Institute for Health and Consumer Protection

European Chemicals Bureau

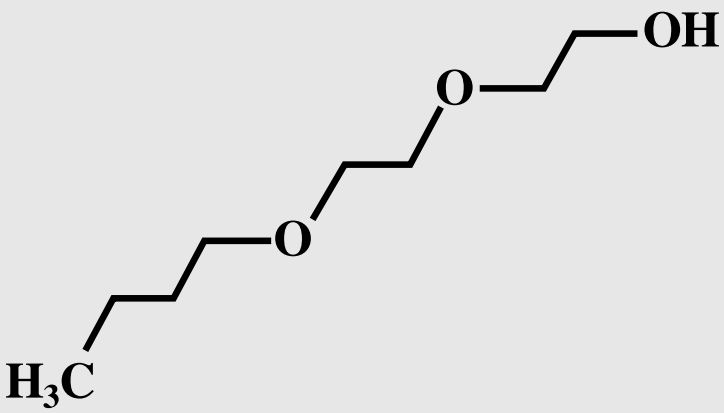
Existing Substances

European Union Risk Assessment Report

CAS No.: 112-34-5

EINECS No.: 203-961-6

2-(2-butoxyethoxy)ethanol



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RISK ASSESSMENT

Cataloguing data can be found at the end of this publication

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RISK ASSESSMENT

Final report, July 1999

The Netherlands

Rapporteur for the risk evaluation of 2-(2-butoxyethoxy)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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Date of Last Literature Search:	**1996**
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.

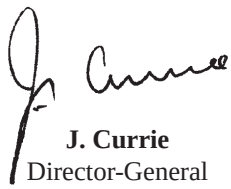
The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[2], which is supported by a technical guidance document[3]. Normally, the "Rapporteur" and individual companies producing, importing and/or using the chemicals work closely 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. 112-34-5
EINECS-No. 203-961-6
IUPAC name 2-(2-butoxyethoxy)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:
- health risks for the consumer are expected to occur due to the use of DEGBE in paint spraying applications.

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:
- eye exposure due to incidental splashing should be avoided when the pure substance is handled.
- local effects on skin cannot be excluded in occupational scenario 4 (manual application of products containing DEGBE) after repeated dermal exposure.
- based upon the present information with regard to anticipated effects after repeated inhalation exposure in workers reduction measures should be taken for occupational exposure scenario 4 (manual application of products containing DEGBE).

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

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.:	112-34-5
EINECS-No.:	203-961-6
IUPAC name:	2-(2-butoxyethoxy)ethanol
Synonyms:	butoxyethoxyethanol, butyl carbitol, butyl diglycol, butyl diglycol ether, butyl digol, butyl dioxitol, diethylene glycol butyl ether, diglycol monobutyl ether, Dowanol DB
Molecular formula:	$C_8H_{18}O_3$
Structural formula:	CH_2-$(CH_2)_3$-O-CH_2-CH_2-O-CH_2-CH_2-OH
Molecular weight:	162.23

Purity/impurities, additives

Purity:	>99% w/w
Impurity:	< 0.5% w/w 2-butoxyethanol (CAS-No. 111-76-2)
	< 0.25% w/w ethanol, 2-(2-propenyloxy) (CAS-No. 111-46-6)
	< 0.2% w/w 2-(2-methylpropoxy)ethanol (CAS No. 204-881-4)
Additives:	0.004-0.006% w/w 2,6-di-tert-butyl-p-cresol (CAS-No 128-37-0)

Physico-chemical properties

Physical state:	liquid
Melting point:	-68 °C
Boiling point:	228-234 °C at 1013 hPa
Relative density:	0.948-0.96 g/cm^3 (20 °C)
Vapour pressure:	0.027 hPa at 20 °C
Water solubility:	miscible
Partition coefficient n-octanol/water (log value):	0.56
Granulometry:	not applicable
Conversion factors (101 kPa, 20 °C):	1 ppm = 6.75 mg/m^3; 1 mg/m^3 = 0.148 ppm
Flammability:	none, based on flashpoint (78-116 °C), autoflammability temperature (210 °C) and structural formula and thermodynamic properties
Explosive properties:	none, based on structural formula and thermodynamic properties
Oxidising properties:	none, based on structural formula and thermodynamic properties

These data were mentioned in Material Safety Data Sheets of BASF AG (1994), BP (1994), Hoechst AG (1992, 1993) and in other references (Patty 1994; Verschueren 1983; Van Leeuwen *et al.* 1992; Funasaki *et al.* 1984; Lipnick *et al.* 1987).

Classification

Classification and labelling according to the 25th ATP of Directive 67/548/EEC:
Classification: Xi; R36
Labelling: Xi R36 S(2-)24-26

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

The chemical 2-(2-butoxyethoxy)ethanol (hereafter referred to as DEGBE) belongs to the group of glycol ethers, which are mainly used as solvents. During 1991-1993 the annual production of DEGBE in the European Union ranged from 20,000 to 80,000 tonnes (IUCLID HEDSET 1994). According to more recent information provided by industry, the total EU production (1994) of all butyl glycol ethers is 181,000 tonnes. Approximately 24-25% of this will be DEGBE i.e. about 44,000 tonnes. This estimate is supported by an actual figure of 46,600 t/yr which is the sum of all actual production tonnage that were individually submitted to the rapporteur. The latter figure will be used in the report (Chapter 3). Virtually no DEGBE is believed to be imported into the EU (OSPA 1995). No data on export are given. The production in the European Union is located at eight different sites (see **Table 2.1**).

Table 2.1 Production sites (larger than 1,000 t/yr) of DEGBE in the EU.

Company	Location
BP Chemicals Ltd	Laverne, France
BASF AG	Ludwigshaven, Germany
ICI Chemicals and Polymers Limited[1]	Wilton (Cleveland), United Kingdom
ICI Chemicals and Polymers France SA[2]	Chocques, France
EniChem S.p.A. Polyurethane Division	Cardano al Campo, Italy
Hoechst AG	Gendorf, Germany
Huels AG	Marl, Germany
Shell Nederland B.V.	Hoogvliet Rt, the Netherlands

[1] Union Carbide Ltd. acquired the ICI (Wilton) glycol ether production facility on 1-2-1995
[2] Contract manufacturer for Union Carbide Ltd since 1-2-1995

DEGBE is produced by the reaction of ethylene oxide and n-butanol with an alkalic catalyst (for details see paragraph 3.1.1.1).

2.2 USE PATTERN

Table 2.2 shows the industrial and use categories of DEGBE. It has a wide range of uses as a (co)solvent with applications in paints, dyes, inks, detergents and cleaners (see also paragraphs 4.1.1.0 and 4.1.1.1). The major function of this agent is to dissolve various components of mixtures in both aqueous and non-aqueous systems.

Table 2.2 Industrial and use categories of DEGBE.

Industrial category	IC no.	Use category	UC no.
- Chemical industry: basic chemical	2	Solvents	48
- Paints, lacquers and varnishes industry	14		
- Chemical industry: chemicals used in synthesis	3	Intermediates	33
- Other	15	Reprographic agents (e.g. dye solvent)	45
- Other	15	Others (component of fire extinguisher foam)	55
- Mineral oil and fuel industry	9	Hydraulic fluids and additives (diluent)	30
- Personal / domestic use	5	Cleaning/washing agents and disinfectants	9
- Public domain	6		
- Metal industry	8		

Average quantitative estimations are available on the use pattern of DEGBE at the EU market (OSPA 1995). These data are summarised in **Table 2.3**.

Table 2.3 Quantitative estimation on the use pattern of DEGBE.

Use	Total (%)	Divided over Industrial and Public (%)	
Cleaning agents (e.g. floor and metal cleaners)	59	Industrial	22
		Public	37
Paints (e.g. surface coatings)	36	Industrial	33
		Public	3
Chemical intermediate (for BDGA[1] production)	5	Industrial	5
		Public	0

[1] BDGA: butyl diglycol acetate.

Table 2.3 shows that about two thirds of the total tonnage of DEGBE is used in a range of formulated detergents, hard surface cleaners and metal cleaners used by professional trades and members of the general public. The second largest usage of DEGBE is as solvent in surface coatings. The different applications in coatings (100%) can be broken down as follows: coil coatings (44%), can coatings (9%), water based car base coats (18%), general industrial coatings (9%) and water based decorative paint (trade 10% and retail 10%) (OSPA 1995).

3 ENVIRONMENT

3.1 EXPOSURE ASSESSMENT

3.1.0 General

DEGBE 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 DEGBE.
General characteristics of DEGBE which are relevant for the exposure assessment are discussed below:

a) Degradation

Hydrolysis
No experimental data are available on hydrolysis. However, alcohols and ethers are generally resistant to hydrolysis (Lyman *et al.* 1990).

Photodegradation
If DEGBE is present in ambient air it is expected to exist almost entirely in the vapour phase, based on a vapour pressure of 0.027 hPa at 20 °C, where vapour phase reactions with photochemically produced hydroxyl radicals may be important. A QSAR-method is applied for a first estimation of primary transformation rates (Atkinson 1985). The overall OH rate constant for DEGBE has been estimated to be $3.62 \cdot 10^{-11}$ cm^3/molecule·second at 25 °C (Cited in HSDB (through Jan. 1994)). The estimated value corresponds to an atmospheric half-life of about 11 hours at an atmospheric concentration of $5 \cdot 10^5$ hydroxyl radicals molecule/cm^3 (Cited in HSDB (through Jan. 1994)).
Since DEGBE does not adsorb ultraviolet radiation within the solar spectrum, direct photolysis in the atmosphere is not expected to occur (Cited in HSDB (through Jan. 1994)).

Biodegradation
The available aerobic biodegradation test results for DEGBE are summarised in **Table 3.1**. A number of tests were carried out according to (international) standard test guidelines. However, the current information on several technical aspects is incomplete for nearly all biodegradation tests. Nevertheless, the total set of information available is regarded as being sufficient to draw conclusions on the degradation potential of DEGBE.

Ready biodegradability tests

The test results of BOD5-tests were not consistent. In the first and fourth test, DEGBE was shown to be readily biodegradable (BOD5/COD > 0.5). However, no information was available on the concentration of inoculum and whether this inoculum was adapted or non-adapted. In the second and third test, no ready biodegradability of DEGBE could be shown. The BOD20 test (test no.5) indicated ready biodegradability of DEGBE.
Two other ready biodegradability tests were carried out. In test no. 6 no ready biodegradability could be shown. The biodegradation was nearly 60% after 28 days, but the BOD was divided by the COD instead of the ThOD. Because the COD is often not as high as the ThOD, this results in falsely high values for the percentage of biodegradation. Besides, this test failed to meet the 10-day window criterion. The DOC die-away test (no.7), however, clearly showed that DEGBE is ready biodegradable.

Table 3.1 Biodegradation test results for DEGBE.

No.	Type of test	Detection	Result	Day	Method	Conc. of TS	Conc. of inoculum	Ref.
1	BOD5-test	O_2 uptake	71 %[3] 43 % 32 %	5 5 5	Unknown	0.8 mg/l 2 mg/l 4 mg/l	Unknown[a]	44
2	BOD5-test	O_2 uptake	11 %[1] (BOD/ThOD)	5	APHA No.219, 1971	Unknown	10 ml[d]	Bridie *et al.* 1979
3	BOD5-test	O_2 uptake	16 % (BOD/COD)	5	other[4]	5, 10, 15 & 20 µl/l	Unknown	Bishopp
4	BOD5-test	O_2 uptake	54 % (BOD/ThOD)	5	APHA, 1980	Unknown	Unknown	Babeu and Vaishonav 1987
5	BOD20-test	O_2 uptake	75 %[1] (BOD/COD)	20	other[4]	2 & 3 µl/l	Unknown[f]	Bishopp
6	Ready biodegr test	O_2 uptake	58 %[1] (BOD/COD)	28	OECD Guideline 301F	100 mg/l	30 mg/l[b]	ICI 1992
7	Ready biodegr. test	DOC die away	94 %[1]	14	OECD301E	20 mg/l DOC	0.5 ml/l[b]	Huels AG
8	Inherent biodegr. test	O_2 uptake	66 %[1]	28	other	100 mg/l	100 mg/l[c]	BP 1992
9	Inherent biodegr. test	DOC	100 %[3]	9	Zahn-Wellens -test	300 mg/l	Unknown	Huels
10	Inherent biodegr. test	COD-determ.	100 % 60 % 19 %	6 5 3	"standversuch Hoechst"	500 mg/l	Unknown[c]	Hoechst AG 1976
11	Inherent biodegr. test	DOC-determ.	99 %	8	other	400 mg/l	Unknown	BASF 1980

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

[1]: non-adapted inoculum
[2]: adapted inoculum
[3]: no information on adaptation or non-adaptation of inoculum available
[4]: Method and materials were found in "Determination of Biochemical Oxygen Demand of Solid and Liquid Organic Chemicals", Method No. KPCQ-A-EA-G-M-3-1, Eastman Kodak Company.

Although some inconsistencies occur in the "full picture" of ready biodegradability tests on DEGBE, the overall conclusion is that the substance can be regarded as ready biodegradable.

Inherent biodegradability test

Four inherent biodegradability tests were conducted. The results were consistent. In test no. 8, 66% biodegradation was measured. In the other three tests DEGBE showed more than 70%

biodegradation. As was expected, DEGBE was inherently biodegradable which is in support of the conclusion on ready biodegradability derived above.

b) Distribution

The Henry's Law constant of $4.4 \cdot 10^{-3}$ Pa.m^{-3}/mol at 20 °C (EUSES) indicates that volatilisation of DEGBE from surface waters and moist soil is expected to be very low.
Using the log K_{ow} of 0.56, according to the TGD a K_{oc} of 3.6 l/kg can be estimated. The K_p for soil is subsequently calculated by multiplying the K_{oc} with a f_{oc} of 0.02 for soil ---> 0.07 l/kg. Based on this K_p DEGBE is expected to be highly mobile in soil. It should be borne in mind, however that the derivation of a K_p from low log K_{ow} values is less reliable.

Whilst physical removal from the atmosphere by precipitation and dissolution in clouds can occur, the short atmospheric residence time suggests that wet deposition is of limited importance.

c) Accumulation

No experimental data on bioaccumulation are available. Therefore, BCF-values for fish and worm are calculated using the log K_{ow} of 0.56 (TGD96). The estimated BCF-values amount to 1.4 (l/kg) and 2.2 (kg/kg) for, respectively, fish and worm (EUSES: see http://ecb.ei.jrc.it). In view of these BCFs, DEGBE is expected to have a low bioaccumulating potential in the environment.

3.1.1 Emission scenarios

3.1.1.1 Releases from production

DEGBE is produced as a by-product of the butylglycolether (BGE) manufacturing. Other products formed during BGE manufacturing are tri, tetra and mixtures of higher glycol ether homologues. The main and side products are separated by distillation. The solid tarry bottoms of the separation process are usually incinerated.

BGE is produced by reacting n-butanol with ethylene-oxide. The catalyst used in this reaction is a strong base, e.g. NaOH, KOH or Na-butylate. Sometimes the catalyst is introduced in water solutions of 50% mass, especially when NaOH or KOH are used. Once introduced in the reactor, the catalyst is recycled during the entire campaign. The water introduced or formed in the first cycle is distilled off during product separation.
With the introduction of 500 kg NaOH in 50% mass solution, the maximum amount of water liberated is 500 (solution) + 225 (liberated at butylate formation) = 725 kg per campaign. This water, that does not contain BGE, is emitted through the effluent system of the site.
As BGE is the desired product, ethylene oxide is introduced in excess. Unreacted ethylene oxide is recycled into the reactor. In view of the physical properties of ethylene oxide (boiling point of 10.7 °C), the reactor systems are closed. Presence of water during the reaction is unbeneficial as this reacts violently with ethylene oxide under the prevailing conditions.
The process can be performed in batches or continuously in a pipe reactor. The companies mentioned in **Table 2.1** all have a continuous reactor for production.
The distillation is performed under reduced pressure. For two plants it is known that the vacuum is generated by a “waterjet pump”. Although this pump is protected by a cold trap, the water may receive some vapours of the products. For the other plants there is no additional information on the vacuum system.

At the end of the campaign the reactor may be emptied and cleaned. A small release of DEGBE to waste water will occur during the cleaning activities.

In conclusion it can be said that DEGBE production is a dry process. Releases to water in the production process of DEGBE may only occur via the vacuum system or following cleaning activities.

Releases to water

Release data to water for the DEGBE production sites in the EU (**Table 2.1**) are presented in **Table 3.2**. (Note: the site numbers in **Table 3.2** do not directly correspond with the order of companies in **Table 2.1**). For seven of the eight (no. 1-7) production sites the exposure assessment is based on actual, site specific data. For one site (no.8), a generic scenario was carried out based on default values (TGD96), because no site specific data were submitted for aquatic releases.
It is assumed that the amounts released to water will enter a sewage treatment plant. During sewage treatment 87 percent is expected to be removed by biodegradation.
Relevant data for the predicted environmental concentration (PEC) calculations in an STP and the aquatic compartment are also presented in **Table 3.2**. The effluent concentration leaving the STP (PEC_{STP}) is calculated by multiplying the daily amount released by the fraction that is not removed from STP and dividing it by the volume of the STP. This PEC_{STP} is divided by a dilution factor to obtain the local PEC in surface water. In formulae:

$$PEC_{STP} = \frac{\text{amount released} \cdot \%\ \text{not-removed in STP} \cdot 1{,}000}{\text{volume STP}} \qquad \textbf{(1)}$$

$$\text{local } PEC_{\text{surface water}} = \frac{PEC_{STP}}{\text{dilution factor}} \qquad \textbf{(2)}$$

where,
- amount released in kg/d
- fraction not-removed in STP is 0.13 for DEGBE
- volume STP in m^3/day
- dilution factor = (flow STP + flow river)/flow STP

Several additional remarks should be made with respect to **Table 3.2**:
- besides production releases, for plants no. 5 and 6 also actual data are given on the releases of DEGBE during processing and/or formulation. (Plant no.6: chemical intermediate and plant no.5: chemical intermediate and formulation in various products, e.g. leather dyes).
- for site number 2 the concentration in the effluent of the STP reflects the total organic carbon content in the unit outfall weir. As at present the fraction of DEGBE in this total organic content is not known, no PEC in the receiving water is calculated.
- for site no.4 the emission amount of 5 kg/day reflects the releases of DEGBE to water due to losses via the vacuum pumps. From all site specific information received, this is the highest release amount during production. No PEC in surface water could be calculated for this site, as the receiving water is sea with an unknown dilution factor.
- the release of 5 kg/day of site no.4 may be used as representative for losses of DEGBE via the vacuum system in plants no. 1-7. For site no. 3 this would give a PEC_{STP} of 0.006 mg/l and a PEC in surface water of $2 \cdot 10^{-6}$ mg/l.

Table 3.2 Aquatic emission data from production sites of DEGBE in the EU.

Site no.	Release to water (kg/day)	Measured Estimate	Size of STP (m^3/day)	Minimal flow of receiv. water (m^3/s)	Dilution in receiv. water	Conc. effluent STP (mg/l) (=PEC_{STP})	Conc. in receiv. water (mg/l) (= PEC surface w.)	Year
1	-	-	no data	no data	no data	-	-	1995
2	-	M	240[2]	no data	50[3]	(1065[4])	Unknown	1994
3	-	-	24,000	590	2100	-	-	Unknown
4	5	M	6000[5]	no data[6]	no data	0.03	unknown	Unknown
5	0.05/167*	E	410,000	734	150	0.01[1]	$6.7 \cdot 10^{-5}$	1993
6	0.1/3.0*	E	7270	3	35	$5 \cdot 10^{-4}$/ 0.01*	$1.4 \cdot 10^{-5}$ /$4 \cdot 10^{-4}$*	1993
7	< 2.7	E	72000	18.4	21.5	< 0.001	$< 5.9 \cdot 10^{-5}$	Unknown
8	50[7]	E	2000 (default)	-	10 (default)	3.2	0.27	1996

* processing data
\- not applicable
no data no data were submitted
1 covers both production and processing
2 there is no STP available, but only a drainage system with a flow of 240 m^3/day.
3 dilution factor was confirmed by the national authority of the producing country
4 during cleaning operations water is drained off into the river without treatment. (Based on TOC in the unit outfall weir) No biodegradation assumed.
5 the flow of process water is 72 m^3/day.
6 release to surface water is allowed in permit. The receiving water is sea. The dilution for marine environment is unknown.
7 based on Tables A1.1 and B1.3 of TGD and input tonnage of 5,000 tonnes, i.e. upper limit of IUCLID tonnage range.

Releases to air

Release data to air for the DEGBE production sites in the EU (**Table 2.1**) are presented in **Table 3.3**. (Note: the site numbers in this table do not directly correspond with the order of sites in **Table 2.1**). All eight production sites submitted actual data on atmospheric releases.

Table 3.3 Atmospheric emissions of DEGBE from production sites in the EU.

Site no.	Release to air (kg/day)	Measured Estimated	Conc.air in mg/m^3 (100 m. from source) (local PEC_{air})	Year
1	0	E	0	Unknown
2	0.07	E	$< 3.9 \cdot 10^{-4}$	1993
3	1.7	E	$3.9 \cdot 10^{-4}$	Unknown
4	0.1	Unknown	$< 3.9 \cdot 10^{-4}$	Unknown
5	0/0.13[1]	E	$< 3.9 \cdot 10^{-4}$	1993
6	0.006/0.07[1]	E	$< 3.9 \cdot 10^{-4}$	1993
7	0.07	E	$< 3.9 \cdot 10^{-4}$	Unknown
8	negligible	E	$< 3.9 \cdot 10^{-4}$	1996

1 processing data.

The highest reported daily release to air, i.e. 1.7 kg/day for site no.3, is initially used for the EUSES calculation of a local PEC in air. The calculation resulted in a DEGBE concentration of $3.9 \cdot 10^{-4}$ mg/m^3 at 100 metres from the source. As this value is very low, no calculations were made for the other site specific scenarios.

Several additional remarks should be made with respect to **Table 3.3**:
- besides production release, for sites no.5 and 6, also actual release data are given for processing.
- for site no.2 the figure of 0.07 kg/day is based on releases during production, storage and road tanker filling operations.
- for site no.3 the release to air was taken from calculations presented in a permit request.

Releases to soil
Several companies stated that sludge from the STP and (solid) waste containing DEGBE are incinerated. Local releases to soil from deposition are assumed to be negligible.
The calculated PEC in soil for the generic production scenario no. 8 is 0.02 mg/kg.

3.1.1.2 Releases from processing, formulation and use

Generic exposure scenarios are used for estimating the releases from processing, formulation and use of DEGBE, as no actual data were obtained from either industry or other bodies (except for some data mentioned in the previous paragraph). The scenarios are based on the two most important use categories of DEGBE, i.e. detergents and paints (see paragraph 2.2). Paints are further subdivided in 1) coil coatings and 2) other paints (can coating, water based car base coats, general industrial coatings, water based decorative paint (trade and retail)).
An overview of the various environmental exposure scenarios for processing, formulation and private use of DEGBE is given in **Table 3.4**.

Table 3.4 Environmental exposure scenarios for processing, formulation and private use of DEGBE.

Scenario	specification
Detergent I	formulation
Detergent II	processing (public domain)
Detergent III	private use
Paints I (coil coatings)	formulation
Paints II (coil coatings)	processing
Paints III (other paints)	formulation
Paints IV (car, can etc. paints)	processing
Paints V (decorative)	public domain
Paints VI (paints)	private use

The exposure assessment is based on the EU-Technical Guidance Documents (TGD 1996) applying the European Union System for the Evaluation of Substances, EUSES (EC 1996). In addition, for the scenarios Detergent I and Paint I/II (coil coating) the use category documents were used for getting more realistic release factors.
The input parameters and results of the EUSES calculations are shown in http://ecb.ei.jrc.it.

Local releases

The local release estimates for formulation, processing and private use of DEGBE for the generic scenarios are given in **Tables 3.5, 3.6 and 3.7**. Local use volumes per scenario are calculated as percentages of the regional tonnage. The percentages mentioned in **Table 2.3** (paragraph 2.2) are used. Following the TGD, the regional tonnage is set at 10 percent of the total EU tonnage, i.e.

Table 3.5 Local releases of DEGBE from formulation, processing and private use of detergent and cleaners.

	Generic scenario detergents (I-IV)		
Scenario	**Detergent I**	**Detergent II**	**Detergent III**
Tonnage	4660 • 0.59 = 2749	4660 • 0.22=1025	4660 • 0.37= 1724
Main category	non-dispersive	wide/non-dispersive	Wide dispersive
Industrial category Use category	6 (Public domain) 9 (Cleaning/washing agents)	6 (Public domain) 9 (Cleaning/washing agents)	5 (Personal/domestic) 9
Life cycle step	formulation	processing	private use
Number of days	300 (Table B2.2)[1] f=0.75	200 (Table B3.3)[1] f=0.002	365 (Table B4.1)[1] f=0.002
Release estimates (%) air water	 0.002 (Table 2)[2] 0.09	 0.25 (Table A3.5)[1] 90	 0 (Table A4.1)[1] 99
Amount released (kg/d) air water	 0.1 6.2	 0.03 9.2	 0 9.4

[1] A and B tables refer to TGD96. Fraction of chemical in formulation is set at 0.1.

[2] Table derived from Emission Scenario Document IC-5 Personal/domestic and IC-6 Public domain (1995/1996).

Table 3.6 Local releases of DEGBE from formulation and processing of paint (coil coatings).

	Generic scenario paints I and II	
Scenario	**paints I (coil coating)**	**paints II (coil coating)**
Tonnage	4660 • 0.16 = 746	4660 • 0.16= 746
Main category	non-dispersive	wide dispersive
Industrial category Use category	14 (paint: coil coating) 48 (solvents)	14 (paint: coil coating) 48 (Solvents)
Life cycle step	formulation	processing
Number of days	300 (Table B2.2)[1] f=1	300 (Table B3.13)[1] f=0.1
Release estimates (%) air water	 - 1 (Table 3.5)[2]	 - 1 (Table 3.5)[2]
Amount released (kg/d) air water	 0 25	 0 2.5

[1] A and B tables refer to TGD96. Fraction of chemical in formulation is set at 0.05.

[2] Table derived from Emission Scenario Document IC-14 Paints, lacquers and varnishes industry (1995/1996).

Table 3.7 Local releases of DEGBE from formulation, processing and private use of paints (others).

	Generic scenario paints			
Scenario	**paints III (others)**	**paints IV (can, car and gen.ind.)**	**paints V (decorative)**	**paints VI (others)**
Tonnage	4660·0.19 = 885	4660·0.13= 606	4660·0.03= 140	4660·0.03= 140
Main category	Multi-purpose equipment III	Wide dispersive		Wide dispersive
Industrial category	14 (Paints, lacquers and varnishes ind.)	14	14	14
Use category	48 (Solvents)	48	48	48
Life cycle step	formulation	processing	processing	private use
Number of days	300 (Table B2.2)[1] f=0.75	300 (Table B3.13) f=0.1	300 f=0.01	300 (Table B4.5)[1] f=0.002
Release estimates (%)				
air	0.25 (Table A2.1)[1]	80 (Table A3.15 WB)[1]	80	80 (Table A4.5)[1]
water	2	10	10	15
Amount released (kg/d)				
air	5.5	162	3.7	0.7
water	44	20.2	0.5	0.1

1 A and B tables refer to TGD96. Fraction of chemical in formulation is set at 0.05.
WB Water based.

0.1·46,600 = 4660 tonnes. This assumption is supported by detailed industry information regarding the consumption of DEGBE throughout Europe (Fax industry 17-10-1996).
For paint scenario V processing of decorative paints it should be noted that this scenario is in fact not covered by the TGD Table 3.13. This **table** refers to industrial painting and not painting by small companies as is meant here. The fraction of main source of 0.15 according to Table 3.13 would result in extremely high amounts of DEGBE containing paints that are being used by small painting trades (1.5 tonnes per day!!). A fraction of main source of 0.01 is therefore considered more realistic. This value is used in the current risk assessment for scenario V.

Regional and continental releases
The regional release includes all relevant life cycle stages of DEGBE. For production it is assumed that there is only one production site in the region. The production scenario site 8 (generic for water) is used as input for the life cycle stage production. The regional releases are estimated to be **1950 kg/d** to air, **5320 kg/d** to waste water and **2280 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 **17,600 kg/d** to air, **47,900 kg/d** to waste water and **20,500 kg/d** 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.

3.1.1.3 Local Predicted Environmental Concentrations

Note: The local predicted environmental concentrations based on the DEGBE releases from production are already given in **Tables 3.2** (water) and **3.3** (air).

Table 3.8 PECs in the effluent of an STP and local PECs in surface water.

Scenario	PEC in STP (mg/l)	Local PEC in surface water (mg/l)
Scenario detergent I - formulation	0.4	0.05
Scenario detergent II - processing	0.6	0.07
Scenario detergent III - private use	0.6	0.07
Scenario paints I (coil coating) - formulation	1.6	0.17
Scenario paints II (coil coating) - processing	0.2	0.03
Scenario paints III - formulation	2.8	0.3
Scenario paints IV (car, can etc.) - processing	1.3	0.14
Scenario paints V (decorative) - processing	0.03	0.02
Scenario paints VI - private use	0.009	0.01

Table 3.9 Local PECs in soil.

Scenario	PEC (mg/kg) terrestrial
Scenario detergent I - formulation	0.004
Scenario detergent II - processing	0.006
Scenario detergent III - private use	0.006
Scenario paints I (coil coating) - formulation	0.01
Scenario paints II (coil coating) - processing	0.003
Scenario paints III - formulation	0.02
Scenario paints IV - processing	0.02
Scenario paints V - processing	0.002
Scenario paints VI - private use	0.002

3.1.1.3.1 Aquatic compartment

The daily amounts released for the generic exposure scenarios, as presented in **Tables 3.5**, **3.6** and **3.7**, are the basis for the calculations of the PECs. The PEC_{STP} and the local PEC in surface water are calculated with the formulae in paragraph 3.1.1.1. Default values of 2,000 m^3/day and 10 are used for the volume of the STP and the dilution factor, respectively.
Table 3.8 gives the PECs for the aquatic compartment.

3.1.1.3.2 Terrestrial compartment

The EUSES model takes into account both the application of STP sludge on agricultural soil and deposition from air for the calculation of DEGBE 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) for the various generic scenarios.

3.1.1.3.3 Atmosphere

The calculated annual average DEGBE concentrations in air are presented in **Table 3.10**.

Table 3.10 Local PECs in air.

Scenario	PEC local (mg/m^3)
Scenario detergent I - formulation	$4.5 \cdot 10^{-5}$
Scenario detergent II - processing	$1.7 \cdot 10^{-5}$
Scenario detergent III - private use	$1.3 \cdot 10^{-5}$
Scenario paints I (coil coating) - formulation	$1.4 \cdot 10^{-5}$
Scenario paints II (coil coating) - processing	$1.3 \cdot 10^{-5}$
Scenario paints III - formulation	$1.3 \cdot 10^{-3}$
Scenario paints IV - processing	0.04
Scenario paints V - processing	0.0009
Scenario paints VI - private use	$1.8 \cdot 10^{-4}$

3.1.1.3.4 Non compartment specific exposure relevant to the food chain

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

Table 3.11 PECs in fish and worm.

Scenario	PEC fish (mg/kg)	PEC worm (mg/kg)
Scenario detergent I - formulation	0.04	0.004
Scenario detergent II - processing	0.04	0.004
Scenario detergent III - private use	0.06	0.004
Scenario paints I (coil coating) - formulation	0.1	0.006
Scenario paints II (coil coating) - processing	0.03	0.004
Scenario paints III - formulation	0.2	0.009
Scenario paints IV - processing	0.1	0.01
Scenario V - processing	0.02	0.004
Scenario paints VI -private use	0.02	0.003

3.1.1.3.5 Measured data

DEGBE concentrations were measured in the influent and effluent of the communal STP in Göteborg, Sweden (Paxéus *et al.* 1992). Average influent concentrations in 1990 and 1991 were found to be, respectively, 42 and 91 µg/l. The upper limit of the influent range was 300 µg/l. The effluent concentrations ranged from not detectable to 3 µg/l. (Clark *et al.* 1991) detected DEGBE (9 µg/l) in the effluent of one out of three sampled communal STPs in New Jersey, USA. On the basis of the results of their own study and those of the Clark study, Paxéus *et al.* 1992 concluded that: "in view of the general trend for introduction of water-soluble based products it may be expected that the quantity of glycol derivatives and similar types of compounds in the influent waste water will increase in the future".

3.1.1.4 Regional PECs

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

Table 3.12 Regional PECs in air, water and soil.

compartment	PEC regional
air	$1.3 \cdot 10^{-5}$ (mg/m^3)
water	0.01 (mg/l)
soil	0.001 (mg/kg)

3.2 EFFECTS ASSESSMENT

3.2.1 Aquatic compartment

3.2.1.1 Short-term toxicity to fish

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

Table 3.13 Short term fish toxicity data of DEGBE.

No.	Species	Duration (h)	LC50 (mg/l) 95% C.I.	Method	References
1	Lepomis marcrochirus	96	1300	Other	Dawson *et al.* 1975
2	Carrassius auratus	24	2700	APHA 1971	Bridie *et al.* 1979
3	Poecilia reticulata	7 d	1150	Other	Koenemann 1981
4	Leuciscus idus melanotus	48	2750	DIN 38412 part 15	Huels AG. Unpublished study
5	Leuciscus idus melanotus	48	1805	Other	Juhnke 1978
6	Leuciscus idus melanotus	48	2305	Other	Juhnke 1978
7	Menidia beryllina[1]	96	2000	Other	Dawson *et al.* 1975/77

[1] marine species

Two out of seven short term toxicity tests (no. 2 and 4) were conducted according to (international) standard test guidelines. Only nominal test concentrations were given.

The lowest LC50, i.e. 1150 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 DEGBE short term toxicity studies for daphnids.

Table 3.14 Short term daphnid toxicity data of DEGBE.

No.	Species	Duration (h)	EC50 (mg/l) 95 % C.I.	Method	References
1	Daphnia magna	48	> 100	OECD No. 202 C2	BP Chemicals Ltd 1992
2	Daphnia magna	24	2850	Other	Bringmann and Kuehn 1977
3	Daphnia magna	24	3200 (2990-3424)	Other	Bringmann and Kuehn 1982
4	Daphnia magna	24	3184 (2783-3644)	DIN 38412 Part II	Huels AG. Unpublished Study

Tests no. 1 and 4 with DEGBE were conducted according to (international) standard test guidelines. Only nominal test concentrations were given. Test no. 1 was a limit test using a concentration of 100 mg/l.

The lowest EC50-value of D. magna, i.e. 2850 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

Table 3.15 shows the algae toxicity studies of DEGBE.

Table 3.15 Algae toxicity data of DEGBE.

Species	Duration	Effect (mg/l)	Method	References
Scenedesmus subspicatus	96 h	EC50 > 100	OECD Guideline 201	BP Chemicals 1992
Microcystis aeruginosa	8 d	NOEC = 53	Growth inhibition test	Bringmann and Kuehn 1976, 1978
Scenedesmus quadricauda	8 d	NOEC = 1000	Growth inhibition test	Bringmann and Kuehn 1978, 1980

The first test was conducted according to (international) standard test guidelines (limit test). Only nominal test concentrations were given. In the second and third test (according to Bringman and Kühn), TGK (Toxische GrenzKonzentration) values were established on the basis of biomass. As the percentage effect at the TGK is 3% to 5%, these values are regarded as NOEC-values.

Blue-green algae (M. aeruginosa) should be counted among the primary producers due to their autotrophic nutrition.
The NOEC-value of 53 mg/l for M. aeruginosa will be taken into consideration with the results from other aquatic toxicity studies when deriving the PNEC for the aquatic compartment.

3.2.1.4 Toxicity to micro-organisms

The DEGBE toxicity studies with micro-organisms are shown in **Table 3.16**.

Table 3.16 Micro-organism toxicity data of DEGBE.

No.	Species	Duration (h)	NOEC (mg/l)	Method	References
1	Chilomonas paramaecium	48	2774	Growth inhibition test	Bringmann *et al.* 1980
2	Pseudomonas putida	16	1170	Growth inhibition test	Huels Unpublished Study
3	Pseudomonas putida	16	255	Growth inhibition test	Bringmann and Kuehn 1976, 1980
4	Entosiphon sulcatum	72	73	Growth inhibition test	Bringmann and Kuehn 1980
5	Uronema parduczi	20	420	Growth inhibition test	Bringmann and Kuehn 1980

All available micro-organism tests, except for test no. 2, concerned Bringmann and Kuhn tests, in which the toxicity thresholds are considered to be equal to a NOEC. Because protozoa are not (directly) involved in the biodegradation of chemicals in a sewage treatment plant, the NOEC-values for this taxonomic group (tests no. 1, 4 and 5) are only used as supportive information for the derivation of the PNEC for micro-organisms. The arithmetic mean of both values for P.putida, i.e. 713 mg/l, is used for deriving the PNEC for micro-organisms.

3.2.1.5 PNEC for the aquatic compartment

The PNEC for the aquatic compartment is extrapolated from the NOEC of 53 mg/l for Microcystis aeruginosa using an extrapolation factor of 50. This factor is chosen because chronic data are available for two trophic levels (algae and micro-organisms) and, additionally, these NOECs seem to cover the most sensitive taxonomic groups. Both taxonomic groups are also represented by a number of species.
Short-term QSAR-values (according to TGD96) for fish and daphnids of, respectively, 2200 and 2300 mg/l, are consistent with the experimental data for both taxonomic groups. However, the experimental NOEC for M.aeruginosa is rather low compared with the short-term QSAR-value for algae of 2600 mg/l (a ratio acute:chronic of 10 would give a NOEC of 260 mg/l). It would be difficult to explain this low value of M.aeruginosa on biological/structural grounds.

The extrapolation leads to a PNEC for the aquatic environment of 1 mg/l.

$PNEC_{aquatic}$ = 1 mg/l

3.2.1.6 $PNEC_{micro-organisms}$

The PNEC for micro-organisms is extrapolated from the NOEC for P. putida (713 mg/l). using an extrapolation factor of 10. This leads to a PNEC of 71 mg/l.

$PNEC_{micro-organisms}$ = 71 mg/l

3.2.2 Terrestrial compartment

Since there are no DEGBE toxicity data for terrestrial organisms, no $PNEC_{terrestrial}$ can be derived directly.

3.2.2.1 PNEC for the 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 $PNEC_{terrestrial}$ 0.2 mg/kg (EUSES).

$PNEC_{terrestrial}$ = 0.2 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)

The PEC/PNEC ratios based on the actual releases of DEGBE at production (**Table 3.2**) are all below 1 (**conclusion ii**). The same is true for the generic production scenario (site no.8; PEC/PNEC ratio of 0.3) and for the few PEC/PNEC ratios that can be calculated based on actual releases from processing (**Table 3.2**).

The local PECs in an STP and surface water for the various environmental exposure scenarios (processing) are presented in **Table 3.8**. The PNECs for micro-organisms and aquatic organisms are, respectively, 71 and 1 mg/l. **Table 3.17** shows the corresponding PEC/PNEC ratios for micro-organisms and aquatic organisms.

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

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

Table 3.17 PEC/PNEC ratios for micro-organisms and aquatic organisms.

Scenario	$PEC/PNEC_{micro\text{-}organisms}$	$PEC/PNEC_{aquatic}$
Scenario detergent I - formulation	0.05	0.05
Scenario detergent II - processing	0.08	0.06
Scenario detergent III - private use	0.08	0.06
Scenario paints I (coil coating) - formulation	0.2	0.1
Scenario paints II (coil coating) - processing	0.02	0.03
Scenario paints III - formulation	0.4	0.3
Scenario paints IV (car, can etc.) - processing	0.2	0.1
Scenario V (decorative) - processing	0.004	0.01
Scenario paints VI - private use	$1 \cdot 10^{-3}$	0.01

3.3.2 Terrestrial compartment (local)

The local PECs in the terrestrial compartment for the various emission scenarios are given in paragraph 3.1.2.2. The PNEC terrestrial is 0.2 mg/kg. **Table 3.18** shows the corresponding PEC/PNEC ratios for the terrestrial compartment.

Table 3.18 shows that in all emission scenarios the PECs do not exceed the PNEC for the terrestrial environment (**conclusion ii**). The same is true for the generic production scenario (site no. 8).

Table 3.18 PEC/PNEC ratios for the terrestrial compartment.

Scenario	$PEC/PNEC_{terrestrial}$
Scenario detergent I - formulation	0.02
Scenario detergent II - processing	0.03
Scenario detergent III - private use	0.03
Scenario paints I (coil coating) - formulation	0.06
Scenario paints II (coil coating) - processing	0.01
Scenario paints III - formulation	0.09
Scenario paints IV - processing	0.1
Scenario V (decorative) - processing	0.01
Scenario paints VI - private use	0.01

3.3.3 Atmosphere (local)

No 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 (local)

In none of the scenarios the PECs in fish or worm exceed the PNEC for predators (**conclusion ii**). For the selected PNEC for predators (50 mg/kg): see conclusion of paragraph 4.1.2.6.

3.3.5 Risk characterisation (regional)

The PECs in water and agricultural soil calculated for the regional scale (**Table 3.12**) do not exceed the corresponding PNECs (**conclusion ii**). No regional 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 DEGBE at 1) the workplace, 2) from use of consumer products and 3) indirectly via the environment.
An overview of the uses of DEGBE (industrial and uses categories) is given in **Table 2.2**.

More specified uses of DEGBE are (Cited in HSDB (through jan 1994)):
- as intermediate for diethylene glycol monobutyletheracetate
- coalescing agent in latex paints
- solvent: for stamp pad inks
  for dyes
  mutual solvent for soap, oil, water in household cleaners
  for high baked enamels
  for nitro-cellulose
- dispersant for vinyl chloride resins in organosols
- diluent for hydraulic brake fluids

The most probable human exposure would be occupational exposure, which may occur through dermal contact or inhalation at workplaces where it is produced or used.

Non-occupational exposure can occur from the use of consumer products containing DEGBE and from the ingestion of contaminated drinking water supplies.
Consumer exposure data are scarce. Drinking water supplies in several US cities found DEGBE as a contaminant, but concentrations were not given (Cited in HSDB (through jan 1994)).

The concentration of DEGBE in indoor is estimated to range from 1-20 µg/m^3 (Lanting and De Mik 1991).
Peak concentrations of DEGBE measured indoor did not exceed 10.8 mg/m^3 (Gibson *et al.* 1991).

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);
- storage, transport and repackaging of chemical products (e.g. paints);
- painters (e.g. paints, paint removers, cleaning agents);
- wood industry (e.g. paints, diluents, cyanoacrylate adhesives);
- basic metal and metal product industries (e.g. paints, cleaning agents, cutting oil, lubricants, anti foaming agents);

- leather industry (e.g. paints, dyes);
- textile industry (e.g. printing inks, dyes, detergents);
- cleaners (e.g. cleaning agents, degreasers, rust removers);
- printing presses (e.g. printing inks, cleaning agents, solvents);
- plastics, plastic articles and rubber articles (stabilisers, lubricants, softeners);
- concrete, etc. articles (thickeners, process regulators);
- car body repair shops (lacquers).

The results of the search for DEGBE in the Swedish product register are presented in Annex 3 (from KEMI (1995)).

The use of products may include:
- transfer of liquids by means of a transfer line and pumping: paints, inks, dyes and other products;
- manual transfer of liquids or pastes: paints, inks, dyes, cleaning agents, anti-corrosion agents and other products;
- manual cleaning or degreasing: cleaning, degreasing, rust removing, lime removing agents used by cleaners, in the basic metals and metal products industry, in the wood and furniture industries, in the food and beverages industries and in several other industries;
- manual painting or application of adhesives using a brush, a roll or spray painting equipment: paints and adhesives applied by painters, in parts of the wood and furniture industry, the construction industry, the basic metals and metal products industry and other industries;
- automated painting and coating using a lacquer curtain, automated spray painting or dipping in the wood industry, the basic metals and metal products industry, metal coating and treatment shops, the leather industry, the textile industry;
- automated printing using printing presses: publishers and in the textile industry;
- high pressure cleaning: food products and beverages industries, pulp and paper industry, publishers and printers, basic metals and metal products industries, wholesale stores and repair facilities.

The routes of exposure are by inhalation of vapours and/or aerosols (spraying of lacquers, high pressure cleaning and printing) 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 DEGBE or of products containing DEGBE, e.g. drumming the (pure) substance or 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 DEGBE and products containing DEGBE;
- workers using products containing DEGBE in the above mentioned industries.

The following data (if available) are used for occupational exposure assessment:
- physico-chemical data of DEGBE and products containing the substance: physical appearance, vapour pressure at room temperature, percentage of DEGBE in products;
- data regarding methods of use and use pattern of the substance and products (potentially) containing DEGBE and exposure control pattern in the relevant industries (from the HEDSET or other sources);
- exposure data for DEGBE 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) and EPA transfer model); in the exposure models the above mentioned types of data are used.

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 effectiveness of PPE in practical situations is very limited. Furthermore, the effectiveness 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 DEGBE is produced and/or used. In many cases, the processes and activities that may lead to emission of DEGBE 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 DEGBE, including quality control sampling and drumming, cleaning of production equipment; handling pure DEGBE;

2 - production of products containing DEGBE, including transferral, mixing, quality control sampling and drumming, cleaning of mixing equipment;
3 - transferral of products containing DEGBE to application equipment (automated or manual) and automated application of products containing DEGBE, including printing (automated application);
4 - manual application of products containing DEGBE, such as spray application, brushing, rolling, cleaning (including manual transferral 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.

A limited number of measured levels of occupational exposure to DEGBE was found in literature (Gibson *et al.* 1991; Vincent *et al.* 1994; Norback *et al.* 1995) and in a German database (BIA 1996). No data for DEGBE were available in a number of other databases (NEDB 1995; Norwegian Exposure Database 1995; AMI 1995; INRS 1995). Confidential information from one producer contains concentrations of the main compound produced (2-butoxyethanol; EGBE) measured in production departments. No information on sampling duration and control measures in use is presented in these data (Company A).

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 4 data from measurements of DEGBE or analogues that will be used for the actual assessment of exposure levels are given. In Annex 5 assumptions and results of relevant calculations using the EPA transfer model are presented.

Scenario 1: production of DEGBE

Production of DEGBE may lead to some emission into the air. Production is in closed systems, except for activities such as sampling and drumming. Drumming of DEGBE 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). According to the producers, drumming (in tank trucks, tank cars or drums) is highly automated and apart from effective local exhaust ventilation, also separation is used as a means of lowering exposure levels (OSPA 1995).

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 is reported to take 40 minutes per tank (Company A).

Measured data

Exposure data for DEGBE are provided by the producers and are found in a German database (OSPA 1996; BIA 1996). Exposure levels presented by the producers generally are below 1 ppm, with the highest value being 1.6 ppm (≈ 11 mg/m^3). All measurements (16 measurements with a duration of more than 1 hour and 1 with a duration less than 1 hour) reported by the German database resulted in levels below the limit of detection (≈ 2 mg/m^3 if the duration of measurement was 2 hours; BIA 1996) These measurements are from the chemical industry and from cleaning of buildings. The number of measurements per industry has not been presented (BIA 1996).

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 (Company A 1994; OSPA 1996; Clapp *et al.* 1984; ECETOC 1994A; Piacitelli *et al.* 1989; Piacitelli *et al.* 1990). According to the producers, exposure to DEGBE will be lower than to the other glycol ethers, not only because of the lower vapour pressure, but also because of a lower percentage of DEGBE in the product stream (Company A 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). Information from one of the producers (OSPA 1996) describes the drum and tank filling processes now in use in Europe in detail, including information on local exhaust ventilation, for other references data on control measures are not available at this moment. Reported short-term exposure levels, with a duration of measurements of approximately 15 minutes, are below 10 mg/m^3 (Piacitelli *et al.* 1989; Piacitelli *et al.* 1990).
The substances mentioned in most of the references have a considerable higher vapour pressure than DEGBE, 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**.

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 0.63 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 (≈ 3.4-20.3 mg/m^3). For non-

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

Type of container	Concentrations (mg/m^3)	
	Typical	Worst case
Rail car	0.01	0.11
Tank truck	0.00	0.06
Drums (200 L)	0.14	12.69
Can (10 L)	0.01	0.63

dispersive use and other patterns of control the following exposure levels are calculated:
- segregation: 3-10 ppm (≈ 20-68 mg/m^3);
- direct handling with dilution ventilation: 10-50 ppm (≈ 68-338 mg/m^3);
- direct handling without dilution ventilation: 50-100 ppm (≈ 338-676 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 DEGBE has a vapour pressure of only 2.7 Pa. Considering this, the measured exposure or concentration levels from one producer (generally below 1 ppm) (OSPA 1996) 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 substantially below the reasonable worst case level (based on data provided by industry). 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, given the information (OSPA 1995) that leaking drums are rare.
Dermal exposure is assessed by EASE.
Based on EASE the estimates of dermal exposure levels of DEGBE are for tank filling activity the following.

- Non-dispersive use with direct handling and intermittent contact: 0.1-1 mg/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 (OSPA 1996).

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. Contact with contaminated drums will lead to a higher area of skin exposed, but will be accidental exposure.
The reasonable worst case exposure becomes 210 mg/day.

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

- Inhalation exposure; reasonable worst case, full shift: ≈ 0.6 mg/m^3;
- Inhalation exposure; reasonable worst case, short term: ≈ 1.3 mg/m^3;
- Inhalation exposure; typical, full shift: << 0.6 mg/m^3;
- Dermal exposure; reasonable worst case: 210 mg/day.

Scenario 2: production of products containing DEGBE
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 (UBA, 1997), but are probably drummed in cans with a volume up to 10 L. Transferral of DEGBE 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, cans or even smaller packings, e.g. ball point ink fillings. The use of very good local exhaust ventilation cannot be assumed in all facilities that mix chemical products. Some of these facilities are relatively small and not very modern.

Duration and frequency of exposure may be full shift and daily, although transfer 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; Guirguis *et al.* 1994; NEDB 1995; Piacitelli and Krishnan 1989; Piacitelli *et al.* 1990). 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).

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 DEGBE: EPA transfer model, correction by fraction of DEGBE in product, assuming at maximum 10% DEGBE.

Type of container	Concentrations (mg/m^3)	
	Typical	Worst case
Cans (10 L)	< 0.01	0.06
Small cans (1 L)	< 0.01	0.06
Drums (200 L)	0.01	1.27

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 0.13 mg/m^3.
Drumming of paint remover (35% DEGBE) in cans of 10 L leads to worst case calculated concentrations, according to the EPA model, of approximately 0.7 mg/m^3. Such very good local exhaust ventilation is not considered to represent the reasonable worst case situation.
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 generally non-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 direct handling with dilution ventilation agree very

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

good with the data for EGEEA and EGBE from Angerer *et al.* (1990). Results from the EPA transfer model appear to be lower than the data from analogues. This may be due to the fact that the analogues have a distinctly higher vapour pressure. On the other hand the EPA transfer model may 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.
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 worst 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 processes due to transfer of DEGBE at the beginning of the process are similar 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. However, it is assumed to be only one exposure moment (incidental exposure), leading to lower exposure levels.

Drumming into rail cars and tank trucks will be done using transfer lines, while drumming into drums or cans may lead to contact with contaminated surfaces due to overflowing, or fill spouts that are not fitted correctly. Based on EASE the upper bound dermal exposure estimate for both activities are the following, assuming 5-10% DEGBE in the product:

- non dispersive use with direct handling and intermittent contact: 0.005-0.1 mg/cm^2; exposed area half of both hands = 420 cm^2: 2-42 mg/day.

Gibson mentions a cleaner containing 9% of DEGBE (Gibson *et al.* 1991), while maximum percentages of glycol ethers in water-borne paints given by Hansen *et al.* (1987) are below 5%. An estimate of 10% DEGBE in such products therefore appears to be appropriate for a reasonable worst case situation.

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

- Inhalation exposure; reasonable worst case, full shift: ≈ 2.5 mg/m^3;
- Inhalation exposure; reasonable worst case, short term: ≈ 5.1 mg/m^3;
- Inhalation exposure; typical, full shift: ≈ 1.3 mg/m^3;
- Dermal exposure; reasonable worst case: 42 mg/day.

Scenario 3: automated application of products containing DEGBE
The application of products containing DEGBE with automated equipment may involve preparation of the product (e.g. blending of different paints to reach a specific colour), transferral 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 transferral. Skin exposure potential will be limited to the transferral 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; Guirguis *et al.* 1994; NEDB 1995; Norwegian Exposure Database 1995; Piacitelli *et al.* 1990; Veulemans *et al.* 1987; Vincent *et al.* 1994). Short-term levels reported (duration of measurements approximately 15 minutes) are in the same range (NEDB 1995; Norwegian Exposure Database 1995; Piacitelli *et al.* 1990).

Models

The applicable result from the EASE model, considering products containing at maximum 10% of DEGBE and application at room temperature is: negligible exposure, since the vapour pressure of DEGBE - corrected by a factor of 10 to take into account the limited fraction of DEGBE in the products - falls into the category “very low” (< 1 Pa).

With the correction for percentage of substance after running the model - as proposed in the Technical Guidance Document - the results would be one-tenth of the following levels:

- non-dispersive; LEV: 0.5-3 ppm (≈ 3.4-20.3 mg/m^3);
- non-dispersive; segregation: 3-10 ppm (≈ 20.3-68 mg/m^3);
- wide dispersive; segregation: 10-50 ppm (≈ 68-338 mg/m^3).

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

For the substances for which measured data are presented in above the levels estimated by EASE (correcting the vapour pressure for 10% of substance in the mixture) would also be 0.5 - 50 ppm, depending on the control pattern.

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 for pure DEGBE in this scenario (0.5 ppm = 3.4 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 transferral of products, either by connection of a transfer line or by manual liquid transfer. Based on EASE the upper bound dermal exposure levels for products containing 5-10% DEGB are the following:

- connecting a transfer line; non-dispersive use; direct handling and incidental contact: 0-0.01 mg/cm^2; exposed area: 420 cm^2: 0-4 mg/day;

- bench scale liquid transfer; non-dispersive use; direct handling and intermittent contact: 0.005-0.1 mg/cm^2; exposure area: 420 cm^2: 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: ≈ 3.4 mg/m^3;
- Inhalation exposure; reasonable worst case, short term: ≈ 17 mg/m^3;
- Inhalation exposure; typical, full shift: < 1 mg/m^3;
- Dermal exposure; reasonable worst case: 42 mg/day.

Scenario 4: manual application of products containing DEGBE

Manual application, such as brushing, rolling and cleaning is a type of wide dispersive use, often 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

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.* (1987) 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 DEGBE in the work area are reported to be 4-5 mg/m^3 with paints reported to contain up to 1.5%. 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.* 1987). 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 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; Guirguis *et al.* 1994; NEDB 1995; Norwegian Exposure Database 1995; Piacitelli *et al.* 1990; Veulemans *et al.* 1987; Vincent *et al.* 1994; Zaebst 1984). 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 in cleaning with undiluted cleaner and manual painting and were between < 1 mg/m^3 and 60 mg/m^3 for more volatile glycol ethers (Gibson *et al.* 1991; Hansen *et al.* 1987). 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 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 from the EASE model as provided in diskette are independent of the vapour pressure of the substance and are:
- spray application; uncontrolled: > 1000 ppm (> 6800 mg/m^3);
- spray application; dilution ventilation present: 500-1000 ppm (≈ 3400-6800 mg/m^3);
- spray application; segregation: 100-200 ppm (≈ 680-1360 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 (1360-3400 mg/m^3);
- spray application; dilution ventilation present: 100-200 ppm (≈ 680-1360 mg/m^3);
- spray application; segregation: 10-50 ppm (≈ 68-340 mg/m^3).

The applicable result from the EASE model for other manual applications is negligible exposure (if the vapour pressure is corrected by a factor of ten before running the model).

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.
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 *et al.* 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 DEGBE (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). The number of data for DEGBE is very limited. However, the available measured data and the observation on very slow decline of concentrations of DEGBE by Norback *et al.* (1995) show that exposure levels of 5-10 mg/m^3 are possible.

Considering the few measured data, the 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 10 mg/m^3 (approximately one-third of the two next highest maximum values for EGBE, similar to values for isocyanate-oligomers) and short-term levels of up to 100 mg/m^3 (ten times the full shift levels) appear to be possible. Typical long-term values may be up to the levels for DEGBE 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 for products containing 5-10% DEGBE are the following:

- bench scale liquid transfer with small volumes; non-dispersive use with direct handling and intermittent contact: 0.005-0.1 mg/cm^2; exposed area = 200 cm^2: 1-20 mg/day;
- limited manual contact; non-dispersive use with direct handling and intermittent contact: 0.005-0.1 mg/cm^2; 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: 0.25-1.5 mg/cm^2; exposed area: two hands, part of the forearms and head = 1300 cm^2: 325-1950 mg/day;
- cleaning; wide-dispersive use with direct handling and incidental contact: 0.005-0.1 mg/cm^2; exposed area is two hands = 840 cm^2: 42-420 mg/day.

The highest value given by EASE will be used for 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: ≈ 10 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.

Scenario	Exposure		Estimated inhalation exposure level (mg/m^3)						Estimated skin exposure level (mg/day)[A]
			Long-term				Short-term		
	Duration (hr/day)	Frequency (day/year)	Typical	Method[B]	Worst-case	Method[B]	Level	Method[B]	
1: production of DEGBE	6-8	100-200	<< 0.6	Data industry	0.6	EPA-LEV	1.3	Expert	210
2: production of products containing DEGBE	6-8 or less	100-200	1.3	EPA Transfer	2.5	Expert	5.1	Expert	42
3: automated application of products containing DEGBE	6-8 inhal. 0-2 skin	100-200	< 1	Expert	3.4	EASE	17	Expert	42
4: manual application of products containing DEGBE	6-8	100-200	5	Hansen *et al.* (1987)	10	Analogues	100	Expert/ Analogues	1950

A) Skin exposure levels estimated by EASE dermal exposure model; reasonable worst case estimates;

B) All measured data and model results are used in choosing this value, however, the following methods formed the direct basis for the quantitative result presented in the table: Expert = Expert judgement; Analogues = Analogy approach; EASE = EASE model; EPA-LEV = EPA transfer model, taking into account the influence of very effective LEV.

4.1.1.2 Consumer exposure

In Sweden the substance is found in 456 products whereof 54 are available to consumers (see also Annex 3) (KEMI 1995). The total volume produced in 1993 for these products was 1656-1741 tonnes. Information from the Danish product register showed that DEGBE is found in 877 products at a total tonnage for 1995 of 831 (The Danish product register 1995). DEGBE is used in many consumer products at typical concentrations of about 5% (OSPA 1996). The identified consumers products are fire extinguishing agents, paints, varnishes, aqueous paints, (dispersion) adhesives, polishing agents, stain removers, cleaning agents and detergents.

With respect to the low vapour pressure (0.027 hPa at 20 °C) as well as the small use volume of DEGBE per event, the major source for consumer exposure could be from its use as a solvent in household cleaners and from its use in latex paints. In Europe DEGBE is used as a coalescing

agent in about 3 - 20% of the aqueous paints at concentrations ranging from 1 to 4% (CEPE 1997). The concentrations of DEGBE used in cleaning products is about 10% (Gibson *et al.* 1991).
The following data (if available) are used for the consumer exposure assessment:

- physical chemical data of DEGBE (molecular weight, log K_{ow}, vapour pressure at room temperature)
- contact parameters
- concentration parameters (e.g. percentage of DEGBE in latex paint and cleaner (or for other glycol ethers used in similar products)
- exposure data for DEGBE (or for other glycol ethers in similar products)
- results from consumer models.

With respect to the above mentioned indicated consumer uses of DEGBE and the availability of information especially about the concentration of DEGBE in the consumers products two exposure scenarios are considered: latex paints and liquid hard surface cleaners.
Inhalation exposure from the use of DEGBE containing paint in a spray application is described for workers (chapter 4.1.1.1: scenario 4). Since also consumers may use this application a risk assessment is carried out based on the outcome of the occupational exposure assessment (worst-case).
Exposure data are available for the use of DEGBE in liquid hard surface cleaner (Gibson *et al.* 1991). Measured exposure data are also available for DGBA (the acetate ester of DEGBE) used in latex paint. The consumer exposure to DEGBE in latex paint is estimated using the CONSEXPO model, version 1.04 (Van Veen 1995). CONSEXPO contains a number of models for the estimation of exposure and uptake (during uses) of substances via the inhalatory, dermal and oral routes. For all scenarios a relative density of 1 g/m^3 was assumed.

Scenario I: Latex paint
When DEGBE is used as an ingredient in latex paints the main exposure routes are by inhalation and by skin contact. The amount of DEGBE in paints is at maximum 5%. Measured exposure data are not available for DEGBE but only for its acetate ester (DGBA). Gingell *et al.* (1993) reported human exposure studies performed under simulated consumer use conditions for the use of DGBA in latex paint. The paint containing 0.6% w/w of DGBA as a coalescing aid was used to paint walls (256 ft^2 ≈ 23.78 m^2) of a small room (11·14 ft [≈ 3.35·4.27m]) by roller at the recommended application rate of 400 ft^2/gallon (≈ 9.8 m^2/l). This took approx 80 min. Three experiments were performed with different room ventilation rates (0.3, 1 and 3 air changes per hr). Personal breathing air and room air monitoring was performed using charcoal tubes and DGBA was determined by gas chromatography. For al three air change rates, personal monitoring indicated a concentration of between the limit of detection [0.03 ppm (≈ 0.2 mg/m^3]) and 0.05 ppm (≈ 0.33 mg/m^3) DGBA. The authors concluded that because DEGBE is less volatile than DGBA, inhalation exposure to DEGBE from use in paint is likely to be less than the estimate for DGBA.

The consumer exposure to DEGBE itself is estimated with the CONSEXPO model using exposure scenario “evaporation from mixture”. For reason of comparison we first used the same scenario as described by Gingell *et al.* 1993 with a latex paint containing 0.6% DEGBE (Gingell *et al.* 1993). Details of the parameters used and the results of the modelling are presented in Annex 6.1a,b & c. The outcome of the modelling has been obtained through a reasonable worst-case approach.
Result of the model
For the 3 different room ventilation rates (0.3, 1 and 3 air changes per hr.) the average inhalatory exposure concentration per event was 0.47, 0.41 and 0.31 mg/m^3, respectively. The dermal

exposure from vapours was estimated to be 6 mg/cm^3. These routes simultaneously result in a total internal dose rate of 14.2 mg/kg b.w./day (yearly average) after inhalation and dermal exposure, assuming 75% and 100% absorption, respectively.
The event-estimates of the inhalatory exposure by CONSEXPO equal the exposure data available for DGBA.

In a second paint scenario (Dutch scenario) the DEGBE content in latex paint was assumed to be 5% (as a worst case) and the room volume was defined at 30m^3 (3·4·2,5). Full details of the parameters used and the results of the modelling are presented in Annex 6.1d. The outcome of the modelling has been obtained through a reasonable worst-case approach.
Result of the model
Assuming the use of paint for 80 min. with 5 kg/event results in an average inhalatory exposure concentration per event of 3.97 mg/m^3. The dermal exposure from vapours, was estimated to be 50 mg/cm^3. These routes simultaneously result in a total internal dose rate of 119 µg/kg b.w./day (yearly average) after inhalation and dermal exposure, assuming 75% and 100% absorption. For the risk characterisation with respect to acute dermal toxicity comparison with the single event exposure (10 cm^3 containing 5% DEGBE, with b.w.=70 kg results in an exposure of 7.14 mg/kg b.w.) is more relevance
The event estimates of the Dutch scenario are used in the risk characterisation for consumers (see 4.1.3.2)

Scenario II: Liquid hard surface cleaners
DEGBE is incorporated into liquid hard surface cleaning products at concentrations of up to 9% to enhance their cleaning effectiveness. Consumers using these cleaners may be exposed by direct dermal contact with the cleaning solution, by inhaling DEGBE vapours during the cleaning task, or by breathing room air after cleaning. Gibson *et al.* (1991) performed several experiments (with restricted airflow, exaggerated cleaner consumption and no rinsing) to estimate potential consumer inhalation exposure to DEGBE in the home. Bath-room air concentrations of DEGBE showed peak values between 1 and 3 hours after the task initiation and decreased thereafter gradually with time. The peak concentrations did not exceed 1.6 ppmv (parts per million by volume)[≈ 10.8 mg/m^3] in all experiments. The total DEGBE concentration in the air at the time of maximum air concentrations accounted for only 1 to 3% of the DEGBE on the washed surfaces.

The person doing the washing task was exposed to average DEGBE concentrations in the breathing zone below 0.8 ppmv (<≈ 5.4 mg/m^3) in all experiments performed.
Supposing the use of DEGBE in hard surface cleaners for 1 hr once in 3 days, the yearly average exposure (based on the average DEGBE concentrations in the breathing zone) is 5.4·1/24·0.3 = 0.068 mg/m^3.

4.1.1.3 Indirect exposure via the environment

DEGBE may be released to the environment via effluents at sites where it is produced or used.
Actual release data for DEGBE production sites in Europe are presented in **Table 3.3**.
The highest calculated DEGBE concentration was 3.9·10^{-4} mg/m^3 at 100 m from the source.
Generic scenarios are used for estimating the releases from formulation, processing and private use of DEGBE. The scenarios are based on the two most important use categories of DEGBE, i.e.

detergent and paint. Paints are further subdivided in 1) coil coating and 2) other paints. An overview of the various environmental scenarios is given in **Table 3.4**.
The calculated total annual average local DEGBE concentrations in air for the different scenarios are presented in **Table 4.4**. The total human intake via air, drinking water and food for all emission scenarios at local scale are given in **Table 4.5**.

From the specific scenarios Detergent I, II & III and Paint I & II it can be calculated that the intake via drinking water is the major route followed by the intake via leaf crops and fish. For the scenarios paint III, IV,V and VI the intake via leaf crops is the major route followed by the intake via drinking water and fish.

On all scenarios for the regional scale air concentrations as well as the total human intake are given. These data are presented below in **Table 4.6**.

Table 4.4 Total annual average local concentration estimates in air.

Scenario	PEC local (mg/m^3)
Scenario detergent I - formulation	$4.5 \cdot 10^{-5}$
Scenario detergent II - processing	$1.7 \cdot 10^{-5}$
Scenario detergent III - private use	$1.3 \cdot 10^{-5}$
Scenario paints I (coil coating) - formulation	$1.4 \cdot 10^{-5}$
Scenario paints II (coil coating) - processing	$1.3 \cdot 10^{-5}$
Scenario paints III - formulation	$1.3 \cdot 10^{-3}$
Scenario paints IV - processing	0.04
Scenario paints V - processing	$9 \cdot 10^{-4}$
Scenario paints VI - private use	$1.8 \cdot 10^{-4}$

Table 4.5 Total daily intake via air, drinking water and food for all emission scenarios at local scale.

Scenario	total daily intake (mg/kg/day)
Scenario detergent I - formulation	1.98E-3
Scenario detergent II - processing	1.8E-3
Scenario detergent III - private use	2.6E-3
Scenario paints I (coil coating) - formulation	4.9E-3
Scenario paints II (coil coating) - processing	1.1E-3
Scenario paints III - formulation	0.0192
Scenario paints IV - processing	0.328
Scenario paints V - processing	8.2E-3
Scenario paints VI -private use	2.2E-3

Table 4.6 Regional scale air concentrations and total human intake for all emission scenarios.

Emission scenarios (generic production, detergent and paint)	Regional scale
PEC-air	$1.3 \cdot 10^{-5}$ mg/m^3
Total human intake	$6 \cdot 10^{-4}$ mg/kg day

4.1.1.4 Combined exposure

Although it is possible that humans are exposed to DEGBE 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, metabolism and excretion, *in vivo*

Absorption, metabolism and excretion were studied in rats dermally exposed to ^{14}C-DEGBE at dose levels of 200 (undiluted and 10% aqueous solution) and 2000 mg/kg bw/d (undiluted) for 24 hours under occlusion at a surface area of 4.3 cm^2 (Boatman *et al.* 1993). After 24 hours ^{14}C was determined in the patch and washing liquid (water). Urine, cage wash and faeces were collected during 7 days in 24 hour samples for ^{14}C determination. At the end of the study 14C was determined in the carcasses and the dermal exposure sites. Total recovery ranged from 81 to 89%. DEGBE was incompletely absorbed. In rats of the low dose group 33 and 30% of the applied dose was absorbed in males and 43 and 54% in females for the diluted and undiluted solutions, respectively. In the males of the high dose group 3.4% of the applied dose was absorbed and in the females 19%. In this dose group dermal absorption rates were 0.73 and 1.46 mg/cm^2/hr for males and females, respectively. In the other dose group the dermal absorption rates varied between 0.25 and 0.32 mg/cm^2/hr. Urinary excretion accounts for the majority of the recovered ^{14}C in both dose groups. In the low dose group urinary excretion was 31% and 27% of the applied dose in males, and 42 and 51% in females for the diluted and undiluted DEGBE, respectively. In the high dose group 3.3% of the applied dose was excreted in urine in males, and 18% in females. The majority was excreted within 24 hours after the start of the study. The major urinary metabolite was 2-(2-butoxyethoxy)acetic acid (61-80% of total urinary radioactivity). The glucuronic acid of DEGBE was present at levels ranging from 5.2 to 8.2% of the urinary ^{14}C.

Dermal absorption, *in vitro*

Absorption through the skin was investigated in two *in vitro* studies. The penetration rate of undiluted DEGBE through abdominal rat skin was 0.51 mg/cm^2/hr (receptor: saline) (Guest *et al.* 1986). The rate of absorption through human epidermis amounted to 0.035 ± 0.025 mg/cm^2/hr with a lag time of ca. 2 hours (undiluted DEGBE, receptor liquid: water) (Dugard *et al.* 1984).

In the draft review by ECETOC (Procter and Gamble 1985) it is mentioned that the *in vitro* penetration rates of DEGBE in cleaning products through human skin were 0.159, 0.065 and 0.0012 mg/cm^2/hr for 100%, 50% and 1.5% dilutions, respectively.

It should be mentioned that data from *in vitro* studies can only be used for comparison of dermal absorption within one test system. Results cannot be used as absolute values for risk assessment purposes.

Conclusion

From the dermal studies it is concluded that complete dermal absorption cannot be excluded. For risk characterisation 100% dermal absorption should be assumed (worst-case estimate). This is stressed by the skin irritating properties of DEGBE after repeated exposure (see chapter 4.1.2.6).

Data on oral and respiratory absorption are lacking, but the high level of dermal absorption might be indicative for a high level of absorption via these routes. Because there in insufficient insight in the factors influencing the extent of respiratory absorption, the default value as given in the TGD is used for risk assessment (i.e., 75%).

4.1.2.2 Acute toxicity

Animal studies
The studies by the oral and dermal route are summarised in **Table 4.7**.

Table 4.7 Summary of acute toxicity data.

Route	Species	LD50	Unity	Reference
Oral	Rat (fed)	9623	mg/kg bw	Eastman Kodak Co. 1984A
Oral	Rat (fasted)	7292	mg/kg bw	Eastman Kodak Co. 1984A
Oral	Mouse (fed)	5526	mg/kg bw	Eastman Kodak Co. 1984A
Oral	Mouse (fasted)	2406	mg/kg bw	Eastman Kodak Co. 1984A
Dermal	Rabbit	2764	mg/kg bw	Eastman Kodak Co. 1984B

It is concluded that DGBE has a low acute toxicity by oral and dermal routes. Signs of toxicity before death in orally treated mice and rats included inactivity, laboured breathing, rapid respiration, anorexia, weakness, tremors and prostration (Eastman Kodak Co. 1984). In dermally treated rabbits anorexia, enlargement of the kidneys, discoloration of the renal pelvis, and oedematous and haemorrhagic lesions in the thymus were observed (Eastman Kodak Co. 1984).
It is mentioned that the substance is “not toxic” by inhalation, possibly due in part to the low vapour concentration that could be generated (Patty 1994). No rats died when exposed for 7 hr to the maximum attainable vapour concentration of DEGBE, estimated to be 18 ppm (120 mg/m^3). However, it is noted that the data available did not allow a definite conclusion on the acute toxicity of DEGBE by inhalation.

Human data
There are no human data on acute toxicity.

Conclusion
The data submitted are acceptable with respect to the basic requirements as specified in Annex VIIA of Directive 67/548/EC. According to the EC criteria the substance needs not be classified on the basis of its acute toxicity.

4.1.2.3 Irritation

Animal studies
Skin
The results of a skin irritation study according EC guidelines indicate that the substance should not be classified as irritating to the skin (Southwood 1987). See also chapter 4.1.2.6 for local skin effects after repeated exposure.

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

Eyes
The eye irritation study in rabbits (Ballantyne 1984) does not fully meet the OECD-guidelines, but given the results this study is acceptable for evaluation of the eye irritating potential (scores are mentioned in the IUCLID Data Sheet added to the report). DEGBE should be classified as irritating to the eyes.

Human data
There are no human data on irritation.

Conclusion
The data submitted are acceptable with respect to the basic requirements as specified in Annex VIIA of Directive 67/548/EC. DEGBE should be classified as irritant to eyes, but not as irritant to the skin. For local effects after repeated exposure, see chapter 4.1.2.6. Classification and labelling as mentioned in Annex I (Xi, R36, S26) is correct.

4.1.2.4 Corrosivity

The substance is not corrosive to the skin, eyes or respiratory tract (see 4.1.2.3).

4.1.2.5 Sensitisation

Animal studies
Despite omissions in the report of Basketter (1985) (results of induction were not reported) the study can be used for evaluation of the skin sensitising potential of DEGBE, because results of a preliminary study indicated that proper dose levels were used. Based on these considerations and because no sensitising potential was observed in this study, it is concluded that DEGBE is not sensitising to skin.

Human data
There are no data on human sensitising potential of DEGBE.

Conclusion
The data submitted are acceptable with respect to the basic requirements as specified in Annex VIIA of Directive 67/548/EC. DEGBE should not be classified as sensitising to the skin.

4.1.2.6 Repeated dose toxicity

Animal data
Results of repeated dose toxicity studies are summarised in **Table 4.8**.

Table 4.8 Summary of repeated dose toxicity studies with DEGBE.

Study	NOAEL	LOAEL	Effects		Ref.
Inhalation toxicity					
Subacute, rat (5 wk, 6 hr/d, 5 d/wk; 0, 13, 39, 117 mg/m^3)	39 mg/m^3	117 mg/m^3	high conc	hepatocyte vacuolisation consistent with fatty change and increased relative liver weight in f; decreased relative liver weight in m	Gushow *et al.* 1984
Subacute, rat (2 wk, 6 hr/d, 5 d/wk; 100 and 350 mg/m^3 vapour, and 1000 mg/m^3 aerosol)	< 100 mg/m^3	100 mg/m^3	all conc mid and high conc	perivascular and peribronchial infiltrate; decreased spleen weight in males increased lung weight	BASF AG 1987
Subacute, female rat (2 wk, 6 hr/d, 5 d/wk; 350 mg/m^3)	< 350 mg/m^3	350 mg/m^3		decreased body weight gain; multifocal perivascular and peribronchial accumulation of granulocytes	BASF AG 1991
Semichronic, rat (90 d, 6 hr/d, 5 d/wk; 13, 40 and 94 mg/m^3)	≥ 94 mg/m^3		all conc	no treatment-related effects	BASF AG 1992
Oral toxicity					
Semichronic, rat (6 wk, males, gavage; 891, 1781, 3564 mg/kg bw/d)	< 891	891	mid and high doses low dose all doses	decrease in red blood cell count, Hb, MCH, increased spleen weights (absolute and relative), increase in liver weight, lesions in spleen and kidneys. increase in relative liver weight hyperkeratosis in stomach[C]	Eastman Kodak Co. 1984C
Semichronic, rat (90-d, 5 d/wk, males and females, gavage; 51-65, 254-327 and 1270-1630 mg/kg bw/d)	< 51-65 mg/kg bw/d	51-65 mg/kg bw/d	high dose mid and low doses	88% and 92 % mortality in m and f dose-related decrease in WBC and lymphocytes in f dose-related increase in creatinine in m	Hobson *et al.* 1987
Dermal toxicity[D]					
Subacute, rabbit (4 wk, 5 d/w, 7 hr/d, without occlusion; 30 mg/kg bw/d)	≥ 30 mg/kg[B]			no treatment-related effects	Elliott *et al.* 1982
Semichronic, rat (13 wk, 5 d/w, 6 hr/d, occlusion; 200, 600 and 2000 mg/kg bw/d); neurotoxicity study	2000 mg/kg bw/d[A]	> 2000 mg/kg bw/d[A]	all doses high dose	no systemic effects; no neurotoxic effects in FOB, no neuropathological changes scab formation at treatment site	Beyrouty *et al.* 1993
Semichronic, rat (13 wk, occlusion; 200, 600 and 2000 mg/kg bw/d)	2000 mg/kg bw/d[A]	> 2000 mg/kg bw/d[A]	all doses	no systemic effects at doses up to 2000 mg/kg. Erythema, concentration dependent in incidence, severity and time of onset. Slightly more severe in females.	Auletta *et al.* 1993

[A] NOAEL and LOAEL for systemic toxicity; the NOAEL and LOAEL for local effects are lower, see text and **Table 4.9**.

[B] Because of the study design this value is only indicative.

[C] not specified but in all likelihood fore-stomach is meant

[D] Systemic effects, see also **Table 4.9** for local effects

Inhalation studies
In a 5-week study in rats, exposed to 13, 39 and 117 mg/m^3 an increased hepatocyte vacuolisation consistent with fatty change was observed in females of the high dose group (Gushow *et al.* 1984). This effect was also observed in females of the control and other treatment groups, but it was less intense. In the high dose group 3/10 females had a pale liver. In the high dose group the relative liver weight was increased in females; in males of the mid and high dose groups the relative liver weight had a dose-related decreased. This effect was not accompanied by microsopic changes. The NOAEL is established at 39 mg/m^3.
In a 2-week range-finding study rats were exposed to 100 mg/m^3 DEGBE vapour and 350 and 1000 mg/m^3 of the aerosol (BASF AG 1987). Exposure to the vapour caused a reduction of spleen weight in males. Exposure to the aerosol caused a dose-related reduction in spleen weight not accompanied with effects on haematology and an increase in lung weight. Histopathological changes including perivascular and peribronchial accumulation of granulocytes as well as minimal bronchiolisation in the lungs were observed in all treatment groups. The NOAEL is established at < 100 mg/m^3.
Local lung effects (perivascular and peribronchial accumulation of granulocytes) and a decreased body weight gain were observed in a study with female rats exposed during 2 weeks, 6 hr/d, 5 d/week to 350 mg/m^3 (BASF AG 1991). After a recovery period of 4 weeks only minimal to slight granulocyte accumulation in the lungs was observed. Regression in severity was evident. The NOAEL is lower than 350 mg/m^3.
In a 90-day study rats were exposed (whole-body) to 0, 13, 40 and 94 mg/m^3 during 6 hr/d (BASF AG 1992). No treatment-related effects (including liver effects) were observed. The NOAEL is established at 94 mg/m^3.

Conclusion
Exposure at 100 mg/m^3 and above (aerosols) causes local lung effects. These effects were not observed in the 90-d study at vapour concentrations up to 94 mg/m^3.
It is noted that most of the studies were performed with whole body exposure and absorption by skin cannot be excluded.
Liver effects as observed in the 5-week inhalation study (13, 39 and 117 mg/m^3) at the high dose group were not observed in rats exposed to 94 mg/m^3 during 90 days. The liver might be considered as target organ after inhalation. For the risk assessment the NOAEL of 94 mg/m^3 (i.e., the highest attainable vapour concentration in this study) is used as starting point. However, the size of the margins of safety and assessment factors should be judged in the light of the liver effects at 117 mg/m^3 and the NOAEL of 39 mg/m^3 found in the subacute inhalation study.

Oral studies
A 6-week gavage study was performed in male rats given doses of 891, 1782 and 3564 mg/kg bw/d (Eastman Kodak Co. 1984C). The high dose level caused decreased food consumption, accompanied by decreased body weight gain. In the mid and high dose groups reduction of red blood cell count, haemoglobin level and mean cell haemoglobin were observed. Increases in spleen weights and histopathological changes in spleen (congestion) and kidneys (protenaceous casts) were found also in these groups. Absolute and relative liver weight were significantly increased at the two higher dose groups, but only relative liver weight was slightly but significantly) increased at the low dose group. No histopathological lesions in the liver were observed in the two highest dose groups; histopathology of the liver was not performed at the low dose group. Hyperkeratosis of the stomach (not specified but in all likelihood fore-stomach is meant) was observed in all rats treated with DEGBE.

Therefore, the NOAEL for systemic and local effects is established to be < 891 mg/kg bw/d. It is noted that the systemic effects at the LOAEL were limited to minor liver effects.
In a gavage study rats (16/sex/group) were given doses of 51-65, 254-327 and 1270-1630 mg/kg bw/d 5 d/wk for 13 weeks (Hobson *et al.* 1987). An interim sacrifice (6 rats/sex/group) was conducted at 6 weeks. Following interim sacrifice the low and mid dose group consisted of 10 rats/sex and the high dose group consisted of 4 males and 4 females due to the increased mortality in this dose group. At study termination mortality in the high dose group was 88% in males and 92% in females; only 2 male rats and 1 female rat survived 13 weeks. In the mid dose group the mortality was 60 and 30% for males and females, respectively. It cannot be excluded that the high mortality was caused by irritation of the fore-stomach (see 6-week study; this organ was not examined pathologically in the 13-week study). In females of the mid and low dose groups a dose-related decrease in white blood cell count (WBC) and lymphocytes was observed. It is noted that this was accompanied by an increased relative kidney weight in the two remaining males of the high dose group. The NOAEL is established at < 51 mg/kg bw/d. The effects observed in this study are not consistent with the toxicity profile of glycol ethers. Furthermore, there are doubts on the quality of the study, because of the high, unclarified mortality.

Conclusion
DEGBE caused effects in liver, spleen, kidneys, and haemotological parameters in oral studies. Given the inconsistency in effects between the studies, clear conclusions on the target organ of DEGBE after oral administration cannot be given. Both studies available have limitations: the 6-weeks study was performed with males only, and the 13-weeks study suffers from a high mortality rate at the highest dose level. The effects on WBC and lymphocytes as observed in the 13-weeks study in females of the low and mid dose group were not observed in the 6-weeks study with males at all dose levels (up to 3564 mg/kg bw/d). The effects observed in this study are not consistent with the toxicity profile of glycol ethers. Given the doubts on the quality of the 13-weeks study the NOAEL of < 891 mg/kg bw/d derived from the 6-weeks study is used as starting point for risk assessment. However for risk assessment it should be weighed that effects were observed in females in the 13-weeks study at dose levels of 51 and 254 mg/kg bw/d and that only males were tested in the 6-weeks study.

Dermal studies
Systemic effects observed in dermal repeated dose studies are summarised in **Table 4.8**. Local effects induced by repeated dosing as were observed in dermal repeated dose studies in rats and rabbits and in the dermal teratogenicity study in rabbits are summarised in **Table 4.9**.
In a 4-week dermal study in rabbits, exposed to a formulation of 1.5% DEGBE in water (30 mg/kg bw/d) no treatment-related local or systemic effects were observed (Elliott *et al.* 1982). The NOAEL for systemic and local effects was ≥ 30 mg/kg bw/d. However, a proper evaluation was not possible because of the poor study design, and, therefore, this level should only be considered as indicative. Severe dermal reactions were observed in rabbits exposed to 1.5% DEGBE in a hard surface cleaner formulation using the same dose schedule. These effects are most probably caused by the formulation, because of the similarity in effects observed in rabbits receiving the hard surface cleaner without DEGBE.
In a 13-week dermal study in rats, exposed to 200, 600 and 2000 mg/kg bw/d, 5 d/week, 6 hr/d no mortality and no effects on body weight, organ weights, pathology and clinical chemistry were observed at all dose levels (Auletta *et al.* 1993). DEGBE caused erythema in all treatment groups at the application site. Incidence, severity and time of onset of the effects were concentration

Table 4.9 Summary of local effects observed after repeated dosing.

Study	Dose levels, duration	Vehicle	Occlusion	Surface area	NOAEL local effects (mg/kg/d)	NOAEL local effects (mg/cm²)[A]
Repeated dose study, rabbit (Elliott *et al.* 1982)	30 mg/kg bw/d; 28 d, 7 hr/d, 5 d/wk	water	-	10% body surface	≥ 30[B]	≥ 0.54[B]
Teratogenicity study, rabbit (Nolen *et al.* 1985)	100, 300, 1000 mg/kg bw/d; 12 d, 4 hr/d	water	-	200 cm²	100	1.5
Repeated dose study, rat (Auletta *et al.* 1993)	200, 600, 2000 mg/kg bw/d; 13 wk, 6 hr/d, 5 d/wk	water	+	9 cm²	< 200	< 5.5
Repeated dose study (neuro), rat (Beyrouty *et al.* 1993)	200, 600, 2000 mg/kg bw/d; 13 wk, 6 hr/d, 5 d/wk	water	+	10% body surface	600[C]	7.5[C]

[A] Calculated with body weight rabbit 3000 g, body weight rat 250 g, body surface rabbit 1680 cm², body surface rat 200 cm²
[B] Because of the study design this value is only indicative.
[C] According to the author. However, given the concise description of the skin effects a NOAEL for local effects cannot be established.

dependent. In the high dose group (undiluted DEGBE, 55 mg/cm²) erythema was observed in 4/10, 7/10, 9/10 and 9/10 female rats after 1, 4, 8 and 13 weeks, respectively. Necrosis and eschar formation were seen in 1/10, 5/10, 1/10 and 4/10 females after 1, 4, 8 and 13 weeks, respectively. In females of the low (5.5 mg/cm²) and mid (16.5 mg/cm²) dose group irritation started after about 5 and 3 weeks, respectively. In males the effects were less severe and started later. The NOAELs for local skin and systemic effects are established at < 200 mg/kg bw/d and at ≥ 2000 mg/kg bw/d, respectively.
In a study in rats, using the same dose schedule no neurotoxic effects (functional observation battery and neuropathology) were observed (Beyrouty *et al.* 1993). In this study local effects were only observed at the highest dose level tested (25 mg/cm²). Because of the brief description of the dermal effects and since no data on the onset of effects were given, these results cannot be used for the establishment of a NOAEL for local effects.
In the dermal teratogenicity study in rabbits skin effects were observed about one week after the start of the application (Nolen *et al.* 1985). No irritation was seen at 1.5 mg/cm². Slight erythema and desquamation were observed at 4.5 mg/cm² and all rabbits treated with 15 mg/cm² showed moderate skin irritation with oedema.

Conclusion
The study from Auletta *et al.* (1993) is considered most suitable for deriving a dermal NOAEL. Dose levels up to 2000 mg/kg bw/d caused no systemic effects in rats. This level can be used for risk characterisation.
As to local effects, it is noted that the NOAELs as derived from the dermal repeated dose studies are within a same range. Given the differences in exposure circumstances and onset of symptoms it is not desirable to set an overall NOAEL for local skin effects to be used in risk characterisation.

The results of the study with the best fit concerning exposure circumstances (duration of exposure, vehicle, occlusion, and concentration per unit skin surface) should be used for this purpose.

Human data
There are no human data on repeated toxicity.

Conclusion repeated dose studies
The data submitted are acceptable with respect to the basic requirements as specified in Annex VIIA of Directive 67/548/EC. DEGBE needs not be classified on basis of the results of the repeated dose studies.
It is noted that the toxic potential of DEGBE after oral administration (NOAEL < 891 mg/kg bw/d; for systemic effects the NOAEL is 891 mg/kg bw/d) is higher than after dermal administration. This might be explained by a lower absorption after dermal than after oral administration, but there are not enough data to exclude differences in metabolism or toxicodynamics. No clear conclusions can be drawn on possible differences in toxic potential after inhalation and oral administration (respiratory NOAEL ≥ 94 mg/m^3, i.e. ≥ 27 mg/kg bw/d; oral NOAEL < 891 mg/kg bw/d).

4.1.2.7 Mutagenicity

The mutagenic potential of DEGBE was investigated by Thompson *et al.* (1984) in several assays. DEGBE does not induce reverse mutations in Salmonella typhimurium TA98, TA100, TA1537 and TA1538, with and without metabolic activation, nor chromosomal aberrations in Chinese hamster ovary cells *in vitro*. DEGBE was negative in the UDS test with primary cultures of rat hepatocytes without metabolic activation. The substance was negative in the *in vitro* mouse lymphoma assay in the presence of metabolic activation, and a weakly positive response was observed without metabolic activation (at toxic dose levels). It does not induce sex-linked recessive lethality in Drosophila.
DEGBE does not induce forward mutations at the HGPRT locus in Chinese hamster ovary cells with and without metabolic activation (Dow Chemical Study 1987A; Gollapudi *et al.* 1993)
DEGBE does not induce micronuclei in bone marrow of mice, after administration of a single oral dose of 330, 1100 or 3300 mg/kg (Gollapudi *et al.* 1993).

Conclusion
The data submitted are acceptable to establish the mutagenic potential of DEGBE and are in accordance with respect to the basic requirements as specified in Annex VIIA of Directive 67/548/EC.
It is concluded that DEGBE 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 reproduction studies and studies on developmental toxicity are summarised in **Table 4.10**.

Table 4.10 Summary of reproduction toxicity studies with DEGBE.

Study	NOAEL (mg/kg bw/d)	LOAEL (mg/kg bw/d)	Effects		Ref.
Oral toxicity					
One-generation repro-study, rat (gavage, 250, 500, 1000 mg/kg bw/d)	parental/ reproduction: 1000 offspring: 500	parental/ reproduction: > 1000 offspring: 1000	high dose	decreased body weight gain of pups during later stages of lactation	Nolen *et al.* 1985
Developmental, rat (feed, 25, 115, 633 mg/kg bw/d, days 0-20 of gestation)	maternal: not established developmental: not established[1]	maternal: not established developmental: not established[1]	high dose	not statistically significant decrease in numbers of implantations[1]	Ema *et al.* 1988
Developmental, mouse (gavage, 500 and 2050 mg/kg bw/d, days 6-13 of gestation)	maternal: not established developmental: not established	developmental: not established maternal: not established	high dose	maternal death (25%)	Hardin *et al.* 1987
Dermal toxicity					
One generation repro-study, rat (2000 mg/kg bw/d, males and females 13-weeks premating; females days 0-20 of gestation, 6 hr/d, 5 d/w, occlusion)	Parental, reproduction and offspring: 2000	Parental, reproduction and offspring: > 2000		no treatment-related effects	Auletta *et al.* 1993
Developmental, rat (s.c.119, 239, 478 and 716 mg/kg bw/d, days 6-15 of gestation)	maternal: 239 developmental: 478	maternal: 478 developmental: 716	two highest	reduced maternal body weight gain, skin effects	Wilson 1983
			highest	developmental effects	
Developmental, rabbit (dermal, 100, 300 and 1000 mg/kg bw/d, 4 hr/d, occlusion, days 8-19 of gestation)	maternal: 1000 developmental: 1000	maternal: > 1000 developmental: > 1000	mid and high	maternal: skin irritation	Nolen *et al.* 1985

[1] The results of this study should be combined with the result of the study of Nolen *et al.* (1985) (see text).

Oral reproduction study

A one-generation reproduction study was performed in rats given doses of 0, 250, 500 and 1000 mg/kg bw/d by gavage (Nolen *et al.* 1985). Untreated males were mated with treated females and vice versa. No signs of parental toxicity or effects on fertility were observed. It is noted that the differences between the NOAELs for parental toxicity in this study and the NOAELs from the oral repeated dose toxicity studies (see chapter 4.1.2.6) might be explained by the only small number of effect parameters which are studied in reproduction toxicity studies. Reduced body weight gain of the pups from the high-dose females was the only treatment-related effect. The number of live-born pups was slight, but not statistically significantly decreased at 1000 mg/kg bw/d. The NOAEL for developmental effects was established at 500 mg/kg bw/d and for parental toxicity and fertility at 1000 mg/kg bw/d.

Dermal reproduction study
In a one-generation reproduction study male and female rats were dosed with 0 and 2000 mg/kg bw/d (occlusion, 10 cm^2) during 13 weeks premating and females were treated through d 20 of gestation (Auletta *et al.* 1993). Male and female mating indices, pregnancy rates, male fertility indices, parturation data, pup body weights, pup survival and viability were not adversely affected before, during or after pregnancy.

Oral developmental studies
In an oral developmental toxicity study mice were dosed by gavage with 0, 500 and 2050 mg/kg bw/d (Hardin *et al.* 1987). Maternal mortality was 25% at the high dose level. There are no indications for other adverse maternal effects, and there are no indications for embryo/foetotoxicity from the parameters studied (litter size, birth weight and neonatal growth). It is noted that the differences between the NOAELs for parental toxicity in this study and the NOAELs from the oral repeated dose toxicity studies (see chapter 4.1.2.6) might be explained by the only small number of effect parameters which are studied in reproduction toxicity studies. However, because no search for malformations or skeletal anomalies was performed, setting a NOAEL for teratogenicity is considered unjustifiable.

In an oral developmental study rats were given 0, 25, 115 and 633 mg/kg bw/d during day 0-20 of gestation (Ema *et al.* 1988). It should be mentioned that the number of animals per dose group was too low (14-16). However, in view of the results observed the study can be used for evaluation. According to the authors reduction in body weight gain as observed at all dose levels was the only sign of maternal toxicity and no effects on developmental toxicity or teratogenic effects were observed. However, the maternal body weight gain was not dose-related reduced and the scatter in the values was high. The statistically insignificant decreases in numbers of implantations (10.4±1.1, 10.7±1.4, 9.4±0.5, 8.8±1.3) and new-borns (9.6±1.5, 10.3±1.6, 8.6±0.9, 8.2±0.8) per litter may be substance-related effects and cannot be ignored, because the effects on the number of live-born pups observed in the one-generation study of Nolen *et al.* (1985) at 1000 mg/kg bw/d. It is not likely that DEGBE causes irreversible structural changes. Based on this study and the study of Nolen *et al.* (1985), it is concluded that the NOAEL for developmental effects is 500 mg/kg bw/d. The marginal effects at 115 mg/kg bw/d are considered not to be toxicologically significant.

Dermal developmental studies
In a dermal developmental toxicity study in rats dosed s.c. with 119, 239, 478 and 716 mg/kg bw/d the NOAEL for embryo/foetotoxicity was 478 mg/kg bw/d (decrease in mean foetal weight and mean placental weight, reduced ossification) and the NOAEL for maternal toxicity was 239 mg/kg bw/d (reduced body weight gain at 478 and 716 mg/kg bw/d, and transient haemoglobinuria at the highest dose level) (Wilson 1983). The developmental effects were considered to be attributable to maternal toxicity.
In a dermal developmental study rabbits were dosed with DEGBE at 0, 100, 300 and 1000 mg/kg bw/d, 4 hr/d at 200 cm^2 without occlusion from day 8 to 19 of gestation (Nolen *et al.* 1985). Maternal body weight gain was slightly reduced at the two higher dose levels (not statistically significant). These dose levels caused skin irritation after about one week, which persisted until the end of the study. There were no indications for developmental or teratogenic effects at any of the dose levels tested. The NOAELs for systemic maternal toxicity and for developmental effects are 1000 mg/kg bw/d.

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

Conclusion reproduction toxicity
The data submitted are acceptable with respect to the basic requirements as specified in Annex VIIA of Directive 67/548/EC.
In a one-generation gavage study with rats the NOAEL for fertility was 1000 mg/kg bw/d (highest dose level tested).
As for developmental effects the oral NOAEL was established at 500 mg/kg bw/d. The only effect observed at the next higher dose level tested was reduced body weight gain of the pups. DEGBE caused no teratogenic effects after oral administration.
No effects were observed in a dermal one-generation study at doses up to 2000 mg/kg bw/d.
Neither systemic maternal toxicity nor developmental or teratogenic effects were observed in rabbits dermally exposed to dose levels up to 1000 mg/kg bw/d. The developmental effects observed in the subcutaneous study with rats were considered to be attributable to maternal toxicity. Because of these results and in view of the high dose levels tested in the dermal teratogenicity study with rabbits it is not deemed necessary to perform a dermal teratogenicity study in another animal species.

4.1.3 Risk characterisation

4.1.3.0 General aspects

The human population may be exposed to DEGBE 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).

There are no human data on toxicity of DEGBE.

From the dermal absorption studies it is concluded that complete dermal absorption cannot be excluded. For risk characterisation 100% dermal absorption should be assumed (worst-case estimate). This is stressed by the skin irritating properties of DEGBE after repeated exposure. Data on oral and respiratory absorption are lacking, but the high level of dermal absorption might be indicative for a high level via these routes. Because there is insufficient insight in the factors influencing the extent of oral respiratory absorption, the default value as given in the TGD is used for risk assessment (i.e., 75%).

DEGBE needs not to be classified on the basis of its acute oral and dermal toxicity. The substance is classified as irritating to the eyes, but not as irritant to the skin. However, repeated dermal exposure to DEGBE caused local skin effects. Classification as sensitising agent is not indicated.

With respect to repeated dose toxicity the NOAEL of 94 mg/m^3 (duration corrected value 17 mg/m^3) as concluded from a 90-day toxicity study in rats is used as starting point for risk characterisation. However, the size of the margins of safety and assessment factors should be judged in the light of the liver effects at 117 mg/m^3 and the NOAEL of 39 mg/m^3 found in the subacute inhalation study.
DEGBE caused effects in liver, spleen, kidneys, and on haematological parameters after oral administration. Both oral toxicity studies available have limitations. The oral NOAEL is

established at < 891 mg/kg bw/d (6-weeks study). For risk assessment it should be weighed that effects were observed in females in the 13-weeks study at dose levels of 51 and 254 mg/kg bw/d and that only males were tested in the 6-weeks study.
In dermal studies dose levels up to 2000 mg/kg bw/d caused no systemic effects in rats (13-weeks study). As for local effects, it is noted that the NOAELs as derived from the dermal repeated dose studies are within a same range. Given the differences in exposure circumstances and onset of symptoms it is not desirable to set an overall NOAEL for local skin effects to be used in risk characterisation. The results of the study with the best fit concerning exposure circumstances (duration of exposure, vehicle, occlusion, and concentration per unit skin surface) should be used for this purpose.

DEGBE is considered to be not genotoxic. Data on carcinogenicity are not available.

In a one-generation gavage reproduction study with rats the NOAEL for fertility was 1000 mg/kg bw/d (highest dose level tested). As for developmental effects the oral NOAEL was established at 500 mg/kg bw/d. The only effect observed at the next higher dose level tested was reduced body weight gain of the pups. DEGBE caused no teratogenic effects after oral administration.
No effects were observed in a dermal one-generation study at doses up to 2000 mg/kg bw/d. Neither systemic maternal toxicity nor developmental or teratogenic effects were observed in rabbits dermally exposed to dose levels up to 1000 mg/kg bw/d.

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 low toxicity observed in the acute inhalation and dermal studies and the anticipated occupational exposure levels it is concluded that DEGBE is of no concern for workers with regard to acute effects (**conclusion ii**).

Irritation
Acute dermal irritation
Given the effects observed in the skin irritation studies with rabbits it is concluded that DEGBE is of no concern for workers with regard to acute skin irritation (**conclusion ii**).

Dermal irritation after repeated dose
Repeated dermal exposure may induce local skin effects. Starting-points for the risk characterisation after repeated dermal exposure with respect to these effects are (a) the results from the repeated dermal studies (see **Table 4.9**) and the (b) the dermal occupational exposure estimates (see chapter 4.1.1.1. and **Table 4.3**). The estimated exposure levels in mg/cm^2/d amounts to approx. 0.05, 0.1, 0.1, and 1.5 mg/cm^2 for scenario 1, 2, 3, and 4, respectively. In the scenario 1, 2, and 4 the duration of exposure is estimated to be 6-8 hr/d and the frequency 100-200 d/year. In scenario 3 the duration of exposure is estimated to be up to 2 hours per day. Given the estimated frequency of exposure (100-200 d/year) chronic exposure is assumed for risk characterisation. These levels are compared with the results from the study of Auletta *et al.* (1993) in which rats were exposed for 13 weeks, 6 hr/d, 5 d/w and in which the lowest dose (5.5 mg/cm^2) caused local skin effects after

5 weeks and the mid-dose (16.5 mg/cm^2) after 3 weeks. The MOSs between the LOAEL and the dermal exposure levels are listed in **Table 4.11**. The MOSs are evaluated by comparison with the minimal MOS (40). 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 4.11**.
Based on the risk assessment for dermal exposure as mentioned in **Table 4.11** it is concluded that health risks for local effects due to repeated dermal exposure are not expected for scenario 1, 2, and 3. For scenario 4 it is concluded that risk reduction measures are indicated (**conclusion iii**).
It is noted that this risk assessment relies on conservative estimates of dermal exposure and the use of PPE is not taken into account. It might be possible that in some industrial premises worker protection measures are already applied.

Table 4.11 Risk assessment for DEGBE for local skin effects after repeated occupational dermal exposure.

Scenario/subscenario	Risk assessment for dermal exposure		
	Estimated dermal exposure (mg/cm^2)	MOS[A]	Conclusion[B]
1: Production of DEGBE	0.05	110	ii
2: Production of products containing DEGBE	0.1	55	ii
3: Automated application of products containing DEGBE	0.1	55	ii
4: Manual application of product containing DEGBE	1.5	4	iii

[A] based on a LOAEL of 5.5 mg/cm^2;

[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 A1.1**) and Annex 2.

Eye irritation
Exposure to the eyes is possible via vapours or accidentally by splashing. Given the effects observed in the acute eye irritation study in rabbits it is concluded that goggles should be worn when the pure substance is handled. It is not clear whether this is recommended by all the companies in their MSDS's. Therefore, **conclusion iii** is applicable.
Because no effects on eyes were reported in repeated dose studies with whole body exposure and because of the low volatility of DEGBE it is concluded that the substance is of no concern for workers with regard to eye irritation by vapours (**conclusion ii**).

Respiratory irritation
At dose levels above 100 mg/m^3 (aerosols) local lung effects cannot be excluded. Because of the estimated dose levels in scenario 4 (spray application) **conclusion iii** is reached for this application.

Corrosivity
Given the results from the skin and eye irritation studies it is concluded that DEGBE is of no concern for workers with regard to corrosivity (**conclusion ii**).

Sensitisation

Given the results from the dermal sensitisation study with guinea pigs it is concluded that DEGBE 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

The dermal 13-week study reveals that prolonged exposure at high dose levels (up to 2000 mg/kg bw/d) does not give rise to systemic effects, while local effects were observed at all dose levels tested. Nevertheless, the risk for systemic effects after repeated skin contact is estimated below. Risk characterisation for local skin effects after repeated exposure to DEGME is described in the paragraph "irritation".

Starting-points for the risk characterisation for workers exposed by skin contact for systemic effects are (a) the NOAEL of 2000 mg/day (highest dose level tested) from the semichronic dermal study with rats, and (b) the estimated inhalation exposure levels for the different occupational scenarios (see chapter 4.1.1.1 and **Table 4.3**). Given the estimated frequency of exposure (100-200 d/year) chronic exposure is assumed for risk characterisation. The MOSs between the NOAEL and the dermal exposure levels are listed in **Table 4.12**. The MOSs are evaluated by comparison with the minimal MOS (54). In Annex 1 the assessment factors used to establish the minimal 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**.

Table 4.12 Occupational risk assessment of DEGBE for repeated dose toxicity (systemic effects).

Scenario/subscenario	Risk assessment for dermal exposure			Risk assessment for inhalation exposure		
	Estimated dermal exposure (mg/day)	MOS[A]	Conclusion[B]	Estimated inhalation exposure (mg/m^3)	MOS[C]	Conclusion[D]
1: production of DEGBE	210	667	ii	0.6	157	ii
2: production of products containing DEGBE	42	3333	ii	2.5	38	ii
3: automated application of products containing DEGBE	42	3333	ii	3.4	28	ii
4: manual application of products containing DEGBE	1950	72	ii	10	9	iii

A calculation based on the NOAEL of 2000 mg/kg bw/d assuming a worker body weight 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 A1.2**) and Annex 2;

C calculation based on the NOAEL of 94 mg/m^3;

D 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.

Based on the risk assessment for dermal exposure as mentioned in **Table 4.12** it is concluded that systemic effects due to repeated dermal exposure are not expected. **Conclusion ii** is reached for all occupational scenarios.

Inhalation exposure
Starting-points for the risk characterisation for workers exposed by inhalation are (a) the NOAEL of 94 mg/m^3 from the semichronic inhalation study with rats, and (b) the estimated inhalation exposure levels for the different occupational scenarios (see chapter 4.1.1.1 and **Table 4.3**). Given the estimated frequency of exposure (100-200 d/year) chronic exposure is assumed for risk characterisation. The MOSs between the NOAEL and the inhalation exposure levels are mentioned in **Table 4.12**. The MOSs are evaluated by comparison with the minimal MOS (36). In Annex 1 the assessment factors used 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 the **Table 4.12**.

Given the risk assessment for inhalation exposure as mentioned in **Table 4.12** it is concluded that, based upon the present information, health risks due to occupational inhalation exposure cannot be excluded for scenario 4. **Conclusion iii** is considered to be applicable for scenario 4.

Combined exposure
With reference to the hazard assessment, there are indications that the toxic potential of DEGBE after oral administration is higher than after dermal exposure, and no clear conclusions on possible differences on the toxic potential after inhalation and oral administration can be drawn. 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 conclusions for scenario 1, 2, and 3 drawn for the dermal and inhalation routes separately, it is assumed that internal exposure of the worker as result from uptake via both routes in these scenarios will not give rise to adverse systemic health effects. A risk was estimated for scenario 4 after inhalation exposure. It cannot be excluded that dermal exposure in this scenario will additionally contribute to that risk.

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

Carcinogenicity
There are no carcinogenicity studies available.
Given the results from the mutagenicity studies and the repeated dose studies with DEGBE it is concluded that there are no clear reasons for concern for workers with regard to carcinogenicity (**conclusion ii**).

Reproductive toxicity
Dermal exposure
Starting-points for the risk assessment with regard to reproductive toxicity for workers exposed by skin contact are the NOAELs from the dermal developmental toxicity study with rabbits (1000 mg/kg bw/d) and from the reproduction study with rats (2000 mg/kg bw/d). Both levels mentioned were the highest dose levels tested and neither reproduction effects nor effects on offspring were

observed. The NOAEL from the developmental subcutaneous study is not used, because the route of administration is not representative for occupational exposure.

From these studies it is concluded that DEGBE is of no concern with respect to these effects after dermal exposure when other systemic effects are avoided (**conclusion ii**).

Inhalation exposure
There are no reproduction toxicity studies by inhalation available. DEGBE caused neither effects on fertility nor developmental effects in dermal studies. As for oral developmental effects a NOAEL of 500 mg/kg bw/d was observed in rats. Fertility effects were not observed after oral administration. DEGBE is not teratogenic. Because it is unclear whether inhalation exposure resembles oral or dermal administration the NOAEL for developmental effects (500 mg/kg bw/d) from the oral studies is used for (worst case) risk characterisation.

The MOS between the NOAEL and the estimated inhalation occupational exposure levels (see section 4.1.1.1 and **Table 4.3**) are mentioned in **Table 4.13**. The MOSs are evaluated by comparison with the minimal MOS (72). In Annex 1 the assessment factors applicable to establish the minimal MOS are given (**Table A1.4**). There is concern when the MOS is lower than the minimal MOS. The conclusions are given in **Table 4.14**.

Based on the risk assessment for inhalation exposure as mentioned in **Table 4.13** it is concluded that developmental effects due to occupational inhalation exposure are not likely to occur. **Conclusion ii** is considered to be applicable.

Table 4.13 Risk assessment of DEGBE for reproduction toxicity after occupational inhalation exposure.

	Risk assessment for long-term inhalation exposure/reproduction toxicity		
Scenario/subscenario	**Estimated inhalation exposure (mg/m^3) worst case**	**MOS[A]**	**Conclusion[B]**
1: production of DEGBE	0.6	5833	ii
2: production of products containing DEGBE	2.5	1400	ii
3: automated application of products containing DEGBE	3.4	1029	ii
4: spray application of products containing DEGBE	10	350	ii

[A] calculation based on a respiratory volume of 10 m^3/workday, a worker body weight of 70 kg, and an oral NOAEL of 500 mg/kg bw/d;
[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 A1.4**) and Annex 2.

4.1.3.2 Consumers

Like for workers (see chapter 4.1.3.1) it is possible that consumers may use spray applications of DEGBE in paint. At dose levels above 100 mg/m^3 (aerosols) local lung effects cannot be excluded. Therefore based on the outcome of the workers exposure assessment (worst case) **conclusion iii** is reached for this possible consumer application.

Scenario I: Latex paint
For the use of DEGBE in latex paint an inhalatory exposure estimate per event was calculated of 3.97 mg/m^3 in an acute scenario ("Dutch"). In paragraph 4.1.2.2. it is mentioned that the 7hr LC_0 in rats is 120 mg/m^3 (maximum attainable vapour concentration) indicating that DEGBE is not toxic via the inhalatory route. Given this low toxicity and the anticipated consumer exposure level it is concluded that there is no concern for consumers with regard to inhalatory acute effects (**conclusion ii**). It is noted that eye exposure (possible via vapours) given the effects observed in the acute eye irritation study in rabbits may result in irritation. However because no effects were reported in repeated dose studies with whole body exposure and because of the low volatility of DEGBE it is concluded that the substance is of no concern for consumers with regard to irritation by vapours (**conclusion ii**). The margin of safety between the dermal LD_{50} of ≥ 2500 mg/kg bw./day (it is noted that DEGBE passes the human skin very quickly) and the single event exposure of 7.14 mg/kg b.w./day. has been calculated to be 350. This margin of safety is considered sufficient to avoid acute effects. Given the effects observed in the skin irritation study with rabbits it is concluded that DEGBE is of no concern. It is noted that dermal irritation occurs only after repeated exposure to DEGBE (liquid) (**conclusion ii**).

Scenario II: Liquid hard surface cleaners
For the use of DEGBE in hard surface cleaners an inhalatory exposure as well as risk assessment was carried out (Gingell *et al.* 1993). When comparing the yearly average inhalatory exposure to DEGBE in hard surface cleaners of 0.068 mg/m^3 with the inhalatory NOAEL of 94 mg/m^3 in the 90d rat study the margin of safety is calculated to be 1382. Taking into account intra- and inter species variation, the use of a NOAEL from a sub-chronic study and the fact that in a semichronic study (NOAEL 39 mg/m^3) liver effects were observed at 117 mg/m^3 this margin of safety is considered to be sufficient (**conclusion ii**).

4.1.3.3 Man exposed indirectly via the environment

Inhalation exposure
Repeated dose toxicity
For the risk characterisation after repeated exposure all exposure estimates for air (see **Table 4.4** are compared with the observed NOAEL of 94 mg/m^3 (17 mg/m^3 corrected for continuous exposure) from the 90-day rat study.

When comparing the local concentration estimates in air with the observed NOAEL from the 90-day rat inhalation study (94 mg/m^3 = 17 mg/m^3 corrected for continuous exposure (DCV)) the lowest the margin of safety is calculated for scenario IV and is 460, all other margins of safety are > 1000. These margins of safety are considered sufficient taken into account 1) the intra- and inter-species variation, 2) the use of a NOAEL (17 mg/m^3) for continuous exposure instead of using the uncorrected NOAEL (94 mg/m^3) and 3) the assumption that car, can and general industrial painting are taken place at the same location is most probably over-conservative (**conclusion ii**).

When comparing the regional scale air concentration 1.3 · E-5 (see **Table 4.6**) with the NOAEL (duration corrected value) of 17 mg/m^3 a margin of safety of 4.1 · E+5 is calculated indicating no concern for human safety indirectly exposed via the environment (**conclusion ii**).

Table 4.14 Margins of safety between the NOAEL from the 90-day rat inhalation study (DCV) and the estimated annual average concentrations in air.

Scenario	Margin of safety
Scenario detergent I - formulation	3.79E+4
Scenario detergent II - processing	9.83E+5
Scenario detergent III - private use	1.26E+6
Scenario paints I (coil coating) - formulation	1.26E+6
Scenario paints II (coil coating) - processing	1.27E+6
Scenario paints III - formulation	1.33E+4
Scenario paints IV - processing	460
Scenario paints V - processing	1.96E+4
Scenario paints VI - private use	9.3E+4

Given the margin of safety between the estimated indoor concentration of DEGBE of 1-20 µg/m^3 and the NOAEL of 17 mg/m^3 (corrected value for continuous exposure) no concern for the public at large is expected (**conclusion ii**).

Reproductive toxicity

There are no reproduction toxicity studies by inhalation available. Because it is unclear whether inhalation exposure resembles oral or dermal administration the NOAEL for developmental effects (500 mg/kg b.w.) from the oral studies is used for (worst-case) risk characterisation. By route-to-route extrapolation (assuming 100% and 75% absorption via the oral and inhalatory route, respectively and 300 mg as rat b.w. with a respiratory rate of 240 ml/min) the oral NOAEL of 500 mg/kg b.w. is equivalent to an inhalatory continuous exposure of 570 mg/m^3 (it is noted that ≈120 mg/m^3 is the maximum attainable vapour concentration).

The calculated margins of safety for all local scenarios are ranging from 1360 - 5E+5. These margins of safety are considered sufficient taken into account intra- and inter-species variation, the use of a NOAEL of 500 mg/kg b.w. in an oral developmental study (equivalent to inhalatory exposure 570 mg/m^3 [taken into account the above given assumptions] (**conclusion ii**).

Intake via drinking water and via all media

Starting point for the risk assessment after repeated exposure is the oral NOAEL of < 891 mg/kg b.w./day from a 6-weeks rat study. At this dose level only minor liver effects were observed and local effects (hyperkeratosis of the stomach) were seen.

The oral NOAEL (500 mg/kg b.w.) from the oral developmental study in rats is used for the risk assessment regarding reproductive effects (at the highest dose: 1000 mg/kg b.w. only a reduced body weight gain of the pups was observed). Fertility effects were not observed after oral administration. DEGBE caused no teratogenic effects after oral administration.
The public at large may be exposed to DEGBE via drinking water since in the USA drinking water supplies have been shown to contain DEGBE (concentrations not given) (Cited in HSDB (through jan 1994)). In the Netherlands DEGBE is identified in the river Meuse but not further quantified, drinking water analysis have not been performed (Van Genderen *et al.* 1994). For the rest of Europe no data of DEGBE occurrence in drinking water are available. A separate risk characterisation has not been carried out since no measured data could be found for DEGBE in drinking water.

For the local scale the margin of safety between the oral NOAEL of < 891 mg/kg b.w./d and the total intake via air, drinking water and food for all scenarios is given in **Table 4.15**.

Table 4.1.5 Margins of safety (MOS) between the oral NOAEL of < 891 mg/kg b.w./d and the estimated total daily intake at the local site.

Scenario	Margin of safety
Scenario detergent I - formulation	4.49E+5
Scenario detergent II - processing	5.05E+5
Scenario detergent III - private use	3.47E+5
Scenario paints I (coil coating) - formulation	1.83E+5
Scenario paints II (coil coating) - processing	8.2E+5
Scenario paints III - formulation	4.63E+4
Scenario paints IV - processing	2.72E+3
Scenario paints V - processing	1.08E+5
Scenario paints VI - private use	4.08E+5

The calculated margins of safety for all local scenarios (as presented in **Table 4.15**) are ranging from 2.72E+3 - 8.2E+5. These margins of safety are considered sufficient taken into account intra- and inter-species variation, the use of a LOAEL in a 6 week study with male rats only (at this dose level no systemic effects occurred but only local effects were observed) and the fact that effects observed in females in the limited 13-weeks study at dose levels of 51 and 254 mg/kg b.w./d (i.e. on

WBC and lymphocytes) were not observed in the 6-weeks study up to 3564 mg/kg bw/d. (**conclusion ii**).

For the regional scale the margin of safety for all emissions scenarios (production, detergent and paint) on the regional scale is 1.48E+5, indicating no concern for human safety after indirect exposure (**conclusion ii**).

Reproductive toxicity
The margins of safety for all scenarios (local and regional) are >> 1000. From these margin of safety it is concluded that DEGBE is of no concern with respect to reproductive effects after oral administration, taken into account intra- and inter-species variations and the use of the NOAEL of 500 mg/kg b.w. for developmental effects (**conclusion ii**).

4.1.3.4 Combined exposure

A risk assessment for humans after combined exposure has not been carried out at this stage of the assessment.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

Flammability, explosive properties and oxidising properties are not considered to form a 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 (e.g. 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:
- health risks for the consumer are expected to occur due to the use of DEGBE in paint spraying applications.

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:
- eye exposure due to incidental splashing should be avoided when the pure substance is handled
- local effects on skin cannot be excluded in occupational scenario 4 after repeated dermal exposure.
- based upon the present information with regard to anticipated effects after repeated inhalation exposure in workers reduction measures should be taken for occupational exposure scenario 4 (manual application of products containing DEGBE).

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

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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.

Aspect	Assessment factors
Interspecies differences[1]	2
Intraspecies differences[2]	2
Differences between experimental conditions and exposure pattern of the worker[3]	2
Type of critical effect	1
Dose-response curve[4]	5
Confidence of the database	1
Minimal MOS	40

Table A1.1 Assessment factors applied for the calculation of minimal MOS for local dermal effects after chronic dermal exposure based on a 13-week dermal toxicity study in rats.

[1] Adjustment via caloric demands is not applicable in case of local effects. An uncertainty factor 2 is considered applicable for local effects for remaining interspecies differences.

[2] A factor 2 is considered applicable for intraspecies differences in case of local effects.

[3] In case of systemic effects the default value for extrapolation from semichronic to chronic exposure amounts 10. In case of local effects a smaller factor is indicated, because it is assumed that the severity of effects will increase with longer exposure times, but the height of the NOAEL will decrease to a lower extent than in the case of systemic effects. A factor 2 is considered applicable.

[4] A factor 5 is considered applicable for extrapolation form LOAEL to NOEL.

Aspect	Assessment factors
Interspecies differences[1]	4·3
Intraspecies differences	3
Differences between experimental conditions and exposure[2] pattern of the worker	3
Type of critical effect	1
Dose-response curve[3]	0.5
Confidence of the database	1
Minimal MOS	54

Table A1.2 Assessment factors applied for the calculation of the minimal MOS for systemic effects after chronic dermal exposure based on a 13-week dermal toxicity study in rats.

[1] Adjustment via caloric demands (4 for rats) together with an uncertainty factor for remaining interspecies differences

[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. The default value for extrapolation from semichronic to chronic exposure is 10. A smaller factor is indicated, because the results of the subacute and semichronic inhalation studies indicate neither more severe adverse effects at similar exposure levels nor lower adverse effect levels by extending exposure times. A factor 3 is considered applicable, because no clear conclusions can be drawn on effects of extending exposure times from semichronic to chronic.

[3] Because no systemic effects were observed and the NOAEL might be 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 systemic effects after chronic inhalation exposure based on a 13-week inhalation toxicity study in rats.

Aspect	Assessment factors
Interspecies differences[1]	3
Intraspecies differences	3
Differences between experimental conditions and exposure pattern of the worker[2]	2
Type of critical effect	1
Dose-response curve	1
Confidence of the database[3]	2
Minimal MOS	36

1 No corrections are made for caloric demands, because extrapolation is based on concentration equivalents. Only an uncertainty factor for remaining interspecies differences 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 subacute and semichronic inhalation studies indicate neither more severe adverse effects at similar exposure levels nor lower adverse effect levels by extending exposure times. Because no clear conclusions on the effect of semichronic to chronic exposure times can be drawn, a factor 2 is considered to be applicable.

3 Given the results from the subacute inhalation study (NOAEL 39 mg/m^3) an extra uncertainty factor 2 is introduced.

Table A1.4: Assessment factors applied for the calculation of the minimal MOS for reproduction effects after inhalation exposure based on a oral developmental toxicity study.

Aspect	Assessment factors
Interspecies differences[1]	4·3
Intraspecies differences	3
Differences between experimental conditions and exposure pattern of the worker	1
Type of critical effect	1
Dose-response curve	1
Confidence of the database[2]	2
Route-to-route extrapolation[3]	1
Minimal MOS	72

1 Adjustment via caloric demands together with an uncertainty factor for remaining interspecies differences

2 An arbitrary factor 2 is introduced for uncertainties introduced by route-to-route extrapolation

3 For rout-to-route extrapolation correction is made by differences between oral and inhalation absorption. Default values for oral and inhalation absorption are used, because data are lacking, i.e. 75% and 75%, respectively. This correction results in a factor 1.

Annex 2 Risk estimation using the minimal MOS-approach 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.

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 so far 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 toxico-kinetic 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 IA of Regulation 1488/94, a HBROEL is calculated and compared with the exposure estimate for workers or sub-populations 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.

Interspecies 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 A2.1 Assessment factors applied for the calculation of HBROELs.

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

[a] 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) toxico-kinetic 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-lives 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 toxico-kinetics 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:

$$\text{HBROEL-derm (mg/d)} = \text{NOAEL}_{\text{dermal, animal}}\ \text{(mg/kg bw/d)} \cdot 1/A \cdot 70\ \text{kg}$$

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:

$$\text{HBROEL-inh (mg/d)} = \text{NOAEL}_{\text{inhalation, animal}}\ \text{(mg/m}^3\text{)} \cdot 1/A \cdot 10\ \text{m}^3$$

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:

$$\text{HBROEL-derm (mg/d)} = \text{NOAEL}_{\text{oral, animal}}\ \text{(mg/kg bw/d)} \cdot X \cdot 1/A \cdot 1/Y \cdot 70\ \text{kg}$$

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);
- a 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:

$$\text{HBROEL-inh (mg/d)} = \text{NOAEL}_{\text{oral, animal}}\ \text{(mg/kg bw/d)} \cdot X \cdot 1/A \cdot 1/Z \cdot 70\ \text{kg}$$

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:

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

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);
- a 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:

$$\text{HBROEL-inh (mg/d)} = \text{NOAEL}_{\text{dermal, animal}}\ (\text{mg/kg bw/d}) \cdot Y \cdot 1/A \cdot 1/Z \cdot 70\ \text{kg}$$

Rationale: the NOAEL from a 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 The occurrence of DEGBE in products according to the Swedish product register

Trades that use products containing 2-(2-butoxyethoxy)-ethanol and product functions.

Trade	Product functions
Other products	Cleaning agent Degreasing agent Developer
Food products and beverages	Cleaning agent High pressure cleaning agent Lime remover Rust remover Anti foaming agent Machine washing-up agent Lubricant additive
Textile	Printing ink Dyes and pigment Detergent Cleaning agent additive Textile colouring agent Solvent intermediate
Tanneries, leather (luggage, handbags, footwear)	Aqueous paint Solvent based paint Dyes and pigment
Wood and wood products	Aqueous paint Solvent based paint Diluent Mordant Adhesives (cyanoacrylates) Anti adhesion agent
Pulp, paper and paper products	Preservative Cleaning agent Degreasing agent High pressure cleaning agent Anti foaming agent
Publishers and printers	Printing ink Solvent based paint Cleaning agent High pressure cleaning agent Cleaning agent additive Solvent Developer Photo chemical
Dyes and pigments	Diluent Solvent
Plastics (in primary form)	Stabiliser

Trade	Product functions
Paint and lacquer fabrication	Paint Solvent based paint Dyes and pigment Thickener Preservative Stabiliser Solvent Paint additive Bactericide Fungicide pH regulator
Soap, detergents, cleaning and polishing agents industry	Cleaning agent Degreasing agent Stain remover Lime remover Cleaning agent (premises) Solvent Surfactant
Perfumes and toilet preparations	Solvent
Other chemical products	Cleaning agent (premises) Wetting agent
Glues and gelatines	Thickener Solvent
Rubber products	Lubricant Softener
Plastic products	Stabiliser
Articles of concrete, plaster and cement	Thickener Process regulator
Basic metals and metal products	Cutting fluid
Basic metals	Aqueous paint Solvent based paint Degreasing agent High pressure cleaning agent
Metal products	Paint Aqueous paint Solvent based paint Cutting fluid Adhesive

Trade	Product functions
	Metal surface treatment agent Cleaning agent Degreasing agent High pressure cleaning agent Rust remover Anti foaming agent Lubricant Diluent Rust prevention agent Inhibitor
Treatment and coating of metals	Paint Metal surface treatment agent Degreasing agent Diluent
Machinery and equipment	Paint Aqueous paint Cutting fluid Cleaning agent Degreasing agent Anti foaming agent Lubricant Rust prevention agent Car care product
Electrical machinery n.e.c.	Cutting fluid Cleaning agent Solvent Electrical insulator Metal surface coating
Radio, television, communication equipment	Printing ink Soldering material Detergent
Furniture industry	Aqueous paint Thickener Stabiliser
Transport equipment	Paint remover Paint Aqueous paint Solvent based paint Cutting fluid Adhesive Cleaning agent Degreasing agent High pressure cleaning agent Anti foaming agent Rust prevention agent Casting compounds
Manufacture for export, export	Aqueous paint Solvent based paint Preservative
	Cutting fluid Polishing agent Cleaning agent Degreasing agent High pressure cleaning agent Anti foaming agent Disperging agent
Construction	Paint remover Paint Aqueous paint Solvent based paint Adhesive Dispersion adhesive Soldering material Cleaning agent (premises) Anti corrosion agent Corrosion inhibitor Sealing agent
Wholesale and retail/repair of motor vehicles and motorcycles and personal and household goods	Fire extinguisher Paint remover Solvent based paint Adhesive Cleaning agent Degreasing agent Stain remover High pressure cleaning agent Lime remover Cleaning agent (premises) Detergent Lubricant Diluent Drying agent Car care product Emulsifier Transmission agent Windscreen washer Foaming agent Carbonisation agent Water repelling agent
Wholesale trade (except motor vehicles and motorcycles)	Degreasing agent Lubricant Car care product Transmission agent Rinsing agent
Agents involved in sale of fuels, ores, metals and industrial chemicals	Fungicide
Wholesale of china, glassware, wallpaper and cleaning materials	Polishing agent Cleaning agent

Trade	Product functions
Wholesale of chemicals	Fire extinguisher Cleaning agent Lime remover Cleaning agent (premises) Solvent Finishing agent
Retail (except motor vehicles), repair of personal and household goods	Dispersion adhesive Degreasing agent Stain remover High pressure cleaning agent Car care product Anti static agent
Paint stores	Paint Aqueous paint
Transport, storage and communication	Cleaning agent Degreasing agent Drying agent Solvent
Services	Fire extinguisher Lime remover Cleaning agent (premises)
Research and development	Laboratory chemical

Trade	Product functions
Cleaning	Paint remover Polishing agent Cleaning agent Degreasing agent Stain remover High pressure cleaning agent Lime remover Cleaning agent (premises) Rust remover Disinfectant
Public authorities, national defence	Cleaning agent Degreasing agent High pressure cleaning agent
Health and social work establishments	Cleaning agent Degreasing agent
Other community and personal services	Rust remover
Laundries and dry cleaning	Cleaning agent Stain remover Detergent Cleaning agent additive Whitening agent
Several trades	Floor covering Decontamination

Annex 4 Exposure levels of DEGBE and other glycol ethers 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						
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.* 1987)
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.* 1987)
EGBE	80	Construction; removing mastic with solvents	8-107 mg/m^3			(Kelly 1993)
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)

Substances	Vapour pressure (Pa)	Industries and tasks	Exposure levels (ppm, unless otherwise stated)		Remarks	References
			Full-shift	Short-term		
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	Miscellaneous manufacturing industries	< 25 < 5 < 5 < 5 < 5		n = 28 n = 32 n = 15 n = 8 n = 4	(Guirguis *et al.* 1994)
EGBE EGEEA EGEE	80 270 530	Rubber manufacturers, other than tires, tubes and footwear	< 25 < 5 < 5		n = 34 n = 21 n = 22	(Guirguis *et al.* (1994)
EGBE EGEEA DPGME	80 270	Jewellery and silverware manufacturers	< 25 2% > 5 < 150		n = 6 n = 82; 2% of samples > 5 ppm n = 6	(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)
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	(Guirguis *et al.* 1994)
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)

Substances	Vapour pressure (Pa)	Industries and tasks	Exposure levels (ppm, unless otherwise stated)		Remarks	References
			Full-shift	Short-term		
DEGBE	2.7	Use of waterborne paint (brushing or rolling)		4 - 5	1.5% of 2EGBEE in paint	(Hansen *et al.* 1987)
DEGME	30			8 - 32	4% of DEGME in paint	
DPGME				30 - 40	1% of DPGME in paint	
EGBE	80			2 - 60	0-1.4% of EGBE in paint	
EGPhE				0 - 0.7	1.7% of EGPhE in paint	
				all in mg/m^3	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 5 Estimation of concentrations due to transfer operations - USEPA Transfer Model[5]

The USEPA transfer model is a 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 by the USEPA 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 transferral is often the activity with the highest levels of emission.

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

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

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 (m^3/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 = 162 p = 2.7
kwc = 0.1 Twc = 293
knorm = 0.5 Tnorm = 293

where wc = worst case and norm = normal or typical case.

The calculations are applicable to the transfer of pure substances. For calculating concentrations of substances emitted from mixtures the results can be corrected for the percentage of substance in the mixture if the mixture can be considered to be an ideal mixture.

The following transferral operations are considered:

a - rail car
b - tank truck
c - drum (200 L)
d - can (10 L)
e - small can (1 L)

[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.

The results are presented in the table below.

Results from the USEPA transfer model:

Worst Case									
	f	M	V	r	P	Tl	Q	k	Cm
a	1.0	162	76.000	1	2.70	293	1203000	0.1	0.11
b	1.0	162	19.000	2	2.70	293	1203000	0.1	0.06
c	1.0	162	0.200	30	2.70	293	850	0.1	12.69
d	1.0	162	0.010	30	2.70	293	850	0.1	0.63
e	1.0	162	0.001	300	2.70	293	850	0.1	0.63
Typical case									
	f	M	V	r	P	Tl	Q	k	Cm
a	1.0	162	76.000	1	2.70	293	4812000	0.5	0.01
b	1.0	162	19.000	2	2.70	293	4812000	0.5	0.00
c	0.5	162	0.200	20	2.70	293	5100	0.5	0.14
d	0.5	162	0.010	20	2.70	293	5100	0.5	0.01
e	0.5	162	0.001	200	2.70	293	5100	0.5	0.01

Annex 6 Consumer exposure

Annex 6a GINGELL SCENARIO

CONSEXPO Monte Carlo Percentile Report

Compound: DEGBE (CAS: 112-34-5)

EXPOSURE

Inhalatory:	4.67e-01 (mg/m^3)	95.0 percentile
Dermal:	6.00e+00 (mg/cm^3)	95.0 percentile
Oral:	Unknown	
Year average:	1.10e-02 (mg/cm^3)	

UPTAKE

Inhalatory:	3.87e+00 (mg/year)	95.0 percentile
Dermal:	3.60e+02 (mg/year)	95.0 percentile
Oral:	Unknown	
Total uptake:	3.64e+02 (mg/year)	95.0 percentile
Dosis:	1.42e-02 (mg/kg bw/day)	95.0 percentile

CONSEXPO report

Generated by CONSEXPO version 1.03

Compound: DEGBE (CAS: 112-34-5)
Subject: person
Weight: 70.000 kg (uninspected default)

CONTACT
Contact scenario: Painting
Parameter definition of scenario:
Duration of contact per event: 160.000 min
Duration of actual use per event: 80.000 min
Frequency of contact: 6.000 1/year
Start of contact: 0.00e+00 min

INHALATION

Exposure
Scenario: evaporation from mixture
Person uses product (volume around person=5 m^3).
Mean event concentration (average case): 4.673e-01 mg/m^3
Year average (average case): 8.528e-04 mg/m^3
Mean event concentration (cumulative worst case): 4.673e-01 mg/m^3
Year average (cumulative worst case): 8.528e-04 mg/m^3

Exposure estimates based on the following parameters:
Release area: 14.300 m^2
Temperature: 25.000 Celsius
Ventilation rate: 10.680 m^3/hr
Room volume: 35.600 m^3
Product amount: 2.420 kg
Weight fraction: 0.600%
Molweight solvent: 150.000 g/mol

Uptake
Model: fraction model
Average case estimate : 3.869e+00 mg/year
: 1.513e-04 mg/(kg.day)
Cumulative worst case estimate : 3.869e+00 mg/year
: 1.513e-04 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 75.000%
Inhalation rate: 11500.000 cm^3/min
Respirable fraction: 1.000 fraction

DERMAL

Exposure
Scenario: fixed volume of product
Mean event concentration (average case): 6.000e+00 mg/cm^3
Year average (average case): 1.095e-02 mg/cm^3
Mean event concentration (cumulative worst case): 6.000e+00 mg/cm^3
Year average (cumulative worst case): 1.095e-02 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: 0.600%
Dilution before use: 1.000 times

Uptake
Model: fraction model
Average case estimate : 3.600e+02 mg/year
: 1.408e-02 mg/(kg.day)
Cumulative worst case estimate : 3.600e+02 mg/year
: 1.408e-02 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 1.000 dimless

ORAL
No exposure

Annex 6b GINGELL SCENARIO

CONSEXPO Monte Carlo Percentile Report

Compound: DEGBE (CAS: 112-34-5)

EXPOSURE

Inhalatory:	4.12e-01 (mg/m^3)	95.0 percentile
Dermal:	6.00e+00 (mg/cm^3)	95.0 percentile
Oral:	Unknown	
Year average:	1.10e-02 (mg/cm^3)	

UPTAKE

Inhalatory:	3.41e+00 (mg/year)	95.0 percentile
Dermal:	3.60e+02 (mg/year)	95.0 percentile
Oral:	Unknown	
Total uptake:	3.63e+02 (mg/year)	95.0 percentile
Dosis:	1.42e-02 (mg/kg low/day)	95.0 percentile

CONSEXPO report

Generated by CONSEXPO version 1.03

Compound: DEGBE (CAS: 112-34-5)
Subject: person
Weight: 70.000 kg (uninspected default)

CONTACT
Contact scenario: Painting
Parameter definition of scenario:
Duration of contact per event: 160.000 min
Duration of actual use per event: 80.000 min
Frequency of contact: 6.000 1/year
Start of contact: 0.00e+00 min

INHALATION

Exposure
Scenario: evaporation from mixture
Person uses product (volume around person=5 m^3).
Mean event concentration (average case): 4.118e-01 mg/m^3
Year average (average case): 7.517e-04 mg/m^3
Mean event concentration (cumulative worst case): 4.118e-01 mg/m^3
Year average (cumulative worst case): 7.517e-04 mg/m^3

Exposure estimates based on the following parameters:
Release area: 14.300 m^2
Temperature: 25.000 Celsius
Ventilation rate: 35.600 m^3/hr
Room volume: 35.600 m^3
Product amount: 2.420 kg
Weight fraction: 0.600%
Molweight solvent: 150.000 g/mol

Uptake
Model: fraction model
Average case estimate : 3.410e+00 mg/year
: 1.334e-04 mg/(kg.day)
Cumulative worst case estimate : 3.410e+00 mg/year
: 1.334e-04 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 75.000%
Inhalation rate: 11500.000 cm^3/min
Respirable fraction: 1.000 fraction

DERMAL

Exposure
Scenario: fixed volume of product
Mean event concentration (average case): 6.000e+00 mg/cm^3
Year average (average case): 1.095e-02 mg/cm^3
Mean event concentration (cumulative worst case): 6.000e+00 mg/cm^3
Year average (cumulative worst case): 1.095e-02 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: 0.600%
Dilution before use: 1.000 times

Uptake
Model: fraction model
Average case estimate : 3.600e+02 mg/year
: 1.408e-02 mg/(kg.day)
Cumulative worst case estimate : 3.600e+02 mg/year
: 1.408e-02 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 1.000 dimless

ORAL
No exposure

Annex 6c GINGELL SCENARIO

CONSEXPO Monte Carlo Percentile Report

Compound: DEGBE (CAS: 112-34-5)

EXPOSURE

Inhalatory:	3.19e-01 (mg/m^3)	95.0 percentile
Dermal:	6.00e+00 (mg/cm^3)	95.0 percentile
Oral:	Unknown	
Year average:	1.10e-02 (mg/cm^3)	

UPTAKE

Inhalatory:	2.64e+00 (mg/year)	95.0 percentile
Dermal:	3.60e+02 (mg/year)	95.0 percentile
Oral:	Unknown	
Total uptake:	3.63e+02 (mg/year)	95.0 percentile
Dosis:	1.42e-02 (mg/kg bw/day)	95.0 percentile

CONSEXPO report

Generated by CONSEXPO version 1.03

Compound: DEGBE (CAS: 112-34-5)
Subject: person
Weight: 70.000 kg (uninspected default)

CONTACT
Contact scenario: Painting
Parameter definition of scenario:
Duration of contact per event: 160.000 min
Duration of actual use per event: 80.000 min
Frequency of contact: 6.000 1/year
Start of contact: 0.00e+00 min

INHALATION

Exposure
Scenario: evaporation from mixture
Person uses product (volume around person=5 m^3).
Mean event concentration (average case): 3.193e-01 mg/m^3
Year average (average case): 5.828e-04 mg/m^3
Mean event concentration (cumulative worst case): 3.193e-01 mg/m^3
Year average (cumulative worst case): 5.828e-04 mg/m^3

Exposure estimates based on the following parameters:
Release area: 14.300 m^2

Temperature: 25.000 Celsius
Ventilation rate: 106.800 m^3/hr
Room volume: 35.600 m^3
Product amount: 2.420 kg
Weight fraction: 0.600%
Molweight solvent: 150.000 g/mol

Uptake
Model: fraction model
Average case estimate : 2.644e+00 mg/year
: 1.034e-04 mg/(kg.day)
Cumulative worst case estimate : 2.644e+00 mg/year
: 1.034e-04 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 75.000%
Inhalation rate: 11500.000 cm^3/min
Respirable fraction: 1.000 fraction

DERMAL

Exposure
Scenario: fixed volume of product
Mean event concentration (average case): 6.000e+00 mg/cm^3
Year average (average case): 1.095e-02 mg/cm^3
Mean event concentration (cumulative worst case): 6.000e+00 mg/cm^3
Year average (cumulative worst case): 1.095e-02 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: 0.600%
Dilution before use: 1.000 times

Uptake
Model: fraction model
Average case estimate : 3.600e+02 mg/year
: 1.408e-02 mg/(kg.day)
Cumulative worst case estimate : 3.600e+02 mg/year
: 1.408e-02 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 1.000 dimless

ORAL
No exposure

Annex 6d DUTCH SCENARIO

CONSEXPO Monte Carlo Percentile Report

Compound: DEGBE (CAS: 112-34-5)

EXPOSURE

Inhalatory:	3.97e+00 (mg/m^3)	95.0 percentile
Dermal:	5.00e+01 (mg/cm^3)	95.0 percentile
Oral:	Unknown	
Year average:	9.13e-02 (mg/cm^3)	

UPTAKE

Inhalatory:	3.29e+01 (mg/year)	95.0 percentile
Dermal:	3.00e+03 (mg/year)	95.0 percentile
Oral:	Unknown	
Total uptake:	3.03e+03 (mg/year)	95.0 percentile
Dosis:	1.19e-01 (mg/kg bw/day)	95.0 percentile

CONSEXPO report

Generated by CONSEXPO version 1.03

Compound: DEGBE (CAS: 112-34-5)
Subject: person
Weight: 70.000 kg (uninspected default)

CONTACT
Contact scenario: Painting
Parameter definition of scenario:
Duration of contact per event: 160.000 min
Duration of actual use per event: 80.000 min
Frequency of contact: 6.000 1/year
Start of contact: 0.00e+00 min

INHALATION

Exposure
Scenario: evaporation from mixture
Person uses product (volume around person=5 m^3).
Mean event concentration (average case): 3.972e+00 mg/m^3
Year average (average case): 7.250e-03 mg/m^3
Mean event concentration (cumulative worst case): 3.972e+00 mg/m^3
Year average (cumulative worst case): 7.250e-03 mg/m^3

Exposure estimates based on the following parameters:
Release area: 35.000 m^2

Temperature: 25.000 Celsius
Ventilation rate: 15.000 m^3/hr
Room volume: 30.000 m^3
Product amount: 5.000 kg
Weight fraction: 5.000%
Molweight solvent: 150.000 g/mol

Uptake
Model: fraction model
Average case estimate : 3.289e+01 mg/year
: 1.286e-03 mg/(kg.day)
Cumulative worst case estimate : 3.289e+01 mg/year
: 1.286e-03 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 75.000%
Inhalation rate: 11500.000 cm^3/min
Respirable fraction: 1.000 fraction

DERMAL

Exposure
Scenario: fixed volume of product
Mean event concentration (average case): 5.000e+01 mg/cm^3
Year average (average case): 9.126e-02 mg/cm^3
Mean event concentration (cumulative worst case): 5.000e+01 mg/cm^3
Year average (cumulative worst case): 9.126e-02 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: 5.000%
Dilution before use: 1.000 times

Uptake
Model: fraction model
Average case estimate : 3.000e+03 mg/year
: 1.173e-01 mg/(kg.day)
Cumulative worst case estimate : 3.000e+03 mg/year
: 1.173e-01 mg/(kg.day)
Uptake estimates based on the following parameters:
Absorbed fraction: 1.000 dimless

ORAL
No exposure

European Commission

EUR 18998 – European Union Risk Assessment Report
2-(2-butoxyethoxy)ethanol, Volume 2

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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The report provides the comprehensive risk assessment of the substance 2-(2-butoxyethoxy)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-butoxyethoxy)ethanol concludes with no concern for the environment, but health risks for the consumer are expected to occur due to the use of the substance in paint spraying applications. Health risks for workers are expected by eye exposure due to incidental splashing when the pure substance is handled, local effects on skin, which can not be excluded after repeated dermal exposure, and with regard to anticipated effects after inhalation during manual application of products 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.

CL-NA-18998-EN-C

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

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