bioavailability via the dermal route is 100%) and the estimated total daily uptake has been calculated to be about 90. Taken into account intra- and inter-species variation and the occurrence of visceral malformations of the cardiovascular system at very high doses, it is indicated that concern for developmental effects cannot be excluded (**conclusion iii**).

Scenario II

The inhalatory exposure concentration when using DEGME containing paint stripper was 148 mg/m^3 as calculated by the CONSEXPO model in an acute scenario. The margin of safety between the 1 hr inhalatory $LC_{50\text{-rat}}$ value of 200 mg/l and the estimated inhalatory concentration/event has been calculated to be about 1300. Taken into account all data available, this margin of safety is judged to be sufficient (**conclusion ii**).

Repeated dose toxicity

The margin of safety between the marginal LOAEL of 40 mg/kg b.w./day (uptake basis assuming the bioavailability via the dermal route is 100%) and the estimated total daily uptake has been calculated to be about 100. Taken into account intra- and inter- species variation and the use of a marginal subchronic marginal effect level, it is indicated that there is concern for consumers (**conclusion iii**).

Reproductive toxicity

The margin of safety between the NOAEL from the dermal developmental study in rabbits (50 mg/kg b.w., uptake basis assuming the bioavailability via the dermal route is 100%) and the estimated total daily uptake has been calculated to be about 133. Taken into account intra- and inter-species variation and the occurrence of visceral malformations of the cardiovascular system at very high doses, it is indicated that concern for developmental effects cannot be excluded (**conclusion iii**).

Scenario III

Repeated dose toxicity and reproductive toxicity

For the use of DEGME as a cleaning agent in windscreen washer liquid an inhalatory exposure concentration of 2.2 mg/m^3 is calculated. The total calculated internal dose (yearly average) is 20 µg/kg b.w/day. The margins of safety between the marginal effect level of 40 mg/kg b.w./day in the semi-chronic guinea pig study and reproductive dermal NOAEL of 50 mg/kg b.w.(uptake basis assuming the bioavailability via the dermal route is 100%) and the estimated total daily uptake have been calculated to be ≥ 2000. Taking into account all data available, this margin of safety is judged to be sufficient (**conclusion ii**).

4.1.3.3 Man exposed indirectly via the environment

Inhalation exposure

Repeated dose toxicity

For the risk characterisation for humans indirectly exposed by inhalation the local concentration estimates in air (100 m from source) are compared with the observed NOAEL of ≥ 1060 mg/m^3 (189 mg/m^3 corrected for continuous exposure) from the 90-day rat study. The local concentration estimates in air are presented in **Table 4.5**. The regional scale air concentrations are presented in **Table 4.7**.

The margins of safety for the local scale are presented in **Table 4.14** and are ranging from 9.2E+3 - 9E+6 indicating no concern for human safety, taken into account intra- and inter-species variation and the use of a NOAEL from a 90-day rat study (**conclusion ii**).

Table 4.14 Margins of safety between the NOAEL from the 90-day rat study and the estimated concentration in air (100 m) from source.

Specific or generic	Margin of safety (MOS)
Specific scenario A - production	3.9 E+6
Specific scenario B - production/processing	3.1 E+5
Generic scenario C - production	5.0 E+4
Generic scenario D - production	9.0 E+6
Generic scenario E1 (Anti-icing agent) - formulation	7.4 E+4
Generic scenario E2 (Basic chemicals) - processing	9.2 E+3
Generic scenario E3 (Chemical intermediate) - formulation	6.8 E+5

When comparing the regional scale air concentration (see **Table 4.7**) with the NOAEL of ≥ 189 mg/m^3 also a very high margin of safety (7E+5) is calculated indicating no concern for human safety (**conclusion ii**).

Reproductive toxicity

There are neither reproduction toxicity studies by inhalation available nor suficient data to perform a quantitative route-to-route extrapolation (e.g. absorption data are lacking). From the available oral repeated dose toxicity study (NOAEL 900 mg/kg b.w.) and the oral embryotoxicity study (NOAEL 200 mg/kg b.w.) it may be concluded that reproduction effects may occur at lower dose levels than the critical effects as observed in the oral repeated dose studies. However since the above calculated margins of safety for exposure by inhalation at local and regional scale are

≥ 7000 it is considered unlikely that reproductive effects due to inhalation exposure will occur. Therefore it is concluded that there are no reasons for concern for humans exposed via the environment with regard to reproductive effects (**conclusion ii**).

Intake via drinking water and total intake

The public at large may be exposed to DEGME via drinking water since in the USA drinking water supplies have been shown to contain DEGME. For Europe no data are available. A separate risk characterisation for drinking water has not been carried out since no measured data could be found for DEGME in drinking water.

The total intakes via air, drinking water and food at local scale are presented in **Table 4.6** and the regional total human intake via air, water and food is given in **Table 4.7**.

Repeated dose toxicity

For the risk characterisation after repeated dose toxicity these intakes are compared with the overall oral NOAEL of 900 mg/kg b.w. from the 6-week rat study. On the local scale the margins of safety (MOS) are given in **Table 4.15**.

Table 4.15 The margins of safety (MOS) between the NOAEL from the 6-week rat study and the estimated total daily intake at the local site.

Specific or generic	Margin of safety (MOS)
Specific scenario A - production	1.2 E+4
Specific scenario B - production/processing	1.1 E+5
Generic scenario C - production	1.3 E+4
Generic scenario D - production	8.2 E+4
Generic scenario E1 (Anti-icing agent) - formulation	2.6 E+4
Generic scenario E2 (Basic chemicals) - processing	2.4.0 E+3
Generic scenario E3 (Chemical intermediate) - processing	6.5 E+4

The calculated margins of safety for all local scenarios are ranging from 2400 - 11000 indicating no concern for human safety following indirect exposure to DEGME, taken into account intra- and inter-species variation and the use of a NOAEL from a 6-week rat study (**conclusion ii**).

When comparing the total intake at regional scale (see **Table 4.7**) with the NOAEL of 900 mg/kg b.w. the margin of safety is 2.05 E+6 indicating no concern for human safety, take into account all data available (**conclusion ii**).

Reproductive toxicity
Starting point for the risk characterisation is the NOAEL from the oral developmental study in rats of 200 mg/kg b.w. and the total daily intakes as presented in **Table 4.16** also used for the calculation of the MOS after repeated oral exposure.

Table 4.16 The margins of safety (MOS) between the NOAEL from the developmental rat study and the estimated total daily intake at the local site.

Specific or generic	Margin of safety (MOS)
Specific scenario A - production	2663
Specific scenario B - production/processing	24600
Generic scenario C - production	2941
Generic scenario D - production	18182
Generic scenario E1 (Anti-icing agent) - formulation	5731
Generic scenario E2 (Basic chemicals) - processing	522
Generic scenario E3 (Chemical intermediate) - processing	14493

It is calculated that the margin of safety for the generic scenarios E2 (basic chemicals)-processing is 522. Taken into account intra- and inter-species variation, the use of a generic scenario and the occurrence of visceral malformations of the cardiovascular system only at very high doses (≥ 1800 mg/kg b.w.), it is concluded that this margin of is sufficient (**conclusion ii**). The margins of safety (all ≥ 1000) for the other local scenarios A, B, C, D and E3 as well as the regional scale are also indicating no concern for developmental effects in humans following indirect exposure to DEGME, taken in acount all data available (**conclusion ii**).

4.1.3.4 Combined exposure

No risk assessment has been carried out for humans at this stage of the assessment.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

Flammability, explosive properties and oxidising properties are not considered to form an hazard. However, it is noted that oxidation by air may involve peroxidation of the substance, which may increase explosive properties. A general warning to this effect is recommended. Use of anti-oxidants reduces the potential to peroxidation. Strong reducing agents (eg. light metals) may lead to decomposition and hazardous gas generation.
There is no need for further information and/or testing with regard to physico-chemical properties (**conclusion ii**).

5 RESULTS

Environment

( ) i) There is need for further information and/or testing
(X) ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied
( ) iii) There is a need for limiting the risks: risk reduction measures which are already being applied shall be taken into account

Consumers

( ) i) There is need for further information and/or testing
( ) ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied
(X) iii) There is a need for limiting the risks: risk reduction measures which are already being applied shall be taken into account

Conclusion (iii) is reached because:
- the risk assessment indicates a possible concern for consumers through the uses of paint or paint stripper containing the substance.

Workers

( ) i) There is need for further information and/or testing
( ) ii) There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied
(X) iii) There is a need for limiting the risks: risk reduction measures which are already being applied shall be taken into account

Conclusion (iii) is reached because:
- based on the information available with respect to anticipated effects after occupational dermal exposure (repeated dose studies) risk reducing measures should be taken for occupational exposure scenarios 1, 2 and 4.
- based on the information available with respect to anticipated effects after occupational dermal exposure (developmental effects) risk reducing measures should be taken for occupational exposure scenario 2 (production of products containing DEGME) and 4 (manual application of products containing DEGME).

It might be possible that in some industrial premises these worker protection measures are already applied.

In relation to all other potential adverse effects and the worker population it is concluded that based on the available information at present no further information/testing on the substance is needed.

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GLOSSARY

Standard term / Abbreviation	Explanation / Remarks and Alternative Abbreviation(s)
Ann.	Annex
AF	assessment factor
BCF	bioconcentration factor
bw	body weight / *Bw, b.w.*
°C	degrees Celsius (centigrade)
CAS	Chemical Abstract System
CEC	Commission of the European Communities
CEN	European Committee for Normalisation
CEPE	European Committee for Paints and Inks
d	day(s)
d.wt.	dry weight / *dw*
DG	Directorate General
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{50lab}	period required for 50 percent dissipation under laboratory conditions (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
$DT_{90field}$	period required for 90 percent dissipation under field conditions (define method of estimation)
EC	European Commission
EC	European Communities
EC_{50}	median effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
EU	European Union
EUSES	European Union System for the Evaluation of Substances
f_{oc}	organic carbon factor (compartment depending)
g	gram(s)
gw	gram weight
GLP	good laboratory practice
h	hour(s)
ha	hectares / *h*
HPLC	high pressure liquid chromatography
IARC	International Agency for Research on Cancer
IC_{50}	median immobilisation concentration or median inhibitory concentration 1 / *explained by a footnote if necessary*

ISO	International Standards Organisation
IUPAC	International Union for Pure Applied Chemistry
kg	kilogram(s)
kPa	kilo Pascals
K_{oc}	organic carbon adsorption coefficient
K_{ow}	octanol-water partition coefficient
Kp	solid-water partitioning coefficient of suspended matter
l	litre(s) / *L*
log	*logarithm to the basis 10*
$L(E)C_{50}$	lethal concentration, median
m	meter
µg	microgram(s)
mg	milligram(s)
MOS	margins of safety
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
OJ	Official Journal
pH	potential hydrogen -*logarithm* (to the base 10) of he 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
Pa	Pascal unit(s)
PEC	predicted environmental concentration
PNEC(s)	predicted no effect concentration(s)
$PNEC_{water}$	predicted no effect concentration in water
(Q)SAR	quantitative structure activity relation
STP	sewage treatment plant
TGD	Technical Guidance Document[3]
UV	ultraviolet region of spectrum
UVCB	Unknown or Variable composition, Complex reaction products or Biological material
v/v	volume per volume ratio
w/w	weight per weight ratio

[3] Commission of the European Communities, 1996. Technical Guidance Documents in Support of the Commission Directive 93/67/EEC on risk assessment for new substances and the Commission Regulation (EC) No. 1488/94 on risk assessment for existing substances. Commission of the European Communities, Brussels, Belgium. ISBN 92-827-801 [1234].

Annex 1 Establishment of the minimal MOSs used for the risk characterisation by the Netherlands

NOTE: This annex represents the views of the Netherlands. In particular it presents the approach used by the Netherlands to determine, in a transparent way, which conclusion is to be drawn for worker risk characterisation base on the magnitude of the MOS.

Table A1.1 Assessment factors applied for the calculation of the minimal MOS for systemic effects after chronic dermal exposure based on a semichronic dermal toxicity study in guinea pigs.

Aspect	Assessment factors
Interspecies differences[1]	3.4 • 3
Intraspecies differences	3
Differences between experimental conditions and[2] exposure pattern of the worker	5
Type of critical effect	1
Dose-response curve[3]	2
Confidence of the database	1
Overall[4]	306 (100)

[1] Adjustment via caloric demands together with an uncertainty factor

[2] A factor for extrapolation from semichronic to chronic exposure is introduced because it is necessary to take into account (a) that in general adverse effect levels will decrease with increasing exposure times, (b) that adverse effects may appear a long time after exposure has been stopped, and (c) other and more serious adverse effects may appear with increasing exposure times. Default value for extrapolation from semichronic to chronic exposure is 10. A smaller factor is indicated, because the results of the oral studies indicate neither more severe adverse effects at similar exposure levels nor lower adverse effect levels by extending exposure times from 11 days (subacute) to 6 weeks (semichronic). A factor 5 is considered applicable, because no clear conclusions can be drawn on extending exposure times from semichronic to chronic.

[3] Factor 2 is applied for starting from a marginal LOAEL instead of a NOAEL

[4] Reasonable worst case estimations are generally used for individual assessment factors. However, because with respect to DEGME, there are only marginal effects observed, and because it cannot be excluded that the factor introduced for differences between experimental conditions and exposure pattern of the worker is too conservative, the resulting overall factor is considered too heigh. Therefore, an overall assessment factor of 100 is justifiable by expert judgement to calculate the minimal MOS.

Table A1.2 Assessment factors applied for the calculation of the minimal MOS for systemic effects after chronic inhalation exposure based on a semichronic inhalation toxicity study in rats.

Aspect	Assessment factors
Interspecies differences[1]	3
Intraspecies differences	3
Differences between experimental conditions and[2] exposure pattern of the worker	5
Type of critical effect	1
Dose-response curve[3]	0.5
Confidence of the database	1
Overall	23

1 No corrections are made for caloric demands, because extrapolation is based on concentration equivalents. Only an uncertainty factor is applied.

2 A factor for extrapolation from semichronic to chronic exposure is introduced because it is necessary to take into account (a) that in general adverse effect levels will decrease with increasing exposure times, (b) that adverse effects may appear a long time after exposure has been stopped, and (c) other and more serious adverse effects may appear with increasing exposure times. Default value for extrapolation from semichronic to chronic exposure is 10. A smaller factor is indicated, because the results of the oral studies indicate neither more severe adverse effects at similar exposure levels nor lower adverse effect levels by extending exposure times from 11 days (subacute) to 6 weeks (semichronic). A factor 5 is considered applicable, because no clear conclusions can be drawn on extending exposure times from semichronic to chronic.

3 Because no (systemic) effects were observed and the LOAEL might be much higher than the highest dose level tested, an arbitrary factor 0.5 is introduced.

Table A1.3 Assessment factors applied for the calculation of the minimal MOS for reproductive effects after dermal exposure based on a dermal developmental toxicity study in rabbits.

Aspect	Assessment factors
Interspecies differences[1]	2.4 • 2
Intraspecies differences	3
Differences between experimental conditions and exposure pattern of the worker	1
Type of critical effect[2]	1
Dose-response curve	1
Confidence of the database	1
Overall	14

1 Adjustment via caloric demands, together with an uncertainty factor. The default value for the uncertainty factor is 3. Because the developmental effects were studied in several species, and there were no indications for large interspecies differences with respect to the kind of effects, a factor 2 is considered to be sufficient.

2 Given the severity of the effects it is not necessary to introduce an additional factor for the effects.

Annex 2 Risk estimation using the minimal MOS-approach by the Netherlands

NOTE: This annex represents the views of the Netherlands. In particular in presents the approach used by the Netherlands to determine, in a transparent way, which conclusion is to be drawn for worker risk characterisation base on the magnitude of the MOS.

For occupational risk assessment the NOAEL/LOAEL to be used as starting point is compared with the estimated exposure levels. The minimal MOS is used for evaluation of the MOS, i.e., the margin between the NOAEL/LOAEL and the estimated occupational exposure levels. The MOS is considered to be insufficient when the minimal MOS/MOS ratio exceeds 1.

Guidance for the calculation of the minimal MOS can be extracted from a report describing the establishment of Health-Based Recommended Occupational Exposure Limits to be used for risk assessment[4]. The minimal MOS is equal to the overall assessment factor applied to calculate the HBROEL, including the corrections made for differences in absorption between routes. Relevant parts of this report are given below. It is noted that HBROEL should actually be read as Health Based Occupational Reference Value (HBORV) for use in risk assessment.

Guidance for the establishment of Health-Based Recommended Occupational Exposure Limits to be used for risk assessment

1. General introduction

1.1 This report describes the methods used for setting Health-Based Recommended Occupational Exposure Levels (HBROELs) to be applied in risk assessment.

1.2 The HBROEL is defined as the maximum amount of a substance to which a worker can be exposed without adverse health effects being expected. In general, it will be expressed as mg per worker per day. For the time being a starting point is that workers may be exposed predominantly, but not exclusively, by two routes: dermally and by inhalation. HBROELs are assessed for both routes separately and for every effect (if possible) as defined in the Technical Guidance Document.

1.3 The methods described in present report are based on the current state of the art. At the moment several studies are being performed at TNO, aimed at improving these methods, which will be regularly revised if new insights necessitate to do so.

2. Hazard identification

2.1 The hazard assessment serves as starting point for the derivation of a HBROEL:

(a) an integrated toxicity profile should be drawn up, indicating the adequacy of the overall data base and identifying possible shortcomings in sofar as these shortcomings hamper, or even prevent, establishment of the HBROELs;

[4] Hakkert BC, Stevenson H, Bos PMJ, van Hemmen JJ, Methods for the establishment of Health-Based Recommended Occupational Exposure Limits for existing substances, TNO-report V96, 463, July 4, 1996, The Netherlands.

(b) description of the toxicity and toxicokinetic studies should be detailed enough to allow the establishment of deviations from default values for assessment factors and absorption rates to be used in setting the HBROELs;

(c) the hazard assessment should focus on identification of those toxicological or epidemiological studies that can be used as starting point for the establishment of the HBROELs;

(d) presentation in a tabular form of all NOAELs and "Lowest-Observed-Adverse-Effect-Levels" (LOAELs), together with the type of effects on which these levels are based, is strongly recommended to facilitate the selection of the NOAEL or NOAELs to be used as starting point for establishing the HBROELs, and for the establishment of appropriate assessment factors.

3. Extrapolation of toxicity data to workers

A *General aspects*

3.1 The (animal) toxicity data must be extrapolated to workers in order to set exposure limits. Where a NOAEL/LOAEL has been identified for any of the effects listed in Annex I A of Regulation 1488/94, a HBROEL is calculated and compared with the exposure estimate for workers or subpopulations of workers. Therefore, the HBROEL may be based on e.g. repeated dose toxicity studies or reproduction toxicity studies. In fact, the NOAEL or NOAELs to be selected for establishing the HBROELs for a defined exposure situation should preferably come from studies corresponding as much as possible with the defined exposure situation.

3.2 For a genotoxic carcinogen no overall NOAEL can be determined and therefore the method to derive a HBROEL as described below cannot be used.

3.3 Because workers are mainly exposed by contact with the skin or by inhalation, an important element of the evaluation of the toxicological database should be its relevancy with respect to these routes of exposure.

3.4 In addition to the route of exposure, the actual duration of exposure or the actual exposure pattern of the worker should be considered and may be taken into account in setting HBROELs. Assessment factors as indicated in 3.5-3.17 should be used. It is noted that, when long-term exposure cannot be excluded, the basis for setting HBROELs should be long-term exposure studies, or, if these are not available, extrapolation to long-term exposure should be applied.

B *Assessment factors*

3.5 To translate the selected NOAEL into a HBROEL, assessment factors compensating for uncertainties inherent to extrapolation of experimental (animal) data to a given human situation and for uncertainties in the toxicological data base, have to be applied. For the sake of clarity in this report the term assessment factor is used and is meant as a general term to cover all factors designated in the literature as safety factor, uncertainty factor, extrapolation factor, adjustment factor, etc.

3.6 Discussion and weighing of the total body of data is an important element in the final choice of the overall assessment factor comprising various (sub)factors related to:

(a) interspecies differences;
(b) intraspecies differences;
(c) differences between experimental conditions and exposure situation (duration, frequency and pattern of exposure) of the worker;
(d) type of critical effect;
(e) dose-response curves;
(f) confidence in the database.

Interpecies differences

3.7 For extrapolation of data from animal studies to workers (interspecies differences) account should be taken of differences in body size and of remaining species-specific differences between animal and human. The first part of the extrapolation which only allows for the differences in body size between experimental animals and humans, is based on caloric requirements or metabolic body size, which is proportional to the 0.75 power of body weight. In order to be able to express the dose in mg/kg bodyweight (to the power 1)- which is the traditional routine designation of the dose - adjustment factors are calculated. The size of these adjustment factors are e.g. 7 for mice, 4 for rats and 1.4 for dogs, etc. Secondly, an assessment factor is applied for remaining uncertainties, for which the default value amounts to 3. For inhalation studies only a factor 3 is used, and no correction is made for differences in body size, because extrapolation is based on toxicological equivalence of a concentration of a chemical in the air of experimental animals and humans; animals and humans breathe at a rate depending on their caloric requirements.
When this method of extrapolation is contra-indicated, scaling across species on the basis of body weight is applied, using a default assessment factor of 10 (i.e. the factor for allometric scaling as well as for remaining uncertainties).

3.8 For local skin and respiratory tract effects the assessment factor for interspecies differences is 3, adjustment for differences in body size is inappropriate.

Intraspecies differences

3.9 Since the worker population does not include the very young, the elderly or the infirm, it is assumed that for workers the intraspecies differences are smaller than for the public at large. Therefore the default value for intraspecies variation for workers is 3, instead of 10 as used for the general population. In case of embryotoxic and/or teratogenic effects a factor 10 should be used, because no distinction should be made between the progeny of the occupational population and the general population.

Differences between experimental conditions and exposure pattern of the worker

3.10 A factor allowing for differences in duration of exposure between the worker and the toxicity study should be considered because it is necessary to take into account

(a) that in general adverse effect levels for specific effects will decrease with increasing exposure times, (b) that adverse effects may appear a long time after exposure has been discontinued, and (c) other and more serious adverse effects may appear with increasing exposure times. This factor should be derived considering the whole toxicity profile. For extrapolation of data from subacute to semichronic exposure this factor ranges generally between 1 and 5 and for extrapolation of semichronic to chronic exposure the same range is indicated.
Only in exceptional cases, when no conclusions can be drawn as to the effect of exposure time on the NOAEL a default factor of 10 should be used for extrapolation from subacute to semichronic exposure and a factor of 10 for semichronic to chronic exposure.

3.11 For local skin or local upper-respiratory tract effects, an assessment factor for the duration of exposure is not warranted (i.e. factor 1), unless the available data indicate otherwise.

Type of critical effect

3.12 The biological significance of the critical adverse effect in terms of its presumable health consequence should be considered in the selection of assessment factors. For instance, a reversible change in a biochemical parameter of doubtful toxicological significance may warrant the use of an additional factor smaller than one (< 1), whereas e.g. microscopically visible brain damage may indicate application of a factor higher than one (> 1). The default value is 1.

Dose-response curve

3.13 When a reliable dose-response curve for the relevant adverse effect has been established, the slope of this curve should be taken into account. The steeper the dose-response curve, the smaller the assessment factor can be. The assessment factor to be used, depends on expert judgement. The default value is 1.

Confidence in the database

3.14 The size, quality, completeness, and consistency of the database should be considered. Major aspects for the evaluation of the quality of the data supporting the NOAEL are:

(a) deviations from official guidelines which are not properly substantiated;
(b) number of animals used;
(c) number of dose levels tested;
(d) adequacy of haematological, biochemical and pathological examinations.

Indications for doubts on the confidence in the database are:

(i) the absence of certain types of studies;
(ii) conflicting results between studies;
(iii) doubts on the reliability of the route-to-route extrapolation.

On the other hand, consistency of results from different studies, consistency of animal and human data and reliable mechanistic data are indicative for a high-confidence database.

Establishment of the overall assessment factor

3.15 A summary of the factors according to the **table** as mentioned below will be described in evaluation report. Deviations from default factors should be explained in footnotes below the **table**.

Table A1.4 Assessment factors applied for the calculation of HBROELs.

Aspect	Assessment factor; default value
Interspecies differences	
- mouse	7[1]·3
- rat	4[1]·3
- rabbit	2.4[1]·3
- dog	1.4[1]·3
Intraspecies differences	3
Differences between experimental conditions and exposure pattern of the worker	1
- chronic to chronic exposure	10
- subacute to semichronic exposure	10
- semichronic to chronic exposure	1
- other aspects	
Type of critical effect	1
Dose-response curve	1
Confidence of the database	1

[1] This is a calculated adjustment factor, allowing for the differences in metabolic body size (see 3.7).

3.16 Principally, the overall factor is established by multiplication of the separate factors, unless the data indicate another method to be used. One should be aware that in practice it is not possible to distinguish all above mentioned factors, and some factors are not independent of each other. Therefore, straightforward multiplication may lead to unreasonably high factors. Discussion and weighing of individual factors is essential to establish a reliable and justifiable overall assessment factor.

C *Prerequisites for the extrapolation of animal studies to derive dermal and inhalation HBROELs*

3.17 For extrapolation there are two possibilities:
(a) direct extrapolation within the same route; this is described in 3.18;
(b) route-to-route extrapolation; this is described in 3.19-3.24

Direct extrapolation of dermal or inhalation toxicity data

3.18 In case adequate toxicity studies are available using repeated dermal or inhalation exposure, these studies are very important for the establishment of the HBROEL. The following aspects should be carefully considered:

(a) duration of exposure and experimental period should be appropriate;

(b) in practice, dermal and inhalation studies hardly ever cover all substance-related potential adverse effects, because teratogenicity, carcinogenicity and reproduction toxicity are studied predominantly after oral administration; if such effects are observed after oral administration, it has to be carefully considered whether these effects could also occur after dermal or inhalation exposure; this means that data obtained by the oral route have to be used to assess possible health risk from exposure by the other routes (route-to-route extrapolation); prerequisites for reliable extrapolation of oral data to other routes of exposure are described in 3.19-3.24;

(c) the critical effect of a substance in a repeated dermal or inhalation exposure study may be a local one. Of course, in such case assessment factors used for extrapolation of local effects are applied (3.5-3.16);

(d) the conditions used in dermal and inhalation studies preferably reflect the worker exposure situation; the test conditions should be considered in order to conclude whether assessment factors have to be applied to compensate for the differences in exposure conditions between animal experiments and worker exposure; examples of such differences are: vehicle used, presence or absence of occlusion, surface area of contamination, applied amount, distribution over the body, size of particles generated, temperature, etc.

Extrapolation of oral toxicity data (route-to-route extrapolation)

3.19 The use of e.g. oral toxicity data to establish a HBROEL for e.g. dermal exposure (route-to-route extrapolation) is an alternative for the use of toxicological data obtained using the appropriate route of exposure. In such cases, route-to-route extrapolation is necessary to bridge the gap between the available data set and the occupational exposure situation (duration, frequency and pattern of exposure) when no adequate toxicity studies are available, using the relevant route of exposure.

3.20 When route-to-route extrapolation is to be used, the following aspects should be carefully considered:

(a) from acute and/or irritation studies it might appear that a substance exerts local (irritating) effects; in such cases, extrapolation of e.g. oral repeated exposure toxicity data to other routes of exposure is allowed only, if also information is provided on the dose-response relationship for the local effects after repeated exposure; in practice, route-to-route extrapolation for locally acting substances is allowed when toxicity data on repeated exposure indicate that systemic effects after oral administration occur at lower dose levels than local effects;

(b) toxicokinetic data (absorption, distribution, metabolism, and elimination); the major factors responsible for differences in toxicity due to route of exposure include:

(i) differences in bioavailability (absorption); description in 3.21;
(ii) differences in metabolism (first pass effects); description in 3.22;
(iii) differences in internal exposure pattern; description in 3.23.

Differences in bioavailability (absorption)

3.21 Differences in bioavailability after oral, dermal, and inhalation exposure, might result in differences in toxicity between the various routes. For these differences corrections can be made, in part, using absorption data from ADME (absorption; distribution, metabolism; excretion) studies, dermal and inhalation absorption studies, or default values for dermal and inhalation absorption.

Differences in metabolism (first pass effects)

3.22 Differences in metabolic processes may result in activation or inactivation of the chemical agent before it reaches the target organ. For example, the majority of orally absorbed substances passes directly to the liver where they can be activated or inactivated before distribution in the body. When absorbed dermally or by the lungs the majority of these substances may be distributed before metabolic activation/ inactivation. Reliable predictions of “safe” exposure levels can be made in such cases only if the rate of production or elimination of active metabolites is known for each route of exposure.

Differences in internal exposure pattern

3.23 Differences in internal exposure pattern between routes of exposure can result in profound differences in toxic activity of a substance, particularly when the half-life is short. These differences may depend, at least partially, on differences in bioavailability, distribution pattern and metabolism. Reliable predictions are possible more frequently with systemically acting substances having relatively long half-lifes and, therefore, accumulate to produce stable blood or tissue concentrations. Therefore, information on the half-life of a test substance is regarded indispensable in case no information is provided on toxicity after repeated exposure using the relevant route of exposure. If a substance has a short half-life it depends on expert judgement whether or not further information should be provided.

3.24 In practice, relevant data on toxicokinetics and metabolism, especially after dermal and inhalation exposure, are frequently missing. As a consequence, corrections can only be made for differences in bioavailability as determined by the percentages of absorption.
When no experimental data on absorption are available, worst case assumptions have to be made, i.e., 100% absorption after dermal and inhalation exposure. More appropriate values for absorption may be derived using physico-chemical properties (molecular weight, octanol/water partition coefficient) and acute toxicity data.

D *Establishment of HBROELs*

3.25 A dermal HBROEL is derived form a dermal study using the following formula:

HBROEL-derm (mg/d) = $NOAEL_{'dermal,\ animal}$ (mg/kg bw/d)·1/A·70 kg

Rationale: the NOAEL from a dermal animal study is translated into a dermal HBROEL by correction of the NOAEL with:
- an overall assessment factor (A) as established in 3.5-3.16;
- a bodyweight for workers of 70 kg.

Note: The aspects as mentioned in 3.18 should be considered.

3.26 An inhalation HBROEL (8 hr-TWA) is derived from an inhalation toxicity study according to the following formula:

HBROEL-inh (mg/d) = $NOAEL_{inhalation,\ animal}$ (mg/m^3)·1/A·10 m^3

Rationale: the NOAEL from a respiratory animal study is translated into a respiratory HBROEL by correction of the NOAEL with:
- an overall assessment factor (A) as established in 3.5-3.16
- a respiratory volume of workers of 10 m^3/8 hr.

Note: The aspects as mentioned in 3.18 should be considered.

3.27 A dermal HBROEL is derived from an oral toxicity study according to the following formula:

HBROEL-derm (mg/d) = $NOAEL_{oral,\ animal}$ (mg/kg bw/d)·X·1/A·1/Y·70 kg

Rationale: the NOAEL from an oral animal study is translated into a dermal HBROEL by correction of the NOAEL with:
- an oral absorption factor (X);
- an dermal absorption factor (Y);
- an overall assessment factor (A) as established in 3.5-3.16;
- a bodyweight for workers of 70 kg.

Note: The aspects as mentioned in 3.19-3.24 should be considered.

3.28 An inhalation HBROEL (8-hr TWA) is derived from an oral toxicity study according to the following formula:

HBROEL-inh (mg/d) = $NOAEL_{oral,\ animal}$ (mg/kg bw/d)·X·1/A·1/Z·70 kg

Rationale: the NOAEL from an oral animal study is translated into a respiratory HBROEL by correction of the NOAEL with:
- an oral absorption factor (X);
- an inhalation absorption factor (Z);
- an overall assessment factor (A) as established in 3.5-3.16;
- a bodyweight for workers of 70 kg.

Note: The aspects as mentioned in 3.19-3.24 should be considered.

3.29 A dermal HBROEL is derived from an inhalation toxicity study according to the following formula:

HBROEL-derm (mg/d) = $NOAEL_{inh,\ animal}$ (mg/m^3) · R · Z · 1/A · 1/Y · 70 kg

Rationale: the NOAEL from a respiratory animal study is translated into a dermal HBROEL by correction of the NOAEL with:
- an adjustment factor, accounting for respiratory volume in experimental conditions (R)
- an inhalation absorption factor (Z);
- an dermal absorption factor (Y);
- an overall assessment factor (A) as established in 3.5-3.16;
- a bodyweight for workers of 70 kg.

Note: The aspects as mentioned in 3.19-3.24 should be considered.

3.30 An inhalation HBROEL (8-hr TWA) is derived from a dermal toxicity study according to the following formula:

HBROEL-inh (mg/d) = $NOAEL_{dermal,\ animal}$ (mg/kg bw/d) · Y · 1/A · 1/Z · 70 kg

Rationale: the NOAEL from an dermal animal study is translated into a respiratory HBROEL by correction of the NOAEL with:
- an dermal absorption factor (Y);
- an inhalation absorption factor (Z);
- an overall assessment factor (A) as established in 3.5-3.16;
- a bodyweight for workers of 70 kg.

Note: The aspects as mentioned in 3.19-3.24 should be considered.

3.31 The 8-hr TWA HBROEL-inh value may be adopted on a case-by-case basis to actual exposure duration per occupational scenario, considering the duration in the experiment and the critical effects observed.

3.32 In cases where oral as well as dermal/respiratory toxicity data are available, the HBROEL-inh and the HBROEL-derm derived from oral toxicity data and from dermal/respiratory toxicity data should be calculated and the reliability of both calculations should be weighed. A motivation for the choice of the HBROEL to be used as starting point in risk assessment should be explicitly stated in the report.

Annex 3 Levels of glycol ethers for manual application used for the actual assessment of exposure levels

Substances	Vapour pressure (Pa)	Industries and tasks	Exposure levels (ppm, unless otherwise stated)		Remarks	References
			Full-shift	Short-term		
Manual application						
EGEE	530	Electrotechnical industry; Cleaning	0.18-0.58		number of samples and sample duration not indicated	Clapp *et al.* 1984
EGMEA	270	Printing department; lacquering	3.5	1.3-19.4	1 full-shift and 3 short-term measurements	Norwegian Exposure Database 1995
EGMEA	270	Ski production; painting	0.3		17 of 18 samples below lod	Norwegian Exposure Database 1995
EGMEA	270	Spray lacquering		2.0 and 4.7	4 of 6 samples below lod	Norwegian Exposure Database 1995
EGEEA	270	Automotive assembly; spray painting and paint belding	< 0.02-0.05	< 0.61	2 short term samples; 10 of 12 full-shift samples below lod	Piacitelli *et al.* 1990
EGEEA	270	Aircraft maintenance; spray painting	0.29-2.69	1.73-11.9	13 full-shift and 5 short-term samples	Piacitelli *et al.* 1990
EGME	800	Aerospace equipment manufacturing; spray painting, paint blending, primer application, wafer coating	< 0.27	< 0.65-1.04	8 full-shift and 2 of 3 short term samples below lod	Piacitelli *et al.* 1990
EGEE	530		< 0.22	< 0.33-0.86	5 full-shift and 1of 3 short-term samples below lod	
EGEEA	270		< 0.23		15 full-shift and 2 short-term samples below lod	
EGEE	530	Shipyard painting, surface preparation, brush painting inside ships, some spray painting inside ships	<lod-21.5		14 of 102 samples below lod; 5 workers not actively painting; 8 spray painting	Sparer *et al.* 1988
EGME	800		<lod-5.6		50 of 102 samples below lod; 7 workers not actively painting, 7 spray painting	
EGBE	80		<lod-1.3		one of 102 samples above lod	
EGMEA EGEE EGEEA EGBE EGBEA	270 530 270 80 50	Various	0.4-143 3.2-1224 0.6-820 0.2-1775 8.9-11.7 (all in mg/m^3)		12 samples, GM: 11.6 11 samples, GM: 17.1 38 samples, GM: 9.9 17 samples, GM: 8.5 3 samples, GM: 10.6 in total (printing, painting, car repair and various) 262 of 2654 samples above lod	Veulemans *et al.* 1978

Substances	Vapour pressure (Pa)	Industries and tasks	Exposure levels (ppm, unless otherwise stated)		Remarks	References
			Full-shift	Short-term		
EGEE EGEEA EGME EGBE	530 270 800 80	Painting Painting Painting Painting	1.4-210 1.2-79 5.6-137 3.4-93.6 (all in mg/m^3)		19 samples, GM: 9.5 66 samples, GM: 9.7 4 samples, GM: 31.3 10 samples, GM: 18.8 in total (printing, painting, car repair and various) 262 of 2654 samples above lod	Veulemans *et al.* 1978
EGBE	80	Shipbuilding and ship repair Electronic component manufacture Retreading and specialist repair of rubber tyres Wooden and unpholstered furniture manufacture Rubber products manufacture	1-7 4.1-8.7 0.2-4.2 1-35 0.2-4		12 samples 2 samples 6 samples 30 samples, including consecutive samples 9 samples	NEDB 1995
EGBE	80	Car washing	average: 1.8		Only limited pooled data presented in the publication	Vincent *et al.* 1994
EGBE	80	Cleaning personnel	average: 0.1		Only limited pooled data presented in the publication	Vincent *et al.* 1994
EGBE EGEEA EGEE EGBEA	80 270 530 50	Sign and display industry	< 25 8% > 5 < 5 < 25		n = 36 n = 24; 8% of samples > 5 ppm n = 6 n = 64	Guirguis *et al.* 1994
EGBE EGEEA EGEE EGME EGMEA	80 270 530 800 270	Miscelaneous manufacturing industries	< 25 < 5 < 5 < 5 < 5		n = 28 n = 32 n = 15 n = 8 n = 4	Guirguis *et al.* 1994
EGBE EGEEA EGEE EGBE EGEEA DPGME	80 270 530 80 270	Rubber manufacturers, other than tires, tubes and footwear Jewellery and silverware manufacturers	< 25 < 5 < 5 < 25 2% > 5 < 150		n = 34 n = 21 n = 22 n = 6 n = 82; 2% of samples > 5 ppm n = 6	Guirguis *et al.* 1994 Guirguis *et al.* 1994
EGBE EGEEA EGBEA	80 270 50	Utilities other than electricity, gas and water	< 25 < 5 < 25		n = 41 n = 41 n = 41	Guirguis *et al.* 1994

Substances	Vapour pressure (Pa)	Industries and tasks	Exposure levels (ppm, unless otherwise stated)		Remarks	References
			Full-shift	Short-term		
EGBE EGEEA EGEE EGME	80 270 530 800	Leather tanneries	< 25 < 5 < 5 < 5		n = 2 n = 2 n = 31 n = 51	Guirguis *et al.* 1994
EGBE EGEEA EGBEA EGMEA	80 270 50 270	Wholesale	< 25 < 5 < 25 < 5		n = 46 n = 31 n = 9 n = 31	Alexandersson *et al.* 1987
DEGBE	2.7	Cleaning of hard surfaces: undiluted Cleaning of hard surfaces: diluted		0.26-0.77 < 0.009	n = 5, experimental study, cleaning for 20 min. in closed rooms with minimal ventilation using 125 to 300 g of cleaners containing 4% or 9% DEGBE n = 1, experimental study, cleaning for 20 min. with 226 g of diluted cleaner, concentration of 2EGBEE in cleaner dilution ≈ 0.06%	Gibson *et al.* 1991
DEGBE	2.7	Use of waterborne paint (brushing or rolling)		4-5	1.5% of 2EGBEE in paint	Hansen *et al.* 1987
DEGME DPGME EGBE EGPhE	30 80 			8-32 30-40 2-60 0-0.7 all in mg/m^3	4% of DEGME in paint 1% of DPGME in paint 0-1.4% of EGBE in paint 1.7% of EGPhE in paint n = 15; no exact data on sampling duration, sampling only during actual application of paint (≈ 20 minutes at a time)	

EGME = ethylene glycol monomethyl ether = 2-methoxyethanol; 1 ppm ≈ 3.1 mg/m^3
EGEE = ethylene glycol monoethyl ether = 2-ethoxyethanol; 1 ppm ≈ 3.7 mg/m^3
EGMEA = ethylene glycol monomethyl ether acetate = 2 methoxyethyl-acetate; 1 ppm ≈ 4.8 mg/m^3
EGEEA = ethylene glycol monoethyl ether acetate = 2-methoxyethyl-acetate; 1 ppm ≈ 5.4 mg/m^3
EGBE = ethylene glycol monobutyl ether = 2-butoxyethanol; 1 ppm ≈ 4.8 mg/m^3
DEGME = diethylene glycol monomethylether = 2-(2-methoxyethoxy)ethanol; 1 ppm ≈ 5.0 mg/m^3
DEGBE = diethtylene glycol monobutylether = 2-(2-butoxyethoxy)ethanol; 1 ppm ≈ 6.8 mg/m^3
EGBEA = ethylene glycol monobutyl ether acetate = 2-butoxyethyl-acetate; 1 ppm ≈ 6.5 mg/m^3
DPGME = di-propylene glycol monomethyl ether;
EGPhE = ethylene glycol phenyl ether;
n = number of samples
lod = limit of detection.

Annex 4 Estimation of concentrations due to transfer operations - USEPA Transfer Model[5]

The USEPA transfer model is model in which the equilibrium concentrations reached in a room during liquid transfer is calculated. The generation of vapours by displacement of air from containers during liquid transfer is calculated. The generation rate of the vapour is then used as an input variable in a mass balance ventilation model. For several input parameters typical and worst case default values have been established from empirical data. If more specific information is lacking, the default values can be used to calculate concentrations. These concentrations are spatially averaged concentrations. To calculate exposure levels from these concentrations the time workers spend in this and other environments and the concentrations in the other environments should be known or estimated. As a worst case assumption it can be assumed that workers spend a whole shift transferring liquids, since transferal is often the activity with the highest levels of emission.

The formula to calculate the concentrations is given in equation 1.

$$\mathbf{C_m = 1000 \cdot (f \cdot M \cdot V \cdot r \cdot P)/(R \cdot Tl \cdot Q \cdot k)} \qquad \mathbf{(1)}$$

f = saturation factor
M = molar weight (mg/mol)
V = volume of container (m^3)
r = fill rate (h^{-1})
P = vapour pressure of subst.(Pa)
R = universal gas constant (= 8.3144 J/mol.K)
T_1= temperature of the liquid (K)
Q = ventilation rate (m3/h)
k = mixing factor
C_m= calculated concentration level (mg/m^3)

The following input data are standard for each assessment in this annex:
M = 120.2; p = 30;
kwc = 0.1; Twc = 293;
knorm = 0.5; Tnorm = 293;
where wc = worst case and norm = normal or typical case.

The following transferal operations are considered:
a - rail car b - tank truck c - drum

The results are presented in the table below

Worst Case									
	f	M	V	r	P	Tl	Q	k	Cm
a	1.0	120	24.00	1	30.00	293	1203000	0.1	0.30
b	1.0	120	19.00	2	30.00	293	1203000	0.1	0.47
c	1.0	120	0.20	30	30.00	293	850	0.1	104.49
Typical case									
	f	M	V	r	P	Tl	Q	k	Cm
a	1.0	120	76.00	1	30.00	293	4812000	0.5	0.05
b	1.0	120	19.00	2	30.00	293	4812000	0.5	0.02
c	0.5	120	0.20	20	30.00	293	5100	0.5	1.16

[5] USEPA. Approaches for developing screening quality estimates of occupational exposure used by the U.S. EPA's Office of Toxic Substances and their applicability to the OECD SIDS Program. USEPA Office of Toxic Substances (Washington, DC) 1991. Appendix I. U.S. New Chemical methods to assess inhalation exposure to vapors and gases using mass balance models.

Annex 5 Consumer exposure

Annex 5.1

SCENARIO I: Paint

CONSEXPO report

Generated by CONSEXPO version 1.04

Compound: DEGME (CAS: 111-77-3)
Subject: person
Weight: 70.000 kg (uninspected default)

CONTACT
Contact scenario: Painting
Parameter definition of scenario:
Duration of contact per event: 6.000 hr
Duration of actual use per event: 3.000 hr
Frequency of contact: 1.000 1/month
Start of contact: 0.00e+00 min

INHALATION

Exposure
Scenario: evaporation from mixture
Mean event concentration (average case): 4.097e+01 mg/m^3
Year average (average case): 3.365e-01 mg/m^3
Mean event concentration (cumulative worst case): 7.043e+01 mg/m^3
Year average (cumulative worst case): 5.785e-01 mg/m^3

Exposure estimates based on the following parameters:
Release area: 40.000 m^2
Temperature: 25.000 Celsius
Ventilation rate: 15.000 m^3/hr
Room volume: 25.000 m^3
Product amount: 5.000 kg
Weight fraction: 1.000 - 10.000%, uniform distribution
Molweight solvent: 150.000 g/mol

Uptake
Model: fraction model
Average case estimate : 1.646e+03 mg/year
: 6.437e-02 mg/(kg.day)
Cumulative worst case estimate : 2.830e+03 mg/year
: 1.107e-01 mg/(kg.day)
Uptake estimates based on the following parameters:

Absorbed fraction: 75.000%
Inhalation rate: 12400.000 $cm^{3/}$min
Respirable fraction: 1.000 fraction

DERMAL

Exposure
Scenario: fixed volume of product
Mean event concentration (average case): 5.500e+01 mg/cm^3
Year average (average case): 4.517e-01 mg/cm^3
Mean event concentration (cumulative worst case): 9.550e+01 mg/cm^3
Year average (cumulative worst case): 7.844e-01 mg/cm^3
Exposure estimates based on the following parameters:
Product amount: 10.000 g
Product volume: 10.000 cm^3
Weight fraction of compound: 1.000 - 10.000%, uniform distribution
Dilution before use: 1.000 times

Uptake
Model: fraction model
Average case estimate : 6.600e+03 mg/year
: 2.581e-01 mg/(kg.day)
Cumulative worst case estimate : 1.146e+04 mg/year
: 4.482e-01 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 1.000 dimless

ORAL
No exposure

Annex 5.2

SCENARIO II: Paint stripper/remover

CONSEXPO report

Generated by CONSEXPO version 1.04

Compound: DEGME (CAS: 111-77-3)
Subject: person
Weight: 70.000 kg (uninspected default)

CONTACT
Contact scenario: Painting
Parameter definition of scenario:
Duration of contact per event: 6.000 hr
Duration of actual use per event: 3.000 hr
Frequency of contact: 1.000 1/month
Start of contact: 0.00e+00 min

INHALATION

Exposure
Scenario: evaporation from mixture
Mean event concentration (average case): 1.481e+02 mg/m^3
Year average (average case): 1.217e+00 mg/m^3
Mean event concentration (cumulative worst case): 1.481e+02 mg/m^3
Year average (cumulative worst case): 1.217e+00 mg/m^3

Exposure estimates based on the following parameters:
Release area: 2.000 m^2
Temperature: 25.000 Celsius
Ventilation rate: 15.000 m^3/hr
Room volume: 25.000 m^3
Product amount: 5.000 kg
Weight fraction: 30.000%
Molweight solvent: 200.000 g/mol

Uptake
Model: fraction model
Average case estimate : 5.951e+03 mg/year
: 2.328e-01 mg/(kg.day)
Cumulative worst case estimate : 5.951e+03 mg/year
: 2.328e-01 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 75.000%
Inhalation rate: 12400.000 cm^3/min
Respirable fraction: 1.000 fraction

DERMAL

Exposure
Scenario: fixed volume of product
Mean event concentration (average case): 3.000e+02 mg/cm^3
Year average (average case): 2.464e+00 mg/cm^3
Mean event concentration (cumulative worst case): 3.000e+02 mg/cm^3
Year average (cumulative worst case): 2.464e+00 mg/cm^3

Exposure estimates based on the following parameters:
Product amount: 1.000 g
Product volume: 1.000 cm^3
Weight fraction of compound: 30.000%
Dilution before use: 1.000 times

Uptake
Model: fraction model
Average case estimate : 3.600e+03 mg/year
: 1.408e-01 mg/(kg.day)
Cumulative worst case estimate : 3.600e+03 mg/year
: 1.408e-01 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 1.000 dimless

ORAL
No exposure

Annex 5.3

SCENARIO III: windscreen washer liquid

CONSEXPO report
Generated by CONSEXPO version 1.04

Compound: DEGME (CAS: 111-77-3)
Subject: person
Weight: 70.000 kg (uninspected default)

CONTACT
Contact scenario: none
Parameter definition of scenario:
Duration of contact per event: 30.000 min
Duration of actual use per event: 1.000 min
Frequency of contact: 3.000 1/day
Start of contact: 0.00e+00 min

INHALATION

Exposure
Scenario: constant concentration
Mean event concentration (average case): 2.222e+00 mg/m^3
Year average (average case): 1.405e-01 mg/m^3
Mean event concentration (cumulative worst case): 2.222e+00 mg/m^3
Year average (cumulative worst case): 1.405e-01 mg/m^3

Exposure estimates based on the following parameters:
Amount released: 500.000 mg
Weight fraction: 1.00e-02 fraction
Room volume: 2.250 m^3

Uptake
Model: fraction model
Average case estimate : 6.875e+02 mg/year
: 2.689e-02 mg/(kg.day)
Cumulative worst case estimate : 6.875e+02 mg/year
: 2.689e-02 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 75.000%
Inhalation rate: 12400.000 cm^3/min
Respirable fraction: 1.000 fraction

DERMAL

Exposure

Scenario: exposure from air
Mean event concentration (average case): 2.222e-06 mg/cm^3
Year average (average case) : 1.405e-07 mg/cm^3
Mean event concentration (cumulative worst case): 2.222e-06 mg/cm^3
Year average (cumulative worst case): 1.405e-07 mg/cm^3

Exposure estimates based on the folowing parameters:
See inhalatory exposure

Uptake
Uptake unknown

ORAL
No exposure

European Commission

EUR 18999 – European Union Risk Assessment Report
2-(2-methoxyethoxy)ethanol, Volume 1

Editors: B.G. Hansen, S.J. Munn, G. Schoening, M. Luotamo, A. van Haelst, C.J.A. Heidorn, G. Pellegrini, R. Allanou, H. Loonen

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This report provides the comprehensive risk assessment of the substance 2-(2-methoxyethoxy)ethanol. It has been prepared by the Netherlands 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 the assessment of risks to man and the environment, laid down in Commission Regulation (EC) No. 1488/94.

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

The risk assessment for 2-(2-methoxyethoxy)ethanol concludes with no concern for the environment, but there is a potential health risk for workers during production and use, and for the consumer which occurs due to the use of paint and paint strippers containing the substance.

The conclusions of this report will lead to risk reduction measures to be decided by the risk management committee of the Commission.

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