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Institute for Health and Consumer Protection
European Chemicals Bureau
I-21020 Ispra (VA) Italy

2-(2-BUTOXYETHOXY)ETHANOL

CAS-No.: 112-34-5

EINECS-No.: 203-961-6

Summary risk assessment report

1999 **Special Publication I.99.207**

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SUMMARY RISK ASSESSMENT REPORT

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.

Contact point:
Chemical Substances Bureau
P.O. Box 1
3720 BA Bilthoven
The Netherlands

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PREFACE

This report provides a short summary with conclusions of the risk assessment report of the substance 2-(2-butoxyethoxy)ethanol that has been prepared by the Netherlands in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances. For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references, the reader is referred to the original risk assessment report that can be obtained from the European Chemicals Bureau[1]. The present summary report should preferably not be used for citation purposes.

[1] http://ecb.ei.jrc.it

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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

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

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

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. 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/y, which is the sum of all actual production tonnages that were individually submitted to the rapporteur. Virtually no DEGBE is believed to be imported into the EU. No data on export are given. The production in the European Union is located at eight different sites. DEGBE is produced by the reaction of ethylene oxide and n-butanol with an alkalic catalyst.

Table 2.1 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. The major function of this agent is to dissolve various components of mixtures in both aqueous and non-aqueous systems.

Table 2.1 Industrial and use categories of DEGBE.

Industrial category	IC no.	Use category	UC no.
- Chemical industry: basic chemical - Paints, lacquers and varnishes industry	2 14	Solvents	48
- 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 - Public domain - Metal industry	5 6 8	Cleaning/washing agents and disinfectants	9

Average quantitative estimations are available on the use pattern of DEGBE at the EU market and summarised in **Table 2.2**.

Table 2.2 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 2.2 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 %).

3 ENVIRONMENT

3.1 EXPOSURE

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: no hydrolysis, an estimated atmospheric half-life through reaction with OH-radicals of about 11 hours (no direct photodegradation), readily biodegradable, a relatively low Henry's Law constant of $4.4 \cdot 10^{-3}$ $Pa.m^{-3}/mol$ at 20°C indicating that volatilisation of DEGBE from surface waters and moist soil is expected to be very low and a relatively low log K_{ow} of 0.56. From this logKow value a K_p for soil 0.07 l/kg is calculated indicating that DEGBE is expected to be highly mobile in soil.
No experimental data on bioaccumulation are available. The estimated BCF-values amount to 1.4 (l/kg) and 2.2 (kg/kg) for fish and worm, respectively, indicating a low bioaccumulating potential in the environment.

For the environmental exposure assessment of DEGBE both site-specific and generic emission scenarios are used for calculating the Predicted Environmental Concentrations (PECs) in the different environmental compartments.

3.1.1 Exposure at production

For seven of the eight production sites the exposure assessment is based on actual, site specific data. For one site, a generic scenario was carried out based on default values because no site specific data were submitted for aquatic releases. All eight production sites submitted actual data on atmospheric releases. The highest reported daily release to air, i.e. 1.7 kg/day is initially used for the calculation of a local PEC in air, resulting in a very low DEGBE concentration of $3.9 \cdot 10^{-4}$ mg/m^3 at 100 metres from the source.

3.1.2 Exposure at processing, formulation and private use

Generic exposure scenarios are used for estimating the releases from processing, formulation and use of DEGBE. The scenarios are based on the two most important use categories of DEGBE, i.e. detergents and paints. 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 3.1**.

Table 3.1 Environmental exposure scenarios for processing, formulation and private use of DEGBE.

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

The exposure assessment is based on the EU-Technical Guidance Document applying the European Union System for the Evaluation of Substances, EUSES. 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.

Local PEC values for the sewage treatment plant range from 0.009 to 2.8 mg/l. Local PEC values for surface water range from 0.01 to 0.3 mg/l DEGBE. Local soil concentrations in the range of 2 -20 µg/kg are estimated for the terrestrial compartment. Estimated concentrations in the air near the emission sources range from 40 µg/m^3 to less than 0.02 µg/m^3.
Estimated regional PEC values are all much lower than the concentrations near the point sources.

3.2 EFFECTS

Short-term toxicity data are available for fish, daphnia and algae and micro-organisms. The PNEC for the aquatic compartment is extrapolated from a 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. The extrapolation leads to a PNEC for the aquatic environment of **1 mg/l.**

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.**

Since there are no data available for directly deriving a PNEC for the terrestrial compartment the PNEC-terrestrial was estimated from the PNEC for aquatic organisms using the equilibrium partitioning approach. This results in a $PNEC_{terrestrial}$ of **0.2 mg/kg.**

The PNEC predators of **50 mg/kg** was estimated from the oral NOAEL of 500 mg/kg b.w./d.

3.3 RISK CHARACTERISATION

The PEC/PNEC ratios based on the actual releases of DEGBE at production are all below 1 **(conclusion ii)**. The same is true for the generic production scenario and for the few PEC/PNEC ratios that can be calculated based on actual releases from processing.

The local PECs in an STP, for surface water and for soil for the various environmental exposure scenarios are presented in **Table 3.2**.

Table 3.2 shows that in all emission scenarios the PECs do not exceed the PNEC for the different environmental compartments **(conclusion ii)**. The same holds true for sediment organisms and predators (data not shown).

Table 3.2 PEC/PNEC ratios for micro-organisms, aquatic organisms and terrestrial organisms.

Scenario	$PEC/PNEC_{micro\text{-}organisms}$	$PEC/PNEC_{aquatic}$	$PEC/PNEC_{terrestrial}$
Scenario detergent I -formulation	0.05	0.05	0.02
Scenario detergent II -processing	0.08	0.06	0.03
Scenario detergent III -private use	0.08	0.06	0.03
Scenario paints I (coil coating) -formulation	0.2	0.1	0.06
Scenario paints II (coil coating) -processing	0.02	0.03	0.01
Scenario paints III -formulation	0.4	0.3	0.09
Scenario paints IV (car, can etc.) -processing	0.2	0.1	0.1
Scenario V (decorative) - processing	0.004	0.01	0.01
Scenario paints VI -private use	$1 \cdot 10^{-3}$	0.01	0.01

4 HUMAN HEALTH

4.1 EXPOSURE

The human population may be exposed to DEGBE at 1) the workplace, 2) from use of consumer products and 3) indirectly via the environment.

4.1.1 Workplace exposure

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).

The exposure assessment is based on measured data (limited), expert judgement, analogy approach, the EPA transfer model and the EASE model (inhalation and dermal exposure assessment). The results for the different scenarios are summarised in **Table 4.1**.

4.1.2 Consumer exposure

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. Hence, in this assessment two exposure scenarios are considered: latex paints and liquid hard surface cleaners. Since inhalation exposure from the use of DEGBE containing paint in a spray application is described for workers (scenario 4) and consumers may also 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 as well as exposure data 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.

Table 4.1 Summary of the occupational exposure assessment

Scenario	Exposure		Estimated inhalation exposure level (mg/m³)						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.

4.1.3 Man exposed indirectly via the environment

DEGBE may be released to the environment via effluents at sites where it is produced or used. The highest local PEC in air is $3.9 \cdot 10^{-4}$ mg/m^3 at 100 metres from the production source. Estimated concentrations in the air near the emission sources for the different use scenarios (see **Table 3.1**) range from 40 µg/m^3 to less than 0.02 µg/m^3. The total human intake via air, drinking water and food for the different emission scenarios at local scale range from $1.1 \cdot 10^{-3}$ to 0.33 mg/kg/day.

4.2 EFFECTS

In the data set for DEGBE no human data on toxicity of DEGBE are available.
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 a 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 the 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 the 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.

4.3 RISK CHARACTERISATION

4.3.1 Workplace

Given the effects observed in the acute toxicity studies, the skin and eye irritation studies, the sensitisation studies and the mutagenicity tests, and the anticipated occupational exposure levels it is concluded that DEGBE is of no concern for workers with regard to acute effects, acute skin irritation, eye irritation by vapours, corrosivity, skin sensitisation and mutagenicity **(conclusion ii).** There are no reasons for concern with regard to carcinogenicity.

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.

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

Repeated-dose toxicity, local and systemic effects
Repeated dermal exposure may induce local skin effects. 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. Given the estimated frequency of exposure (100-200 d/year) chronic exposure is assumed for risk characterisation. These levels are compared with a LOAEL in rats of 5.5

mg/cm^2 from the 13-week dermal study. The MOS between this LOAEL and the dermal exposure levels ranged from 4 to 110. It is concluded that health risks for local effects due to repeated dermal exposure are not expected for scenarios 1, 2 and 3. Given the margin of safety in scenario 4 (spray application), it is concluded that risk reduction measures are indicated for this scenario **(conclusion iii).**

Starting-point for the risk characterisation for workers exposed by skin contact for systemic effects are the NOAEL of 2000 mg/day (highest dose level tested) from the semichronic dermal study with rats. Given the estimated frequency of exposure (100-200 d/year) chronic exposure is assumed for risk characterisation. The MOS between the NOAEL and the dermal exposure levels ranges from 72 to 3333. It is concluded that systemic effects due to repeated dermal exposure are not expected for all occupational scenarios (**conclusion ii**).

Starting-point for the risk characterisation for workers exposed by inhalation is the NOAEL of 94 mg/m^3 from the semichronic inhalation study with rats. The MOSs between the NOAEL and the inhalation exposure levels range from 9 to 157. It is concluded that, based upon the present information, health risks due to occupational exposure in cannot be excluded for scenario 4 (manual application of products containing DEGBE) (**conclusion iii**).

Reproductive toxicity

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). Since both levels mentioned were the highest dose levels tested and neither reproduction effects nor effects on offspring were observed 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).**

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. The NOAEL for developmental effects (500 mg/kg bw/d) from the oral studies is used for a (worst case) risk characterisation. The MOS between this NOAEL and the estimated inhalation occupational exposure levels range from 350 to 5833. It is concluded that developmental effects due to occupational inhalation exposure are not likely to occur (**conclusion ii**).

4.3.2 Consumers

Like for workers it is possible that consumers may use spray applications of DEGBE in paint. Therefore **conclusion (iii)** is reached for this possible consumer application.

For scenario I “Latex paint” it is concluded that there is no concern for consumers with regard to inhalatory or dermal acute effects, irritation by vapours or skin irritation (**conclusion ii)**. For the use of DEGBE in hard surface cleaners (scenario II) an inhalatory exposure as well as risk assessment was carried out. 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 results in a margin of safety of 1382 which is considered to be sufficient (**conclusion ii)**.

4.3.3 Man indirectly exposed via the environment

For the risk characterisation after repeated exposure all exposure estimates for air 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. 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 (**conclusion ii)**. 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 applying route-to-route extrapolation. The calculated margins of safety for all local scenarios range from 1360 - 5E+5 and are considered sufficient (**conclusion ii)**.
For the local scale the margins 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 range from $2.72 \cdot 10^{+3}$ to $8.2 \cdot 10^{+5}$. These margins of safety are considered sufficient **(conclusion ii)**. The margins of safety for reproductive toxicity are >> 1000 for all scenarios (local and regional) (**conclusion ii)**.

5 RESULTS OF THE RISK ASSESSMENT

Environment

(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

Consumers

(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

(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.