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2-BUTOXYETHANOL
CAS N°: 111-76-2

COVER PAGE**SIDS Initial Assessment Report**
for
6th SIAM

(Paris, 9-11 June 1997)

Chemical Name: 2-Butoxyethanol**CAS No.:** 111-76-2**Sponsor Country:** Australia

National SIDS Contact Point in Sponsor Country:

Ms. Lesley Onyon

HISTORY:

The SIDS Dossier was sent to members on 13 August 1996. No further testing has been recommended.

no testing (X)
testing ()

COMMENTS:

For discussion at SIAM 6.

The SIAR is based on a national assessment conducted under the *Industrial Chemicals (Notification & Assessment) Act 1989 of 2-butoxyethanol* in cleaning products and additional exposure information from Member countries.

Deadline for circulation:

Date of circulation: 28 February 1997
(To all National SIDS Contact Points and the OECD Secretariat)

SIDS INITIAL ASSESSMENT PROFILE

CAS NO.	111 - 76 - 2
CHEMICAL NAME	2-BUTOXYETHANOL
STRUCTURAL FORMULA	CH ₃ CH ₂ CH ₂ CH ₂ OCH ₂ CH ₂ OH
<u>RECOMMENDATION OF THE SPONSOR COUNTRY</u>	
2-Butoxyethanol is considered of low priority for further work.	
<u>SHORT SUMMARY OF THE REASONS WHICH SUPPORT THE RECOMMENDATION</u>	
<p>The main use is for 2-butoxyethanol is in paints and surface coatings, followed by cleaning products and inks. Other products which contain 2-BE include acrylic resin formulations, asphalt release agents, firefighting foam, leather protectors, oil spill dispersants and photographic strip solutions.</p> <p>The principal health effects following acute exposure to 2-butoxyethanol are irritation of the eyes and respiratory tract. The critical effect identified in repeated dose animal studies is haematotoxicity. The lowest reliable NOAEL for haemolysis in the most sensitive species, the rat, is 24.6 ppm (22.5 mg/kg/day). The haematological effects are transient at lower doses and there are large species differences in the haematological response to 2-butoxyethanol exposure, with evidence to show that humans are less sensitive than rats. 2-Butoxyethanol is readily absorbed through the skin.</p> <p>Taking into account the nature of the critical effect and the species difference, a comparison of estimated occupational exposures with the NOAEL for haemolytic effects indicates that the potential risk is generally low. However, for printing and cleaning, where there is prolonged exposure to high concentrations of 2-butoxyethanol, there are some concerns and adequate control measures are needed.</p> <p>Due to low and intermittent exposure, the public health risk from the use of products containing 2-butoxyethanol is low. 2-Butoxyethanol is relatively non-volatile, miscible in water, readily biodegradable and non-bioaccumulative. There is no apparent risk to any of the environmental compartments.</p>	
<u>IF FURTHER WORK IS RECOMMENDED, SUMMARISE ITS NATURE</u>	
No further testing is recommended in the context of SIDS. An NTP 2-year inhalation study in rats and mice and an epidemiological study in France are currently being conducted. Given the potential for risk to human health in some situations, further work on the extent of dermal absorption would be useful.	

FULL SIDS SUMMARY

CAS NO: 111-76-2		SPECIES	PROTOCO L	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point			- 77°C
2.2	Boiling Point			170.8°C
2.3	Density			0.90 kg/m ³
2.4	Vapour Pressure			1.17 hPa at 25°C
2.5	Partition Coefficient (Log Pow)			0.81
2.6	Water Solubility			miscible
A				
	pH			7
B				
2.7	Flash Point			62°C (closed cup)
2.8	Autoignition temperature			230-245°C
2.9	Flammability limits			1.10-12.7%
ENVIRONMENTAL FATE/BIODEGRADATION				
3.1.	Photodegradation			Not expected to undergo direct photolysis
1				
3.1.	Stability in Water			Not expected to undergo hydrolysis
2				
3.1.	Stability in Soil			K _{oc} of 67 indicates high mobility in soil
3				
3.2	Monitoring Data			In air: 1-8 µg/m ³ ; In ground water: 23 µg/L; In surface water: 1.3-5.7 ppm (contam. site)
3.3	Transport and Distribution		Calculated (Fugacity Level 1 type)	In water 84%, air 16%, sediment/soil 0.1% No significant transport expected from water to organic matter in sediments and suspended solids.

3.5	Biodegradation		OECD 301	Readily biodegradable
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	Fath'd min. Sh'ph'd m. Oyster W. shrimp		4d LC ₅₀ = 2137 mg/L 4d LC ₅₀ = 116 mg/L 4d LC ₅₀ = 89 mg/L 4d LC ₅₀ = 130 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates (<i>Daphnia</i>)	D. magna		2d LC ₅₀ = 835 mg/L
4.3	Toxicity to Aquatic Plants e.g Algae	Sel.capricornutum		7d EC ₅₀ > 1000 mg/L
4.5.1	Chronic Toxicity to Fish	Fathead minnow		32d MATC = 135 mg/L (QSAR result)
4.5.2	Chronic Toxicity to Aquatic Invertebrates (<i>Daphnia</i>)			
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	rat mouse guinea-pig rabbit	OECD 401	LD ₅₀ = 530-3000 mg/kg LD ₅₀ = 1230 mg/kg LD ₅₀ = 950-1414 mg/kg LD ₅₀ = 320-370 mg/kg
5.1.2	Acute Inhalation Toxicity	rat mouse guinea-pig	OECD 403	LC ₅₀ = 450-486ppm(2.2-2.4 mg/L) (4h) LC ₅₀ = 700 ppm (3.4 mg/L) (7h) LC ₅₀ = > 690 ppm (3.4 mg/L) (1h)
5.1.3	Acute Dermal Toxicity	rabbit guinea-pig	OECD 402	LD ₅₀ = 100-610 mg/kg LD ₅₀ = 210-> 3000 mg/kg
5.2.1	Skin Irritation	rabbit guinea-pig	OECD404	Moderate irritant Irritant
5.2.2	Eye Irritation	rabbit	OECD405	Irritant
5.2.3	Respiratory Irritation	mouse	Alarie test	Weak irritant
5.3	Sensitisation	guinea-pig	Maximisation	Non-sensitising
5.4	Repeat Dose Tox. - oral (d/w)	rat		90d NOAEL (m) = 129 mg/kg/d; LOAEL (f) = 82 mg/kg/d (haematotox.)
	- oral	rat		6 wk LOAEL (m) = 222 mg/kg/d

	(gav) - inhalation - dermal	rat rabbit		(haematotox.) 9d NOAEL = 20 ppm (haematotox.); 90d NOAEL = 24.6 ppm (haematotox.) 2 wk NOAEL = 90 mg/kg/d (haematotox.); 90d NOAEL = 150 mg/kg/d (haematotox.)
5.5	Genetic Toxicity In Vitro			
A	Bacterial Test (Gene Mutation)	<i>S. typhimur</i> <i>E. coli</i> Ch.hamster V79 cells	OECD 471	TA100, 1535, 1537, 97, 98 negative with and without metabolic activation Negative Negative (with and without m. activation) Positive at high doses
B	Non-Bacterial In Vitro Test - Chromosomal aberrations - Sister chromatid exchange - Unscheduled DNA synthesis	Ch.hamster Ch.hamster V79 cells rat liver		Negative (with and without m. activation) Negative (with and without m. activation) Weakly positive at high doses Inconclusive
5.6	Genetic Toxicity In Vivo - Mouse micronucleus - DNA binding	mouse rat, mouse		Negative Negative
5.8	Toxicity to Reproduction - oral (d/w)	rat (m) mouse		60d NOAEL (parental) = 443 mg/kg/d NOAEL (parental) = 720 mg/kg/d
5.9	Developmental Toxicity/ Teratogenicity - oral (gav) - inhalation - dermal	rat rat rabbit rat		NOAEL = 350 mg/kg/d (maternal tox.); 650 mg/kg/d (embryo-, foetotoxicity) NOAEL = 200 ppm NOAEL = 100 ppm (maternal tox., embryotox.); 200 ppm (foetotoxicity NOAEL = 1760 mg/kg/d
5.11	Experience with Human			Irritation of the eyes, nose and

	Exposure		throat. Headache and nausea.
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SIDS INITIAL ASSESSMENT REPORT**1. IDENTITY**

Name: 2-Butoxyethanol

CAS number: 111-76-2

IUPAC name: Ethylene glycol butyl ether

EINECS number: 203-905-0

Molecular formula: C₆H₁₄O₂.

Structural formula: CH₃CH₂CH₂CH₂OCH₂CH₂OH.

Synonyms: 2-BE, Butoxyethanol, n-Butoxyethanol, 2-Butoxy-1-ethanol, Butyl ethoxol, O-Butyl ethylene glycol, Butyl glycol, Butyl monoether glycol, EGBE, Ethylene glycol butyl ether, Ethylene glycol n-butyl ether, Ethylene glycol monobutyl ether, Ethylene glycol mono-n-butyl ether, Glycol butyl ether, Glycol monobutyl ether, Monobutyl glycol ether, 3-Oxa-1-heptanol.

2-Butoxyethanol is known commercially under the following trade names. Butyl Cellosolve[®], Butyl Icinol[®], Butyl Oxitol[®], Dowanol EB[®], Eastman[®] EB Solvent, Gafcol EB[®], Glycol ether EB[®], Jeffersol EB[®], Poly-Solv EB[®].

Purity: When 2-butoxyethanol (2-BE) is manufactured from ethylene oxide and n-butanol, other glycol ethers such as the di- and triethylene glycol ethers are produced. Consequently, commercial 2-BE may contain small concentrations of other glycol ethers, n-butanol and ethylene glycol. A stabiliser, 2,6-bis(1,1-dimethylethyl)-4-methylphenol, is often added at approximately 0.01% to prevent the formation of peroxides.

Physical and chemical properties: These properties are summarised in the table in the Full SIDS Summary. 2-BE is relatively non-volatile and miscible in water.

Hazard classification: The current European Union (EU) classification is R20/21/22 (Harmful by inhalation, in contact with skin, and if swallowed) and R37 (Irritating to respiratory system). Based on this assessment, risk phrase R36 (Irritating to eyes) is appropriate. The following concentration cut-offs apply: 12.5% for R20/21/22 and 20% for R36 and R37.

EEC classification number is 603-014-00-0.

2. GENERAL INFORMATION ON EXPOSURE

2-Butoxyethanol (2-BE) is used in many different applications. The main use is in paints and surface coatings, followed by cleaning products and inks. Other products which contain 2-BE include acrylic resin formulations, asphalt release agents, firefighting foam, leather protectors, oil

spill dispersants and photographic strip solutions. 2-BE is also used as a feedstock in the manufacture of other chemicals, for example, butyl glycol acetate (BGA).

In international databases, 2-BE is also listed as a solvent for greases, oils, dyestuffs and nitrocellulose resins and enamels. It has been used as an ingredient in agricultural chemicals, cosmetics and brake oils, and as a raw material in the production of phthalate and stearate plasticisers.

In Europe, the total EU production of all butyl glycol ethers is given in CEFIC statistics as 181,000 tonnes. Process chemistry predicts that approximately 50% of this will be 2-BE, that is approximately 90,000 tonnes. Virtually no 2-BE is believed to be imported into the EU (CEFIC, 1995).

The best estimates available for supplies of 2-BE to EU markets are presented in Table 1 (in tonnes per year). The final column gives the typical maximum 2-BE concentration in formulated products.

Table 1 - Volume* of 2-BE in the EU (by Product Type)

Product Type	Total	Industrial	Public	Typical Max %
Surface Coatings	70000	59600	10400	
- Anticorrosion coatings	2600	2600		1
- Can coating	9000	9000		7
- Coil coating	6500	6500		7
- Decorative retail (water based)	10400		10400	1.5
- Decorative trade (water based)	15500	15500		1.5
- General industrial (water based)	16800	16800		3
- Auto OEM (solvent based)	1300	1300		2
- Auto OEM (water based)	6500	6500		8
- Wood coating (water based)	1300	1300		2
Detergents and Cleaners	4000	3000	1000	10
Inks	5000	5000	0	20
Feedstock for BGA Production	11000	11000		
TOTALS	90000	78600	11400	

* tonnes per year

In an analysis of the use patterns of glycol ethers in Sweden over the period 1986-1993, the usage of 2-BE in 1993 was 2100 tonnes, of which 1680 tonnes were imported as 2-BE and the remainder imported in chemical products, mainly paints (Johanson and Rick 1996). In data from the Products Register, 666 products containing 2-BE were listed, with the use pattern (in terms of tonnes 2-BE) being 68% as solvent, 23% in paints and lacquers, 3% in binders, 3% in cleaning agents, and 3% in other uses.

An analysis of the uses of the 434 cleaning products identified during the national assessment in Australia revealed a wide variety of applications (as stated on the Material Safety Data Sheet and/or the label for each product). The main uses are tabled below.

Table 2 - Main Types of 2-BE Cleaning Products in Use in Australia

Use	Number	% of total	2-BE	
			min.	% max.
surface cleaner	214	49	0.57	71
floor stripper	49	11	< 1	30.5
glass/window cleaner	47	10	< 1	40
carpet cleaner	40	9	< 1	10-30
laundry detergent	15	4	< 1.5	10-30
rust remover	11	3	< 10	30-60
oven cleaner	11	3	< 1	10-30
ink/resin remover	9	2	1	10-93
others	38	9	< 10	94

Information from Europe indicates that usage of 2-BE in cosmetics is low. It is used as a solvent in hair products such as hair dyes.

3. ENVIRONMENT

3.1 Environmental Exposure

3.1.1 General Discussion

2-BE will enter the environment via effluent at sites where it is formulated into products and via the disposal of any wash water used in cleaning, printing and surface treatment processes. It will also enter the atmospheric compartment due to evaporation. Release to water is the predominant pathway for cleaning processes, whereas evaporation is the main pathway for the other major use, paints/surface coatings.

Biodegradation studies indicate that 2-BE will be readily degraded by micro-organisms present at sewage treatment plants. Ready biodegradability tests showed that 2-BE achieved a biodegradation rate of greater than 77% after 3 days and 100% after 7 days. A 20-day biochemical oxygen demand test and an Organisation for Economic Cooperation and Development (OECD) 28-day closed bottle test gave 2-BE degradation rates of 75% and 88% respectively. Literature data confirm these results.

Any 2-BE that passes through sewage treatment plants and enters receiving waters is likely to remain in the water column until biodegraded by micro-organisms present in the water. Accordingly 2-BE half-lives in surface water range from 4 weeks to 7 days. The complete miscibility of 2-BE in water suggests that volatilisation, adsorption and bioconcentration are not important fate processes. 2-BE is expected to have a short residence time in the atmosphere.

Disposal of waste 2-BE to landfill may result in contamination of groundwater. A K_{oc} of 67 for 2-BE indicates that it will be highly mobile in soil, and unlikely to partition from the water column to

organic matter contained in sediments and suspended solids. 2-BE has been detected in aquifers underlying a municipal landfill and a hazardous waste site in the USA.

2-Butoxyethanol was detected at 8 ug/m³ in 1 of 6 samples selected for GC-MS from indoor air samples collected from 14 homes and 1 small office in Italy (De Bortoli et al., 1986). The Environmental Protection Agency's volatile organic compounds national ambient database includes data on indoor air showing an average for 14 samples of 0.214 ppb (Shah & Singh, 1988)

2-Butoxyethanol is listed as a contaminant in drinking water samples analysed between September 1974 and January 1980 in a survey of US cities (Lucas, 1984). In Kentucky, USA, 2-BE was detected in ground water at a concentration of 23 ug/L in 1/7 samples collected in February 1974 near the Valley of Drums (Stonebreaker & Smith, 1980)

In Japan, 2-BE was detected in surface water at a concentration of 1310 and 5680 ppb in the water of the Hayashida River as a contaminant from leather industry effluents. The values represent levels after steam and vacuum distillation respectively (Yasuhura et al., 1981).

3.1.2 Predicted Environmental Concentration

The predicted environmental concentrations (PECs) were calculated on the basis of data available for the national Australian assessment, that is, a total volume of approximately 2500 tonnes, with 40% into cleaning products, approximately 50% in paints and surface coatings, and the remainder in inks and other applications. A daily output of 250 million litres from the sewage treatment plant was assumed.

In other countries, the use and release patterns may differ. For example, data from Europe indicates that the greater percentage of 2-BE goes into paints/surface coatings (see Table 1) and that the daily output from a sewage treatment plant may be 2 million litres. In these circumstances, the PECs may be different from the following concentrations calculated for a large metropolis.

In the following estimates, the PEC of 2-BE in water was calculated according to the methods in the Technical Guidance Document and formula from the USES model.

The assumptions used for calculating the PECs included:

- . All 2-BE used is released to the environment.
- . When used in cleaning products, 90% is released to water, with 10% to the atmosphere. All release to water is via the sewage treatment plant.
- . When used in paints/surface coatings; inks; and other uses, 10% is released to sewer, with 90% to the atmosphere due to evaporation.
- . 300 days per year of 2-BE handling.
- . Manufacture of 2-BE occurs on 300 days per year (at one site only), with 1% released to sewer, that is, a daily release of 67 kg.
- . In the absence of data, 40% use of 2-BE will be assumed to occur in the Sydney metropolitan area, for which the PEC_{local} is calculated.

Based on these assumptions, the following daily release figures through end use have been calculated.

Table 3 - Estimated Daily Release of 2-BE for End Use

	Cleaning products	Paints/surface coatings	Inks and other
Use per day (continental)	3.33 te	4.17 te	0.83 te
Amount to sewer (continental)	3000 kg	416.7 kg	83.3 kg
Amount to sewer (local)	1200 kg	166.7 kg	33.3 kg

PEC_(local)

The PEC_(local) for water can be calculated using the equation:

$$PEC_{\text{local(water)}} = C_{\text{eff}} / ((1 + K_{\text{p(susp)}}) \cdot C_{\text{(susp)}} \cdot D)$$

C_{eff} = the concentration of the chemical in the sewage treatment plant;

$K_{\text{p(susp)}}$ = suspended matter-water adsorption coefficient;

C_{susp} = concentration of suspended matter in receiving waters (default value 15 mg/L);

D = dilution factor (= 10).

$$C_{\text{eff}} = W \cdot (100 - P) / (100 \cdot Q)$$

where

W = emission rate (see values in Table 4);

Q = volume of waste water (= 250 million litres/day);

P = % removal in the sewage treatment plant (= 91%).

$$K_{\text{p(susp)}} = F_{\text{oc(susp)}} \cdot K_{\text{oc}}, \quad K_{\text{oc}} = a \cdot P_{\text{ow}} \quad (a = 0.411)$$

where

$F_{\text{oc(susp)}}$ = fraction organic carbon in suspended matter (= 100 mg/L);

P_{ow} = octanol-water partition coefficient (= 6.46).

For the Australian case, PEC_(local) is based in Sydney, where the Sewage Treatment Plant is assumed to carry a daily output of 250 million litres.

Because of the biodegradability of 2-BE, a high percentage could reasonably be expected to be removed from the Sewage Plant prior to release to receiving waters. According to the SIMPLETREAT model, 91% is eliminated in the Sewage Plant.

These equations have been used to calculate PEC_{local} for the water compartment based on release of 2-BE through its use as cleaning agents, in paints/surface coatings, and in inks and other applications. The PECs calculated are given in Table 4. The PEC value calculated for production is probably conservative as a release of 1% is used. Production is carried out in a closed system, with product being recovered during purging processes being recycled.

The PEC_{effluent} is equivalent to the $PEC_{\text{local}}(\text{surface water})$ before dilution. A dilution rate of 10 is used so values for PEC_{effluent} have also been calculated and are in Table 4.

Table 4 - Local PECs Calculated for the Aquatic Environment

Process	Emission rate to sewer (kg/day)	PEC_{local} ($\mu\text{g/L}$)	PEC_{effluent} ($\mu\text{g/L}$)
Production	67	2.4	24
Total use	1400	50.4	504
- in cleaning products	1200	43.2	432
- in paints/surface coatings	166.7	6	60
- in inks/other	33.3	1.2	12

NB: Figures are based on a total annual use of 2500 tonnes of 2-BE.

PEC (continental)

A continental PEC has been calculated based on an Australian population of 18 million people, with a total sewer output of 2700 million litres per day (150 L per person).

Assuming all 2-BE used is released, the daily continental release is 8.3 tonnes. Of this, 3.5 tonnes is released to sewer through end use activities. Based on these estimates, the continental concentration of 2-BE in receiving waters was estimated to be 12 $\mu\text{g/L}$.

Atmosphere

It has been estimated that 10% of 2-BE used in cleaning agents is released to the atmosphere, while 90% used in paints; inks; and other applications is released to the atmosphere through volatilisation.

A PEC (local) for air release of 2-BE from end uses can be calculated. The following equation can be used to calculate the concentration in air at 100 m from the site.

$$C_{\text{air}} = \text{Emission} \times C_{\text{stdair}}$$

where C_{air} = concentration in air at 100 m from a point source (kg/m^3);
 Emission = emission rate to air (kg/sec); and
 C_{stdair} = standard concentration in air at source strength of 1 kg/sec ($= 24 \times 10^{-6}$).

Table 5 - Local PECs Calculated for the Atmospheric Environment

Process	Emission to air (kg/day)	$PEC_{\text{local}}(\mu\text{g/m}^3)$
Use in cleaning products	133.3	37
Use in paints/surface coatings	1500	417

Use in inks/other	300	83
Total	1933	537

These are conservative estimates as they assume all release is from a single point source.

2-BE is expected to have a short half-life in air through reaction with hydroxyl radicals, with a half-life of less than 1 day. The level 1 Mackay fugacity model indicates that, at equilibrium, 84% of 2-BE will partition to water, and 16% will partition to air.

3.2 Effects on the Environment

3.2.1 Aquatic Effects

The results of aquatic toxicity studies are summarised in table 6.

Table 6 - Aquatic Toxicity Results

Test	Species	Result (mg/L)	Reference
Acute toxicity	Fish		
	Fathead minnow (F)	4d LC ₅₀ = 2137	Dow Chemical (1979)
	Sheepshead minnow (S)	4d LC ₅₀ = 116	US EPA (1984)
	Inland silverside (F)	4d LC ₅₀ = 1250	AQUIRE
	Invertebrates		
	Oyster (S)	4d LC ₅₀ = 89	US EPA (1984)
	White shrimp (S)	4d LC ₅₀ = 130	US EPA (1984)
	Brine shrimp (S)	24h LC ₅₀ = 1000	AQUIRE
	<i>Daphnia magna</i> (F)	2d LC ₅₀ = 835 24h EC ₅₀ = 1815	Dow Chemical (1979) AQUIRE
Growth inhibition	Algae		
	Green algae	7d EC ₅₀ > 1000	Dow Chemical USA (1988)
	Blue-green algae	EC ₅₀ > 35	AQUIRE
	Micro-organisms		
	Sewage bacteria	16h IC ₅₀ > 1000	Union Carbide Chemicals and Plastics Co. Inc. (1989)

F=Freshwater species; S=Saltwater species

The lowest definitive LC₅₀ result was for the oyster (*Crassostrea virginica*) and was 89.4 mg/L. This was chosen over the result obtained for testing on blue green algae, as this result is a toxicity threshold and was therefore considered inappropriate to base a PNEC on. A good range of test results are available. Even so, an assessment factor of 1000 was used. While this is very conservative, it will demonstrate the potential hazard of 2-BE in a worst case situation. Applying the assessment factor of 1000, the PNEC is 89.4 µg.L⁻¹.

3.2.2 Terrestrial Effects

No data available.

3.3 Initial Assessment for the Environment

Aquatic Compartment

PEC/PNEC ratios for the aquatic compartment can be calculated using the worst-case local scenario, in this instance, the PEC (local) of 52.8 µg/L. This was based on a worst case emission factor from 40% of all 2-BE being released in the Sydney metropolitan area.

The PEC/PNEC ratio has been calculated for local and continental compartments as follows:

$$\text{PEC/PNEC}_{\text{local}} = 0.59$$

$$\text{PEC/PNEC}_{\text{continental}} = 0.13$$

These ratios suggest that 2-BE is unlikely to cause adverse effects in the aquatic environment.

The risk of 2-BE to sewage micro-organisms is considered to be minimal as the $\text{PEC}_{\text{effluent}}$ figure of approximately 528 µg/L (Table 4) is several orders of magnitude below the only available test result of 16h $\text{IC}_{50} > 1000$ mg/L.

4. HUMAN HEALTH

4.1 Human Exposure

4.1.1 Occupational Exposure

The major routes of exposure to 2-BE are inhalation and skin absorption. 2-BE is a liquid which is miscible with water. It is readily absorbed through the skin, including absorption from aqueous solution, and in vapour and aerosol form. The total exposure of workers to 2-BE must take into account the inhalation uptake of vapours and aerosols and the dermal absorption of 2-BE in liquid, vapour and aerosol form.

Exposure estimates were calculated from the available monitoring data and by modelling. Measured data were limited, particularly for dermal exposure. The worst-case estimates generated in this exposure assessment are considered to be 'feasible' worst-case estimates, as they describe high end or maximum exposures in 'feasible but not unrealistic' situations. The estimates are not intended to account for extreme or unusual use scenarios which are unlikely to occur in the workplace. The vast majority of occupational exposures are expected to be well below these estimates.

For occupational exposure to vapours, a respiratory rate of 1.3 m³/h and a bioavailability of 0.75 were assumed. Based on toxicological data, it was assumed that an additional 20% of the vapour uptake was due to dermal absorption. For the dermal absorption of 2-BE liquid, a skin absorption rate of 0.2 mg/cm²/h and a skin surface area of 1000 cm² were assumed. For all occupational exposure estimates, a body weight of 70 kg was assumed. Details of occupational exposure estimates are given in Appendix 1.

4.1.1.1 Exposure during manufacture

2-BE is manufactured by the reaction of n-butanol and ethylene oxide. The process is enclosed as extensive precautions are taken to prevent and minimise exposure to workers in the production area, due to the toxicity of the ethylene oxide feedstock.

2-BE is stored in sealed tanks which are banded to contain any spills.

Exposure during manufacture is low as the process is sealed. Exposure during transfer to tankers or drums is generally minimised by the use of automated filling, where the operator is segregated from the area during transfer, and the use of local exhaust ventilation. Incidental exposure may occur when the process is breached or when spills occur. Exposure may occur during maintenance activities, however, the purging of plant and equipment is generally standard practice.

Atmospheric monitoring for 2-BE is usually conducted regularly by manufacturers in their plant areas (see table 7).

Table 7 - Measured Inhalation Data for Manufacture

Manufacturer	Monitoring Area	No. of readings	Mean ppm	Maximum ppm
BASF (EU)	Production	97	0.09	1.2
	Filling	66	1.3	5.3*
	Technical unit	9	0.25	1.2
	Laboratory	14	1.3	11*
	Various	8	0.5	2.7
BP (EU)	All	311	< 0.1	1.6
Eastman (US)	Production	16		< 0.04
	Tanker loading	11	< 0.25	1.8
Huls (EU)	Production	30	< 0.14	0.31
	Filling	10	< 0.14	0.22
	Laboratory/Sampling	20	< 0.38	1.1
ICI (Australia)	All (personal monitoring)		0.1	1.8
	Maintenance (area)			

* These values are reported as outliers by the department of Work Safety (Germany).

The above results are supported by monitoring data available for a US plant. For a similar process, where the manufacturing operation is also enclosed, the highest results were obtained during drum filling, with a time-weighted average (TWA) reading of 1.7 ppm (8.3 mg/m³) obtained in area monitoring. The highest personal monitoring reading was 0.1 ppm (0.5 mg/m³). During drum filling, local exhaust ventilation was in place to minimise inhalation exposure in case of spills.

Taking 3 ppm (14.7 mg/m³) as a maximum atmospheric concentration (taken from Table 7, where highest maximum reading was 2.7 ppm), the estimated daily dose for exposure to 2-BE vapours (inhalation and dermal) during manufacture is 2.0 mg/kg/day.

For dermal exposure to 2-BE liquid during manufacture, it is assumed that skin contact will be incidental, that is, for 1% of the work period. The estimated dermal exposure is 0.2 mg/kg/day.

Therefore, the combined dermal and inhalation exposure during manufacture would not be expected to exceed 2.2 mg/kg/day.

4.1.1.2 Exposure during formulation

During the formulation of products containing 2-BE, workers may be exposed to 2-BE during preweighing before mixing, during transfer to the mixing tank, during mixing and during the filling of containers with product. The whole operation is generally carried out at room temperature.

The potential exposure of workers to 2-BE during mixing is variable as the process may be enclosed or relatively open. When the transfer of 2-BE to the mixing vessel is carried out in a sealed system, potential exposure will be minimal, but when the operator adds the raw materials directly by drum to the mixing tank, exposure may be greater due to possible splashing and vapour and/or aerosol generation. Information obtained from the national assessment of 2-BE in Australia indicated that a number of formulators of cleaning products containing 2-BE use the latter procedure and that approximately 50% of formulators carry out mixing in open top tanks, with greater potential for exposure.

There is potential for worker exposure during the product filling operation. The design of the filling operation will influence exposure, for example, if the packing line is enclosed at the point of filling, then inhalation exposure will be reduced. If filling is an automatic operation with containers pneumatically filled, then exposure is likely to be lower.

Little measured data were available for exposure during the formulation of products containing 2-BE. In exposure data supplied by one large UK formulator, Holden (part of the ICI group), 2-BE was detected in 15 cases out of 89 personal monitoring samples, with the mean 0.7 ppm and the maximum 1.5 ppm. In personal monitoring data from Germany, 2-BE was generally below the analytical detection limit, with and without mechanical ventilation. In 204 measurements during weighing and filling operations (bead mills), 95% of samples were below 2.5 ppm (12 mg/m³).

In the scientific literature, in the only data available for formulation, the maximum TWA air concentration for workers in a varnish production plant was 8.1 ppm (39.7 mg/m³), the 2-BE content in the product(s) not being stated.

Occupational exposures were calculated for a range of 2-BE concentrations. As operators are generally involved in both mixing and filling, the estimates of exposure are for the formulation process as a whole. Considering the process and the tasks during formulation where exposure may occur, inhalation exposure is assumed to be continuous and dermal exposure intermittent (skin contact for 20% of the work time). Inhalation estimates were based on the available monitoring data for formulation and cleaning operations. The following combined inhalation and dermal estimates (in mg/kg/day) were calculated for an 8-hour work period (Table 8).

Table 8 - Exposure Estimates for Formulation*

% 2-BE	Max. 2-BE in air (ppm)	Max. daily dose (est.) (mg/kg/d)
10	2	1.9

30	10	8.2
60	10	9.5

* See Appendix 1

4.1.1.3 Exposure during use of products containing 2-BE

A considerable amount of atmospheric monitoring data for 2-BE is available for exposure during use of the various products containing the chemical. In some cases, biological monitoring (for the major metabolite of 2-BE, 2-butoxyacetic acid (BAA), has also been conducted. The available atmospheric monitoring data for 2-BE is summarised in table 9.

Table 9 - Atmospheric Monitoring Data for 2-BE during Product Use

Operation	% 2-BE	Mean ppm	Max. ppm	Reference
<i>Cleaning</i>				
Car window cleaning	5.7-21.2	1.8	7.3	Vincent (1993)
Office cleaning	0.9-9.8	0.3	0.7	Vincent (1993)
Floor scrubbing	0.3		1.6	NIOSH (1979)
Cleaning of floors		n.d	<9.6 ¹	BGAA (1996)
General window cleaning		< 0.2		NIOSH (1983)
Schoolroom cleaning	0.25	< 0.7		NICNAS (1996)
Cleaning print machines	10-50	5.2	9.7	NIOSH (May 1987)
Cleaning printing press rollers		0.3	0.5	NIOSH (1990)
Surface cleaning		n.d	<4.9 ¹	BGAA (1996)
<i>Printing</i>				
General printing		0.6	0.8	Sakai et al (1993)
Printing (various)		0.8		Veulemans et al (1987)
		0.2	0.7	Vincent et al (1996)
		4	5	NIOSH (1986)
Silk screening	100	25 ²	36	NIOSH (Dec 1987)
	100	63 ²	169	NIOSH (Dec 1987)
	to 45%	6.8		NIOSH (1985)
		0.2	1.6	Vincent et al (1996)
	n/a	n.d	<1.6 ³	BGAA (1996)

<i>Painting/Surface treatment</i>			
General painting		4	Veulemans et al (1987)
House painting		0.01	0.015 Norback et al (1996)
Painting (various)		0.1	0.8 Vincent et al (1996)
Fabrication of paints		0.4	45 Vincent et al (1996)
Cataphoresis		0.8	6.2 Vincent et al (1996)
Staining/varnishing		5	71 Denkhaus et al (1986)
		0.2	2.4 Vincent et al (1996)
Floor making		2.6	NIOSH (1985)
Spray painting	to 55%	0.4	Winder & Turner (1992)
Spray painting (manual)		n.d.	<3.1 ¹ BGAA (1996)
Surface coating (manual)		n.d.	<8.4 ¹ BGAA (1996)
Car repair		1.2	BGAA (1996)
Car coating		0.1	0.1 Veulemans et al (1987) Vincent et al (1996)
<i>All uses</i>			< 25 Guirguis et al (1994)

n.d. non-detectable

n/a not available

1 95% samples below this value

2 In this study, only 2 samples for both personal monitoring and area monitoring were analysed.

3 90% samples below this value

Biological monitoring was also conducted in several studies by Vincent and Sakai. Post-shift readings for BAA in urine (expressed as mg/g creatinine) are listed in Table 10.

Table 10 - Biological Monitoring Data for 2-BE during Product Use

Operation	% 2-BE	Mean BAA	Max. BAA	Reference
<i>Cleaning</i>				
Car window cleaning	5.7-21.2	96.5	371	Vincent (1993, June)
Office cleaning	0.9-9.8	< 2	3.3	Vincent (1993, June)
<i>Printing</i>				
General printing		3.9	9.9	Sakai et al (1993)
Printing (various)		2.2	7.1	Vincent et al (1996)
Silk screening		n.d.	n.d.	Vincent et al (1996)
<i>Painting/Surface treatment</i>				
Painting (various)		4	63	Vincent et al (1996)
Fabrication of paints		3.9	60	Vincent et al (1996)
Cataphoresis		17.9	210	Vincent et al (1996)
Staining/varnishing		4	34	Vincent et al (1996)
Car coating		2.3	28	Vincent et al (1996)
<i>Cosmetics</i>	< 0.5-5	n.d.	n.d.	Vincent et al (1996)

<i>Use of cutting oils</i>	1-5	3.2	8.3	Vincent et al (1996)
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n.d. non-detectable

Cleaning

A large number of cleaning products contain 2-BE, so a large number of workers are potentially exposed to the chemical. Exposure to 2-BE during cleaning is extremely variable, due to differences in frequency and duration of use, strength of solution used, method of application and precautions taken during use.

The strength of solution used in the cleaning process is generally low as the product is usually diluted substantially before use, for example, most surface cleaners specify a dilution ratio in the range 1:3 to 1:100, depending on the application and the soil loading. A large proportion of cleaning products contain less than 10% 2-BE, so the final strength of solution is often less than 1%. In the national Australian assessment, a random survey of 20 general surface cleaning products containing < 10% 2-BE indicated that the dilution ratio ranged from 1:1 to 1:250, with most ratios in the 1:5 to 1:100 range. Some products are sold as high level concentrates (> 50% 2-BE) which must be diluted with large volumes of water before use.

A number of different methods are used to apply the cleaning solution, for example, washing, wiping, mopping and spraying. In the national Australian assessment, approximately half of the cleaning products were used in spray form, with a small number marketed in aerosol spray cans or trigger packs.

Occupational exposures were calculated for a range of 2-BE concentrations. Both inhalation and dermal exposure were assumed to be continuous over the whole work period. Inhalation estimates were based on the available monitoring data for cleaning activities (see Table 9). Dermal estimates assumed continuous skin contact over the work period. The following combined inhalation and dermal exposure dose estimates (in mg/kg/day) were obtained for an 8-hour work period (table 11).

Table 11 - Exposure Estimates for Use of Cleaning Products*

% 2-BE	Max. 2-BE in air (ppm)	Max. daily dose (mg/kg/d)
0.1	2	1.4
1.0	2	1.6
10	4	5.0
30	10	13.7

*See Appendix 1

Printing

2-BE is used as a coupling solvent in a range of specialist inks including silk screen inks used by professional trades. The inks contain high levels of solids and up to approximately 20% 2-BE.

Some monitoring data are available for exposure during the use of inks containing 2-BE (see Table 9). However, some of the data are not representative of typical work scenarios in printing, for example, in the NIOSH (1987) study, the workers were exposed to neat 2-BE in open spray troughs and wash table areas. Consequently, the other data were used in calculating exposure during silk

screening and general printing tasks using inks containing 2-BE. Dermal estimates assumed continuous skin contact over the work period. The following combined inhalation and dermal exposure estimates (in mg/kg/day) were obtained for an 8-hour work period.

Table 12 - Exposure Estimates for Use of 2-BE in Printing*

Activity	% 2-BE	Max. 2-BE in air (ppm)	Max. daily dose (mg/kg/d)
Silk screening	50	10	18.2
General printing	20	2	6.0

* See Appendix 1

Paints/Surface coatings

2-BE is used in a wide variety of paints and surface coatings, particularly in water-based type. The concentration of 2-BE varies from one product to another, with European exposure data indicating that up to 8% 2-BE is used in the various formulations (see Table 1). Due to high volume use, a large number of workers are potentially exposed to 2-BE.

Exposure to 2-BE during painting is extremely variable, due to differences in frequency and duration of use, concentration of 2-BE in the paint, method of application and precautions taken during use. This variation is reflected in the atmospheric monitoring data available for 2-BE during painting and surface treatment (see Table 9).

Assuming a maximum atmospheric concentration of 10 ppm (49 mg/m³) TWA for use of a paint/surface coating containing 10% 2-BE, an estimate for exposure to vapours is 6.8 mg/kg/day.

Dermal estimates assumed continuous skin contact over the work period (8 hours). This resulted in an estimate for dermal exposure to liquid 2-BE of 2.3 mg/kg/day.

Therefore, the combined inhalation and dermal daily dose of 2-BE during an 8 hour work period would not be expected to exceed 9.1 mg/kg/day.

4.1.1.4 Exposure during use as feedstock

2-BE is used as a chemical intermediate to produce butyl glycol acetate (BGA). As the transfer to reaction vessels is via a sealed system, exposure is negligible.

4.1.2 Consumer Exposure

Cleaning

Consumers are potentially exposed to 2-BE during the use of cleaning products containing the chemical, for example, during general surface cleaning. Cleaning products for consumer use which contain 2-BE generally contain less than 10% 2-BE are diluted substantially before use. Some trigger packs containing low concentrations of 2-BE are available to consumers. Inhalation and dermal exposure may arise during use. Details of consumer exposure estimates are given in Appendix 1.

Assuming a maximum atmospheric concentration of 4 ppm (19.6 mg/m³), a respiratory rate of 0.8 m³/h and a body weight of 60 kg, the estimate for exposure to vapours for a cleaning time of one hour is 0.25 mg/kg/event.

For dermal exposure, assuming a skin absorption rate of 0.2 mg/cm²/h, a skin surface area of 1000 cm², and continuous skin contact over a one hour cleaning period, the estimate for dermal exposure to a 10% solution is 0.33 mg/kg/event. Therefore, the combined inhalation and dermal exposure for use of a 10% cleaning solution for one hour would not be expected to exceed 0.58 mg/kg/event.

Paints/Surface coatings

Consumers are potentially exposed to 2-BE during the use of paints containing the chemical. European exposure data indicates that paints available for consumer use which contain 2-BE typically contain less than 1.5% 2-BE (see Table 1). Inhalation and dermal exposure may arise during use.

Assuming a maximum atmospheric concentration of 2 ppm (9.8 mg/m³), a respiratory rate of 0.8 m³/h and a body weight of 60 kg, the estimate for exposure to vapours for a painting time of 6 h/day is 0.75 mg/kg/day.

For dermal exposure, assuming a skin absorption rate of 0.2 mg/cm²/h, a skin surface area of 1000 cm², and continuous skin contact over a 6 hour painting period, the estimate for dermal exposure to a paint containing 1.5% 2-BE is 0.3 mg/kg/day. Therefore, the combined inhalation and dermal exposure for use of a paint containing 1.5% 2-BE for 6 hours would not be expected to exceed 1.05 mg/kg/day.

Cosmetics

2-BE is listed as being used as a solvent in cosmetics, although EU data indicates that usage may be very low in Europe. According to the Cosmetic Ingredient Dictionary, it is used in hair dyes. Solvents in hair dye formulations can be present at concentrations up to 10%.

The EU Scientific Committee on Cosmetology (SCC) advise that the quantity of hair dye used is likely to be approximately 100 mL (= g) once a month for permanent dyes and 35 mL once a week for semi-permanent dyes. The amount of 2-BE applied would therefore be 10/28 = 0.36 g/day for permanent dyes and 3.5/7 = 0.5 g/day for semi-permanent dyes.

It is estimated that 10% of the product remains on the head after rinsing, of which 10% is available for absorption through the scalp (the other 90% remains with the hair), that is, 1% of the amount applied may be absorbed. Therefore, exposure may be up to 3.6 mg/day for permanent dyes and up to 5 mg/day for semi-permanent dyes.

4.1.3 Indirect Exposure via the Environment

Indirect exposure of the public at large to 2-BE via the environment is restricted to the use of products containing 2-BE in public places, for example, paints and cleaning agents in public buildings. Due to the low concentration of 2-BE in paints and cleaning solutions (generally less than 10%), the low volatility of 2-BE and its ready biodegradability in the environment, indirect exposure is likely to be minimal.

4.2 Effects on Human Health

4.2.1 Kinetics and Metabolism

The toxicokinetics of 2-BE have been well investigated in laboratory animals, particularly the F344 rat, and some studies have been conducted on human volunteers. The results of many of the studies have been reported in the open literature. In order to optimise the extrapolation of data from one species to another, pharmacokinetic models have been developed.

2-BE is well absorbed via the inhalation, oral and dermal routes. Absorption studies in various species, including humans, have shown that 2-BE is rapidly absorbed through the skin, including absorption from aqueous solution. There is some evidence to indicate that 2-BE in aqueous solution is more readily absorbed than from neat liquid (Bartnik et al., 1987; Johanson & Fernstrom, 1988). Dermal studies in humans and human skin specimens indicate that the dermal absorption rate is most likely in the order of 0.2 mg/cm²/h (Dugard et al., 1984). From the results of several inhalation studies in volunteers, the respiratory uptake was approximately 57-78% of the inspired amount (Johanson et al., 1986; Johanson & Boman, 1991). Recent human studies and predictions from the physiologically-based pharmacokinetic (PBPK) model of Corley et al (1994) indicate that the dermal absorption of vapour may contribute up to approximately 20% of the total vapour uptake.

Animal studies have shown that 2-BE is rapidly distributed to all tissues via the blood stream. In a gavage study in F344 rats with ¹⁴C-labelled 2-BE, the highest levels of radioactivity were found in the forestomach, then the liver, kidneys, spleen and glandular stomach (Ghanayem et al., 1987 (b)). In a dermal study in male Wistar rats, ¹⁴C-labelled 2-BE was distributed widely to all tissues, with the greatest level of radioactivity in the spleen and thymus, followed by the liver (Bartnik et al., 1987).

Studies in animals and humans have indicated that the major metabolic pathways of 2-BE are similar in various species. In the different species, 2-BE is efficiently metabolised, mainly to BAA, which is formed by oxidation by alcohol/aldehyde dehydrogenase. In animals, smaller amounts of the glucuronide and sulfate conjugates and ethylene glycol can be formed by other metabolic pathways, following exposure at high doses. In human studies, the glutamine conjugate of BAA has been detected in urine following exposure to 2-BE, and suggests an additional detoxification pathway in humans (Rettenmeier et al., 1993). 2-BE is removed from the blood, with an elimination half-life of approximately 40 to 80 minutes in humans (Johanson et al., 1986). The major metabolite BAA is rapidly excreted in urine in animals and humans with an urinary excretion half-life of approximately 3-6 hours in humans (Johanson et al., 1986). In human studies, wide variations in absorption and excretion rates between subjects have been found.

A number of different PBPK models have been proposed for 2-BE to enable the extrapolation of the effects observed in one species to another, in particular the effects in the rat to humans. Johanson et al (1986) proposed a PBPK model for the inhalation of 2-BE in humans, but recent developments of the model by Shyr et al (1993) and Corley et al (1994) have incorporated more data, including that from rat studies and other routes of exposure. The Corley model is a dual 2-BE-BAA model developed to incorporate more physiological and biochemical information on BAA, the principal metabolite of 2-BE. The model also incorporates the other metabolic pathways identified in metabolism studies. In validation work against a wide variety of test results, including data from rat and human studies and data from different exposure routes, values predicted by the model generally agreed well with experimental data. The physiologically-based pharmacokinetic model developed by Corley et al (1994), successfully estimated the disposition of 2-butoxyethanol and BAA under a

variety of exposure scenarios. Based on data from absorption studies indicating that 2-butoxyethanol was more readily absorbed from aqueous solution, and assuming that 10% of body area was exposed (approximately 2000 cm²), Corley et al's model predicted as a worst-case scenario that the skin absorption of undiluted 2-butoxyethanol over 6h would lead to a BAA blood concentration of 0.37 mM, and that absorption of a 40% solution would result in 1.3 mM BAA.

4.2.2 Human Health Effects

Exposure to 2-BE vapour may result in irritation of the eyes, nose and throat, headache and nausea. In controlled studies in volunteers, nose and eye irritation were observed at 113 ppm, nausea and headache at 100 ppm (Carpenter et al., 1956), but no adverse effects were noted at 20 or 50 ppm (Johanson et al., 1956; Johanson & Boman, 1991). Workers using 2-BE cleaning products have reported respiratory irritant effects, nausea, headaches and tiredness, however the atmospheric levels were unknown. Isolated cases of skin reddening and dermatitis have been reported in workers using cleaning products on a regular basis, however, as the products contain many ingredients, the irritant effects cannot be solely attributed to 2-butoxyethanol. In general, occupational case studies have not identified skin irritancy as a significant effect in exposed persons. In a patch test in volunteers, 2-BE was not a skin sensitiser (TKL Research Inc., 1992).

In a study conducted in human volunteers (2 men, 1 woman) the red blood cell fragility was unaffected. Exposure was to 195 ppm for two four-hour periods. BAA was excreted in the urine of the woman and 1 male but only a trace was detected in the second male. Symptoms included irritation of the eyes, nose and throat, unpleasant taste and headache (Carpenter et al., 1956).

Haemolytic effects have only been observed in humans who have ingested large quantities (30-60g) of 2-BE (Rambourg-Schepens et al., 1988; Gijzenbergh et al., 1989). The ingestion of large quantities of 2-BE (30-106g) may also result in coma, metabolic acidosis, shock and respiratory distress (Rambourg-Schepens et al., 1988; Gijzenbergh et al., 1989; Bauer et al., 1992). Respiratory distress was observed in one case report and may have occurred as a result of aspiration of refluxed stomach contents rather than being directly attributable to exposure to 2-BE (Bauer et al., 1992).

4.2.3 Effects in Experimental Animals and *In Vitro* Test Systems

The large number of good quality studies conducted in animals and *in vitro* test systems have enabled the health effects of 2-BE to be well characterised. The main effect observed in both acute and repeated dose animal toxicity studies is haematotoxicity, with the principal haemolytic agent being BAA. The species differences in susceptibility to this effect are considerable, with rats and mice the most susceptible, rabbits less susceptible and humans and guinea-pigs the least susceptible. *In vitro* studies indicate that there is an order of magnitude difference in the susceptibility to BAA of rat red blood cells compared to humans, with rats being more susceptible.

Acute toxicity

The acute toxicity of 2-BE is moderate by all routes of exposure and is, in general, higher than other glycol ethers. The oral LD₅₀ (rat) is 530-3000 mg/kg, dermal LD₅₀ (rabbit) is 100-610 mg/kg, and inhalation 4h LC₅₀ (rat) is 2.2-2.4 mg/L (450-486 ppm) (ECETOC, 1994). The dermal LD₅₀ of 100 mg/kg (Duprat and Gradski, 1979) is lower than (no observable adverse effect level) NOAELs and (lowest observable adverse effect level) LOAELs of short-term repeated dose studies and is therefore considered questionable. Death was generally caused by narcosis or respiratory failure and congestion and damage to the kidney, liver, lungs and spleen were often observed at necropsy.

Haemolytic effects were observed in most acute studies. Acute dermal studies show that 2-BE is readily absorbed through the skin.

Irritant effects

2-BE is a severe eye irritant (Bushy Run Research Centre, 1980 ; Carreon, 1981; Kennah et al., 1989; Jacobs, 1992). Results of skin irritation studies are conflicting, however, 2-BE is considered to be a mild to moderate skin irritant in test animals (Tyler, 1984; Gingell et al., 1994; ECETOC, 1994). The results of one sensory irritation study in mice indicate that 2-BE vapour may be irritating to the nose and throat (Kane et al., 1980). Skin sensitisation studies were negative (Unilever Research, 1989; Zissu 1995), and immunotoxicity studies in the rat and guinea pig did not result in any significant effect on the immune response (Grant et al 1985; Bartnik et al., 1987; Ghanayem et al., 1987 (b); Crevel et al., 1990).

Repeated dose toxicity

Several short-term and subchronic repeated dose studies in animals by all routes of exposure have been performed. The critical effect seen in repeated dose studies is haematotoxicity. The main signs of toxicity at high doses include anaemia (decreased red blood cell count and haematocrit, decreased mean cell haemoglobin concentration and increased mean cell volume) and haemoglobinuria due to haemolysis of the red blood cells. At low doses, haemolytic effects are transient, generally occurring during the first days of exposure only (Werner et al., 1943; Carpenter et al., 1956; Dodd et al., 1983). There is some evidence of haemopoiesis occurring as a compensatory mechanism, such as spleen hyperplasia. In addition, this transience could be due in part to the replacement of older red blood cells with younger more resistant ones, as *in vitro* test results indicate that younger red blood cells are more resistant to haemolysis than older ones. Haematotoxicity in rats appears to be age-related, with the effects more severe in older rats.

The repeated dose studies also indicate that there are significant species differences in the susceptibility to the haemolytic effects of 2-BE. Rats appear to be the most sensitive species (Carpenter et al., 1956). The most relevant inhalation studies and the haemolytic effects observed are summarised in table 13.

In a 90-day inhalation study in rats, the NOAEL was 24.6 ppm. In this study 16 male and 16 female Fischer 344 rats were exposed (whole body) to 2-BE vapours at 0, 5.0, 24.6 or 77 ppm. Ten animals/sex/dose were exposed for 6 hrs/day for 13 weeks while the other 6 rats/sex/dose were sacrificed after 6 weeks for blood analysis. Haematological effects were observed in rats exposed to 77 ppm, particularly the females. After 6 weeks of exposure statistically significant decreases were observed in haemoglobin, red blood cell count and haematocrit and an increase in mean corpuscular (or cell) volume (MCH). These effects were noted only in the females. At the end of 13 weeks statistically significant decrease in the red blood cell count was seen in male and female rats and an increase in MCH in female rats. A small but not statistically significant decrease in haemoglobin and haematocrit and an increase in white blood cells was observed in male rats. There was no sign of blood in the urine of the animals. No effect on red blood cell osmotic fragility was observed. No significant gross or microscopic lesions were observed at necropsy and there were no significant effects on the lungs, liver, kidney or testes (Snellings et al., 1981).

Table 13 - Summary of *In Vivo* Haematological Studies (Inhalation)

<i>Study</i>	<i>Species</i>	<i>Dose/Duration</i>	<i>Haemolytic Effect</i>
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Carpenter et al (1956)	rat	62 ppm/4h	Increased RBC fragility
		54-432 ppm/7h, 30d	Increased fragility (all doses) Haemoglobinuria (≥ 203 ppm)
		113 ppm/4h	Increased fragility
	mouse	112-400 ppm/7h, 30-90d	Increased fragility (all doses) Haemoglobinuria (≥ 200 ppm)
	rabbit	125, 197 ppm/7h	Increased fragility (both doses)
	guinea pig	665 ppm/8h	No effect
	human	113 ppm/4h	No effect
		195 ppm/8h	No effect
Longo & Dodd (1981)	rat	20 ppm/6h, 9d	No effect
		86 ppm/6h, 9d	Haemolysis
Snellings et al (1981)	rat	25 ppm/6h, 90d	No effect
		77 ppm/6h, 90d	Haemolysis
Johanson (1994)	rat	20 ppm/12d	No haemolysis
		100 ppm/12d	No haemolysis

In a 90-day dermal study in rabbits, the NOAEL was 150 mg/kg/day (WIL Research Laboratories Inc., 1983). In a 90-day drinking water rat study conducted by the US National Toxicology Program (NTP), the NOAEL was 129 mg/kg/day for male rats, but no NOAEL could be established for the females as slight anaemia was observed at the lowest dose (82 mg/kg/day) (NTP, 1993).

Effects other than haemolysis which have been observed in repeated-dose studies include changes to the liver, kidney, spleen and thymus, with these effects considered secondary to haemolysis as they are seen at levels at or above haematotoxic doses.

Fertility and reproductive toxicity

In fertility studies, minor changes in sperm concentration and the oestrous cycle were noted in a drinking water rat study but adverse effects have been observed only at or above doses which are toxic in other respects (NTP, 1993). In a continuous breeding study in mice, significant adverse effects were observed only at very high dose levels which caused severe maternal toxicity (Morrissey et al., 1989; Heindel et al., 1990). These results for 2-BE are in contrast to the lower molecular weight homologues, 2-methoxyethanol and 2-ethoxyethanol, which both cause testicular degeneration (Nagano et al., 1984; Morrissey et al., 1989; Exon et al., 1991). In other reproductive studies, developmental effects were observed only at maternally toxic doses. No evidence of teratogenicity was observed in any studies, again in contrast to 2-methoxyethanol and 2-ethoxyethanol (Tesh, 1976; Bushy Run Research Center, 1984; Wier et al., 1987; Sleet et al., 1989; Working & Mattison, 1993).

Genotoxicity

2-BE has tested negative in a wide variety of well-conducted *in vitro* assays, including gene mutation (Chiewchanwit & Au, 1995), chromosomal aberration (Villalabos-Pietrini et al., 1989); and DNA effect assays. These assays were generally conducted at both cytotoxic and non-cytotoxic doses. In a recent study, 2-BE was a weakly positive inducer of gene mutations, sister chromatid exchanges and aneuploidy in V79 cells at high doses (Elias et al., 1996). 2-BE was negative in an *in vivo* mouse micronucleus assay (Elias et al., 1996). Based on the available data, 2-BE is unlikely to be genotoxic.

Carcinogenicity

No 2-year carcinogenicity studies were available but an NTP inhalation study in rats and mice is under way.

In vitro Haematological Studies

In vitro studies have confirmed the species differences observed in *in vivo* studies (see Table 14). In particular, the studies have shown that human red blood cells are at least ten times less sensitive than rat red blood cells to the haemolytic effects of BAA (Bartnik et al., 1987; Ghanayem, 1989). Studies demonstrated that haemolysis is preceded by swelling, increased osmotic fragility and decreased cell deformability of red blood cells. Therefore, the evidence indicates that the haemolytic effects are a result of changes to the cell membrane, rather than effects on the bone marrow (Ghanayem et al., 1990; Udden & Patton, 1994). The haemolytic resistance of red blood cells from potentially susceptible humans was studied. The red blood cells from healthy young adults, aged persons, patients with sickle cell disease and persons with hereditary spherocytosis were treated with 2mM BAA for 4 hrs. Haemolysis in treated cells was higher than controls for aged adults, but the difference was not statistically significant. The deformability of red cells from persons with sickle cell disease or hereditary spherocytosis was reduced, but BAA had no added effect (Udden, 1994).

Table 14 - Summary of *In Vitro* Haematological Studies

<i>Study</i>	<i>Species</i>	<i>Exposure Duration</i>	<i>Dose (mM BAA)</i>	<i>Effect</i>
Bartnik et al (1987)	rat	1h	7.5	Haemolysis
	human	1h	15	No effect
	rat	3h	3.75	Haemolysis
	human	3h	5	No effect
Ghanayem (1989)	rat	4h	0.5	Haemolysis
	human	4h	2	No effect
			4	Slight swelling
			8	Slight haemolysis

Ghanayem & Sullivan (1993)	rat	4h	2	Haemolysis
	rabbit		2	Swelling
	human		2	No effect
Udden & Patton (1994)	rat	6h	0.2	Slight haemolysis preceded by swelling
		4h	2	Significant haemolysis preceded by swelling

4.3 Initial Assessment for Human Health

4.3.1 General Aspects

The critical effects identified for acute exposure to 2-BE are eye and respiratory irritation, with irritation observed in controlled studies at 113 ppm but not at 100 ppm. In most work situations, the risk of irritant effects is low as the concentration of 2-BE is low in most products and 2-BE has a low volatility. However, the risk may be increased where aerosols are generated, heat is used, or where products are used in spray form. Based on human evidence, 2-BE is not classified as a skin irritant, but slight irritation may occur after repeated skin contact. It has been demonstrated that skin absorption can occur in the absence of irritation.

The critical effect (that is, the most sensitive endpoint) identified in animal studies for repeated or prolonged exposure to 2-BE is haematotoxicity. As the haematological effects are transient at lower doses and 2-BE does not bioaccumulate, they are considered more of an acute than a chronic nature. The lowest reliable NOAEL for haemolysis in the most sensitive species (the rat) is 24.6 ppm (22.5 mg/kg/day) from a 90-day inhalation rat study. The NOAEL in mg/kg/day is derived by assuming 100% absorption, the average weight of rat of 215g and rat respiratory rate of 0.16 m³/day. The NOAEL, 24.6 ppm (121 mg/m³), represents an absorbed dose of:

$$\frac{121\text{mg/m}^3 \times 0.16 \text{ m}^3/\text{day} \times 6\text{h}}{0.215 \text{ kg} \times 24\text{h}} = 22.5 \text{ mg/kg/day}$$

From the results of controlled and case studies in humans, animal *in vivo* studies, and *in vitro* studies using animal and human red blood cells, humans may be less sensitive to the haemolytic effect of 2-BE than rats. For example, increased red blood cell fragility was observed in rats exposed to 54 ppm 2-BE for 7 hours, however, no effect was observed in human volunteers exposed to 195 ppm for 8 hours. *In vitro* studies indicate that human red blood cells are at least ten times less sensitive than rat red blood cells to the haemolytic effects of BAA, and that the red blood cells of the aged and persons with hereditary blood disorders are not significantly more sensitive to the effects of BAA than red blood cells from humans not similarly afflicted.

The conclusion that humans may be considerably less sensitive than rats to the haemolytic effects of 2-BE is supported by Corley's PBPK model, which successfully estimated the disposition of 2-BE

and BAA under a variety of exposure scenarios. Corley's model predicted as a worst-case scenario that the skin absorption of undiluted 2-BE over 6h would lead to a BAA blood concentration of 0.37 mM, and that absorption of a 40% solution would result in 1.3 mM BAA. These values are below the BAA concentration (2 mM) at which no haemolysis was observed in human cells *in vitro* and well below the concentration at which haemolysis was observed (8 mM BAA).

The risk of haemolytic effects in humans was determined for each scenario by comparing the estimated human daily dose with the rat NOAEL (22.5 mg/kg/day), and then taking into account the following parameters: the human population exposed, the nature and severity of the effect, inter- and intraspecies variability, and uncertainties in the risk assessment process such as the quality and completeness of the database. A knowledge of the mechanism of action of BAA on red blood cells in different species (including humans) may allow for a refinement in intraspecies extrapolations.

4.3.2 Occupational

The risk to human health from exposure to 2-BE has been characterised by estimating the margin of safety (MOS). The MOS is derived by comparing the NOAEL (for the critical effect) with the estimated human dose. The most reliable NOAEL for the critical effect (haemolysis) is 24.6 ppm (22.5 mg/kg/d) in a 90 day inhalation rat study. In deciding whether a MOS is considered sufficient, a number of parameters are taken into account, including the human population exposed, the nature and severity of the effect, interspecies and intraspecies variability, and completeness and quality of the database

Manufacture

The manufacture of 2-BE is an enclosed process so typical worker exposure is very low. Single exposures may occur during activities such as plant maintenance, drum filling off and transference from storage vessels to road tankers, however, as inhalation exposure is low (maximum reading 11 ppm, most readings below 3 ppm TWA) and effective control measures are in place, the risk of acute effects, such as irritant effects, are low.

The calculated MOS for haemolytic effects is $22.5 \text{ mg/kg/d} / 2.2 \text{ mg/kg/d} = 10$, with a high degree of confidence in the estimate due to sufficient reliable data. Taking into account the lower susceptibility of humans to haemolysis by 2-BE compared with rats, there is no cause for concern regarding the risk of haemolytic effects in workers exposed to 2-BE during manufacture.

Formulation

In most work situations, vapour and aerosol concentrations are unlikely to be high enough to result in acute effects such as respiratory and eye irritation, headache and nausea. However, eye and respiratory irritation may occur in certain work situations where aerosols are generated or where high vapour concentrations occur, for example, during the handling of spills, during maintenance, or if heat is applied.

Based on the exposure estimates in Table 8, the MOS for haemolytic effects is 12 for exposure during the formulation of a product containing 10% 2-BE, 2.7 for a 30% formulation and 2.4 for a 60% product. Taking into account the lower susceptibility of humans to haemolysis by 2-BE compared with rats, there is little cause for concern regarding the risk of haemolytic effects in workers exposed to 2-BE during the formulation of products containing up to 60% 2-BE.

Cleaning

In well-controlled work situations, the risk of acute effects in cleaners is of low concern. However, cleaning products containing 2-BE may be used in workplaces where control measures are poor, for example, without adequate ventilation and personal protective equipment, and therefore exposure may be greater. Also, many of the cleaning products are deliberately used in spray form and, in some cases, users are advised to apply heat during dilution of the product. The resultant periodic generation of vapour and/or aerosols may lead to a greater risk of respiratory and eye irritation, particularly in workplaces with inadequate ventilation. Most of the reports of irritation in cleaners have been associated with the use of cleaning products in spray form.

Based on the exposure estimates in Table 11, the MOS for haemolytic effects is 16 for exposure during the use of a cleaning solution containing 0.1% 2-BE, 14 for a 1% solution, 4.5 for a 10% solution, and 1.6 for a 30% solution. Taking into account the lower susceptibility of humans to haemolysis by 2-BE compared with rats, there is little cause for concern regarding the risk of haemolytic effects in workers exposed to 2-BE during the use of cleaning solutions containing up to 30% 2-BE. However, there may be a concern in situations where there is prolonged exposure (particularly dermal exposure) to solutions containing high concentrations (30% or more) of 2-BE.

Printing

In most work situations where 2-BE is used in printing in diluted form, vapour concentrations are unlikely to be high enough to result in acute effects such as respiratory and eye irritation (see Table 9). However, eye and respiratory irritation may occur in certain work situations where aerosols are generated or where high vapour concentrations occur. Acute effects may also arise during the use of high concentrations of 2-BE. In monitoring data available for exposure to 2-BE during silk screening, very high vapour concentrations (up to 169 ppm) were obtained during the use of 100% 2-BE.

Based on the exposure estimates in Table 12, the MOS for haemolytic effects is 3.7 for general printing (for use of a 20% 2-BE formulation). Taking into account the lower susceptibility of humans to haemolysis by 2-BE compared with rats, there is little cause for concern regarding the risk of haemolytic effects in workers exposed to 2-BE during general printing tasks using formulations containing up to 20% 2-BE.

The MOS for haemolytic effects is 1.2 for silk screening (for use as a 50% 2-BE formulation). Other much lower readings have been obtained during silkscreening (see Table 9). Where workers are exposed to high concentrations of 2-BE during silkscreening, the MOS of 1.2 indicates that there may be some concern regarding the risk of haemolytic effects.

Paints/Surface Coatings

In well-controlled work situations, the risk of acute effects during painting and surface treatment is of low concern. However, paints and surface treatment products containing 2-BE may be used in workplaces where control measures are poor, for example, without adequate ventilation and personal protective equipment, and therefore exposure may be greater. Also, some products are applied in spray form. The resultant periodic generation of vapour and/or aerosols may lead to a greater risk of respiratory and eye irritation, particularly in workplaces with inadequate ventilation.

The calculated margin of safety (MOS) for haemolytic effects is $22.5/9.1 = 2.5$, based on European data that paints and surface coatings contain less than 10% 2-BE (see Table 1). Taking into account the lower susceptibility of humans to haemolysis by 2-BE compared with rats, there is little cause

for concern regarding the risk of haemolytic effects in workers exposed to 2-BE during painting and surface treatment.

Use as a Feedstock

As exposure is negligible during the use of 2-BE as a feedstock for BGA, there is no risk to human health.

4.3.3 Consumers

In most situations concerning consumers, vapour and aerosol concentrations are unlikely to be high enough to result in acute effects such as respiratory and eye irritation, headache and nausea. However, eye and respiratory irritation may occur in certain situations where aerosols are generated or where high vapour concentrations occur, for example, during spray painting or during the use of cleaning solutions containing high concentrations of 2-BE.

Comparison of exposure estimates for consumers for the use of cleaning solutions (MOS = 22.5/0.58) and paints (MOS = 22.5/1.05) with the NOAEL indicates that there is no cause for concern regarding the risk of haemolytic effects.

Similarly, for the minor use of 2-BE in cosmetics, there is no cause for concern regarding the risk to human health.

4.3.4 Indirect Exposure via Environment

As exposure to 2-BE is minimal via the environment, there is no cause for concern regarding the risk to human health.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

Human Health

From the risk assessment, there may be concern for the health of workers in some work situations where exposure to 2-BE occurs. There may be a risk of acute effects, eye and respiratory irritant effects in the following situations:

- . where formulations or solutions containing high concentrations of 2-BE are used;
- . where products are used in spray form, particularly without adequate ventilation;
- . where heat may be applied, for example, during dilution;
- . where aerosols may be generated;
- . during the handling of spills; and
- . during maintenance procedures if proper precautions are not taken.

The risk of adverse health effects is greater for any of the above situations when accompanied by poor work practices.

For most work situations, the risk of haemolytic effects in workers potentially exposed to 2-BE is minimal. Monitoring data indicated that typical inhalation exposures were well below the estimates used for calculation of MOS. However, it was concluded that prolonged exposure to products containing high 2-BE concentrations (> 30% for products used in cleaning and 50% for products used in printing) should be treated with some caution, particularly where dermal exposure may occur, as there is still conjecture regarding the degree of dermal absorption for differing strengths of 2-BE solutions.

In general, products available to the public contain lower concentrations of 2-BE than those used industrially, so the risk to consumers of haemolytic effects are low. However, there may be a risk of eye and respiratory irritant effects, headache and nausea in situations where 2-BE vapours or aerosols are generated, for example, during spray use.

Environment

2-BE will predominantly enter the environment from the disposal of wash water from cleaning and surface treatment processes and also via effluent at sites where it is formulated into paints, inks and cleaning products. 2-BE will be readily degraded by micro-organisms present at sewage treatment plants and in the receiving waters and is unlikely to bioaccumulate. 2-BE is relatively non-volatile, however, due to the use pattern, some 2-BE will enter the atmospheric compartment.

2-BE disposed to landfill may leach to groundwater due to its expected high mobility in soil and low adsorption potential.

From a considerable body of results, 2-BE can be classified as being practically non-toxic to fish, aquatic invertebrates and sewage micro-organisms, slightly to practically non-toxic to algae and slightly toxic to oysters.

As noted above, 2-BE will be readily biodegraded by sewerage micro-organisms and by micro-organisms present in receiving waters. With allowance for dilution by waste streams, it is estimated that the concentration of 2-BE in sewage plants will be in the order of ppm. Further dilution in the receiving waters is likely to result in sub-ppm concentrations. Such levels do not constitute a significant environmental hazard, and will be further reduced by biodegradation during sewage treatment. In the atmospheric compartment, 2-BE has a short residence time.

5.2 Recommendations

No further toxicity testing of 2-BE is recommended. A 2-year inhalation study in rats and mice is currently being conducted under the NTP, and an epidemiological study in workers exposed to glycol ethers, including 2-BE, is under way in France.

Skin absorption is a significant route of exposure and there is a degree of uncertainty in the estimates of dermal exposure in this assessment. Therefore, further study, including biological and atmospheric monitoring would provide useful information and a more thorough understanding of the extent of skin absorption of 2-BE in workers. The establishment of a Biological Exposure Index should be considered.

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APPENDIX 1

EXPOSURE ESTIMATES

1. FORMULAE FOR EXPOSURE CALCULATIONS

For 2-butoxyethanol, the total body dose (D) is the sum of doses resulting from absorption of vapours (D_v) and dermal absorption of liquid (D_{dl}). That is,

$$D = D_v + D_{dl} \quad (\text{equation 1})$$

As vapour absorption (D_v) comprises absorption across the lungs (D_{iv}) and dermal absorption of vapours (D_{dv}), that is, $D_v = D_{iv} + D_{dv}$, where

$$D = (D_{iv} + D_{dv}) + D_{dl} \quad (\text{equation 1a})$$

Exposure to vapours

The daily dose arising from the inhalation of vapours (D_{iv}) is as follows:

$$D_{iv} = \frac{C \times R \times E \times B}{BW} \quad \text{mg/kg/day} \quad (\text{equation 2})$$

where C = concentration of substance in air (mg/m^3),
 R = inhalation rate (m^3/h),
 E = exposure duration (h/day),
 B = bioavailability of vapours across the lungs (1 = 100%),
 BW = average body weight of worker/consumer (kg).

In addition, 2-butoxyethanol vapours are also absorbed across the skin. From the results of recent studies in volunteers (Corley et al., 1995) and PBPK modelling (Corley et al., 1994), the dermal absorption of 2-butoxyethanol vapours (D_{dv}) comprises up to 20% of the total absorption of vapours (D_v). That is, for 2-butoxyethanol, D_{iv} is approximately 80% of D_v .

That is, $D_{iv} = 0.8 D_v$, or $D_v = \frac{D_{iv}}{0.8}$. (equation 3)

Therefore, combining equations 2 and 3, the daily dose arising from vapour exposure (D_v), inhalational plus dermal, is as follows:

$$D_v = \frac{C \times R \times E \times B}{0.8 \times BW} \quad \text{mg/kg/day} \quad (\text{equation 4})$$

For vapour exposure, the bioavailability (B) is the proportion of inhaled substance which is absorbed through the lungs, for example, some of the substance is exhaled. In inhalational (breathing zone) tests in volunteers, 57-78% of the inspired amount of 2-butoxyethanol was absorbed. As these values are similar to the default value of 0.75 (75%) often used in international assessments, a value of 0.75 was used in this report.

For consistency with international assessments, a value of $1.3 \text{ m}^3/\text{h}$ was used for the inhalation rate (R) and a value of 70 kg was used for body weight (BW), for occupational exposure during light work activities.

Similarly for consumer exposure, values of 0.8 m³/h and 60 kg were used for the respiratory rate and the body weight respectively.

Exposure to liquid

The daily total dose arising from liquid exposure (D_{dl}) is as follows:

$$D_{dl} = \frac{W \times S \times A \times E \times F}{BW} \text{ mg/kg/day} \quad (\text{equation 5})$$

where: W = weight fraction of substance in product, for example, 0.1 for a 10% solution,
 S = skin absorption rate (mg/cm²/h),
 A = skin surface area exposed (cm²),
 E = exposure duration (h/day)
 F = skin contact time (as fraction of exposure duration, for example, 0.2 for 20% of time),
 BW = average body weight of worker/consumer (kg).

For skin absorption rate (S), the value of 0.2 mg/cm²/h, based on human in vitro data, was used.

In this assessment, it was considered that dermal exposure would reasonably consist of no more than exposure to both hands (840 cm²) or a hand and a forearm (1000 cm²). For consistency, a value of 1000 cm² for was considered appropriate.

For the case of dermal exposure to aerosols, for example, during spray use, exposed parts of the body may include the face, neck, hands and forearms. However, as exposure to aerosols would not be expected to occur simultaneously with exposure to liquid 2-butoxyethanol (as a solution), the skin surface area of 1000 cm² was considered appropriate.

Liquid 2-butoxyethanol can be in contact with the skin for various fractions (F) of the exposure duration (E), so skin contact with liquid can be extensive, intermittent or incidental. For the purposes of this assessment, extensive dermal exposure is taken as continuous contact (F=1) with the skin. Taking into account assumptions made in the UK EASE (Estimation and Assessment of Substance Exposure) model* for dermal exposure, intermittent exposure is taken as being skin contact for 20% of the time (F=0.2), and incidental exposure as skin contact for 1% of the time (F=0.01).

* *The EASE model is the second version of the knowledge based system developed by the UK Health and Safety Executive (HSE).*

2. CALCULATED EXPOSURES FOR VARIOUS SCENARIOS

Using the formulae detailed in Section 1, Occupational Exposures (Table 1) and Consumer Exposures (Table 2) for various scenarios have been estimated.

Table 1. Occupational Exposure

2- BE (%)	W	C ppm	E mg/m ³	F	Daily Dose		
					D _v	D _{dl}	D _v + D _{dl}

Manufacture	100	1	3	14.7	8	0.01	2.0	0.2	2.2
Formulation	10	0.1	2	9.8	8	0.2	1.4	0.5	1.9
	3	0.3	10	49	8	0.2	6.8	1.4	8.2
	60	0.6	10	49	8	0.2	6.8	2.7	9.5
Cleaning	0.1	0.001	2	9.8	8	1	1.4	0.02	1.4
	1	0.01	2	9.8	8	1	1.4	0.2	1.6
	10	0.1	4	19.6	8	1	2.7	2.3	5.0
	30	0.3	10	49	8	1	6.8	6.9	13.7
Silk Screen Printing	50	0.5	10	49	8	1	6.8	11.4	18.2
General Printing	20	0.2	2	9.8	8	1	1.4	4.6	6
Paints/Surface Coatings	10	0.10	10	49	8	1	6.8	2.3	9.1

Table 2. Consumer Exposure

	2-BE (%)	W	C ppm	C mg/m ³	E	F	Daily Dose		
							D _v	D _{dl}	D _v + D _{dl}
Cleaning	10	0.1	4	19.6	1	1	0.25	0.33	0.58
Paints/ Surfaces	1.5	0.015	2	9.8	6	1	0.75	0.3	1.05

Key: *W* = weight fraction of 2-BE in product
C = concentration of 2-BE in air (mg/m³ and ppm)
E = duration of exposure (h/day)
F = fraction of the exposure duration
D_v = dose resulting from absorption of vapours
D_{dl} = dose resulting from dermal absorption of liquid

SIDS DOSSIER
ON THE HPV PHASE 4 CHEMICAL

2-BUTOXYETHANOL

CAS No. 111-76-2

Sponsor Country: AUSTRALIA

DATE: 13 August 1996
(revised 1 November 1996)

SIDS PROFILE

DATE: 13 August 1996

1.01 A	CAS No.	111-76-2
1.01 C	CHEMICAL NAME (OECD Name)	2-BUTOXYETHANOL
1.01 D	CAS DESCRIPTOR	
1.01 G	STRUCTURAL FORMULA	CH ₃ CH ₂ CH ₂ CH ₂ OCH ₂ CH ₂ OH
	OTHER CHEMICAL IDENTITY INFORMATION	Empirical formula C ₆ H ₁₄ O ₂ Molecular weight 118.2
1.5	QUANTITY	200 000 - 500 000 tonnes
1.7	USE PATTERN	Based on European and Australian data: 70-75% in paints, surface coatings, 5-10% in cleaning products 5-10% in inks 10-15% as feedstock
1.9	SOURCES AND LEVELS OF EXPOSURE	Diffuse releases to atmosphere, municipal waste systems, and occasionally ground waters. Indoor air: 0.214 ppb (US EPA), 8 µg/m ³ (Italian study). Ground water: 23 µg/L at US contaminated site. Surface water: 1310-5680 ppb (Japan). Occupational exposure considerable in cleaning services industry, paint, lacquer and varnish industry, hospitality industry, printing. Exposure in other industries and product formulation minor. Some consumer exposure through use of cleaning products, some paints, cosmetics.
ISSUES FOR DISCUSSION (IDENTIFY, IF ANY)	No further SIDS testing required.	

SIDS SUMMARY

CAS NO: 111-76-2		Information Available	OECD Study	GLP	Other Study	Estimation Methods	Acceptable	SIDS Testing Required
STUDY		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL-CHEMICAL								
2.1	Melting Point	Y	N	-	N	N	Y	N
2.2	Boiling Point	Y	N	-	N	N	Y	N
2.3	Density	Y	N	-	N	N	Y	N
2.4	Vapour Pressure	Y	N	-	N	N	Y	N
2.5	Partition Coefficient	Y	Y	-	N	N	Y	N
2.6	Water Solubility	Y	N	-	N	N	Y	N
	pH and pKa values	Y	N	-	N	N	Y	N
2.12	Oxidation : Reduction potential	Y	N	-	N	N	Y	N
OTHER P/C STUDIES RECEIVED		N	-	-	-	-	Y	N
ENVIRONMENTAL FATE and PATHWAY								
3.1.1	Photodegradation	Y	N	-	N	N	Y	N
3.1.2	Stability in water	Y	N	-	-	Y	Y	N
3.2	Monitoring data	Y	-	-	-	-	Y	N
3.3	Transport and Distribution	Y	N	-	-	Y	Y	N
3.5	Biodegradation	Y	Y	-	Y	N	Y	N
OTHER ENV FATE STUDIES RECEIVED		Y	N	-	Y	N	Y	N
ECOTOXICITY								
4.1	Acute toxicity to Fish	Y	N	-	Y	N	Y	N
4.2	Acute toxicity to Daphnia	Y	N	-	Y	N	Y	N
4.3	Toxicity to Algae	Y	N	Y	Y	N	Y	N
4.5.2	Chronic toxicity to Daphnia	N	-	-	N	-	-	N
4.6.1	Toxicity to Soil dwelling organisms	N	-	-	-	-	-	N
4.6.2	Toxicity to Terrestrial plants	N	-	-	-	-	-	N
4.6.3	Toxicity to Other non-mammalian terrestrial organisms	N	-	-	-	-	-	N
OTHER ECOTOXICITY STUDIES RECEIVED		Y	N	-	Y	N	Y	N
TOXICITY								
5.1.1	Acute Oral	Y	Y	-	Y	N	Y	N
5.1.2	Acute Inhalation	Y	Y	-	Y	N	Y	N
5.1.3	Acute Dermal	Y	Y	-	Y	N	Y	N
5.4	Repeated Dose	Y	Y	Y	Y	N	Y	N
5.5	Genetic Toxicity in <i>in vitro</i>							
	. Gene Mutation	Y	Y	Y	Y	N	Y	N
	. Chromosomal aberration	Y	N	Y	Y	N	Y	N
5.6	Genetic Toxicity <i>in vivo</i>	Y	Y	-	Y	N	Y	N
5.8	Reproductive Toxicity	Y	Y	Y	Y	N	Y	N
5.9	Development/Teratogenicity	Y	Y	Y	Y	N	Y	N
5.11	Human experience	Y	-	-	Y	N	Y	N
OTHER TOXICITY STUDIES RECEIVED		Y	Y	Y	-	-	Y	N

1. GENERAL INFORMATION**1.01 SUBSTANCE INFORMATION**

- A. CAS number** 111-76-2
- B. Name (IUPAC name)** ETHYLENE GLYCOL BUTYL ETHER.
- C. Name (OECD name)** . 2-BUTOXYETHANOL
- D. CAS Descriptor (where applicable for complex chemicals)**
- E. EINECS-Number** 203-905-0
- F. Molecular Formula** C₆H₁₄O₂
- G. Structural Formula** CH₃CH₂CH₂CH₂ OCH₂CH₂OH
- H. Substance Group**
- I. Substance Remark**
- J. Molecular Weight** 118.2

1.02 OECD INFORMATION

- A. Sponsor Country:** AUSTRALIA
- B. Lead Organisation**
 Name of Lead Organisation: Worksafe Australia
 National Industrial Chemicals Notification and Assessment
 Scheme (NICNAS)
 Contact person: Ms Lesley Onyon
 Address:
 Street: 92 Parramatta Road
 Town: CAMPERDOWN
 SYDNEY
 State/Territory: NSW
 Postcode: 2050
- Tel: 61 2 9577 9417 Fax: 61 2 9577 9465
- C. Name of responder**
- Name: ICI Australia Operations Pty Ltd
 Address: 1 Nicholson St, Melbourne, Victoria
 Australia 3000
- Tel.: 61 3 9665 7227 Fax: 61 3 9665 7929

D. Other participating companies

Union Carbide Chemicals (Australia) Pty Ltd
 Suite 1, 1st floor
 1-7 Jordan St Gladesville
 Sydney, New South Wales
 Australia, 2111

BP Chemicals Ltd
 Belgrave House
 76 Buckingham Palace Rd
 SW1 WOSU London
 United Kingdom

1.1 General Substance Information

Substance type: organic
Physical status: liquid
Purity: greater than 95%

1.2 Synonyms

beta.-Butoxyethanol
 2-BE
 BG
 BGE
 Butilglicole, eteremonobutilico del glicole monoetilenico, butilcellosolve
 Butoxyethanol
 2-Butoxy-1-ethanol
 2-n-Butoxyethanol
 Butyl Cellosolve®
 Butyl ethoxol
 Butyl glycol
 Butyl glycol ether
 Butyl Icinol®
 Butyl monoether glycol
 Butyl Oxitol®
 Dowanol EB®
 Eastman® EB Solvent
 EGBE
 Emkanol BG®
 Ethanol, 2-butoxy
 Ethylene glycol butyl ether
 Ethylene glycol mono-n-butyl ether
 Ethylene glycol monobutyl ether
 Ethylene glycol n-butyl ether
 Ethylenglykolmono-n-butylether
 Glycol butyl ether
 Glycol monobutyl ether
 1-Hydroxy-2-n-butoxyethan

Monobutyl glycol ether
 O-Butyl ethylene glycol
 3-Oxa-1-heptanol
 Solvenon EB

1.3 Impurities

Commercial 2-BE may contain small concentrations of other glycol ethers, n-butanol and ethylene glycol.

1.4 Additives

A stabiliser, 2,6-bis(1,1-dimethylethyl)-4-methylphenol, may be added at approx. 0.01% to prevent peroxide formation.

1.5 Quantity

Based on EU figures, 200 000 - 500 000 tonnes per year produced worldwide (EU 90 000 te/year, Australia 2000 te/year).

1.6 Labelling and Classification

Type: as in EC Directive 67/548/EEC
Labelling:
Symbols (classification): Xn (harmful)
Category of danger: Harmful, Irritant
Specific limits: 12.5%
R-Phrases: (20/21/22) Harmful by inhalation, in contact with skin and if swallowed;
 (37) Irritating to respiratory system;
 (36) Irritating to eyes
S-Phrases: (2) Keep out of reach of children;
 (24/25) Avoid contact with skin and eyes

1.7 Use Pattern**A. General**

Type of use	Category
Solvent in surface coatings and paints	Wide dispersive use Paints, lacquers and varnishes industry
In cleaning/washing agents	Wide dispersive use Public domain
Solvent in inks	Wide dispersive use Other (printing industry)
Other (feedstock)	Used in closed system Chemical industry - in synthesis
Other	Bead mills (195)

B. Use in Consumer Products

Function	Amount present	Physical state
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Cleaning/washing agents	1-10%	liquid
Paints and surface coatings	< 1.5%	liquid
Cosmetics	< 10%	liquid

1.8 Occupational Exposure Limit Values

Type of limit: MAC (NL)
Limit value: 100 mg/m³ [20 ppm]
Short term expos.
Limit value: 200 mg/m³ [40 ppm]
Schedule: 15 minute (1)

Type of limit: MAK (DE)
Limit value: 20 ppm [100 mg/m³]
Short term expos.
Limit value: 40 ppm [200 mg/m³]
Schedule: 30 minute
Frequency: 4 times
Remark: H = danger of skin absorption; pregnancy: Group C (no reason to fear risk of damage to the developing embryo when adhering to MAK or BAT values)
Reference: Deutsche Forschungsgemeinschaft, List of MAK and BAT Values 1995, VCH Verlagsgesellschaft, Weinheim, 1995.

Type of limit: BAT (biological exposure index)
Limit value: 100 mg/L
Remark: Value expressed as mg 2-BE per litre of urine.
 Monitoring based on measurement of 2-butoxyacetic acid in urine.
Reference: Deutsche Forschungsgemeinschaft, List of MAK and BAT Values 1996, VCH Verlagsgesellschaft, Weinheim, 1996.

Type of limit: MEL - TWA (UK)
Limit value: 120 mg/m³ [25 ppm]
Remark: (a) Skin notation;
 (b) a proposed amendment to COSHH Regulations changes the MEL to an OES - reason: CNS effect threshold established.

Type of limit: TLV - TWA (US - ACGIH)
Limit value: 121 mg/m³ [25 ppm]
Remark: Skin notation (7)

Type of limit: PEL-TWA (US - OSHA):
Limit value: 50 ppm [40 mg/m³]
Remark: Skin notation (9)

Type of limit: REL - TWA (US - NIOSH)

Limit value: 5 ppm [24 mg/m³]
Remark: Skin notation (5)

Type of limit: TWA (Australia)
Limit value: 25 ppm [121 mg/m³]
Remark: Skin notation (8)

1.9 Sources of Exposure

Remark: As the quantities of this substance placed on the EU market by Union Carbide Benelux N.V. are normally sourced from the manufacturing facilities of its U.S. parent company, no exposure can arise within the EU from the manufacture of these quantities. The comments below on exposure are restricted to uses for which Union Carbide believes its customer use this substance.

Major use(s): As solvent in paints and cleaners.

Sources of human exposure: Intermittent exposure of general public via inhalation and skin contact. Quantitative estimates are not available.

Sources of environmental exposure: Diffuse releases to atmosphere, municipal waste systems and occasionally ground waters. Substance is inherently biodegradable and degrades to carbon dioxide and water. Quantitative estimates of releases to the two compartments are not available.

Source: Union Carbide Benelux Antwerpen
Source: Eastman Chemical AG Zug

Remark: 1) The majority of BP Chemicals' material is used as a solvent in industrial coatings, inks and adhesives. All are used industrially and exposure will be controlled by effective local exhaust ventilation.

2) Some BP Chemicals' material is used as an intermediate in chemical synthesis. It is used in closed systems and the only potential for exposure is due to opening of containment for filling of transport vessels. This is controlled by effective local exhaust ventilation.

3) Some BP Chemicals' material is used as a minor constituent of water-based cleaning and washing agents used industrially and possibly by the public. The dilution, circumstances of use, and frequency and duration of potential exposure normally result in insignificant patterns of exposure to users.

Source: BP Chemicals Ltd. London
Source: Eastman Chemical (Deutschland) GmbH Koln

Remark: In data from the Products Register in Sweden, 666 products containing 2-BE were listed, with 68% being used as solvent, 23% in paints and lacquers, 3% in binders, 3% in cleaning agents, and 3% in other uses.

Reference: Johanson and Rick, 1996 (169)

Remark: In Australia, 434 cleaning products containing 2-BE were identified, with a wide variety of applications.
Source: NICNAS 1996 (11)

1.13 Additional Remarks

Remark: TRANSPORT INFORMATION

Delisted by UN as a dangerous good in 1994
 Identification Number: NA 1993
 Class: C1 (combustible liquid)
 Packing Group: III
 Proper Shipping Name: Combustible liquid

Sea (IMO)
 Class: C1
 Packing Group: III
 Symbol: Harmful
 Marine Pollutant (Y/N): No

Rail/Road (RID/ADR)
 Class: C1
 Item: 13(c)
 Symbol: Harmful
 Kemler Plate: 60/2369

Air (IATA/ICAO)
 Class: C1
 Packing Group: III
 Symbol: Harmful

Source: Shell Nederland Chemie B.V. Hoogvliet-Rotterdam
 NICNAS 1996 (11)

Remark: Disposal: Incinerate in a furnace where permitted under national and local regulations. At very low concentrations in water, this product is biodegradable in a biological wastewater treatment plant.

Transport: 2-Buthoxyethanol is shipped in road/rail tankcars, tankcontainers/ISOtanks and smaller packages (e.g. drums).

Source: Union Carbide Benelux Antwerpen

Remark: Transport Road/rail Tankers/isotanks drums
 Disposal in accordance with local, state or national regulations

Source: ICI Chemicals & Polymers Limited Runcorn, Cheshire ICI C&P France SA Chocques

Remark: 2-Butoxyethanol is shipped either in bulk or in steel drums. The bulk shipments are in tank trucks, rail tank cars, or rail tank containers. Our warehouses check that the transporters have the necessary papers and equipment available in case of an emergency.

Source: Eastman Chemical AG Zug

Remark: Transport: 2-Butoxyethanol (2-BE) was listed as a Class 6.1(b) substance in Packaging Group III until late 1994. However, 2-BE was delisted by the UN Committee of Experts on the Transport of Dangerous Goods at its November 1994 meeting.

Source: United Nations (1995) (13)

Remark: 2-Butoxyethanol is shipped either in bulk or in steel drums. The bulk shipments are in tank trucks, rail tank cars, or rail tank containers. Our warehouses check that the transporters have the necessary papers and equipment available in case of an emergency.

Source: Eastman Chemical (Deutschland) GmbH Ko1n

2. Physico-chemical Data

CAS-No.: 111-76-2

2.1 Melting Point

Value: = -75 degree C

GLP: no data

Source: BP Chemicals Ltd. London (17)

Value: = -70 degree C

GLP: no data

Source: BP Chemicals Ltd. London (18)

Value: = -77 degree C

GLP: no data

Source: NIOSH, USA (5)

2.2 Boiling Point

Value: = 167 - 173 degree C at 1013 hPa

Method: other: DIN 53171

GLP: no data

Remark: Min 95E (v/v)

Source: Hoechst AG (15) (21)

Value: = 170.8 degree C

Remark: Adapted from values in literature

Source: NIOSH, USA (5)

Value: = 170.2 - 172 degree C

Remark: Range of values selected from references.

Source: BP Chemicals Ltd. London (17) (23)

2.3 Density

Type: density

Value: = 0.899 - 0.904 g/cm³ at 20 degree C

Method: other: DIN 51757

GLP: no data
Source: Hoechst AG (15) (21)

Type: relative density
Value: = 0.897 at 25 degree C
GLP: no
Source: Eastman Kodak USA (25)

2.4 Vapour Pressure

Value: = 1.17 hPa at 25 degree C
Remark: From selected references.
Source: ECETOC, 1994 (122)

Value: = 4 hPa at 40 degree C
GLP: no data
Source: BASF (27)

2.5 Partition Coefficient

log Pow: = 0.74
Method: other (calculated): using computer program by CompuDrug Ltd.
GLP: no data
Source: BASF (28)

log Pow: = 0.81 at 25 degree C
Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
GLP: no data
Source: BASF (29)

log Pow: = 0.83
Method:
Source: BP Chemicals Ltd. London (30)

2.6 Water Solubility

Value: miscible at 20 degree C
GLP: no data
pH: = 7
Source: Hoechst AG (15)

2.7 Flash Point

Value: = 60 degree C
Type:
Method: other: DIN 51755
GLP: no data
Source: Hoechst AG (21)

Value: = 62 degree C

Type: closed cup
Method: other: ASTM D56
GLP: no
Source: Eastman Kodak USA (32)

Value: = 63 degree C
Type: closed cup
Method: other: ASTM D3278 (Setaflash)
GLP: no
Source: Eastman Kodak USA (34)

Value: = 65 degree C
Type:
Method: other: DIN 5178
GLP: no data
Source: Hoechst AG (15)

Value: = 70.1 degree C
Type: Cleveland open cup
Method:
Source: Sax and Lewis (19)

Value: = 70 degree C
Type: open cup
Method: other: ASTM D56
GLP: no
Source: Eastman Kodak USA (25)

2.8 Auto Flammability

Value: = 230 degree C
Method: other: DIN 51794
GLP: no data
Source: BASF (27)

Value: = 235 degree C
Method: other: ASTM D2155
GLP: no
Source: Eastman Kodak USA (34)

Value: = 238 - 245 degree C
Remark: Range of values selected from references.
Source: BP Chemicals Ltd. London (35) (36)

2.9 Flammability

Result: other: Lower flammable limit value 1.10% at 93 degree C.
Method: other: ASTM E681
GLP: no
Source: Eastman Kodak USA (34)

Result: other: Upper flammable limit value 12.78% at 135 degree C.
Method: other: ASTM E681
GLP: no
Source: Eastman Kodak USA (34)

2.10 Explosive Properties

Result: not explosive
Method: other: ASTM E537 (Differential Thermal Analysis).
GLP: no
Source: Eastman Kodak USA (34)

2.11 Oxidizing Properties

2.12 Additional Remarks

Remark: Soluble in mineral oil and most organic solvents (The Merck Index). Mixes in all proportions with acetone, benzene, carbon tetrachloride, ethyl ether, n-heptane and water; miscible in all proportions with many ketones, ethers, alcohols, aromatic paraffins and halogenated hydrocarbons (HSDB).
Source: BP Chemicals Ltd. London (23)(18)

Remark: Surface tension = 27.4 mN/m at 25 degreeC.
Source: BP Chemicals Ltd. London (18)

Remark: Henry's Law Constant = 2.08×10^{-7} atm/m³/mole at 25 degree C.
Source: BP Chemicals Ltd. London (39)

Remark: Henry's Law constant - 2.08×10^{-8} atm/m³/mole at 25 degree C.
Source: BP Chemicals Ltd. London (39)

Remark: Coefficient of cubical expansion = 9.5×10^{-4} at 55 degree C.
Source: BP Chemicals Ltd. London

Remark: Viscosity = 6.4 cP at 20 degree C.
Source: BP Chemicals Ltd. London

Remark: Equilibrium vapour concentration in air is 1300 ppm [6283 mg/m³] at 20 degree C
Source: BP Chemicals Ltd. London

Remark: Combustion with limited access to atmosphere may cause carbon monoxide formation.
Source: BP Chemicals Ltd. London

Remark: Refractive index 1.422 at 25 degree C
Source: Dow USA (20)

Remark: Forms peroxides.

Source: Eastman Kodak USA (34)

Remark: Undergoes reactions typical of glycol ethers

Source: Dow USA (20)

3. Environmental Fate and Pathways

CAS-No.: 111-76-2

3.1.1 Photodegradation

Type: air
Light source: other: U.V. fluorescent lights
Light spect.: = 345 - 355 nm
Conc. of subst.: .00967 mg/l at 30 degree C
INDIRECT PHOTOLYSIS
Sensitizer: NO3
Conc. of sens.: 1 mg/l
Degradation: = 0 % after 6 hour
Method: other (measured): Studied in a 12 m³ smog chamber with 55% relative humidity. Analysis by GC/UV.
GLP: no data
Test substance: other TS
Reference: Yanagihara et al, 1977 (40)

Type: air
Conc. of subst. at 25 degree C
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm³
Rate constant: = $2.3 \times 10^{-11} \text{ cm}^3/(\text{molecule} * \text{sec})$
Method:
GLP: no data
Test substance: other TS
Remark: This rate constant yields an atmospheric half life of about 17 hours.
Reference: Atkinson, 1987 (41)

Type:
Method:
Test substance:
Remark: 2-Butoxyethanol does not absorb light in the environmentally significant range (>290 nm) therefore would not be expected to undergo direct photolysis.
Source: BP Chemicals Ltd. London (42)

Type:
Method:
Test substance:
Remark: Based on its vapour pressure, 2-butoxyethanol would be expected to exist entirely in the vapour phase in air and reactions with photochemically produced hydroxyl radicals may be important.
Source: BP Chemicals Ltd. London (18)

Type:
Method:
Test substance:

Remark: Alcohols and ethers are generally resistant to hydrolysis and do not absorb UV light in the environmentally significant range (> 290 nm). Therefore, 2-BE is not expected to undergo hydrolysis or direct photolysis.

Source: NICNAS 1996 (11)(22)

3.1.2 Stability in Water

Type:
Method:
Test substance:
Remark: 2-Butoxyethanol does not absorb light of wavelength >290 nm and would therefore not be expected to undergo hydrolysis in aquatic environments.

Source: BP Chemicals Ltd. London (18)

Type:
Method:
Test substance:
Remark: Because 2-butoxyethanol is miscible in water, and based on an estimated Henry's Law constant of 2.08×10^{-8} atm/m³/mole at 25 degree C, volatilisation from natural bodies of water is not expected to be an important fate process.

Source: BP Chemicals Ltd. London (18)

3.1.3 Stability in Soil

Type:
Radiolabel:
Concentration:
Cation exch. capacity:
Microbial biomass:
Method:
GLP:
Test substance:
Remark: Biodegradation is likely to be the most important removal mechanism from aerobic soil.

Source: BP Chemicals Ltd. London (18)

Type:
Radiolabel:
Concentration:
Cation exch. capacity:
Microbial biomass:
Method:
GLP:
Test substance:
Remark: Limited monitoring data has shown that it may leach to ground water. A soil adsorption coefficient of 67 (Syracuse Research Council, 1988) indicates that 2-butoxyethanol will be highly mobile in soil and it should not partition from the water column to organic matter contained

Source: in sediments or suspended solids.
BP Chemicals Ltd. London (18)

3.2 Monitoring Data (Environment)

Type of measurement: background concentration
Medium: air
Remark: 2-Butoxyethanol was detected at 8 ug/m³ in 1 of 6 samples selected for GC-MS from indoor air samples collected from 14 homes and 1 small office in Italy.
Reference: De Bortoli, 1986 (44)

Type of measurement: background concentration
Medium: air
Remark: The Environmental Protection Agency's volatile organic compounds national ambient database includes data on indoor air (not industrial space) showing an average for 14 samples of 0.214 ppb.
Reference: Shah and Singh, 1988 (45)

Type of measurement: concentration at contaminated site
Medium: drinking water
Remark: 2-Butoxyethanol is listed as a contaminant in drinking water samples analysed between September 1974 and January 1980 for a survey of US cities including Pomona, Escondido, Lake Tahoe, Orange Co., Dallas, Washington DC, Cincinnati, Philadelphia, Miami, New Orleans, Ottumwa and Seattle. Values specified in Volume 2.
Reference: Lucas, 1984 (46)

Type of measurement: concentration at contaminated site
Medium: ground water
Remark: 2-Butoxyethanol was detected at a concentration of 23 ug/l in 1/7 samples collected in February 1974 near the Valley of Drums, Kentucky, USA, a contaminated site.
Reference: Stonebreaker and Smith, 1980 (47)

Type of measurement: concentration at contaminated site
Medium: surface water
Remark: 2-Butoxyethanol was detected at concentrations of 1310 and 5680 ppb in the water of the Hayashida River (Hyogo prefecture, Japan) as a contaminant from leather industry effluents. The values represent levels after steam and vacuum distillation respectively. Date of study: 2 April 1980.
Reference: Yasuhara, 1981 (48)

3.3.1 Transport between Environmental Compartments

Type: adsorption
Media: soil - air
Method: other: calculated by equation 4-8 in Lyman, W.J. et al. (1982), Handbook of chemical property estimation methods.
Year: 1982

Remark: The soil adsorption coefficient Koc was estimated as 67.
Source: BP Chemicals Ltd. London (38)

3.3.2 Distribution

Media: water - air
Method: other (measurement): by headspace chromatography.
Year: 1988

Remark: Partition coefficient from salt water was 7051 at 37 degree C.
Source: BP Chemicals Ltd. London (50)

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, domestic, non-adapted
Concentration: 10 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 95% after 28 days
Result: readily biodegradable
Method: OECD Guideline 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: 1981
GLP: no
Test substance: other TS: Huels AG
Source: BP Chemicals Ltd. London (51)

Type: aerobic
Inoculum: activated sludge, domestic, non-adapted
Concentration: 500 mg/l related to test substance
Degradation: = 100% after 28 days
Result: inherently biodegradable
Method: OECD Guideline 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 1981
GLP: no
Test substance: other TS: Huels AG
Source: BP Chemicals Ltd. London (51)

Type: aerobic
Inoculum: activated sludge, industrial, non-adapted
Concentration: 450 mg/l related to test substance
Degradation: = 100% after 5 days
Result: inherently biodegradable
Kinetic: 1 day = 22%
 3 day = 63%
 5 day = 100%
Method: OECD Guideline 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"

Year: 1976
GLP: no
Test substance: other TS: Hoechst AG
Source: BP Chemicals Ltd. London (52)

Type: aerobic
Inoculum: activated sludge
Concentration 100 mg/l related to Test substance
Degradation = 96% after 14 days
Result: inherently biodegradable
Method: other: MITI-Test (BOD of ThOD).
Year:
GLP: no data
Test substance: other TS
Test condition: Concentration of sludge: 30 mg/l
Source: BP Chemicals Ltd. London (53)

Type: aerobic
Inoculum: domestic sewage, adapted
Degradation:
Result: readily biodegradable
Method: other: No 219. American Public Health Association Inc. COD determined by ASTM 1974.
Year: 1979
GLP: no data
Test substance: other TS: as marketed by Shell.
Remark: Theoretical Oxygen demand = 2.31 g/g; BOD₅ = 0.71 g/g (31% of theoretical oxygen demand); COD = 2.20 g/g. With seeding adapted, BOD = 1.68 g/g (73% of theoretical oxygen demand).
Reference: Bridie et al, 1979 (54)

Type: aerobic
Inoculum: domestic sewage, adapted
Concentration: 10 mg/l related to Test substance
Degradation: = 88% after 20 days
Result: readily biodegradable
Kinetic: 5 day = 26%
 10 day = 74%
 15 day = 82%
 20 day = 88%
Method: other: not specified
Year: 1974
GLP: no data
Test substance: other TS
Remark: A 20 day test in fresh water (these results) and salt water (see next record). Butoxyethanol concentrations were 3, 7 and 10 mg/l. Theoretical Oxygen demand was 2.3 mg/mg and measured chemical oxygen demand (COD) was 2.25 mg/mg.
Reference: Price et al, 1974 (55)

Type: aerobic

Inoculum: domestic sewage, adapted
Concentration: 10 mg/l related to test substance
Degradation: = 10- 75% after 20 days
Result: readily biodegradable
Kinetic: 5 day = 26%
 10 day = 74%
 15 day = 82%
 20 day = 88%
Method: other: not specified.
Year: 1974
GLP: no data
Test substance: other TS
Remark: This record for biodegradation in salt water complements the previous record for fresh water.
Reference: Price et al, 1974 (55)

Type: aerobic
Inoculum: mixed activated sludge and secondary effluent
Concentration: 0.8 ml/100 ml
Degradation: = 77.7% after 3 days, 100% after 7 days
Result: readily biodegradable
Method: ISO 7827, based on OECD Guidelines 301A and 301E
Year: 1984
GLP: no
Test substance:
Source: ICI Australia Operations (24)

Type: aerobic
Inoculum: domestic sewage
Concentration: 0.8 ml/100 ml
Degradation: = 88% after 28 days
Result: readily biodegradable
Kinetic: 5 day = 25%
 10 day = 60%
 20 day = 75%
 28 day = 88%
Method: OECD TG 301 C, 301 D
Year:
GLP:
Test substance:
Source: ICI Australia Operations (31)

3.6 BOD5, COD and BOD5/COD Ratio

B O D 5
Method: other
Year: 1979
GLP: no
Concentration: 3 µg/l related to Test substance
BOD5: = 1300 mgO₂/l
C O D

Method: other
Year: 1979
GLP: no
COD: = 2180 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: = 0.6

Result: TOD = 2300 mg O₂/ml. BOD₂₀ = 1800 mg O₂ at 3 ul/l.

Test condition: Method similar to BOD Method 405.1, U.S. EPA (EPA-600/4-79-020, 1979) and COD Method 410.1, U.S. EPA (EPA-600/4-79-020, 1979). Concentration units expressed as 3 ul/l, not ug/l. Test medium was activated sludge under aerobic conditions.

Source: Eastman Kodak USA (56)

B O D 5

Method: other: fresh water using non-acclimated seed.

Year:

GLP: no data

BOD5: = 598 mgO₂/l

C O D

Method: other: measured value taken from Bridie et al.

Year:

GLP: no data

COD: = 2200 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: <= 0.27

Remark: BOD5 value taken from BP Chemicals Limited source.

Source: BP Chemicals Ltd. London

B O D 5

Method: other: not specified; seeding adapted.

Year:

GLP: no data

BOD5: = 0.17 mgO₂/l

C O D

Method: other: not specified.

Year:

GLP: no data

COD: = 2200 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: = 0.76

Reference: Bridie et al, 1979 (54)

B O D 5

Method: other: not specified; seeding not adapted

Year:

GLP: no data

BOD5: = 0.71 mgO₂/l

C O D

Method: other: not specified
Year:
GLP: no data
COD: = 2200 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: = 0.32

Reference: Bridie et al, 1979 (54)

B O D 5

Method: other: salt water using non-acclimated seed.
Year:
GLP: no data
BOD5: = 667 mgO₂/l

C O D

Method: other: measured value from Bridie, A.L. et al.
Year:
GLP: no data
COD: = 2200 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: <= 0.3

Remark: BOD5 value from BP Chemicals Ltd source.

Reference: Bridie et al, 1979 (54)

3.7 Bioaccumulation

Species: other: not specified

Exposure period:

Concentration:

BCF: = 2.51

Elimination:

Method: other: not specified

Year:

GLP: no data

Test substance: other TS

Remark: 2-Butoxyethanol should not bioconcentrate among aquatic organisms.

Source: BP Chemicals Ltd. London (18)

Species: other: specified as aquatic species only.

Exposure period:

Concentration:

BCF: = 2.5

Elimination:

Method: other: Calculated from log K_{ow}

Year:

GLP: no data

Test substance: other TS

Remark: Calculated using equation 5.2 in Lyman, W. J. et al. 1982.

Source: BP Chemicals Ltd. London (38)

3.8 Additional Remarks

Remark: No data identified from literature searched.
Source: BP Chemicals Ltd. London

4. Ecotoxicity CAS-No.: 111-76-2**AQUATIC ORGANISMS****4.1 Acute and Prolonged Toxicity to Fish**

Type: other: not specified
Species: *Poecilia reticulata* (Fish, fresh water)
Exposure period:
Unit: µmol/l
Analytical monitoring: no data
LC50: = 14791
Method: other: guideline followed not recorded.
Year:
GLP: no data
Test substance: other TS
Remark: The value was calculated according to Litchfield, J.F. and Wilcoxon, F. (1949). in *J. Pharmacol Exp. Ther.* 96, 99, or by estimation from a log/probit plot.
Source: BP Chemicals Ltd. London (61)

Type: semistatic
Species: *Poecilia reticulata* (Fish, fresh water)
Exposure period: 7 day
Unit: µmol/l
Analytical monitoring: no data
LC50: = 8318
Method: other: guideline followed was not recorded.
Year: 1981
GLP: no data
Test substance: other TS: acetone or propan-2-ol were used as the solvent vehicle.
Remark: Groups of 8, 2-3 mth-old fish were exposed to each concentration tested. Water hardness was 25 mg/l as calcium carbonate and oxygen content was >5 mg/l. Temperature was 22 (+/-1) degree C.
Source: BP Chemicals Ltd. London (61)

Type: static
Species: *Carassius auratus* (Fish, fresh water)
Exposure period: 24 hour
Unit: mg/l
Analytical monitoring: yes
LC50: = 1700

Method: other: Standard methods for the examination of water and wastewater. Method No 231, American Public Health Association Inc., NY.
Year: 1971
GLP: no data
Test substance: other TS
Remark: Test conducted in tap water.
Source: BP Chemicals Ltd. London (63)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour
Unit: mg/l
Analytical monitoring: no data
LC50: = 1490
Method: other: not specified.
Year:
GLP: no data
Test substance: other TS
Remark: Tests conducted in potable well water, 23 degreeC with mild aeration applied after 24 hr. It is reported that some test substances in the study were diluted with water or a solvent described as having relatively low toxicity
Source: BP Chemicals Ltd. London (64)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour
Unit: mg/l
Analytical monitoring: no
LC50: = 1880
Method: other: DIN 38412 part 15
Year: 1982
GLP: no
Test substance: other TS: Huels AG.
Source: BP Chemicals Ltd. London (65)

Type: static
Species: Leuciscus idus melanotus (Fish, fresh water)
Exposure period: 48 hour
Unit: µmol/l
Analytical monitoring: no data
LC0: = 1170 - 1350
LC50: = 1395 - 1575
LC100: = 1490 - 1620
Method: other: Deutsche Einheitsverfahren zur Wasser-, Abwasser - und Schlamm-Untersuchung L15: Fischtest.
Year: 1976
GLP: no data

Test substance:	other TS	
Source:	BP Chemicals Ltd. London	(66)
Type:	static	
Species:	Menidia beryllina (Fish, estuary, marine)	
Exposure period:	96 hour	
Unit:	mg/l	
Analytical monitoring:	no data	
LC50:	= 1250	
Method:	other: not specified	
Year:	1975	
GLP:	no data	
Test substance:	other TS	
Remark:	Tests carried out in potable well water at 20 degreeC with added sea salt mix. It is reported that some test substances evaluated in the study were diluted in water or a solvent described as having relatively low toxicity.	
Source:	BP Chemicals Ltd. London	(64)
Type:	static	
Species:	Pimephales promelas (minnow, fathead)	
Exposure period:	96 hour	
Unit:	mg/l	
Analytical monitoring:	no data	
LC50:	2137	
Method:	other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. USEPA, Corvallis, Oregon, USA.	
Year:	1975	
GLP:	no data	
Test substance:	other TS	
Remark:	Raw lake water dechlorinated with activated carbon used in test aquariums.	
Reference:	Bartlett, 1979	(37)
Source:	Dow Chemical, USA	
Type:	static	
Species:	Cyprinodon variegatus (minnow, sheepshead)	
Exposure period:	96 hour	
Unit:	mg/l	
Analytical monitoring:	no data	
LC50:	116	
Method:	other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. USEPA, Corvallis, Oregon, USA.	
Year:	1975	
GLP:	no data	
Test substance:	other TS	
Remark:	Dilution water used was synthetic sea water, 25.0 ppt, pH = 8.3.	
Source:	Amoco Corporation, USA	(43)

Species: Brine shrimp
Exposure period: 24 hour
Unit: mg/l
Analytical monitoring: no data
LC50: 1000
Method: other:
Year:
GLP: no data
Test substance: other TS
Remark:
Source: AQUIRE (183)

4.2 Acute Toxicity to Aquatic Invertebrates (e.g Daphnia)

Species: Artemia salina (Crustacea)
Exposure period: 24 hour
Unit: mg/l
Analytical monitoring: no data
TLM : = 1000
Method: other: a static test at 24.5 degree C.
Year:
GLP: no data
Test substance: other TS
Remark: TLM is the concentration causing 50% mortality and was determined graphically from measurements at an unspecified number of concentrations.
Reference: Price et al, 1974 (55)

Species: Crangon crangon (Crustacea)
Exposure period: 96 hour
Unit: mg/l
Analytical monitoring: no data
LC50 : = 550 - 950
Method: other: not specified
Year:
GLP: no data
Test substance: other TS
Source: Verscheuren, 1983 (69)

Species: Crangon crangon (Crustacea)
Exposure period: 48 hour
Unit: mg/l
Analytical monitoring: no data
LC50 : = 600 - 1000
Method: other: not specified.
Year:

GLP:	no data	
Test substance:	other TS	
Source:	Verscheuren, 1983	(69)
Species:	Daphnia magna (Crustacea)	
Exposure period:	24 hour	
Unit:	mg/l	
Analytical monitoring:	yes	
EC0:	= 1283	
EC50:	= 1698 - 1940	
EC100:	= 2500	
Method:	other: 20 degree C, immobilisation in artificial fresh water.	
Year:		
GLP:	no data	
Test substance:	other TS	
Remark:	Analytical monitoring consisted of checking pH at the end of the study to check that it was within the range tolerated by Daphnia magna and checking oxygen concentration.	
Source:	BP Chemicals Ltd. London	(71)
Species:	Daphnia magna (Crustacea)	
Exposure period:	24 hour	
Unit:	mg/l	
Analytical monitoring:	no	
EC50:	= 5000	
Method:	other: DIN 38412 part 11	
Year:	1982	
GLP:	no data	
Test substance:	other TS	
Source:	BP Chemicals Ltd. London	(72)
Species:	Daphnia magna (Crustacea)	
Exposure period:	24 hour	
Unit:	mg/l	
Analytical monitoring:	no data	
EC0:	= 1140	
EC50:	= 1720	
EC100:	= 2500	
Method:	other: not specified.	
Year:		
GLP:	no data	
Test substance:	other TS: 2-butoxyethanol diluted with tap water.	
Remark:	24-hour old Daphnia were exposed to a series of dilutions of 2-BE in tap water and swimming ability was measured after 24 hour. The EC50 value was calculated for E0 and E100.	
Source:	BP Chemicals Ltd. London	(73)
Species:	Daphnia magna (Crustacea)	

Exposure period:	24 hour	
Unit:	mg/l	
Analytical monitoring:	no data	
LC50:	835	
Method:	other: Method for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, USEPA, Corvallis, Oregon, USA	
Year:	1975	
GLP:	no data	
Test substance:	other TS	
Remark:	Raw lake water dechlorinated with activated carbon used in test aquariums.	
Reference:	Bartlett, 1979	(37)
Source:	Dow Chemical, USA	
Species:	Daphnia magna (Crustacea)	
Exposure period:	24 hour	
Unit:	mg/l	
Analytical monitoring:	no data	
EC50:	1815	
Method:	other:	
Year:		
GLP:	no data	
Test substance:	other TS	
Remark:		
Source:	AQUIRE	(183)
Species:	Other aquatic mollusc (Crassotera virginicas)	
Exposure period:	96 hour	
Unit:	mg/l	
Analytical monitoring:	no data	
LC50:	89.4	
Method:	other: Method for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, USEPA, Corvallis, Oregon, USA	
Year:	1975	
GLP:	no data	
Test substance:	other TS	
Remark:	Dilution water used was synthetic sea water, 25.0 ppt, pH = 8.3	
Source:	Amoco Corporation, USA	(43)
Species:	Other aquatic crustacea (Panaeus setiferus)	
Exposure period:	96 hour	
Unit:	mg/l	
Analytical monitoring:	no data	
LC50:	130	
Method:	other: Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, USEPA, Corvallis, Oregon, USA	
Year:	1975	

GLP: no data
Test substance: other TS
Remark: Dilution water used was synthetic sea water, 25.0 ppt, pH = 8.3
Source: Amoco Corporation, USA (43)

4.3 Toxicity to Aquatic Plants (e.g. Algae)

Species: Microcystis aeruginosa (Algae, blue, cyanobacteria)
Endpoint: growth rate
Exposure period: 8 day
Unit: mg/l
other: = 35
Analytical monitoring: no data
Method: other: cell multiplication inhibition test
Year:
GLP: no data
Test substance: other TS
Remark: Result is given as the toxicity threshold.
Test condition: Test conducted in static conditions at 27 degree C.
Source: BP Chemicals Ltd. London (74)

Species: Scenedesmus quadricauda (Algae)
Endpoint: growth rate
Exposure period: 7 day
Unit: mg/l
Analytical monitoring: no
LOEC: = 900
Method: other: cell multiplication inhibition test
Year:
GLP: no data
Test substance: other TS: 2-butoxyethanol in double-distilled water.
Source: BP Chemicals Ltd. London (75)

Species: Selenastrum capricornutum (Green algae)
Endpoint: growth rate
Exposure period: 7 day
Unit: mg/l
EC50: > 1000
Analytical monitoring: no data
LOEC: = 125
Method: other: Based on US EPA, The Selenastrum capricornutum Printz Algal Assay: Bottle Test EPA-600/9-78-018. Corvallis, Oregon, USA.
Year: 1978
GLP: yes
Test substance: as prescribed by 1.1-1.4
Reference: Dill and Minazzo, 1988 (57)
Source: Dow Chemical, USA

4.4 Toxicity to Micro-organisms (e.g. Bacteria)

Type: aquatic
Species: Entosiphon sulcatum (Protozoa)
Exposure period: 72 hour
Unit: mg/l
Analytical monitoring: no
LOEL : 91
Method: other: cell multiplication inhibition test
Year:
GLP: no data
Test substance: other TS: 2-butoxyethanol in double-distilled water.
Test condition: At 25 degree C.
Source: BP Chemicals Ltd. London (75)

Type: aquatic
Species: other bacteria: Chilomonas paramecium
Exposure period: 48 hour
Unit: mg/l
Analytical monitoring: no data
EC5 : 911
Method: other: cell multiplication inhibition test.
Year:
GLP: no data
Test substance: other TS: 2-butoxyethanol in double-distilled water.
Remark: Result value gave a decrease in cell count of 5% at most.
Test condition: Test conducted at 20 degreeC and at pH 6.9.
Source: BP Chemicals Ltd. London (76)

Type: other
Species: Pseudomonas putida (Bacteria)
Exposure period: 16 hour
Unit: mg/l
other : = 700
Analytical monitoring: no
Method: other: cell multiplication inhibition test
Year:
GLP: no data
Test substance: other TS: 2-butoxyethanol in double-distilled water.
Remark: Result expressed as the toxicity threshold.
Test condition: Butoxyethanol solution was added to culture medium at pH 7 and 25 degree C. Endpoint measured by extinction.
Source: BP Chemicals Ltd. London (75)(77)

Type: other
Species: Bacteria from domestic sewage
Exposure period: 16 hour
Unit: mg/l

IC50 :	> 1000	
Analytical monitoring:	no	
Method:	other: Growth inhibition test from Alsop et al, J. Water Pollut. Control Fed., vol. 52(10), Oct. 1980	
Year:	1980	
GLP:	no data	
Test substance:	other TS:	
Remark:	Result expressed as the toxicity threshold.	
Reference:	Waggy et al, 1989	(58)
Source:	Union Carbide Chemicals	

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates (e.g. Daphnia)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

4.6.2 Toxicity to Terrestrial Plants

4.6.3 Toxicity to Other Non-mammalian Terrestrial Organisms

Remark:	NO RELEVANT DATA.
Source:	BP Chemicals Ltd. London

4.7 Biological Effects Monitoring

Remark:	NO RELEVANT DATA.
Source:	BP Chemicals Ltd. London

4.8 Biotransformation and Kinetics Excluding Mammals

Remark:	NO RELEVANT DATA.
Source:	BP Chemicals Ltd. London

4.9 Additional Remarks

Remark:	NO RELEVANT DATA.
Source:	BP Chemicals Ltd. London

5. Toxicity CAS-No: 111-76-2

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

- Type:** LD50
Species: rat
Value: = 1190 - 2800 mg/kg bw
Method: other: Butoxyethanol administered by oral gavage to 5 males/group.
Year:
GLP: no data
Test substance: other TS
Remark: Tests carried out in 8 different laboratories.
Reference: Weil and Wright, 1967 (79)
- Type:** LD50
Species: rat
Value: = 1150 - 1910 mg/kg bw
Method: other: administered at concentrations \leq 10% by gavage to groups of 10 male rats.
Year:
GLP: no data
Test subs.: other TS: commercial grade in water
Remark: Effects on kidneys rarely proceeded as far as blood-stained urine and free blood beneath the capsule at the highest doses.
Reference: Smyth et al, 1941 (80)
- Type:** LD50
Species: rat (male)
Value: = 1746 mg/kg bw
Method: other: Eastman Kodak Company, Health, Safety and Human Factors Lab. Protocol
Year:
GLP: no
Test subs.: other TS
Remark: Groups of 5 fed and 5 fasted rats received one of 5 different doses and were observed for 14 days. The LD50 was the same in both fed and fasted rats. Clinical signs included inactivity and weakness. Haemoglobinuria was evident in both fed and fasted animals at the highest dose level and blood was noted in the urine and gastrointestinal tract in animals dying before scheduled necropsy.
Reference: Eastman Kodak Co, 1981 (81)
- Type:** LD50
Species: rat
Value: = 530 - 3000 mg/kg bw
Method: other: no details; observation period of 14 days.
Year:
GLP: no data
Test subs.: other TS: commercial material.
Remark: Results are for several studies conducted over 16 years. Doses at or above the LD50 value caused sluggishness, ruffled fur, prostration and narcosis. Autopsy of rats showed congested or haemorrhaged lungs, mottled livers, severely congested kidneys and haemoglobinuria. Tolerance to single doses decreased with age; LD50's in weanlings, 6-

- week-old and yearling rats were 3000, 2400 and 560 mg/kg respectively.
- Reference:** Carpenter et al, 1956 (82)
- Type:** LD50
Species: rat
Value: = 1950 mg/kg bw
Method: other: keine Angaben
Year: 1966
GLP: no
Test subs.: other TS: Hoechst AG
Remark: Mixed strains, female.
Source: BP Chemicals Ltd. London (83)
- Type:** LD50
Species: rat (male)
Value: = 2410 mg/kg bw
Method: other: gavage at 4 doses 1.25 - 10 ml/kg
Year: 1980
GLP: no
Test subs.: other TS: 2-BE in water
Remark: Observed effects included breathing difficulty, bloody saliva; liver, kidney and adrenal discolouration; distended stomach, intestinal blood.
Reference: Bushy Run, 1980 (59)
Source: Union Carbide Chemicals USA
- Type:** LD50
Species: rat (female)
Value: = 1000-2000 mg/kg bw
Method: other: gavage at 5 doses 130 - 2000 mg/kg
Year: 1981
GLP: no
Test subs.: other TS: crude Dowanol EB in water
Remark: Observed effects included breathing difficulty and necrosis of tails.
Source: Dow Chemical, USA (62)
- Type:** LD50
Species: mouse
Value: = 1519 - 2005 mg/kg bw
Method: other: Eastman Kodak Company, Health, Safety and Human Factors Laboratory Protocol.
Year:
GLP: no
Test subs.: other TS: Eastman Kodak Company.
Remark: Groups of 5 fed and 5 fasted mice received one of 5 different dose levels and were observed for 14 days. The first value in the LD50 range is for fasted mice and the second is for fed mice. Haemoglobinuria was noted at intermediate dose levels in fed mice and blood was found in the stomach and intestines.
Reference: Eastman Kodak Co, 1981 (81)

Type:	LD50	
Species:	mouse	
Value:	= 1230 mg/kg bw	
Method:	other: gavage, observation period of 14 days.	
Year:		
GLP:	no data	
Test subs.:	other TS: commercial material.	
Remark:		
Reference:	Carpenter et al, 1956	(82)
Type:	LD50	
Species:	rabbit (male)	
Value:	= 320 - 370 mg/kg bw	
Method:	other: gavage, observation period 14 days.	
Year:		
GLP:	no data	
Test subs.:	other TS: commercial material.	
Remark:		
Reference:	Carpenter et al, 1956	(82)
Type:	LD50	
Species:	guinea pig	
Value:	= 1200 mg/kg bw	
Method:	other: no details. Observation period 14 days.	
Year:		
GLP:	no data	
Test subs.:	other TS: commercial material.	
Remark:		
Reference:	Carpenter et al, 1956	(82)
Type:	LD50	
Species:	guinea pig	
Value:	= 960 - 1500 mg/kg bw	
Method:	other: in water at ≤10%, by gavage	
Year:		
GLP:	no	
Test subs.:	other TS	
Reference:	Smyth et al, 1941	(80)
Type:	LD50	
Species:	guinea-pig	
Value:	1414 mg/kg bw	
Method:	OECD TG 401	
Year:		
GLP:	yes	
Test subs.:	purity 99.8%	
Remark:	Test conducted in males and females. At necropsy, necrosis and haemorrhage in the gastric mucosa observed. No signs of haematotoxicity were seen in the study.	
Reference:	Eastman Kodak Co, 1994	(87)

Type: other: study to show effect of age on toxicity and metabolism.
Species: rat (male)
Value:
Method: other: Gavage at doses of 32, 63, 125, 250 or 500 mg/kg 2-BE in water.
Year: 1987
GLP: no data
Test subs.: other TS: 99% pure.
Remark: Older rats significantly more susceptible. There was a dose-dependent decrease in circulating red blood cell count, haemoglobin concentration and haematocrit together with an increase in free haemoglobin in blood and subsequent haemoglobinuria. Histopathological changes were found in the liver and kidney. There were significant increases in relative spleen weights at 125 and 500 mg/kg.
Reference: Ghanayem et al, 1987 (84)

Type: other: haematotoxicity study.
Species: rat
Value:
Method: other: doses (by gavage) of 50-500 mg/kg and blood samples taken after 0.5, 2, 4 hours
Year: 1992
GLP: no data
Test subs.: other TS
Remark: Scanning microscopy of erythrocytes showed a change from discocyte to spherocyte and flow cytometric analysis showed an increase in mean cell volume and decreased mean cell haemoglobin concentration compared with the controls. Whole blood viscosity increased at doses of 50 and 100 mg/kg and decreased at higher dosages due to haemolysis.
Reference: Kurantsin-Mills and Lessin, 1990 (85)

Type: other: haematotoxicity study.
Species: rat
Value:
Method: other: 250 mg/kg by gavage, blood sampled at 2, 8 or 24 hours
Year: 1993
GLP: no data
Test subs.: other TS: Aldrich Chemical Co., >99% pure.
Remark: Mean cell volume and haematocrit values were raised immediately after treatment and decreased with time following exposure. Haemolysis and decreased haemoglobin concentrations and red cell numbers occurred.
Reference: Ghanayem and Sullivan, 1993 (86)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Exposure time: 4 hours
Value: = 2.2 - 2.4 mg/l [450 - 486 ppm]

- Method:** other: rats exposed to 202, 523 or 867 ppm; observation period 14 days.
- Year:** 1983
- GLP:** no data
- Test subs.:** other TS: commercial Butyl Cellosolve
- Remark:** Lowest value in range is for females; highest value for males. Signs of toxicity included rapid, shallow breathing, loss of coordination and red staining around the urogenital area. Autopsy of animals that died revealed enlarged, discoloured kidneys and red fluid in the bladder. Tail lesions observed in survivors at 523 ppm.
- Reference:** Bushy Run, 1980 (90)
- Source:** Union Carbide Chemicals USA
- Type:** other: inhalation hazard test.
- Species:** rat
- Expos. time:** 7 hours
- Value:**
- Method:** OECD TG 403
- Year:** 1981
- GLP:** no data
- Test subs.:** other TS: 99%
- Remark:** Values are expressed as the zero lethality time = 3 hour (5 laboratories) and = 1 hour (1 laboratory). Exposure times were 3 min to 7 hour.
- Reference:** Klimisch et al, 1988 (91)
- Type:** other: single exposure toxicity test.
- Species:** rat
- Expos. time:** 18 hours
- Value:**
- Method:** other: Groups of male and female rats exposed to 500 or 800 ppm for up to 18 hours or to saturated air (4500 mg/m³) for up to 9 hours.
- Year:**
- GLP:** no data
- Test subs.:** other TS
- Remark:** Death occurred in 0/6, 2/6 and 4/6 males after exposure to 4500 mg/m³ for 2, 4 and 9 hours respectively. 1/12 female rats died after 8 hours of exposure to < 800 ppm (3.8 mg/l). Haemoglobinuria was evident. 3/6 females died at 800 ppm for 18 hours and 1/6 females died at 500 ppm (2.4 mg/l) for 4 hours. Haemoglobinuria was evident. 11/13 males and 23/23 females died after exposure to 375 ppm (1.8 mg/l) for 7 hours. Haemoglobinuria was evident.
- Reference:** Carpenter et al, 1956 (82)
- Type:** LC50
- Species:** mouse
- Expos. time:** 7 hours
- Value:** = 3.4 mg/l [700 ppm]
- Method:** other: concentrations of 1.87, 2.71, 3.22, 3.72, 4.46 and 5.86 mg/l used and animals observed for 3 weeks.
- Year:** 1943
- GLP:** no data

Test subs.:	other TS: described as relatively pure	
Remark:	Dyspnoea and severe haemoglobinuria were seen at near lethal concentrations. Mortality was seen 7-32 hours after start of exposure and toxic effects were evident on the spleen.	
Reference:	Werner, 1943	(92)
Type:	other: single exposure toxicity test.	
Species:	guinea pig	
Expos. time:	4 hours	
Value:		
Method:	other: exposure to concentrated vapour.	
Year:		
GLP:	no data	
Test subs.:	other TS	
Remark:	Animals were exposed to concentrated vapour; saturated air contains 0.093% butoxyethanol which, at 25 degree C, is equivalent to 4500 mg/m ³ . One animal died. No haemoglobinuria was observed.	
Reference:	Carpenter et al, 1956	(82)
Type:	other: single exposure toxicity test	
Species:	guinea-pig	
Expos. time:	1 hour	
Value:		
Method:	OECD TG 403, except one hour exposure instead of 4 hours	
Year:		
GLP:	yes	
Test subs.:	2-BE vapour, purity of 2-BE 99.9%	
Remark:	No mortality or clinical signs of toxicity resulted when male and female animals were exposed (whole body) to 633 or 691 ppm (3.1 or 3.4 mg/L) 2-butoxyethanol.	
Reference:	Bushy Run, 1994	(95)
Source:	Union Carbide Chemicals USA	

5.1.3 Acute Dermal Toxicity

Type:	other: single dermal application toxicity.	
Species:	rat	
Value:		
Method:	other: single doses of 200, 260, 320, 375 or 500 mg/kg applied to dorsal shaved skin and covered with a glass capsule.	
Year:	1987	
GLP:	no data	
Test subs.:	purity 99%	
Remark:	Percutaneous absorption, metabolism and haemolytic activity study. 500 mg/kg caused haemolytic effects and/or haemoglobinuria within 6 hours of application. Some effects were seen at lower doses but not at 200 mg/kg.	
Reference:	Bartnik et al, 1987	(93)
Type:	LD50	
Species:	rabbit	

Value: = 610 mg/kg bw
Method: other: as described in 21 CFR 191.10 but with abraded skin.
Year:
GLP: no data
Test subs.: other TS: Eastman Organic Chemicals
Reference: Roudabush et al, 1965 (94)

Type: LD50
Species: rabbit (male)
Value: = 400 - 500 mg/kg bw
Method: other: applied to male rabbits for 24 hours, covered intact and observed for 14 days.

Year:
GLP: no data
Test subs.: other TS
Remark: Animals that died showed extreme congestion of the kidneys, haemoglobinuria, pale liver and engorged spleen. Animals tolerated higher doses when a single dose was rubbed onto uncovered skin (2.0 ml killed 2/4 rabbits over a period of 14 days).
Reference: Carpenter et al, 1956 (82)

Type: LD50
Species: rabbit
Value: = 99 mg/kg bw
Method: other: Applied to clipped backs (area 1.54 cm²) for 8 hours and observed for 15 days. Doses were 0.08, 0.10, 0.12, 0.15, 0.20 or 0.25 ml/kg.

Year:
GLP: no data
Test subs.: other TS: > 99.5%
Remark: Signs before death were prostration, hypothermia and haemoglobinuria. Early deaths were caused by narcosis, respiratory failure or possibly cardiac failure. Late deaths were due to renal impairment. In animals that died there were changes in the liver, spleen, lung and kidney tissues including haemoglobinuria, nephrosis and interstitial reaction. Skin damage occurred at all dose levels. There were no changes in surviving animals treated at 0.08 and 0.10 ml/kg. There were persistent kidney lesions in other groups.
Reference: Duprat and Gradiski, 1979 (96)

Type: LD50
Species: rabbit
Value: = 435 mg/kg bw
Method: other: Eastman Kodak Company, Health, Safety and Human Factors Laboratory Protocol (similar to OECD TG 402).

Year:
GLP: no
Test subst.: other TS: Eastman Kodak Company
Remark: Clipped and abraded skin was exposed to dosages of 153, 307, 614 or 1239 mg/kg for 14 days under occlusive wrap. Moderate irritation of the skin was noted. Clinical signs included reduced activity, salivation,

nasal discharge, cyanosis, iritis and prostration. Findings at necropsy included discoloration of the kidney and liver, increased vascularization of the small and large intestines, and haemoglobinuria. No treatment-related gross effects were noted at the two lowest dose levels.

Reference: Eastman Kodak Co., 1981 (97)

Type: LD50
Species: rabbit
Value: 567 mg/kg (male): 636 mg/kg (female)
Method: other: 4 animals at 2 dose levels (0.5 and 1.0 ml/kg) were used.
Year:
GLP no data
Test subst.: commercial Butyl Cellosolve
Remark:. The effects observed at necropsy were; discoloured liver, kidneys, adrenals and intestines, and bloated stomach. Haemoglobinuria was observed in animals at both doses. Nystagmus was seen in two high dose females some hours after exposure.

Reference: Bushy Run, 1980 (99)
Source: Union Carbide Chemicals, USA

Type: LD50
Species: guinea pig
Value: = 210 mg/kg (intact skin), 270 mg/kg bw (abraded skin)
Method: other: As described in 21 CFR 191.10 but with abraded skin. Applied neat on a cellulose pad to intact or abraded skin.

Year:
GLP no data
Test subst.: other TS: Eastman Organic Chemicals
Remark:.
Reference: Roudabush et al, 1965 (94)

Type: LD50 (limit dose)
Species: guinea pig
Value: > 2000 mg/kg bw
Method: OECD TG 402 (limit test)
Year:
GLP yes
Test subst.: purity 99.8%
Remark:. No clinical signs of toxicity observed during study. No effects on organs noted at necropsy.
Reference: Eastman Kodak Co. 1994 (102)

5.1.4 Acute Toxicity, Other Routes

Type: LD50
Species: rat (female)
Route of admin.: i.p.
Value: = 300 - 850 mg/kg bw
Method: other:
Year:

GLP	no data	
Test subst.:	other TS: neat	
Reference:	Carpenter, 1956	(82)
Type:	LD50	
Species:	rat	
Route of admin.:	i.v.	
Value:	= 290 - 500 mg/kg bw	
Method:	other	
Year:		
GLP:	no data	
Test subst.:	other TS: neat or as a 3% solution in 0.75% NaCl solution.	
Remark	Value presented is for the preparation in saline. Neat butoxyethanol gave an LD50 value of 270-340 mg/kg and caused haemolysis	
Reference:	Carpenter et al, 1956	(82)
Type:	LD50	
Species:	mouse	
Route of admin.:	i.v.	
Value:	= 1130 mg/kg bw	
Method:	other	
Year:		
GLP	no data	
Test subst.:	other TS: neat or as a 3% solution in 0.75% NaCl solution.	
Remark:	LD50 value is for preparation in saline.	
Reference:	Carpenter et al, 1956	(82)
Type:	LD50	
Species:	rabbit	
Route of admin.:	i.v.	
Value:	= 380 - 650 mg/kg bw	
Method:	other	
Year:		
GLP:	no data	
Test subst.:	other TS: neat or as a 3% solution in a 0.75% NaCl solution.	
Remark:	LD50 value given is for a solution in saline. Neat butoxyethanol gave an LD50 of 280 mg/kg.	
Reference:	Carpenter et al, 1956	(82)
Type:	other: single injection toxicity study.	
Species:	rat	
Route of admin.:	i.v.	
Value:	25, 37.5, 50, 62.5 or 75 mg/kg	
Method:	other: doses of 25, 37.5, 50, 62.5 or 75 mg/kg in 5 ml/kg solution infused at 1 ml/min.	
Year:		
GLP:	no data	
Test subst.:	other TS: possibly in phosphate buffered saline.	
Remark:	Haemolysis detected only at the highest dosage.	
Reference:	Bartnik et al, 1987	(93)

Type: LD50
Species: rat (female Sprague-Dawley)
Route of admin.: i.p.
Value: The respective LD50 values for n-Butyl Oxitol and Dowanol EB were 252 mg/kg (confidence limits 203-312) and 317 mg/kg (confidence limits 241-417).
Method: other
Year:
GLP: no data
Test subst.: 2 brands of 2-butoxyethanol - n-Butyl Oxitol and Dowanol EB
Remark: Haemoglobinuria and bloody nasal discharge were observed in all animals. In surviving animals at 398 or 500 mg/kg bw, tremors were noted at 22 hours after injection. Body weight gains seemed normal in surviving animals after the two-week post-exposure period. There were no controls in the study.
Source: Dow Chemical, 1972 (109)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Result: not irritating
EC classif.: not irritating
Method: other: BASF AG Test
Year:
GLP: no
Test subst.: other TS: BASF AG
Source: BASF (100)

Species: rabbit
Result: slightly irritating
EC classif.: irritating
Method: other: undiluted material, 4 hour unoccluded application.
Year:
GLP: no data
Test subst.: other TS
Reference: Tyler, 1984 (101)

Species: rabbit
Result: Response was described as slight erythema, with slight oedema after the seventh application.
EC classif.: No firm conclusion can be drawn from this study as only a single rabbit was tested.
Method: no data
Year:
GLP: no data
Test subst.: 2-Butoxyethanol (undiluted)
Remark: 0.5 mL was applied to the clipped intact skin under an occlusive wrap for a series of ten applications over 14 days
Source: Dow Chemical, USA (62)

Species:	rabbit	
Result:	moderate irritant	
EC classif.:	insufficient data	
Method:	other: Eastman Kodak Company, Health, Safety and Human Factors Laboratory Protocol	
Year:		
GLP:	no data	
Test subst.:	Other TS; 2-Butoxyethanol(undiluted)	
Remark:	2-BE applied under an occlusive dressing for 24 hours at a dose just below the mortality level (at 0.3 g/kg bw).	
Reference:	Eastman Kodak Co., 1981	(97)
Species:	New Zealand albino rabbit	
Result:	irritating	
EC classif.:	irritant	
Method:	EEC method (similar to OECD Test Guideline 404)	
Year:		
GLP:	no data	
Test subst.:	Other:	
Remark:	Individual data were not reported for the 3 animals used per substance in the study	
Reference:	Zissu 1995	(67)
Species:	rabbit (male, New Zealand White)	
Result:	irritating	
EC classif.:	irritant	
Method:	EEC method (similar to OECD Test Guideline 404)	
Year:		
GLP:	no data	
Test subst.:	2-butoxyethanol	
Remark:	0.5 mL of 2-butoxyethanol was applied to 6 animals for 4 hours. Skin reactions were scored at 5 hours; 1 day; 3 days and 7 days. The results were variable, with severe and persistent erythema with eschar and severe oedema observed in 3 rabbits and very slight oedema and erythema observed in the others. No oedema was observed in any rabbit after 7 days.	
Reference:	Rohm and Haas, 1983	(70)
Species:	guinea pig	
Result:	irritating	
EC classif.:	irritating	
Method:	other: Eastman Kodak Company, Health, Safety and Human Factors Laboratory Protocol	
Year:		
GLP:	no	
Test subst.:	other TS: undiluted 2-BE	
Remark:	Depilated skin was exposed to doses of 1, 5, 10 or 20 ml/kg for 24 hours under an occlusive wrap. The response was described as 'strong irritant'.	
Reference:	Eastman Kodak Co., 1981	(97)

Species: guinea-pig
Result: 25% solution irritating, 10% non-irritating
EC Classif.: insufficient data
Method: other:
Year:
GLP: no data
Test subs.: other TS; 10% and 25% 2-butoxyethanol in 0.9% saline
Remarks: Conducted as a preliminary occluded patch irritation test designed to determine dose levels for the main skin sensitisation study.
Reference Unilever Research, 1989 (107)

5.2.2 Eye Irritation

Species: rabbit
Result: highly irritating
EC classif.: irritating
Method: Draize Test
Year: 1944
GLP no data
Test subst.: other TS: butoxyethanol in polyethylene glycol.
Remark: Scores for different concentrations tested at 24 hours post-instillation were 100% - 66; 70% - 49; 30% - 39; 20% -2 and 10% - 1 by the Texaco single-digit toxicity classification system (De Sousa et al. (1984) Toxicol. Appl. Pharmacol. 76, 234). In assessment by measurement of corneal thickness, highest concentration still classified as severely irritating, 70% concentration moderately irritating and others mildly irritating.
Reference: Kennah et al, 1989 (103)

Species: rabbit
Result: irritating
EC classif.: irritating
Method: other: Directive 79/83/EEC Annex V part B with lesions evaluated by Directive 83/467/EEC Annex VI, part IID.
Year: 1979
GLP: no data
Test subs.: other TS: 99%, neat.
Remark: Mean erythema scores and % corneal thickening indicated that the substance should be classified as irritant.
Reference: Jacobs and Martens, 1989 (104)

Species: rabbit
Result: not irritating
EC classif.: not irritating
Method: other: BASF test
Year:
GLP: no data
Test subs.: other TS: BASF AG
Source: BASF, 1956 (106)

Species:	rabbit	
Result:	strong irritant	
EC classif.:	irritating	
Method:	other: Instillation of 0.1 mL. Only one animal used.	
Year:		
GLP:	no data	
Test subs.:	2-Butoxyethanol (undiluted)	
Remark:	Severe conjunctivitis, iritis and corneal opacity, with irritation still obvious 21 days after exposure	
Source:	Dow Chemical, USA	(62)
Species:	rabbit	
Result:	strong irritant	
EC classif.:	irritating	
Method:	Other: Internal protocol used.	
Year:		
GLP:	no data	
Test subs.:	2-butoxyethanol (undiluted & aqueous)	
Remark:	0.005 mL of undiluted 2-BE caused severe corneal injury and iritis, 0.5 mL of a 15% aqueous solution caused moderate corneal injury, no effects with 0.5 ml of 5% aq. solution.	
Reference:	Bushy Run, 1980	(59)
Source:	Union Carbide Chemicals, USA	

5.2.3 Respiratory Irritation

Type:	RD50	
Species:	mice (male)	
Result:	weak respiratory irritant [RD50 = 2825 ppm]	
EC Classif.:	insufficient data	
Method:	Alarie test	
Year:		
GLP:	no data	
Test subs.:	2-BE vapour	
Remarks:	Animals exposed to vapour concentrations up to approx. 1100 ppm, so result obtained by extrapolation.	
Reference	Kane et al, 1980	(78)

5.3 Sensitisation

Type:	Magnusson and Kligman guinea-pig maximisation test	
Species:	guinea-pig	
Result:	not sensitising	
EC Classif.:	not sensitising	
Method:	other: minor deviations from OECD Test Guideline 406	
Year:		
GLP:	yes	
Test subs.:	other TS; aqueous solutions of 2-BE in 0.9% saline	
Remarks:	In induction phase, group of 6 male and 4 female animals treated intradermally with 0.5% 2-BE in 0.9% saline, followed by dermal application of 25% solution (in 0.9% saline) 7 days later under an	

occlusive wrap. Animals then challenged twice with 10% 2-BE, firstly at 13 days after induction, and then a week later.
Reference: Unilever Research, 1989 (107)

Type: Magnusson and Kligman guinea-pig maximisation test
Species: guinea-pig
Result: not sensitising
EC Classif.: not sensitising
Method: Magnusson and Kligman protocol
Year: 1969
GLP: no data
Test subs.: other TS; purity 99%
Remark: Sensitising and challenge concentrations 1% 2-BE.
Reference: Zissu, 1995 (67)

Type: repeated insult patch test
Species: human
Result: not sensitising
EC Classif.: not sensitising
Method: Induction phase: 0.2 ml of 10% aqueous solution of 2-BE applied under a patch for 24 hours to the backs of the subjects for a total of 9 times over a 3-week period
 Challenge phase: 10% 2-BE applied to previously unexposed sites two weeks later
Year:
GLP: yes
Test subs.: other TS;
Remark: The skin sensitisation potential of a 10% aqueous solution 2-butoxyethanol (2-BE) was tested by repeated insult patch test on 200 volunteers. In the induction phase, a slight redness (without swelling) was observed in 4 subjects after the first application. By the eighth application, 40 subjects exhibited slight erythema and in another 14, erythema was more definite. In the challenge phase, slight erythema was noted in 7 subjects after 48 hours and in 12 subjects after 72 hours.
Reference: TKL Research, 1992 (175)
Source: CMA USA

5.4 Repeated Dose Toxicity

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 9 days
Frequency of treatment: 6 hours/day for 5 days, 2 days non-exposure and 6 hours/day for 4 days.
Post obs. period: 14 days
Doses: 0.97, 0.415 and 1.183 mg/l [20, 86, 245 ppm]
Control Group: yes, concurrent vehicle
NOAEL: = 0.97 mg/l [20 ppm]
Method: similar to OECD TG 412.

Year:	
GLP:	no data
Test subst.:	other TS: commercial Butyl Cellosolve, purity > 99%
Result:	8 animals/sex/group. No deaths occurred. Treatment-related observations were audible respiration and nasal discharge and reduced body weight gain in rats of one or both sexes at the highest or intermediate dose levels. At 245 ppm, red stained urine was seen in both sexes of the highest concentrations after first and second exposures but not subsequently. Haematological effects including decreased red blood cell counts, haemoglobin concentrations and mean corpuscular haemoglobin concentration and increased mean corpuscular volume (MCV), nucleated red blood cells and, in males only, reticulocytes. A substantial recovery was observed after 14 days, but the decrease in erythrocyte count and the increases in MCV and haemoglobin were still apparent. At 86 ppm, the haematological effects were less marked. Relative liver weights in both sexes were increased at 245 ppm, and in females only at 86 ppm. These changes were not apparent at 14 days. There were no gross lesions. At 20 ppm, no significant effects were observed.
Reference:	Bushy Run 1981; Dodd et al 1983 (88)(108)
Source:	Union Carbide Chemicals USA
Species:	rat
Sex:	male/female
Strain:	Fischer 344
Route of admin.:	inhalation
Exposure period:	42 or 90 days
Frequency of treatment	6 hours/day, 5 days/week
Post obs period:	not specified
Doses:	0.024, 0.121 and 0.372 mg/l [5.0, 24.6, 77 ppm]
Control Group:	yes, concurrent vehicle
NOAEL:	= 0.121 mg/l [24.6 ppm]
Method:	Similar to OECD TG 413. Some rats killed after 42 days and the remainder maintained to 90 days. Gross and histopathological examinations conducted in rats from controls and highest dosage groups.
Year:	
GLP:	no data
Test subst.:	other TS: commercial Butyl Cellosolve, purity > 99%
Result:	16 animals/sex/group. There were no deaths or signs of toxicity. Decrease in bodyweight gain during weeks 2-4 in high dose females was transient. Haematological effects were observed at 77 ppm only, with the effects greater at 6 weeks than at 13 weeks. These effects included decreases in red blood cell count, haemoglobin and haematocrit, and an increase in mean corpuscular haemoglobin. There were no significant treatment-related changes in gross or microscopic lesions or in serum chemistry or urinalysis observations.
Reference:	Bushy Run 1981; Dodd et al 1983 (60)(108)
Source:	Union Carbide Chemicals USA

Species:	rat	
Sex:	male/female	
Strain:	Fischer 344	
Route of admin.:	drinking water	
Exposure period:	2 weeks	
Frequency of treatment:	continuous	
Post obs period:	none	
Doses:	males: 0, 73, 108, 174, 242, 346 mg/kg/day females: 0, 77, 102, 152, 203, 265 mg/kg/day	
Control Group:	yes	
NOAEL:	males: 346 mg/kg/day, females: 203 mg/kg/day	
LOAEL:	females: 265 mg/kg/day	
Method:	other: clinical observations, water consumption, complete necropsies, organ weight measurements.	
Year:		
GLP:	yes	
Test subst.:	other TS: Aldrich Chemical Co. Ltd.	
Result:	5 animals/sex/group. None of the animals died during treatment and there were no treatment-related changes in body weight of males. Female rats had lower weight gain in the highest dosage group. Water consumption was lowered at the highest dosages in both sexes; this resulted in lower target dosages. A slight decrease in thymus weight was observed in female rats at highest dose. Microscopic examination of the testis and epididymis was only conducted in the lower dose group and controls.	
Reference:	NTP, 1993	(110)
Species:	rat	
Sex:	male/female	
Strain:	Sprague-Dawley	
Route of admin.:	drinking water	
Exposure period:	21 days	
Frequency of treatment:	continuous	
Post obs period:	none	
Doses:	180, 506 mg/kg/day in males; 204, 444 mg/kg/day in females.	
Control Group:	yes, concurrent vehicle	
Method:	other: toxicity including immunotoxicity study following injection with Keyhole Limpet haemocyanin on day 20.	
Year:		
GLP:	no data	
Test subst.:	other TS: 97%.	
Result:	Body weights were decreased in males at the highest dosage and in females at both dosages. No treatment-related effects occurred in absolute or relative organ weights and no pathological changes were seen in thymus, testes, liver or kidneys. Natural killer cell activity was enhanced at the low dose level in both males and females but there was no effect on the production of antibody, interferon, interleukin-2 or splenocytes, or evidence of delayed-type hypersensitivity reaction.	
Reference:	Exon et al, 1991	(111)

Species: rat
Sex: male/female
Strain: Fischer 344
Route of admin.: drinking water
Exposure period: 13 weeks
Frequency of treatment: continuous
Post obs period: none
Doses: males: 0, 69, 129, 281, 367, 452 mg/kg/day
 females: 0, 82, 151, 304, 363, 470 mg/kg/day
Control Group: yes
NOAEL: males: 129 mg/kg/day, females: not reached
LOAEL: males: 281 mg/kg/day, females: 82 mg/kg/day
Method: other: clinical observations, body weight changes, water consumption, haematology and clinical chemistry evaluations, urinalysis, complete necropsy examinations and histopathology of tissues were recorded.

Year:

GLP:

Test subst.:

Result:

other TS: Aldrich Chemical Co.
 None of the animals died during the exposure period. Bodyweights were decreased in both sexes in the top two dose levels. Dose-related decrease in water consumption in females resulting in reduced target dosages. Diarrhoea was noted. Males showed mild decreases in haemoglobin levels at dosages ≥ 129 mg/kg/day, mild anaemia, moderately increased reticulocyte counts and mild-markedly increased leukocyte counts at 281 mg/kg/day. Thrombocytopaenia and mild increases in bone marrow cellularity were noted at ≥ 367 mg/kg/day. In females, there was mild-moderate anaemia at all doses and mild increases in bone marrow cellularity, transient changes in platelet counts and marked leukocytosis at ≥ 304 mg/kg/day.

There were transient changes in total protein, albumin and alkaline phosphatase activity in males and/or females at dosages >129 mg/kg/day. Urine volumes and specific gravity were raised. Uterine atrophy was secondary to a decrease in bodyweight gain.

Histopathological lesions of the liver, spleen and bone marrow in both males and females were recorded. The report concluded that butoxyethanol was relatively nontoxic at the doses tested and affected only the erythroid series of the haematopoietic system.

Reference:

NTP, 1993

(110)

Species: rat
Sex: male
Strain: other: COBS CD(SD)BR
Route of admin.: gavage
Exposure period: 6 weeks
Frequency of treatment: 5 days/week
Post obs period: no data

Doses:	222, 443 and 885 mg/kg bw d
Control Group:	yes, concurrent vehicle
NOAEL:	not reached
LOAEL:	222 mg/kg/day
Method:	other: blood and histopathology of tissues examined.
Year:	
GLP:	no data
Test subst.:	other TS: 99.5%, neat.
Result:	10 animals/group. 2/10 rats in the high dosage and 1/10 in the intermediate dosage group died. Body weight gains and feed consumption were decreased at the highest dosage. Haemoglobinuria observed at all doses, particularly at two highest doses and particularly after first two days. At all doses, there was a dose-dependent decrease in red blood cell count and haemoglobin concentration and an increase in mean corpuscular haemoglobin. At the two higher doses, there was a decrease in mean corpuscular haemoglobin concentration, and an increase in mean corpuscular volume. Serum alanin eaminotransferase and alkaline phosphatase levels were slightly increased and serum glucose was reduced. Body weight-relative liver weights were raised at all dosages whereas increases in kidney, heart, brain and spleen weights increased only at the two highest dosages. Clinical observations included lethargy, rough coats, weakness and inactivity. Enlarged, dark spleens, hepatocytomegaly, focal haemosiderin deposition, minimal haemosiderin accumulation in kidneys and splenic congestion were seen in some animals at upper dosage levels. No adverse effects were observed on the testes, thymus, white blood cells or bone marrow.
Reference:	Krasavage, 1986 (112)
Species:	rat
Sex:	male
Strain:	Fischer 344
Route of admin.:	gavage
Exposure period:	12 days
Frequency of treatment:	daily
Post obs period:	24 hours
Doses:	0, 125 mg/kg/day
Control Group:	yes
Method:	other: treatment for 1,2,3,6 or 12 days. Blood analyses and spleen and liver weights recorded.
Year:	
GLP:	no data
Test subst.:	other TS: Aldrich Chemical Co.
Result:	There were signs of significant haemolysis which became more pronounced up to the third day of dosing. Gradual recovery followed up to day 12. Mean cell volume, ATP concentration, reticulocyte numbers and body weight-relative spleen weights increased up to the sixth day of dosing and declined thereafter. Body weight-relative liver weights were slightly lowered on days 3 and 6 and slightly raised on day 12.

Reference: Ghanayem et al, 1992 (113)

Species: rat
Sex: male
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 4 days
Frequency of treatment: daily
Post obs period: 1-22 days
Doses: 500 or 1000 mg/kg bw d
Control Group: yes, concurrent vehicle
Method: other: rats killed on days 1, 4, 8 and 22 after last treatment; blood and tissues examined.

Year:
GLP: no data
Test subst.: other TS: 99.9%
Result: Body weight gain was reduced at the highest dosage. Relative spleen, liver and kidney weights were increased dosage-relatedly and thymus weight decreased on day 1; changes in spleen and liver weights returned to normal by day 22. Marrow hyperplasia and splenic extramedullary haemopoiesis on day 1 were not evident on day 8. Reduced red blood cell count, haematocrit and haemoglobin and raised mean corpuscular volume, mean corpuscular haemoglobin and reticulocyte counts were transient except for mean corpuscular volume and mean corpuscular haemoglobin which were still elevated at day 22. Changes at 500 mg/kg were mild.

Reference: Grant et al, 1985 (114)

Species: rat
Sex: male
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 3 days
Frequency of treatment: daily
Post obs period: 7 days
Doses: 0, 125, 250 mg/kg bw d
Control Group: yes
Method: other: treatment resumed after recovery period at 125 or 250 mg/kg bw d. Blood after 2, 8 or 24 hour and spleens examined.

Year:
GLP: no data
Test subst.: other TS: Aldrich Chemical Co.
Result: Treated/recovered rats were less sensitive to the haemolytic effects of subsequent treatment than untreated rats. Treatment-related mean cell volume and ATP depletion were less evident in pretreated animals as was an increase in spleen weight/body weight ratio. It was concluded that tolerance to butoxyethanol-induced haemolysis occurred following repeated exposure.

Reference: Ghanayem et al, 1992 (113)

Species: rat
Sex: female
Strain: Sprague-Dawley
Route of admin.: oral unspecified
Exposure period: 7 days
Frequency of treatment: daily
Post obs period: none
Doses: 125 and 1500 mg/kg/day
Control Group: yes, concurrent vehicle
Method: other: sublethal dose given for 6 days and then lethal dose given on day 7.
Year:
GLP: no data
Test subst.: other TS: purity not specified.
Result: Survival rate in pretreated rats was 60% higher than in challenged controls. Protection from lethality and changes in haematocrit values suggested an autoprotective mechanism.
Source: BP Chemicals Ltd. London (116)

Species: mouse
Sex: male/female
Strain: CD-1
Route of admin.: drinking water
Exposure period: 7 days pre-mating and 98 days as breeding pairs.
Frequency of treatment: continuous
Post obs period: none
Doses: 0, 700, 1300, or 2000 mg/kg bw/day
Control Group: yes
NOAEL: = 700 mg/kg/day
Method: other: NTP continuous breeding protocol, NTIS No PB89152425/AS. Heindel, J.J. et al.
Year: 1989
GLP: yes
Test subst.: other TS: >99%.
Result: 8 animals /sex/group. 13/20 females in high-dose group and 6/20 females in mid-dose group died during the study. Toxic effects were decreased body weight gain, increased kidney and liver weights and dose-related decreases in water consumption. No treatment-related histopathological lesions were found in the kidneys of females receiving 1300 mg/kg.
Remark: See comments also in section 5.8 (Toxicity to reproduction)
Reference: Heindel et al, 1990 (117)

Species: mouse
Sex: male/female
Strain: B6C3F1
Route of admin.: drinking water
Exposure period: 2 weeks

Frequency of treatment:	continuous	
Post obs period:	none	
Doses:	males: 93, 148, 210, 370 or 627 mg/kg/day females: 150, 237, 406, 673, 1364 mg/kg/day	
Control Group:	yes	
NOAEL:	males: 210 mg/kg/day, females: 406 mg/kg/day	
LOAEL:	males: 370 mg/kg/day, females: 673 mg/kg bw	
Method:	other: clinical observations, water consumption, complete necropsies and organ weight measurements.	
Year:		
GLP:	yes	
Test subst.:	other TS: Aldrich Chemical Co. Ltd	
Result:	5 animals/sex/group. No deaths were noted and there were no effects on body weights and body weight gains. Water consumption was decreased at all dosages except the highest dosage in females. At two highest doses, thymus weights were decreased in males and dehydration was observed in both sexes. Histopathological examinations were not performed.	
Reference:	NTP, 1993	(110)
Species:	mouse	
Sex:	male/female	
Strain:	B6C3F1	
Route of admin.:	drinking water	
Exposure period:	13 weeks	
Frequency of treatment:	continuous	
Post obs period:	none	
Doses:	males: 118, 223, 553, 676, 694 mg/kg/day females: 185, 370, 676, 861, 1306 mg/kg/day	
Control Group:	yes	
NOAEL:	males: 223 mg/kg/day, females: 370 mg/kg/day	
LOAEL:	males: 676 mg/kg/day, females: 553 mg/kg/day	
Method:	other: clinical observations, water consumption, complete gross necropsies, organ weight measurements and histopathological examination of tissues were recorded.	
Year:		
GLP:	yes	
Test substance:	other TS	
Result:	No treatment related deaths, effects on water consumption, clinical observations or effects on organ weights were recorded. Reduced body weight gain at the 3 highest dosages in both males and females. There were no treatment-related gross or microscopic lesions.	
Reference:	NTP, 1993	(110)
Species:	mouse:	
Sex:	male	
Strain:	ICR	
Route of admin.:	oral (gavage)	
Exposure period:	5 weeks	

Frequency of treatment:	5 days/week	
Post obs period:	none specified	
Doses:	500, 1000 or 2000 mg/kg	
Control Group:	yes	
Method:	other:	
Year:		
GLP:	no data	
Test substance:	other TS	
Result:	5 mice/group. All mice at the highest dose level died. Red blood cell counts were decreased at 500 and 1000 mg/kg whereas white blood cell counts, packed cell volume and haemoglobin concentrations were unaffected.	
Reference:	Nagano et al, 1979	(119)
Species:	guinea pig	
Sex:		
Strain:		
Route of admin.:	dermal	
Exposure period:	5-7 days	
Frequency of treatment:	continuous	
Post obs period:	28 days	
Doses:	0.5 or 2.0 ml in covered depots	
Control Group:	no data specified	
Method:	other: single dermal application left in place for 5-7 days.	
Year:		
GLP:	no data	
Test substance:	other TS: 99%	
Result:	20 animals/group. 0/20 died after 0.5 ml; 13/20 died after 2.0 ml (all deaths by day 7). There were no treatment-related effects on body weight gain.	
Reference:	Wahlberg and Boman, 1979	(120)
Species:	rabbit	
Sex:	male & female	
Strain:	New Zealand White	
Route of admin.:	dermal	
Exposure period:	9 days	
Frequency of treatment:	6 hr a day, 5 day a week	
Post obs period:	14 days	
Doses:	18, 90, 180, 360 mg/kg/day	
Control Group:	control group treated with distilled water.	
NOAEL:	90 mg/kg/day	
LOAEL:	180 mg/kg/day	
Method:	5 rabbits/sex/dose were treated with 1 mL/day of undiluted 2-butoxyethanol or aqueous solutions (5%, 25%, 50%).	
Year:		
GLP:	no data	
Test substance:	commercial Butyl Cellosolve	

Result:	With 25% solution (90 mg/kg/day), erythema only was noted. At 180 mg/kg/day, necrosis was seen in 1/5 males and 4/5 females and haemoglobinuria (in all animals) by day nine. With undiluted 2-BE, severe necrosis was seen in all animals, accompanied by oedema and erythema, plus haemoglobinuria and haematological changes (reduced red blood cell count and haemoglobin and increased mean corpuscular haemoglobin). Haematological parameters returned to normal by the end of the 14-day post-exposure observation period. At 100%, a clour change of the kidney was noted in 3/5 females. In a preliminary study at approx. 225 mg/kg/day, histologic examination of the kidneys at necropsy revealed changes consistent with the late stages of haemoglobinuric nephrosis.
Reference:	Bushy Run 1980 (99)
Source:	Union Carbide Chemicals USA
Species:	rabbit
Sex:	male & female
Strain:	New Zealand White
Route of admin.:	dermal
Exposure period:	13 weeks
Frequency of treatment:	6 hours/day, 5 days/week
Post obs period:	
Doses:	2.8%, 14.3% or 42.8% aqueous solutions, equivalent to 10, 50 and 150 mg/kg bw respectively.
Control Group:	control group treated with distilled water
NOAEL:	150 mg/kg/day
Method:	10 rabbits/sex/dose were treated with 1 mL/day of aqueous solutions of 2-butoxyethanol
Year:	
GLP:	yes
Test substance:	commercial Butyl Cellosolve
Result:	Haematological and clinical chemistry parameters were measured at weeks 4 and 12 during the study and a comprehensive histopathological examination was conducted on all animals at necropsy. There were no significant findings. Slight erythema was noted intermittently in all animals, including the controls.
Reference:	WIL Research Laboratories 1983 (68)
Species:	various
Sex:	male and female
Route of admin.:	inhalation
Exposure period:	4 days
Frequency of treatment:	7 hours/day
Post obs period:	2 weeks
Doses:	57-58 ppm or 100 ppm
Control Group:	no controls were used
Method:	other
Year:	
GLP:	no data

Test substance:	2 brands of 2-butoxyethanol - n-Butyl Oxitol and Dowanol EB	
Result:	Dose groups comprised 2 Beagle dogs, 6 guinea-pigs and 8 rats. At 57-58 ppm, one guinea-pig died of respiratory failure during the study but there were no other deaths and no significant clinical observations. At necropsy (guinea-pigs and rats), no treatment-related gross pathological changes were observed. At 100 ppm, haemoglobinuria observed in rats (after the first exposure only), female guinea-pigs died after the second day, and one of the dogs displayed unusual behaviour after the second exposure.	
Source:	Dow Chemical 1972	(109)
Species:	various	
Sex:	male and female	
Route of admin.:	inhalation	
Exposure period:	30, 60 or 90 days	
Frequency of treatment:	7 hr per day	
Post obs period:	no data	
Doses:	up to 494 ppm	
Control Group:	no data	
Method:	other	
Year:		
GLP:	no data	
Test substance:	commercial Butyl Cellosolve	
Result:	Test animals included rats, mice, guinea-pigs, dogs and monkeys. Haemoglobinuria and/or increased red blood cell fragility were observed in all species except the guinea-pig, with the animals generally returning to normal overnight. Older animals were more susceptible to haemolytic effects. Increased relative liver and kidney weights were noted at and above 107 ppm in rats and increased relative kidney weight at and above 203 ppm in guinea-pigs.	
Reference:	Carpenter, 1956	(82)
Species:	laboratory animal	
Sex:	no data	
Strain:	no data	
Route of admin.:	inhalation	
Exposure period:	9 days	
Frequency of treatment:	6 hour/day	
Post obs period:		
Doses:	537 ppm (2,645 mg/l)	
Control Group:	no data specified	
Method:	other: BASF Test	
Year:		
GLP:	no data	
Test substance:	other TS: BASF AG	
Remark:	Dose groups comprised 2 cats, 2 rabbits, 10 guinea pigs, 10 rats and 20 mice.	
Result:	Eine Katz starb nach 7 Expositionen, die beiden Kaninchen starben nach 2 Expositionen, die meisten Ratten starben nach der 2. - 5.	

Exposition und etwa die Haelfte der Maeusen wurde eine starke Haemoglobinurie festgestellt, die zu toedlicher Anaemia fuehrte. Die Katzen und Meerschweinchen zeigten keine Anzeichen einer Haemolyse.

Source: BP Chemicals Ltd. London (121)

5.5 Genetic Toxicity in Vitro

Type: Ames test
Test system: S.typhimurium strains TA100, TA1535, TA1537, TA97, TA98.
Concentration: 0, 100, 333, 1000, 3333 or 10000 ug/plate
Metabolic activation: with and without
Result: negative
Method: OECD Test Guideline 471
Year:
GLP: yes
Test substance: other TS: Aldrich Chemical Co, >99%
Reference: NTP 1993 (110)

Type: Cytogenetic assay
Test system: Chinese hamster ovary (CHO) cells
Concentration: 2513, 3750 and 5000 ug/ml
Met. activation: with and without
Result: negative
Method: other: Galloway et al. (1987). Environ. Mol. Mutagen. IO (Suppl. 10), 1-175
Year: 1987
GLP: yes
Test substance: other TS: Aldrich Chemical Co; 99%
Remark: 2-Butoxyethanol induced cell cycle delay but not chromosomal aberrations.
Reference: NTP 1993 (110)

Type: Sister chromatid exchange assay
Test system: Chinese hamster ovary (CHO) cells
Concentration: 500-5000 ug/ml
Met. activation: with and without
Result: negative
Method: other: Galloway et al. (1987). Environ. Mol. Mutagen. IO (Suppl 10) 1-175.
Year: 1987
GLP: yes
Test substance: other TS: Aldrich Chemical Co.
Remark: The highest test concentrations were toxic in systems without metabolic activation but not in the presence of S9.
Reference: NTP 1993 (110)

Type: other: mutagenic effect on bacteriophage T4D.
System of testing: induction of rapid lysis mutants of bacteriophage T4D in bacterial strains of E. coli B, CR63 and K12 lambda-h measured.
Concentration: not specified

Met. activation:	no data	
Result:	negative	
Method:	other: as specified above	
Year:		
GLP:	no data	
Test substance:	other TS	
Remark:	Butoxyethanol had a severe toxic effect upon phage yield.	
Reference:	Kvelland, 1988	(124)
Type:	point mutation assay	
Test system:	Chinese hamster ovary (CHO) cells	
Concentration:	140-9000 µg/mL	
Met. activation:	with and without	
Result:	negative	
Method:	local protocol	
Year:		
GLP:	no data	
Test substance:	commercial Butyl Cellosolve	
Remark:	Cells were exposed for 5 hours. At the highest dose, 2-butoxyethanol was cytotoxic with S9, but non-toxic without S9.	
Reference:	Bushy Run 1980	(89)
Source:	Union Carbide Chemicals USA	
Type:	Sister chromatid exchange (SCE) assay	
Test system:	Chinese hamster ovary (CHO) cells	
Concentration:	63-2250 µg/mL	
Met. activation:	with and without	
Result:	negative	
Method:	Based on method of Perry and Wolff in Nature 251, p.156 (1974)	
Year:		
GLP:	no data	
Test substance:	commercial Butyl Cellosolve	
Remark:		
Reference:	Bushy Run 1980	(89)
Source:	Union Carbide Chemicals USA	
Type:	Unscheduled DNA Synthesis (UDS) assay	
Test system:	rat hepatocytes	
Concentration:	0.9-900 µg/mL	
Met. activation:		
Result:	positive	
Method:	Cells treated for 2 hr in the presence of tritiated thymidine. UDS activity determined by measurement of radioactivity in liver cell nuclei	
Year:		
GLP:	no data	
Test substance:	commercial Butyl Cellosolve	
Remark:	A statistically significant induction of UDS was observed at the two lowest doses, with the maximum effect at 9 µg/mL. This assay should be regarded as inconclusive as there was no clear dose-related response and various experimental problems occurred during the study.	
Reference:	Bushy Run 1980	(89)

Source:	Union Carbide Chemicals USA	
Type:	Ames test	
Test system:	<i>S.typhimurium</i> strains TA1538, TA1537, TA1535, TA100 and TA98	
Concentration:	up to 5000 µg/plate	
Met. activation:	with and without	
Result:	negative	
Method:	conducted in accordance with OECD Test Guideline 471	
Year:		
GLP:	no data	
Test substance:	T-3722 (3M product), containing 18% 2-butoxyethanol	
Remark:	Other components in the product included isopropyl alcohols (18%) and a fluorochemical salt (27%).	
Reference:	SRI International 1985	(98)
Type:	Ames test	
Test system:	<i>S.typhimurium</i> strains TA97a, TA98, TA100 and TA102	
Concentration:	no data	
Met. activation:	with and without	
Result:	positive response to TA97a (2.2 mg/plate) with and without S9 negative response to TA98, TA100 and TA102	
Method:	no data	
Year:		
GLP:	no data	
Test substance:	2-butoxyethanol	
Remark:	The metabolite 2-butoxyacetic acid and the intermediate metabolite 2-butoxyacetaldehyde were negative to all strains.	
Reference:	Hoflack et al 1995	(115)
Type:	gene mutation assay	
Test system:	CHO-AS52 cells	
Concentration:	up to 0.1% v/v (7.6 mM) 2-butoxyethanol up to 0.2% v/v (15.2 mM) 2-butoxyacetaldehyde (BAL)	
Met. activation:	without	
Result:	negative	
Method:	cells treated with 2-BE or BAL in plain F12 medium for 5 hours	
Year:		
GLP:	no data	
Test substance:	2-BE - Aldrich Chemical Co.; BAL purity > 98%	
Remark:	2-BE is metabolised to BAL 2-BE cytotoxic at 0.5%, BAL cytotoxic at 0.26%	
Reference:	Chiewchanwit and Au 1995	(118)
Type:	Ames test	
System of testing:	<i>S. typhimurium</i> strains TA97a & TA100 and the <i>E. coli</i> strain WP2uvrA	
Concentration:	up to 10 mg/plate	
Met. activation:	with and without	
Result:	negative	
Method:	standard OECD and EC protocols, except a higher dose used	
Year:		

GLP: no data
Test substance: purity 99%
Remark: Assay includes repeat of assay by Hoflack et al 1995
Reference: Gollapudi et al 1995 (123)
Source: CMA, USA

Type: sister chromatid exchange (SCE) assay
Test system: human lymphocytes
Concentration: 500, 1000, 2000, 3000 ppm
Met. activation: without
Result: positive
Method: no data

Year:
GLP: no data
Test substance:
Remark: As the assays were conducted without metabolic activation or positive controls, no firm conclusions can be drawn.
Reference: Villalabos-Petrini et al 1989 (125)

Type: chromosomal aberrations
Test system: human lymphocytes
Concentration: 500, 1000, 2000, 3000 ppm
Met. activation: without
Result: negative
Method: no data

Year:
GLP: no data
Test substance:
Remark: As the assays were conducted without metabolic activation or positive controls, no firm conclusions can be drawn.
Reference: Villalabos-Petrini et al 1989 (125)

Type: Various
Test system: V79 cells
Concentration: no data
Met. activation: no data
Result: positive at high 2-BE concentrations
Method: no data

Year:
GLP: no data
Test substance:
Remark: 2-BE induced mutations at the HGPRT locus. In other tests, 2-BE was a weak inducer of SCEs and aneuploidy at high doses, and at non-cytotoxic doses 2-BE elicited a dose-dependent inhibitory effect on intercellular communication. Metabolites BAA and BAL also tested.
Reference: Elias et al 1996 (131)

5.6 Genetic Toxicity in Vivo

Type: Micronucleus assay (bone marrow)
Species: mice

Strain:	CD-1	
Route of admin.:	intraperitoneal injection	
Exposure period:	24, 48 and 72 hr	
Doses:	2-BE: single doses 150-1000 mg/kg; BAL 50-200 mg/kg.	
Method:	Other: Eight (4/sex) test animals were used per test group.	
Year:		
GLP:		
Result:	negative	
Test substance:		
Remark:	There was no induction of micronucleated polychromatic erythrocytes in bone marrow for 2-BE or BAA. The P/N ratio 1.7 at 1000 mg/kg (2-BE) and 0.78 at 200 mg/kg (BAA) indicating that BAA was more toxic to erythropoiesis than 2-BE.	
Reference:	Elias et al, 1996	(131)
Type:	DNA adduct formation	
Species:	rat	
Strain:		
Route of admin.:		
Exposure period:	single dose	
Doses:	120 mg/kg	
Method:	Other: Animals killed 24 hours after dosing	
Year:		
GLP:		
Result:	DNA adducts were not detected and methylation status was unaltered in the all organs	
Test substance:		
Remark:	3 treated and 3 control animals were used in study. No DNA binding in liver, brain, kidney, spleen and testis observed (using ³² P postlabelling) following exposure.	
Reference:	Keith et al, 1996	(132)
Type:	DNA adduct formation	
Species:	mouse	
Strain:	Transgenic (carrying the v-Ha-ras oncogene)	
Route of admin.:	subcutaneous	
Exposure period:	2 weeks	
Doses:	1500 mg/kg (approximately 120 mg/kg/day)	
Method:	Other: animals (8 to 24 per group) were used and killed at between 5 and 120 days	
Year:		
GLP:		
Results:	DNA adducts were not detected and methylation status was unaltered in all organs following exposure.	
Test substance:	2-butoxyethanol.	
Remark:	No DNA binding in liver, brain, kidney, spleen and testis observed (using ³² P postlabelling) following exposure. Animals were also examined for tumour formation at 120 days with no statistical difference from controls.	
Reference:	Keith et al, 1996	(132)

5.7 Carcinogenicity

Remark: No chronic studies have been completed. NTP started chronic inhalation studies in rats and mice in 1993.

Source: BP Chemicals Ltd. London (122)

5.8 Toxicity to Reproduction

Type: two generation study

Species: mouse

Sex: male/female

Strain: CD-1

Route of admin.: drinking water

Exposure Period:

Frequency of treatment: continuous

Premating Exposure Period: male and female: 7 days

Test duration: For 105 days

Doses: continuous breeding phase: 0, 720, 1340, 2050 mg/kg/day; crossover mating phase: 1830 mg/kg/day; final phase: 950 mg/kg/day

Control Group: yes

Method: other: Continuous breeding protocol in CD-1 mice. NTIS No PB89152425/AS, Heindel et al, Fund. Appl. Toxicol. vol. 15, p.683-696, 1990. Continuous breeding of Fo for 14 weeks then cross-over mating with control and mid-dose groups then assessment of F1 fertility in low dose group

Year: 1989

GLP: no data

Test substance: other TS: >99%

NOAEL Parental: = 720 mg/kg/day

Result: Effects in Fo include high mortality in high-dose (13/20) and medium-dose (6/20) females and body weight loss in both sexes. Water consumption was lowered dose-relatedly in all groups. At 1% and 2%, dose-related decrease in litter size, pup viability and live pup weight. At 0.5%, slight decrease in live pup weight

At crossover mating, no effect on mating index but fertility index and number of live pups/litter reduced when treated females mated with control males. Results suggest that fertility effects primarily due to effects on female mice.

In final phase, no significant fertility and reproductive effects observed in F1 animals as indicated by proportion of successful copulation and fertile females, litter size, pup viability and live pup weights. No treatment-related changes in weights of reproductive organs, sperm motility, morphology, and the oestrous cycle and frequency. However, significant increase in relative kidney weight in females, and significant increase in relative liver weights in males.

Remark: Females were more sensitive to the reproductive toxicity of 2-butoxyethanol. The high dose was too toxic to be used to determine reproductive toxicity.

Reference: Heindel et al, 1990
(117)

Type: other: effects on reproductive organs
Species: mouse
Sex: male
Strain: JCL-ICR
Route of admin.: gavage
Exposure Period:
Frequency of treatment: 5 days/week
Test duration: 5 weeks
Doses: 500, 1000 and 2000 mg/kg
Control Group: yes
Method: other: effects on testes and associated structures determined.
Year:
GLP: no data
Test substance: other TS
Result: All mice died at the highest dosage. There were no significant effects on the relative weights of the testes or seminal vesicles and coagulating gland.

Reference: Nagano et al, 1984 (126)

Type: other: effects on reproductive organs.
Species: rat
Sex: male
Strain: Fischer 344
Route of admin.: drinking water
Exposure Period:
Frequency of treatment: continuous
Test duration: 60 days
Doses: 0, 1500, 3000 or 6000 ppm [0, 124, 234, 443 mg/kg/day]
Control Group: yes
NOAEL Parental: = 443 mg/kg bw
Method: other: Stop exposure study. Testes and epididymides were removed for weighing and examination.
Year:
GLP: yes
Test substance: other TS: Aldrich Chemical Co.
Remark: 30 animals/dose
Result: No deaths occurred. Treatment changes included loss of bodyweight and decreased water intake. Testes and epididymides weights normal and no apparent treatment-related lesions.

Reference: NTP, 1993 (110)

Type: other: effects on reproductive organs.
Species: rat
Sex: male/female
Strain: Fischer 344

Route of admin.:	drinking water
Exposure Period:	
Frequency of treatment:	continuous
Test duration:	13 weeks
Doses:	males: 0, 281, 367, 452 mg/kg/day females: 0, 304, 363, 470 mg/kg/day
Control Group:	yes
NOAEL Parental:	males: 452 mg/kg/day; females: 304 mg/kg/day
Method:	other: Morrissey, R.E. et al. (1988). Fund. appl. Toxicol. 11, 343-358.
Year:	1988
GLP:	yes
Test substance:	other TS: Aldrich Chemical Co.; 99%
Result:	Water consumption was lowered resulting in lower than target dosages. Epididymal weights were lowered in mid- and high-dosage males but these were related to reduced body weight changes. Small but significant reduction in sperm concentration at all 3 doses, but not dose-dependent; no other changes in sperm morphology parameters. In females, oestrous cycle length was unchanged but, in mid- and high-dose groups, differences in length of various stages of oestrous cycle noted.
Remark:	Reproductive tissue evaluations on 10 animals/sex/dose at 3 highest concentrations and controls from main study.
Reference:	NTP, 1993 (110)
Type:	other: effects on reproductive parameters.
Species:	mouse
Sex:	male/female
Strain:	B6C3F1
Route of admin.:	drinking water
Exposure Period:	
Frequency of treatment:	continuous
Test duration:	13 weeks
Doses:	males: 0, 553, 676, 694 mg/kg/day females 0, 676, 861, 1306 mg/kg/day
Control Group:	yes
NOAEL Parental:	males: 694 mg/kg/day; females: 1306 mg/kg/day
Method:	other: Morrissey, R.E. et al. (1988). Fund. appl. Toxicol. 11, 343-358.
Year:	1988
GLP:	yes
Test substance:	other TS: Aldrich Chemical Co. 99%
Result:	Slight decreases in sperm motility and testis weight but not dose-dependent.
Remark:	Reproductive tissue evaluations on 10 animals/sex/dose at 3 highest concentrations and controls from main study.
Reference:	NTP, 1993 (110)

5.9 Developmental Toxicity/Teratogenicity

Species: rat

Sex:	female
Strain:	Fischer 344
Route of admin.:	inhalation
Exposure period:	days 6-15 of gestation
Frequency of treatment:	6 hours/day
Test duration:	to day 21 of gestation
Doses:	25, 50, 100, 200 ppm [0.12, 0.24, 0.48, 0.97 mg/l]
Control Group:	yes
NOAEL Maternal:	= 50 ppm
NOAEL Developmental:	= 50 ppm
NOAEL Teratogenicity:	= 200 ppm
Method:	other: Internal protocol.
Year:	
GLP:	yes
Test substance:	other TS: 99.6%
Remark:	The NOAEL for teratogenicity does not account for skeletal variations.
Result:	Maternal toxicity included evidence of haemoglobinuria at 100 and 200 ppm. Haematological effects included increases in haemoglobin and haematocrit values, mean corpuscular volume and mean corpuscular haemoglobin, and decreases in red blood cell count and mean corpuscular haemoglobin concentration. Body weights, body weight gains and food consumption values were reduced at higher doses. At necropsy, gravid uterus weights were reduced and relative spleen and kidney weights were increased at the highest dosage.
	Embryotoxic effects significantly increased in resorbed litters at 200 ppm. Foetotoxic effects minimal with evidence of delayed skeletal ossification at 100, 200 ppm.
Reference:	Tyl et al, 1984 (127)(135)
Species:	rabbit
Sex:	female
Strain:	New Zealand white
Route of admin.:	inhalation
Exposure period:	day 6-18 of gestation
Frequency of treatment:	6 hours/day
Test duration:	up to day 29 of gestation
Doses:	25, 50, 100, 200 ppm [0.12, 0.24, 0.48, 0.97 mg/l]
Control Group:	yes
NOAEL Maternal:	= 100 ppm
NOAEL Developmental:	foetotoxicity: = 200 ppm embryotoxicity: = 100 ppm
NOAEL Teratogenicity:	= 200 ppm
Method:	OECD TG 414
Year:	
GLP:	yes
Test substance:	other TS: 99.6%
Result:	At highest dose, signs of maternal toxicity included mortality, increased number of abortions and reduced body and uterus weight. No significant dose-dependent haematological changes.

Embryotoxic effects were a reduction in the number of total and viable implantations/litter at the highest dose.

Fusion of the papillary muscles in the left ventricle of 5 foetuses in 4/19 litters at 100 ppm only suggests that this was not a foetotoxic effect of 2-butoxyethanol treatment.

Reference: Tyl et al, 1984 (127)(135)

Species: mouse
Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: 8-14 days of gestation
Frequency of treatment: daily
Test duration: dams sacrificed on day 18 of gestation
Doses: 0, 350, 650, 1000, 1500 or 2000 mg/kg/day
Control Group: yes
NOAEL Maternal: = 350 mg/kg/day
NOAEL Developm.: = 650 mg/kg/day
NOAEL Teratogen.: = 650 mg/kg/day
Method: other: teratology; implantation sites, resorptions and live and dead foetuses and foetuses weighed and examined at day of gestation.

Year:

GLP: no data

Test substance: other TS: 97%

Result: Maternal toxicity included mortality (6/6 and 3/6 at 2000 and 1000 mg/kg bw/day respectively). There was a distinctive green-brown or red-brown staining of cage papers at dosages of 650 mg/kg bw/day and above. Treatment-related clinical observations were lethargy, failure to right, abnormal breathing and green or red vaginal discharge, the latter at 1500 mg/kg bw and above. Developmental toxicity was increased embryo resorption at 1000 mg/kg bw/day and above.

Reference: Wier et al, 1987 (128)

Species: mouse
Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: 8-14 days of gestation
Frequency of treatment: daily
Test duration: dams and offspring sacrificed on post-natal day 22
Doses: 0, 650 and 1000 mg/kg/day
Control Group: yes
NOAEL Maternal: = 650 mg/kg/day
NOAEL Teratogenicity: = 1000 mg/kg/day
Method: other: Post-natal study - dam and offspring toxicity
Year:
GLP: no data
Test substance: other TS: 97%

Result:	Reduction in body weight gain of dams at high dose. No effects on survival and body weight gain of offspring. No adverse reproductive or developmental effects observed.	
Reference:	Wier et al, 1987	(128)
Species:	rat	
Sex:	female	
Strain:	Sprague-Dawley	
Route of admin.:	dermal	
Exposure period:	days 6-15 of gestation	
Frequency of treatment:	0.12 ml 4 times per day	
Test duration:	up to day 20 of gestation	
Doses:	total per day approx. 1760 mg/kg bw/day	
Control Group:	yes	
NOAEL Teratogenicity:	= 1760 mg/kg bw/day	
Method:	other: a two-replicate study of maternal toxicity, embryotoxicity and teratogenicity.	
Year:		
GLP:	no data	
Test substance:	other TS: Fisher Scientific	
Remark:	Preliminary dosage of 0.35 ml 4 times daily was reduced in second replicate because of high mortality.	
Result:	At the lower dose, body weight was slightly reduced, and there was no evidence of embryo- or foetotoxicity, gross malformations or variations. Haemoglobinuria was observed at the preliminary dose, but not at 1760 mg/kg/day.	
Reference:	Hardin et al, 1984	(129)
Species:	rat	
Sex:	female	
Strain:	Fischer 344	
Route of admin.:	oral (gavage)	
Exposure period:	days 9-11 or 11-13 of gestation	
Frequency of treatment:	daily	
Test duration:	20 days	
Doses:	group 1 (gd 9-11): 0, 30, 100 or 200 mg/kg/day group 2 (gd 11-13): 0, 30, 100 or 300 mg/kg/day	
Control Group:	yes	
NOAEL Maternal:	= 30 mg/kg/day	
NOAEL Developmental:	= 100 mg/kg/day	
NOAEL Teratogenicity:	= 200 mg/kg/day	
Method:	OECD TG 414, except for restricted exposure period	
Year:		
GLP:	yes	
Test substance:	other: Radian Corp.	
Results:	Groups of 27-33 animals were dosed with 2-BE (in distilled water) during the critical periods of cardiovascular development. Dose-related changes in haematological parameters were observed in the dams of both groups at the two highest doses (100 and 200 mg/kg or 100 and 300 mg/kg). The effects were more obvious in the early days after dosing and the effects included decreases in red blood cell	

count, haemoglobin, haematocrit and MCHC, and increases in MCV, MCH, reticulocytes and white blood cell count. Other signs of toxicity in the dams included dose-related reductions in body weight gain and food and water consumption. The relative spleen weights were increased at 100 and 200/300 mg/kg, relative kidney weights were increased at 200/300 mg/kg and relative liver weights at 200/300 mg/kg. The NOAEL for maternal toxicity was 30 mg/kg/day.

An increase in non-viable and adversely-affected implants, post-implantation loss and resorptions per litter resulted in the animals at 200 mg/kg/day (group 1 only). In the foetus, a decreased platelet count was noted at 300 mg/kg/day (group 2 only). No foetal malformations, and in particular no cardiovascular malformations, were observed at any dose.

Remark: The study was conducted under the NTP after the results of Tyl's inhalational rat study indicated that 2-BE may adversely affect cardiovascular development.

Reference: Sleet et al, 1989 (139)

Species: rat
Sex: female
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: day 7-15 of gestation
Frequency of treatment: 7 hours/day
Test duration: 20 days
Doses: 150 or 200 ppm
Control Group: yes
NOAEL Maternal: not reached
NOAEL Developm.: = 200 ppm
NOAEL Teratogenicity: = 200 ppm
Method: other: embryotoxicity, foetotoxicity and teratogenicity

Year:
GLP: no data
Test substance: Other TS: Eastman Kodak - purity 98-99.5%
Result: Haemoglobinuria was noted (on first day only) in the dams at both doses, but no evidence of embryotoxicity, foetotoxicity or teratogenicity was observed.

Reference: Nelson et al 1984 (137)

Species: mouse
Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: 7-14 days of gestation
Frequency of treatment: once per day
Test duration: 20 days
Doses: 0, 1180 mg/kg/day
Control Group: yes
NOAEL Maternal: not reached

Method:	other: Screening study - dam and offspring toxicity	
Year:		
GLP:	no data	
Test substance:	other TS: 99%	
Result:	Maternal mortality 20%. Viable litters 77%. No significant difference from controls in number of live pups/litter, pup weight, pup post-natal survival, and pup weight gain.	
Reference:	Schuler et al, 1984	(162)
Species:	rat	
Sex:	female	
Strain:	CD	
Route of admin.:	subcutaneous injection	
Exposure period:	day 6-15 of gestation	
Frequency of treatment:	daily	
Test duration:	21 days	
Doses:	0, 45, 90 or 180 mg/kg/day	
Control Group:	yes	
NOAEL Maternal:	= 45 mg/kg/day	
NOAEL Developm.:	= 180 mg/kg/day	
NOAEL Teratogenicity:	= 180 mg/kg/day	
Method:	OECD TG 414. Groups of 20 pregnant animals were used.	
Year:		
GLP:	no data	
Test substance:	other TS:	
Result:	No mortality resulted. Haemoglobinuria and body weight loss were observed in the medium and high dose dams after the first 2 injections only. Pre-implantation loss was evident at maternally toxic doses, but not dose-dependent and within laboratory's normal range. In the foetuses, a slight increase in rib effects and a dose-dependent increase in incomplete ossification of cranial bones were observed but such effects were not considered as malformations. No significant pathological findings were noted at necropsy.	
Reference	Tesh, 1976	(26)
Species:	rat	
Sex:	female	
Strain:	other: albino Crl:CD	
Route of admin.:	other: in vitro	
Exposure period:		
Frequency of treatment:		
Test duration:		
Doses:	0, 3.12, 6.25, 12.5 or 25 mM	
Control Group:	yes	
NOAEL Embryotoxicity:	= 3.12mM	
Method:	other: Explanted embryos were cultured for 48 hours in Trowell medium containing 2-BE at stated concentrations. Embryos were examined histologically and by total protein content.	
Year:		
GLP:	no data	
Test substance:	other TS: Janssen Chimica; >98%	

- Result:** Embryonic development was blocked at 25 mM; at 12.5 mM there were severe dysmorphic effects and at 6.25 mM there was a reduction in somite numbers and of protein/embryo ratio. Extensive necrosis in the neuroepithelium and its derivatives and in the neuromesenchyma of the branchial arches was noted in embryos exposed to 12.5 mM.
- Reference:** Giavini et al, 1993 (130)

5.10 Other Relevant Information

A. Specific toxicities

- Type:** Other: cytotoxicity to haemopoietic cells *in vitro*
- Remark:** 2-Butoxyacetic acid (BAA) had markedly higher haemolytic activity than 2-BE *in vitro*. After 1 hour 7.5 mM BAA completely lysed rat erythrocytes compared to 175-200 mM for 2-BE. Human erythrocytes incubated for up to 180 min. showed haemolysis by 2-BE at 225 mM and BAA did not cause haemolysis at max. concentration (15 mM). For 180 min. incubation, BAA caused total haemolysis of rat cells at 3.75 mM. The findings show that human erythrocytes are less susceptible than rat cells to haemolysis of red blood cells.
- Reference:** Bartnik et al, 1987 (93)

- Type:** Other: cytotoxicity to haemopoietic cells *in vitro*
- Remark:** In a comparative study in rat and human red blood cells, haemolysis was observed in rat cells exposed for 4h to BAA at the lowest dose (0.5mM). No effects were observed in human cells exposed to 2mM BAA for 4h, but slight swelling of the cells was noted at 4mM, and slight but significant haemolysis was observed at 8mM BAA.
- Reference:** Ghanayem et al, 1989 (133)

- Type:** Other: cytotoxicity to haemopoietic cells *in vitro*
- Remark:** Blood from different animals was incubated with 0, 1 or 2 mM BAA (the primary metabolite of 2-BE) *in vitro*. Blood parameters were measured after incubation for 1, 2 and 4 hr. The studies confirmed the haemolytic effect of BAA *in vitro* in mice and rats (at 1mM BAA), and the yellow baboon (at 2mM), but no significant effect was observed in the red blood cells of guinea-pigs, dogs, cats, domestic pigs and humans after exposure to 2mM BAA for 4h. Rabbit and hamster cells swelled at 2mM, but no haemolysis occurred. These findings demonstrate species differences in BAA-dependent haemolysis; human erythrocytes are less sensitive to this effect.
- Reference:** Ghanayem and Sullivan, 1993 (86)

- Type:** Other: cytotoxicity to haemopoietic cells *in vitro*
- Remark:** In a study on blood cells from human, rat, dog and rabbit, 2-butoxyacetic acid (BAA) lysed rat erythrocytes at 0.05%. Erythrocytes from the other species were stable up to the maximum concentration of 2% BAA.

- Reference:** Hext 1985 (33)
Source: ICI, UK
- Type:** Other: cytotoxicity to haemopoietic cells *in vitro*
Remark: Red blood cells from humans and Fischer 344 rats were treated with 2-butoxyacetic acid (BAA). On exposure to 2 mM for 4 hr, the rat cells exhibited significant haemolysis, preceded by a decrease in red cell deformability (noted at 1 hr); whereas no haemolysis or change in deformability occurred in human cells. On exposure to 0.2 mM for 6 hours, the rat cells exhibited very slight haemolysis and a significant decrease in red cell deformability (noted at 4 hr).
- Reference:** Udden and Patton 1994 (167)
- Type:** Other: cytotoxicity to haemopoietic cells *in vitro*
Remark: Red blood cells from 9 healthy young adults (5m,4f), 9 aged persons (5m,4f), 7 patients with sickle cell disease and 3 persons with hereditary spherocytosis were treated with 2 mM 2-butoxyacetic acid (BAA) for 4 hr. Haemolysis in treated cells was higher than controls for aged adults, but the difference was not statistically significant. The deformability of red cells from persons with sickle cell disease or hereditary spherocytosis was reduced, but BAA had no added effect. No other haemolytic or morphological changes were observed.
- Reference:** Udden 1994 (166)
- Type:** Cytotoxicity
Remark: Measured IC50 concentrations of 2-BE were 53, 44 and 60 mM respectively in the MTT, leucine incorporation and neutral red assays in rabbit corneal epithelial cells *in vitro*. Measured IC50 concentrations of 2-BE were 40 and 45 mM respectively in the MTT and leucine incorporation assays in Chinese hamster lung fibroblast (V79) cell cultures.
- Reference:** Sina et al, 1992 (134)
- Type:** other: Cytotoxicity to haemopoietic cell lines *in vitro*.
Remark: The IC50 of 2-BE to growth-factor dependent or leukaemic mouse, rat or human haemopoietic cell lines *in vitro* was determined. 2-BE inhibited growth of the human promyelocytic line NB4 (96 hour IC50 = 0.1 mM) and the growth factor dependent line DA1 (48 hour IC50 = 0.08 mM). The authors concluded that the toxicity of 2-BE towards certain haemopoietic cells was in the same concentration range as benzene and phenol. However, it is noted that that these conclusions are contrary to *in vivo* data (from 90-day studies) which show that 2-BE is not toxic to bone marrow (Teheux 1994 - ref 150). Due to doubts about the purity of reagents used in the study, the authors have publicly withdrawn the conclusions (Boiron et al 1994 - ref 168).
- Reference:** Ruchaud et al, 1992 (149)
- Type:** Immunotoxicity
Remark: See Section 5.4 of this dossier for results of a toxicity study which

- contained an immunotoxicology component. Butoxyethanol enhanced natural killer cell activity evoked by Keyhole Limpet haemocyanin injection in rats but had no effects on antibody, interferon or interleukin-2 production or on splenocyte numbers or delayed-type hypersensitivity.
- Reference:** Exon et al, 1991 (111)
- Type:** Immunotoxicity
- Remark:** 2-Butoxyethanol did not suppress the primary plaque-forming cell response to trinitrophenol-lipopolysaccharide in male F344 rats at gavage doses ranging 50 to 400 mg/kg.
- Reference:** Smialowicz et al, 1992 (140)
- Type:** Immunotoxicity
- Remark:** Cultured guinea-pig lymphoid cells were exposed (48 hours) to 2-butoxyethanol (2-BE) or 2-butoxyacetic acid (BAA) in the presence of the mitogen phytohaemagglutinin (PHA) at 2.5-10 µg/mL or concanavalin A (Con A) at 5-20 µg/mL) or an antigen (tuberculin at 25-100 µg/mL). Doses of 2-BE and BAA were 0.4, 2.0 and 10mM and 0.2, 1.0 and 5.0mM respectively.
- No significant effects on lymphocyte proliferation were observed for 2-BE, apart from slight reductions at the two highest PHA doses. At the cytotoxic dose of 10mM, a significant reduction in proliferative capacity resulted, particularly for PHA and tuberculin. No significant effects were observed for BAA at any dose tested.
- Reference:** Crevel et al 1990 (139)
- Source:** Unilever UK
- Type:** Behavioural effects
- Remark:** No effect on growth-rate or behavioural performance occurred in female rats exposed by inhalation to 50, 100, 200 or 400 ppm 2-butoxyethanol for 4 hours/day, 5 days/week for 10 days. Behavioural effects were measured using a conditioned avoidance-escape test. Transient haemoglobinuria was observed at 200 and 400 ppm.
- Reference:** Golberg et al 1964 (49)

B. Toxicodynamics, toxicokinetics

- Type:** Metabolism
- Remark:** Treatment of rats with pyrazole (alcohol dehydrogenase inhibitor) protected rats against 2-BE induced haemotoxicity and inhibited 2-BE metabolism to BAA, with inhibition accompanied by increased metabolism to the 2-BE glucuronide (BEG) and sulfate (BES). There was a 10-fold decrease in the ratio of BAA to (BEG+BES) in the urine of rats treated with pyrazole+2-BE compared to rats treated with 2-BE alone. Pretreatment of rats with cyanamide (aldehyde dehydrogenase inhibitor) also significantly protected rats and against 2-BE BE induced haemotoxicity and modified 2-BE

metabolism in a manner similar to pyrazole. Administration of equimolar doses of 2-BE, the intermediate 2-butoxyacetaldehyde (BAL), or the ultimate metabolite BAA caused similar haematotoxic effects. Cyanamide also protected rats against BAL-induced haemotoxicity.

Reference: Ghanayem et al, 1987 (141)

Type: Toxicokinetics

Remark: Radiolabelled 2-BE (125 or 500 mg/kg/day by gavage) was rapidly absorbed and distributed in all organs, the highest levels were found in the forestomach, liver, kidneys, spleen and glandular stomach. Radioactivity was also detected in the lung, heart, skin, testes, muscle, blood and fat. The major route of elimination was in urine followed by exhaled air. The major metabolites in urine were BAA (75% of label) followed by the glucuronide conjugate (BEG). Sulphate conjugate and unchanged 2-BE were found in the urine of low-dose but not high-dose animals. There was evidence of saturation of 2-BE metabolising enzymes. At the high dose, rats eliminated 8% of labelled substance in the bile within 8 hours, this being mainly BEG then BAA.

Reference: Ghanayem et al, 1987 (142)

Type: Metabolism

Remark: After receiving 28, 47 or 140 mg/kg bw/day of radiolabelled 2-BE in drinking water for 24 hours, male rats eliminated 50-60% of the label in urine as BAA, 10% as ethylene glycol and 8-10% as CO₂ in exhaled breath. There was no difference in excretion pattern for the three doses, with >75% of label excreted over 72 hour. Ethylene glycol, a previously unreported metabolite, was thought to arise from the dealkylation of 2-BE.

Reference: Medinsky et al, 1990 (143)

Type: Metabolism

Remark: In a gavage study, young rats (4-5 weeks old) eliminated a higher proportion of administered dose of radiolabelled 2-BE as exhaled CO₂ and in urine than older rats (9-13 weeks old). Older rats eliminated a higher ratio of BAA to conjugated 2-BE in urine and retained more radiolabelled 2-BE in their tissues.

Reference: Ghanayem et al, 1987 (144)

Type: Toxicokinetics

Remark: Following nose-only inhalation exposure to radiolabelled 2-BE at doses of 0.024, 0.24 or 2.16 mg/l for 6 hours, the body burden in male Fischer 344 rats ranged from 21-26% of the inhaled dose and 17-24% was metabolised. The majority (64-76%) was eliminated in the urine, 1.2-2.3% in the faeces and 5.9-7.6% exhaled as CO₂. The carcass contained 12.9-19.8% up to 66 hours postexposure at all concentrations. 2-Butoxyacetic acid was eliminated in urine as the major metabolite at all dosages. Uptake and metabolism was proportional to exposure. Ethylene glycol, the glucuronide conjugate and two unknown minor metabolites were also found.

Urinary excretion was highest at the low dosages. Analysis of whole blood showed the majority of the label in plasma and 20% in the red blood cell fraction after 2 hours exposure.

Reference: Sabourin et al, 1992 (136)

Type: Toxicokinetics

Remark: Following occluded dermal application of radiolabelled 2-BE at 14.4, 43.4 and 76.8 mg/rat for 23 hours, Fischer 344 rats absorbed and metabolized about 20-26% of the dose over 72 hours. 82-83% was excreted in the urine, 2.9-5.6% in the faeces, 3.0-5.0% in exhaled air and 8.3-9.7% remained in the carcass. The application site retained about 0.3-2%. 2-Butoxyacetic acid (BAA) was the major metabolite with evidence of glucuronide conjugate and ethylene glycol. No dose-related trend was apparent in type or quantity of metabolites produced. More than 80% of the label was found in blood plasma and < 20% was found in the red blood cell fraction; 53-75% of the plasma label was associated with BAA.

Reference: Sabourin et al, 1992 (137)

Type: Toxicokinetics

Remark: A physiologically-based pharmacokinetic model of human metabolism, excretion and disposition of inhaled 2-BE was reported. Modelled and observed data were in agreement. Increased physical activity and co-exposure to ethanol were predicted to influence the kinetics of 2-BE. The model indicated that 2-BE is unlikely to accumulate in the body.

Reference: Johanson, 1986 (146)

Type: Absorption

Remark: In an occlusive study in 10 female guinea-pigs using undiluted 2-butoxyethanol, the mean absorption rate obtained was 1.77 mg/cm²/h (range 0.35-3.3), measured by analysing blood samples at intervals up to 2h after application.

Reference: Johanson and Fernstrom, 1986 (170)

Type: Absorption

Remark: In a later study by the same authors using aqueous solutions of 2-butoxyethanol (5-80%) and undiluted chemical, higher absorption rates were obtained for the aqueous solutions (range 0.52-0.73 mg/cm²/h) than for undiluted 2-BE (0.27 mg/cm²/h). Only 2 guinea-pigs per concentration were used (except for 40% solution - 4 animals). Following this initial exposure, all animals (14) were then exposed to 100% 2-BE for 2h and a mean uptake rate of 0.94 mg/cm²/h (range 0.45-2.9) was obtained.

Although the mean absorption rates varied between studies and the individual rates varied within a study, it was clearly demonstrated that 2-butoxyethanol is significantly absorbed through the skin of the guinea-pig, that uptake is rapid, and that absorption is high from aqueous solution.

Reference: Johanson and Fernstrom, 1988 (147)

- Type:** Absorption
Remark: In a study in male and female Wistar rats, 200 mg/kg of radiolabelled 2-BE (undiluted) was applied to the skin under a perforated glass capsule for 48h. Of the applied dose, 29% was absorbed in males within 48h and 25% in females. The maximum radioactivity in blood and plasma occurred after 2h. As the study was conducted under nonocclusive conditions, some 2-BE may have evaporated.
- Reference:** Bartnik et al, 1987 (93)
- Type:** Absorption (dermal - in vitro)
Remark: A series of in vitro tests was conducted (using both undiluted 2-butoxyethanol and aqueous solutions) in different species. The results indicated that absorption through rat skin is high and rapid. Absorption through pig and human skin was lower but significant. The percentage dose absorbed from aqueous solutions was higher than for undiluted 2-butoxyethanol, but the applied dose was much lower. The effects on the rate of skin absorption of 2-butoxyethanol by two ingredients typical of those normally used in cleaning product formulations were also evaluated (separately) in rat and pig skin. The addition of 5% isopropanol and 5% linear sodium dodecylbenzene sulfate to 3.5% and 10% aqueous 2-butoxyethanol solutions did not significantly affect the absorption rate of 2-butoxyethanol.
- Reference:** Bartnik et al 1987 (93)
- Type:** Skin absorption in vitro
Remark: Absorption rate of 2-butoxyethanol across isolated human epidermis in vitro was 0.20 mg/cm²/hour. Undiluted 2-BE was allowed to permeate for 8 hours across a hydrated section of tissue held in a glass diffusion cell.
- Reference:** Dugard et al, 1984 (148)
- Type:** other: *in vitro* percutaneous absorption
Remark: Three sections of stratum corneum from human abdominal skin were exposed to 2-butoxyethanol via Franz-type diffusion cells. Dulbecco's phosphate buffered saline was used as receptor and control solutions. The rate of increase in concentration of 2-butoxyethanol in receptor solution was used to calculate a permeability constant and an absorption rate. The experiment was conducted twice under GLP conditions. Mean dermal absorption rate in the first experimental run was 0.857 +/- 0.282 mg/cm²/hour and in the second run was 1.52 +/- 0.37 mg/cm²/hour. The overall mean dermal absorption rate was 1.19 +/- 0.472 mg/cm²/hour, with the range 0.57-1.91. The variability between experiment runs was due to varying degrees of skin damage caused by the test material. The overall mean absorption rate excludes data from diffusion cells in which the mean damage ratio was greater than 5.
- Reference:** Barber et al, 1991 (151)
Source: Eastman Kodak USA

Type: Distribution and Excretion
Remark: Following subcutaneous injection with 118 mg/kg radiolabeled 2-BE, male rats excreted label in the urine (79%), exhaled air (10%) and faeces (0.5%) after 72 hours. The carcass retained about 5% and high levels were found in the spleen and thymus and, to a lesser extent, in the liver and fat.
Reference: Bartnik et al 1987 (93)

Type: Toxicokinetics (inhalation)
Remark: The mean uptake rate in male Sprague-Dawley exposed continuously to 20 or 100 ppm 2-BE (for periods up to 12 days) was 1.53 mg/h (3.5 mg/kg/h) and 7.73 mg/h (17.8 mg/kg/h) respectively. The rate was independent of duration of exposure.

Mean concentrations (in $\mu\text{mol/kg}$) of 2-BE and 2-butoxyacetic acid (BAA) (the principal metabolite) in tissues were (for 20 and 100 ppm): 2-BE - blood (15.1, 72.3), muscle (9.1, 30.4), testes (3.9, 2.6), liver (10.8, 83.8); BAA - blood (41.0, 179.0), muscle (9.3, 36.2), testes (14.1: 26.7), liver (16.4, 85.2).

The total blood clearance of 2-BE was approx. 2.6 L/h/kg throughout the exposure period and was independent of vapour concentration. The mean renal clearance values for BAA were 0.49 L/h/kg (mean excretion rate 0.98 mg/h) at 20 ppm, and 0.58 L/h/kg (5.3 mg/h) at 100 ppm.

Reference: Johanson 1994 (171)

Type: Elimination (in vitro)
Remark: In a study of the elimination kinetics of 2-butoxyethanol in perfused rat liver, the hepatic blood clearance of 2-butoxyethanol was reported as approximately 2.0 L/h/kg. The elimination rate was clearly dependent on concentration. The addition of 0.1% ethanol drastically reduced the elimination rate, supporting the hypothesis that 2-butoxyethanol is normally oxidised by alcohol dehydrogenase in the liver.

Reference: Johanson 1988 (172)

Type: Elimination/excretion
Remark: In a human study, five male volunteers were exposed to 2-BE by immersing four fingers of one hand in the chemical (undiluted) for 2 hours. The elimination half-life of 2-BE from blood was approx. 80 min. The BAA concentration in urine reached a maximum at about 3 hours after exposure, with a mean half-life of 3.1 hours. A wide variation in results existed between subjects in the study.

Reference: Johanson et al 1988 (156)

Type: Elimination/excretion
Remark: In a 2-hour inhalational study in human volunteers, the mean elimination half-life of 2-BE in the blood was 40 min., with a total blood clearance of 1.2 L/min. and a steady-state volume of

- distribution of 54 L. The concentration and excretion rate of BAA in urine was variable between subjects, with the respective maxima attained after 5-12 hours and 2-10 hours. The mean elimination half-life for BAA in urine after exposure was 5.8 hours.
- Reference:** Johanson et al 1986 (155)
- Type:** Elimination/excretion
- Remark:** In human inhalation studies, 13-27% of the absorbed dose was excreted as BAA in urine and less than 1% eliminated as 2-BE.
- Reference:** Van Vlem 1987 (173)
- Type:** Absorption (dermal)
- Remark:** In a human study, five male volunteers were exposed to 2-BE by immersing four fingers of one hand in the chemical (undiluted) for 2 hours. The mean dermal absorption rate from 12 measurements was 0.142 mg/cm²/h, with individual results quite variable (range 0.05-0.68 mg/cm²/h). There was little or no delay in detecting 2-BE in the bloodstream, with the concentration in blood continuing to increase after exposure in most cases.
- Reference:** Johanson et al 1988 (156)
- Type:** Absorption (dermal)
- Remark:** Six male volunteers exposed one arm to 50 ppm of 2-BE for 2 hours. The dermal absorption of vapours was not more than 21% of the total uptake. Blood was sampled from the exposed arm using the finger-prick method and from the unexposed arm using a catheter. The results indicated that sampling via the finger-prick method (as used by Johanson & Boman, 1991) was not representative of systemic blood concentrations of 2-BE.
- Reference:** Corley et al 1995 (194)
- Type:** Toxicokinetics (inhalation)
- Remark:** In a study carried out in an inhalational chamber, seven male volunteers were exposed to 20 ppm of 2-BE for 2 hours during light exercise at 50 watts (mean breathing rate 22.6 L/min.). The mean respiratory absorption rate was estimated as 71.6 mg/h (range 54.7-97.1), equivalent to 57.3% of the inspired amount. The uptake was rapid and remained relatively constant during exposure. In the study, 41% of the absorbed dose was excreted as BAA in the urine in 24 hours and only 0.03% as 2-BE.
- Reference:** Johanson et al 1986 (155)
- Type:** Absorption
- Remark:** Four male volunteers were exposed to 50 ppm 2-BE for 2 hours, first by inhalation (mouth only), and then skin only (the volunteers wore shorts and an air respirator). At ambient temperature (23°C), the inhalational absorption rate was 70.2 mg/h (range 58.9-78.1) whereas the dermal absorption rate was 227 mg/h (range 61.8-348). The results suggest that dermal uptake accounts for approximately 75% of the total uptake during whole-body exposure to 2-BE vapours. Average absorption rates at raised temperature and

humidity were higher (not statistically significant) and breathing rates were slightly higher with heart rates about the same.

Reference: Johanson and Boman 1991 (154)

Type: Absorption (inhalation)

Remark: In an inhalational study in male volunteers, 67-78% of the inspired amount was absorbed after exposure to 12.6 or 25.2 ppm 2-BE, either at rest or during light exercise at 30 watts. The volunteers wore face masks during the 4 hour exposure. The mean respiratory absorption rate at 25.2 ppm (at rest) was 31 mg/h. At 12.6 ppm the mean uptake (at rest) was 15.5 mg/h, and under a 30 watts workload, it was 33 mg/h.

Reference: Van Vlem, 1987 (173)

Type: Metabolism

Remark: In a gavage study in the F344 rat, 2-butoxyacetic acid (BAA) was the major metabolite in urine (approx. 65% of ¹⁴C-2-butoxyethanol at dose of 126 mg/kg) with concentrations of approx. 15% and 4% of the glucuronide conjugate and ethylene glycol respectively.

Reference: Corley et al 1994 (174)

5.11 Experience with Human Exposure

Type: Case report

Remark: A 50-yr-old woman ingested 250-500 ml of a window cleaning product containing 12% 2-BE (30-60 g 2-BE ingested). Main effects were coma, absence of response to pain stimulus, breathing difficulties, metabolic acidosis, hypokalemia, rise in serum creatinine and increased urinary excretion of oxalate. Treatment was effective against hydroelectrolytic disturbances but haemoglobinuria, inducing progressive erythropenia, ensued on days 3-6. Her condition improved gradually and she was discharged on day 10.

Reference: Rambourg-Schepens, 1988 (157)

Type: Case report

Remark: A 23-yr-old woman ingested 500 ml of a window cleaning product containing 12.7% 2-BE (dose approx. 60 g) and 3.2% ethanol. Main effects were coma, dilated pupils, obstructive respiration, hypotension, metabolic acidosis, hyperventilation, depression of blood haemoglobin concentration from 11.9 g/dl to 8.9 g/dl over 2 days and haemoglobinuria. The main metabolite of 2-BE, 2-butoxyacetic acid, was detected in urine but no oxaluria was observed. She was discharged from hospital on day 8.

Reference: Gijsenbergh et al, 1989 (158)

Type: Case report

Remark: A 53-yr-old male ingested 500 ml of a cleaning fluid containing 9.1% 2-BE (dose 45.5 g) and 2.5% ethanol. He was admitted to hospital about 10 hours later in a state of coma with metabolic acidosis, shock and noncardiogenic pulmonary oedema. His heart

rate was increased, blood pressure was decreased and there were transient polyuria and hypoxaemia. Non-haemolytic hypochromic anaemia was evident with haemoglobin concentration of 9.1 g/dl, haematocrit 25% and thrombopenia (platelet count 85000). The patient was discharged after 15 days.

Reference: Bauer et al, 1992 (159)

Type: Case report

Remark: 24 Children (7 months to 9 years) ingested at least 5 ml of glass/window cleaners containing 2-BE at concentrations ranging 0.5 to 9.9%. Most of the quantities swallowed were small, but one child ingested 30 ml of cleaner containing < 10% 2-BE and another 300 ml of an 8% solution. Children underwent gastric emptying. No signs of haemolysis, metabolic acidosis or CNS depression were observed

Reference: Dean and Krenzelok, 1992 (161)

Type: Case report

Remark: Ingestion of a cleaning product containing 22% 2-BE resulted in symptoms consistent with metabolic acidosis. No signs of haemolysis were apparent. The estimated dose was 80-106 g 2-BE, equivalent to 1.1-1.5 g/kg bw. In a repeat of the incident two weeks later, similar symptoms were observed.

Reference: Gualtieri 1995 (160)

Type: Case report

Remark: A carpet cleaner using a solution containing an unknown concentration of 2-BE experienced dizziness, blurred vision, and red urine towards the end of his 8-hour shift a number of times.

Reference: Pesticide and Toxic Chemical News, USA, 1993 (176)

Source: US EPA

Type: Controlled study

Remark: Three experiments were conducted by Carpenter on human volunteers, with the results as follows:

- . When 2 men were exposed to 113 ppm for 4 hours, no effect on RBC fragility was observed. The men suffered nasal and eye irritation, nasal discharge and a nasty taste in the mouth. At 4-6 hours after exposure, one man was still unwell.

- . When 2 men and one woman were exposed to 195 ppm for two 4-hour periods, the RBC fragility was unaffected. 2-Butoxyacetic acid (BAA) was excreted in the urine of the woman and one male, but only a trace was detected in the second male. Symptoms included irritation of the eyes, nose and throat, unpleasant taste, and headache.

- . When 2 men and 2 women were exposed to 100 ppm for 8 hours, BAA was excreted in all volunteers and no RBC fragility was observed. Symptoms noted were headache and nausea.

- Reference:** Carpenter et al, 1956 (82)
- Type:** Exposure monitoring
- Remark:** An analytical method to determine the absorption of 2-BE following use of formulated products by car window cleaners and office cleaners was reported. The window cleaning agents contained 1-21% 2-BE and the time weighted average (TWA) exposure concentrations ranged from < 0.1 ppm to 7.3 ppm 2-BE. 2-Butoxyacetic acid (BAA) in urine ranged from < 2-371 mg/g creatinine. Office cleaners used products containing between 1-10% 2-BE, with mean exposure approx. 0.3 ppm. BAA in urine ranged from < 2-3.3 mg/g creatinine. Urinary BAA results did not correlate well with atmospheric 2-BE concentrations. The results indicated that inhalation exposure was a minor component of the systemic dose and that dermal absorption of liquid formulations was a major contributor.
- Reference:** Vincent et al, 1993 (163)
- Type:** Exposure monitoring
- Remark:** Exposure measurements were made in 55 French firms covering 18 sectors of activity, including the principal end-use categories of products containing glycol ethers: paints, inks, diluents and varnishes, cleaning products, cosmetics and solvents. Exposure levels were measured in each of the facilities using personal atmospheric monitoring for 2-BE and urinary samples (at the beginning and end of each shift) for the major metabolite, 2-butoxyacetic acid (BAA). The highest exposures were obtained where paints, inks, varnishes and cleaning products were used. In some cases, skin absorption was chiefly responsible for the exposures.
- Reference:** Vincent et al, 1996 (193)
- Type:** Exposure monitoring
- Remark:** Post-shift urine samples from 6 healthy lacquerers exposed to 2-butoxyethanol-containing detergent contained 2-butoxyacetic acid (0.13-5.91 mmol/l) and its glutamine conjugate (0.12-2.45 mmol/l). Pre-shift urine samples contained only traces of these metabolites.
- Reference:** Rettenmeier et al, 1993 (152)
- Type:** Exposure monitoring
- Remark:** Post-shift urine samples from a sub-group of 9 workers (in the printing and electrical industries) exposed to 2-butoxyethanol at a time weighted average range of 0.4-0.8 ppm (mean 0.64 ppm) showed 2-butoxyacetic acid concentrations in the range 1.3-9.9 mg/g creatinine (mean 3.9 mg/g).
- Reference:** Sakai et al, 1993 (153)
- Type:** Exposure Monitoring
- Remark:** Occupational exposure monitoring of school cleaners (in Australia) to products (liquid and sprays) containing 0.25% 2-BE revealed worker airborne exposures below the detection limit (0.7 ppm for

- Reference:** personal monitoring & 0.2 ppm for area monitoring conducted in the classroom 1-1.5 hours after application of the cleaning solution).
NICNAS 1996 (11)
- Type:** Exposure Monitoring
Remark: In a silkscreening operation in Virginia, USA, workers exposed to undiluted 2-BE reported irritation and discomfort. In the subsequent inspection of the workplace, atmospheric concentrations of 2-BE in the range 13-169 ppm were obtained. The mean exposure from personal monitoring was 25 ppm whereas the mean from area monitoring was 69 ppm. Workers used 2-BE in open spray troughs without adequate ventilation or protective equipment.
- Source:** NIOSH 1987 (177)
- Type:** Exposure Monitoring
Remark: Occupational exposure monitoring of print machine operators using a cleaning solvent containing 10-50% 2-BE revealed mean (personal monitoring) levels of 5.2 ppm 2-BE in air (range 1.7-9.7 ppm).
- Source:** NIOSH 1987 (178)
- Type:** Exposure Monitoring
Remark: Occupational exposure monitoring of a cleaner (in USA) carrying out mechanical floor scrubbing with a product containing 0.3% 2-BE, revealed 1.6 ppm 2-BE in air (personal monitoring - 95 min sampling time).
- Source:** NIOSH 1979 (179)
- Type:** Exposure Monitoring
Remark: Occupational exposure monitoring of hospital window cleaners (in USA) using a spray product containing 2-BE revealed < 0.2 ppm 2-BE in air (personal monitoring - sampling over whole shift).
- Source:** NIOSH 1979 (180)
- Type:** Exposure Monitoring
Remark: Occupational exposure monitoring of printing press operators (in USA) cleaning the rollers with a product containing 2-BE revealed < 0.15-0.53 ppm 2-BE in air (personal monitoring - sampling time 4-6 hours).
- Source:** NIOSH 1990 (184)
- Type:** Exposure Monitoring
Remark: In a survey of workers at a number of screen printing shops, personal monitoring of silkscreeners using products containing up to 45% 2-BE resulted in a mean of 6.8 ppm 2-BE in air (16 samples). Personal monitoring of spray painters in the shops using products containing up to 55% 2-BE resulted in a mean of 2.6 ppm 2-BE in air (5 samples). Air sampling during specific tasks resulted in the following mean 2-BE in air: screening 9.1 ppm, spray painting 3.1 ppm, hand cleaning 1.8 ppm, metal coating 0.1 ppm, and blast cleaning 115 ppm.

- Source:** NIOSH 1985 (186)
- Type:** Exposure Monitoring
- Remark:** A silk-screen printer in a fishing rod factory (in USA) experienced headache, throat and nose irritation, including bleeding of the nose. The worker used a cleaning solvent containing 2-BE, cyclohexanol and petroleum distillates. Occupational exposure (personal monitoring) revealed 3-5 ppm (mean 4 ppm) 2-BE in air (sampling time 3-7 hours). The solvent was used in spray form and ventilation was poor.
- Source:** NIOSH 1986 (185)
- Type:** Exposure Monitoring
- Remark:** In occupational exposure monitoring of varnish production workers, a mean of 1.1 ppm 2-BE in air (personal monitoring) was obtained, with a mean BAA level of 10.5 mg/L urine. For individual results, no correlation between 2-BE in air and BAA in urine was seen. The 2-BE content in the product(s) was not stated. Repeat monitoring of the same group of workers gave a mean of 0.6 ppm 2-BE in air (personal monitoring), with a mean BAA level of 8.2 mg/L urine).
- Reference:** Angerer et al 1990, Sohnlein et al 1993 (181)(182)
- Type:** Exposure Monitoring
- Remark:** In a survey of 9 parquet floor makers exposed to a variety of organic solvents, including 2-BE, the mean TWA 2-BE in air was 5.0 ppm, with results up to 71 ppm.
- Reference:** Denkhaus et al, 1986 (187)
- Type:** Exposure Monitoring
- Remark:** In a survey industries and workshops in Belgium, 2-BE was detected in 25/94 air samples in the printing industry, 10/81 in the paint industry, 1/20 car repair shops, and 17/67 other operations. Mean 2-BE in air results were as follows: 0.8 ppm (range 0.3-5.5) in printing, 3.8 ppm (range 0.7-19) in painting, 1.2 ppm in car repair, and 1.7 ppm in other industries.
- Reference:** Veulemans et al, 1987 (188)
- Type:** Exposure Monitoring
- Remark:** In a 2-BE manufacturing process, the highest results were obtained during drum filling, 1.7 ppm (area monitoring).
- Reference:** Clapp et al 1984 (164)
- Type:** Exposure Monitoring
- Remark:** In a survey of house painters in Denmark, the 2-BE in air concentration was in the range 0-12 ppm.
- Reference:** Hansen et al 1987 (189)
- Type:** Exposure Monitoring
- Remark:** In a survey of house painters in Sweden, the 2-BE in air concentration was in the range 0-0.015 ppm, with a mean of 0.01 ppm.

- Reference:** Norback et al 1996 (190)
- Type:** Exposure Monitoring
- Remark:** In a survey of automotive spray painters (in Australia) exposed to a mixture of solvents, the mean TWA 2-BE concentration was 0.4 ppm.
- Reference:** Winder and Turner, 1992 (165)
- Type:** Exposure Monitoring
- Remark:** At a 2-butoxyethanol (2-BE) manufacturing plant in Australia, personal monitoring results (for 2-BE) were generally < 0.1 ppm for both STEL and TWA measurements. The highest monitoring results were obtained during maintenance activities, where a TWA level of 1.8 ppm has been recorded in area monitoring.
- Source:** NICNAS 1996 (11)
- Type:** Exposure Monitoring
- Remark:** In a survey of workers exposed to glycol ethers in a wide variety of industries in Ontario, Canada over the period 1983-1993, 2-BE was detected in 1404 area monitoring samples and 1683 personal monitoring samples. All 2-BE results were less than 25 ppm TWA.
- Reference:** Guirguis et al, 1994 (191)
- Type:** Exposure Monitoring
- Remark:** Personal monitoring results of workers in a wide variety of industries in Germany over the period 1991-1995. Results (expressed as % of measurements below certain threshold (TWA) concentrations) were presented for 3 types of work (formulation; surface coating & cleaning) involving exposure to 2-BE. Of 204 measurements (in 71 companies) during formulation, 5% were > 12 mg/m³ (2.4 ppm); of 115 measurements (in 47 companies) during screen printing (without mechanical ventilation), 10% were > 8 mg/m³ (1.6 ppm); of 200 measurements (in 116 companies) during spray-painting (manual), 5% were > 15 mg/m³ (3.1 ppm); of 59 measurements (in 38 companies) during surface coating (manual), 5% were > 41 mg/m³ (8.4 ppm); of 54 measurements (in 17 companies) during floor cleaning, 5% were > 47 mg/m³ (9.6 ppm) and of 53 measurements (in 31 companies) during surface cleaning (without ventilation), 5% were > 24 mg/m³ (4.9 ppm).
- With each set of measurements at least 50% were below the analytical detection limit (range 0.2-5.0 mg/m³).
- Comment:* TWA measurements were based on a 1 hour sampling period.
- Reference:** Berufsgenossenschaftlicher Arbeitskreis Altstoffe (BGAA),1996 (195)
- Type:** Health survey

Remark: In a qualitative survey of school cleaners in New South Wales, Australia, several reports of eye and throat irritation, headache and nausea were received from cleaners using products containing 2-butoxyethanol (amongst other cleaning products). In most cases, the products were being used in spray form.

Source: NICNAS 1996 (11)

Type: Case report

Remark: Adverse effects observed in cleaners using floor strippers containing high levels of 2-butoxyethanol included eye irritation and drowsiness when the ventilation was poor. Some reddening of the skin and contact dermatitis occurred when the proper safety gloves were not worn.

Source: NICNAS 1996 (11)

Type: Review

Remark: ECETOC has critically reviewed the health and toxicological properties of 2-BE to assist the European Commission in the setting of an exposure standard (Indicative Limit Value).

Haemolysis during the first few days of exposure is the primary indicator of toxicity in rodents. A NOAEL of 25 ppm (equivalent to 121 mg/m³) has been reported for rats exposed over 90 days (Dodd et al. 1983) whereas other mammals, including man, are less susceptible. The metabolite 2-butoxyacetic acid is responsible for 2-BE-induced haemolysis. This produces lysis of rat red blood cells in vitro at 2 mM whereas only very slight effects (no haemolysis) are seen at 8 mM in red cells from humans susceptible to haemolytic disorders. It was concluded that human erythrocytes are more resistant than blood cells from the rat.

The rat NOAEL of 25 ppm was considered by ECETOC as directly relevant to the setting of a workplace exposure standard for 2-BE. This NOAEL also takes account of concurrent dermal absorption occurring during whole body inhalation exposure. In applying this animal data, no uncertainty factor is needed for extrapolation from subchronic to chronic exposure since haemolysis is transient, seen only during the first few days of exposure. A physiologically-based pharmacokinetic model (PBPK model) predicts that the concentration of butoxyacetic acid in blood of humans exposed to 20-25 ppm 2-butoxyethanol will be approximately 0.03 uM. This is 270-fold less than the concentration needed to cause minimal changes in human red blood cells in vitro.

No haemolysis was reported in human volunteers exposed to 50 ppm for 2 hours or 100 or 195 ppm for 8 hours (although irritation of the eyes and respiratory tract were seen at concentrations of 100 ppm and above).

On the basis of the above data, ECETOC concluded that a long term occupational exposure standard (8 hour TWA) of 20 ppm would be

Source:	protective of human health. BP Chemicals Ltd. London	(122)
Type:	Review	
Remark:	In a safety assessment of 2-butoxyethanol for its use in cosmetics, the review panel concluded that, on the basis of animal and clinical data, 2-BE is safe in hair and nail products at concentrations up to 10%.	
Source:	The Cosmetic, Toiletry, and Fragrance Association USA	(192)

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EXTRACT FROM IRPTC LEGAL FILES

file: 17.01 LEGAL rn : 100247
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : 2-Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : ARG type : REG

subject	specification	descriptor
AIR	OCC	MPC

8H-TWA: 120MG/M3 (25PPM). SKIN ABSORPTION.
 entry date: OCT 1991

effective date: 29MAY1991

title: LIMIT VALUES FOR CHEMICAL SUBSTANCES IN THE WORKING ENVIRONMENT-RESOLUTION NO. 444/1991 OF THE MINISTRY OF WORK AND SOCIAL SECURITY (AMENDING REGULATION DECREE NO. 351/1979 UNDER LAW NO. 19587/1972: HYGIENE AND SAFETY AT WORK)
 original : ARGOB*, BOLETIN OFICIAL DE LA REPUBLICA ARGENTINA(ARGENTIAN OFFICIAL BULLETIN), 24170 , I , 1 , 1979
 amendment: ARGOB*, BOLETIN OFICIAL DE LA REPUBLICA ARGENTINA(ARGENTIAN OFFICIAL BULLETIN), 27145 , I , 4 , 1991

file: 17.01 LEGAL rn : 300534
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : 2-Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : CAN type : REG

subject	specification	descriptor
AIR	OCC	TLV

TWA: 25 ppm, 120 mg/m3; skin absorption. Prescribed by the Canada Occupational Safety and Health Regulations, under the Canada Labour Code (administered by the Department of Employment and Immigration). The regulations state that no employee shall be exposed to a concentration of an airborne chemical agent in excess of the value for that chemical agent adopted by ACGIH (American Conference of Governmental Industrial Hygienists) in its publication entitled: "Threshold Limit Value and Biological Exposure Indices for 1985-86". The regulations also state that the employer shall, where a person is about to enter a confined space, appoint a qualified person to verify by means of tests that the concentration of any chemical agent or combination of chemical agents will not result in the exposure of the person to a concentration in excess of the value indicated above. These regulations prescribe standards whose enforcement will provide a safe and healthy workplace.
 entry date: OCT 1994 effective date: 24MCH1994

amendment: CAGAAK, CANADA GAZETTE PART II, 128 , 7 , 1513 , 1994

file: 17.01 LEGAL rn : 301897
 systematic name: Ethanol, 2-butoxy-

common name :Ethylene glycol monobutyl ether
 reported name :Ethylene glycol monobutyl ether
 cas no :111-76-2 rtecs no :KJ8575000
 area : CAN type : REG

subject	specification	descriptor
TRNSP		CLASS
		RQR
LABEL		
PACK		

Schedule II, List II - Dangerous Goods other than Explosives: PIN
 (Product Identification No.): UN2369. Class (6.1): Poisonous. Packing
 group III, (I=Great danger, III=Minor danger). Passenger Vehicles: 60 L.
 Prescribed by the Transportation of Dangerous Goods Regulations, under
 the Transportation of Dangerous Goods Act (administered by the
 Department of Transport). The act and regulations are intended to
 promote safety in the transportation of dangerous goods in Canada, as
 well as provide comprehensive regulations applicable to all modes of
 transport across Canada. These are based on United Nations
 recommendations. The act and regulations should be consulted for
 details. Information is entered under the proper shipping name found in
 the regulations; this may include general groups of chemical substances.
 entry date: OCT 1994 effective date: 02DEC1993

amendment: CAGAAK, CANADA GAZETTE PART II, 127 , 25 , 4056 , 1993

file: 17.01 LEGAL rn : 302515
 systematic name:Ethanol, 2-butoxy-
 common name :Ethylene glycol monobutyl ether
 reported name :Ethylene glycol monobutyl ether
 cas no :111-76-2 rtecs no :KJ8575000
 area : CAN type : REG

subject	specification	descriptor
USE	OCC	RQR
STORE		
LABEL		

Ingredient Disclosure List - Concentration: 1% weight/weight. The
 Workplace Hazardous Materials Information System (WHMIS) is a national
 system providing information on hazardous materials used in the
 workplace. WHMIS is implemented by the Hazardous Products Act and the
 Controlled Products Regulations (administered by the Department of
 Consumer and Corporate Affairs). The regulations impose standards on
 employers for the use, storage and handling of controlled products. The
 regulations also address labelling and identification, employee
 instruction and training, as well as the upkeep of a Materials Safety
 Data Sheet (MSDS). The presence in a controlled product of an ingredient
 in a concentration equal to or greater than specified in the Ingredient
 Disclosure List must be disclosed in the Safety Data Sheet.
 entry date: APR 1991 effective date: 31DEC1987

amendment: CAGAAK, CANADA GAZETTE PART II, 122 , 2 , 551 , 1988

file: 17.01 LEGAL rn : 522981
 !!! WARNING - not original IRPTC record - WARNING !!!
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : Ethylene glycol mono-n-butyl ether
 cas no : 111-76-2 rtecs no : KJ8575000
 area : DEU type : REG

subject	specification	descriptor
AQ		CLASS
USE	INDST	RQR

This substance is classified as moderately hazardous to water (Water Hazard Class: WHC 1). (There are 3 water hazard classes: WHC 3 = severely hazardous; WHC 2 = hazardous; WHC 1 = moderately hazardous; and the classification is "not hazardous to water"). The purpose of the classification is to identify the technical requirements of industrial plants which handle substances hazardous to water.
 entry date: SEP 2001 effective date: 01JUN1999

title: Administrative Order relating to Substances Hazardous to Water (Verwaltungsvorschrift wassergefaehrdende Stoffe)
 original : BUANZ*, Bundesanzeiger, 51 , 98a , 1 , 1999

file: 17.01 LEGAL rn : 532419
 !!! WARNING - not original IRPTC record - WARNING !!!
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : 2-Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : DEU type : REG

subject	specification	descriptor
AIR	EMI	MPC

THIS SUBSTANCE BELONGS TO CLASS II. THE AIR EMISSIONS OF ORGANIC COMPOUNDS MUST NOT EXCEED (AS THE SUM OF ALL COMPOUNDS IN ONE CLASS) THE FOLLOWING MASS CONCENTRATIONS: CLASS I - 20 MG/M3 AT A MASS FLOW OF >= 0.1 KG/H; CLASS II - 100 MG/M3 AT A MASS FLOW OF >= 2 KG/H; CLASS III - 150 MG/M3 AT A MASS FLOW OF >= 3 KG/H. IF COMPOUNDS FROM DIFFERENT CLASSES ARE PRESENT, THE MASS CONCENTRATION MUST NOT EXCEED 150 MG/M3 AT A TOTAL MASS FLOW OF >= 3 KG/H.
 entry date: JAN 1995 effective date: 01MCH1986

title: Technical Instructions on Air Quality Control (Technische Anleitung zur Reinhaltung der Luft)
 original : GMSMA6, Gemeinsames Ministerialblatt, , 7 , 93 , 1986

file: 17.01 LEGAL rn : 540383

!!! WARNING - not original IRPTC record - WARNING !!!
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : Ethylene glycol monobutyl ether
 cas no : 111-76-2 rtecs no : KJ8575000
 area : DEU type : REC

subject	specification	descriptor
AIR	OCC	MAK

MAK value (8-hour time-weighted average): 20 ml/m³ (ppm) or 98 mg/m³ (20 C, 1013 hPa). Peak limitation category II,1: Substance with systemic effects; onset of effect within 2 h; half-life < 2 h; excursion factor = 2 (peak level is 2 x MAK); maximum duration of peaks is 30 min, average value; maximum frequency 4x/shift. - Danger of cutaneous absorption. - Pregnancy risk group C: There is no reason to fear a risk of damage to the embryo or foetus when MAK and BAT values are observed.
 entry date: MAY 2001

title: List of MAK and BAT Values 2000. Maximum Concentrations and Biological Tolerance Values at the Workplace. (MAK- und BAT-Werte-Liste 2000. Maximale Arbeitsplatzkonzentrationen und Biologische Arbeitsstofftoleranzwerte.)
 original : MPGDFD, Mitteilung der Senatskommission zur Pruefung gesundheitsschaedlicher Arbeitsstoffe, 36 , , , 2000

file: 17.01 LEGAL rn : 542509

!!! WARNING - not original IRPTC record - WARNING !!!
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : 2-Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : DEU type : REG

subject	specification	descriptor
AIR	OCC	BAT

Parameter: Butoxyacetic acid. BAT value: 100 mg/l. Assay material: Urine. Sampling time: For long-term exposures: after several shifts. - The BAT value (biological tolerance value for occupational exposures) is defined as the concentration of a substance or its metabolites or the deviation from the norm of biological parameters induced by the substance which generally does not affect the health of the employees adversely.
 entry date: JUN 2001 effective date: 01APR2001

title: Technical Regulations for Hazardous Substances (TRGS 903): Biological Tolerance Values for Occupational Exposures. (Technische Regeln fuer Gefahrstoffe (TRGS 903): Biologische Arbeitsplatztoleranzwerte - BAT-Werte -.)
 original : BNDS6, Bundesarbeitsblatt, , 4 , 52 , 2001

file: 17.01 LEGAL rn : 606999
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : ethylene glycol butyl ether
 cas no : 111-76-2 rtecs no : KJ8575000
 area : GBR type : REG

subject	specification	descriptor
TRNSP	MARIN	RQR
AQ	MARIN	RQR
AQ	EMI	RQR

CLASSIFIED AS A NON-POLLUTING LIQUID SUBSTANCE. DOCUMENTARY EVIDENCE OF ASSESSMENT AND APPROVAL REQUIRED BY A CARRIER. DISCHARGE INTO THE SEA IS NOT PROHIBITED.

entry date: 1992 effective date: 06APR1987

title: THE MERCHANT SHIPPING (CONTROL OF POLLUTION BY NOXIOUS LIQUID SUBSTANCES IN BULK) REGULATIONS 1987, SCHEDULE 2

original : GBR SI*, STATUTORY INSTRUMENTS, 551 , , 15 , 1987

amendment: GBR SI*, STATUTORY INSTRUMENTS, 2604 , , 2 , 1990

file: 17.01 LEGAL rn : 700489
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : IND type : REG

subject	specification	descriptor
MANUF		RQR
SAFTY		RQR
STORE		RQR
IMPRT		RQR

These rules define the responsibilities of occupiers of any industrial activity in which this toxic and hazardous substance may be involved. These responsibilities encompass: (a) assessment of major hazards (causes, occurrence, frequency); (b) measures to prevent accidents and limit eventual impairment to human health and pollution of the environment; (c) provision of relevant factual knowledge and skills to workers in order to ensure health and environmental safety when handling equipments and the foregoing chemical; (d) notification of the competent authorities in case of major accidents; (e) notification of sites to the competent authorities 3 months before commencing; (f) preparation of an on-site emergency plan as to how major accidents should be coped with; (g) provision of competent authorities with information and means to respond quickly and efficiently to any off-site emergency; (h) provision of information to persons outside the site, liable to be affected by a major accident; (i) labelling of containers as to clearly identify contents, manufacturers, physical, chemical and toxicological data; (j) preparation of a safety data sheet including any significant information regarding hazard of this substance and submission of safety reports to the competent authorities; (k) for the import of a hazardous chemical to India, importers must supply the competent authorities with specified information regarding the shipment.

entry date: SEP 1992

effective date: 27NOV1989

title: THE MANUFACTURE, STORAGE AND IMPORT OF HAZARDOUS CHEMICALS RULES.
1989

original : GAZIN*, THE GAZETTE OF INDIA, 787 , , , 1989

file: 17.01 LEGAL rn : 1010486

systematic name:Ethanol, 2-butoxy-

common name :Ethylene glycol monobutyl ether

reported name :2-Butoxyethanol

cas no :111-76-2

rtecs no :KJ8575000

area : MEX

type : REG

subject	specification	descriptor
AIR	OCC	MXL

AT ANY WORKPLACE WHERE THIS SUBSTANCE IS PRODUCED, STORED OR HANDLED A
MAXIMUM PERMISSIBLE LEVEL OF 120MG/M3 (26PPM) MUST BE OBSERVED FOR A
PERIOD OF 8 HOURS OR 360MG/M3 (75PPM) FOR 15 MINUTES FOUR TIMES A DAY
WITH INTERVALS OF AT LEAST 1 HOUR.

entry date: DEC 1991

effective date: 28MAY1984

title: INSTRUCTION NO.10 RELATED TO SECURITY AND HYGIENIC CONDITIONS AT
WORKPLACES. (INSTRUCTIVO NO. 10, RELATIVO A LAS CONDICIONES DE SEGURIDAD
E HIGIENE DE LOS CENTROS DE TRABAJO).

original : DOMEX*, DIARIO OFICIAL, , , , 1984

file: 17.01 LEGAL rn : 1105361

systematic name:Ethanol, 2-butoxy-

common name :Ethylene glycol monobutyl ether

reported name :2-Butoxyethanol

cas no :111-76-2

rtecs no :KJ8575000

area : RUS

type : REG

subject	specification	descriptor
AIR	OCC	MAC

CLV: 5.0MG/M3 (VAPOUR) HAZARD CLASS: III

entry date: MAY 1990

effective date: 01JAN1988

amendment: GOSTS*, GOSUDARSTVENNYI STANDART SSSR (STATE STANDARD OF
USSR), 12.1.005 , , , 1988

file: 17.01 LEGAL rn : 1143058

systematic name:Ethanol, 2-butoxy-

common name :Ethylene glycol monobutyl ether

reported name :ethylene glycol butyl ether

cas no :111-76-2

rtecs no :KJ8575000

area : RUS type : REG

subject	specification	descriptor
AIR	OCC	PSL

CLV: 5.0MG/M3 (VAPOUR)

entry date: MAY 1990

effective date: APR1988

amendment: OBUVR*, ORIENTIROVOCHNYE BEZOPASNYE UROVNI VOZDEISTVIYA
(OBUV) VREDNYKHVESHCHESTV V VOZDUKHE RABOCHEI ZONY (TENTATIVE
SAFE EXPOSURE LEVELS OF HARMFUL SUBSTANCES IN OCCUPATIONAL
AIR), 4613-88 , , , 1988

file: 17.01 LEGAL rn : 1200089

systematic name: Ethanol, 2-butoxy-

common name : Ethylene glycol monobutyl ether

reported name : 2-Butoxyethanol

cas no : 111-76-2

rtecs no : KJ8575000

area : SWE

type : REG

subject	specification	descriptor
AIR	OCC	HLV

1D-TWA: 100MG/M3 (20PPM), 15MIN-STEL: 250MG/M3 (50PPM), SKIN ABSORPTION.

entry date: 1992

effective date: 01JUL1991

title: HYGIENIC LIMIT VALUES.

original : AFS***, ARBETARSKYDDSSTYRELSENS FOERFATTNINGSSAMLING, 1990:13
, , 5-64 , 1990

file: 17.01 LEGAL rn : 1301142

systematic name: Ethanol, 2-butoxy-

common name : Ethylene glycol monobutyl ether

reported name : 2-n-Butoxyethanol

cas no : 111-76-2

rtecs no : KJ8575000

area : USA

type : REG

subject	specification	descriptor
MANUF	REQ	PRMT
USE	OCC	PRMT
SAFTY	OCC	MXL

; Summary - THE FOLLOWING CHEMICAL IS INCLUDED ON A LIST OF CHEMICALS
AND MIXTURES FOR WHICH REPORTING IS CURRENTLY REQUIRED UNDER THE TOXIC
SUBSTANCES CONTROL ACT SECTION 2607A. THIS TOXIC SUBSTANCE IS SUBJECT TO
PRELIMINARY ASSESSMENT INFORMATION RULES ON PRODUCT ION QUANTITIES,
USES, EXPOSURES, AND ADVERSE EFFECTS. MANUFACTURERS INCLUDING IMPORTERS
MUST SUBMIT A REPORT FOR THIS LISTED CHEMICAL MANUFACTURED AT EACH SITE.
entry date: OCT 1991 effective date: 1982

title: PRELIMINARY ASSESSMENT INFORMATION RULES

original : FEREAC, FEDERAL REGISTER, 47 , , 26998 , 1982
 amendment: CFRUS*, CODE OF FEDERAL REGULATIONS, 40 , 712 , 30 , 1990

file: 17.01 LEGAL rn : 1322104
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : 2-Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : USA type : REG

subject	specification	descriptor
CLASS	PESTI	RQR
MANUF	PESTI	PRMT
FOOD	ADDIT	RQR

CASE NAME CELLOSOLVE ESTERS; Summary - THIS SUBSTANCE IS INCLUDED ON A LIST OF ACTIVE INGREDIENTS CONTAINED IN A PRODUCT FIRST REGISTERED BEFORE NOVEMBER 1, 1984, FOR WHICH A REGISTRATION STANDARD HAS NOT BEEN ISSUED. PUBLICATION OF THIS LIST INITIATES AN ACCELERATED REREGISTRATION AND DATA C ALL-IN FOR PRODUCTS CONTAINING THE LISTED ACTIVE INGREDIENTS. IN PARTICULAR THE LIST INCLUDES A NUMBER OF ACTIVE INGREDIENT CASES HAVING INDIRECT FOOD OR FEED USES.

entry date: JAN 1992 effective date: 1988

title: FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT PESTICIDES REQUIRED TO BE REREGISTERED; LIST C.

original : FEREAC, FEDERAL REGISTER, 54 , 140 , 30846 , 1989
 amendment: FEREAC, FEDERAL REGISTER, 54 , 140 , 30846 , 1989

file: 17.01 LEGAL rn : 1325174
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : Ethylene glycol mono-n-butyl ether
 cas no : 111-76-2 rtecs no : KJ8575000
 area : USA type : REC

subject	specification	descriptor
SAFTY	OCC	MXL
USE	OCC	MXL

700 PPM

entry date: OCT 1991 effective date: JUN1990

title: POCKET GUIDE TO CHEMICAL HAZARDS

original : XPHPAW, US PUBLIC HEALTH SERVICE PUBLICATION, 90 , 117 , 50 , 1990
 amendment: XPHPAW, US PUBLIC HEALTH SERVICE PUBLICATION, 90 , 117 , 50 , 1990

file: 17.01 LEGAL rn : 1340162
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : Ethylene glycol mono-n-butyl ether
 cas no : 111-76-2 rtecs no : KJ8575000
 area : USA type : REC

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|subject|specification|descriptor|
|-----+-----+-----|
| AIR   |   OCC   |   TLV   |
|-----+-----+-----|
  
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Time Weighted Avg (TWA) 25 ppm, 121 MG/M3, skin; Summary - THIS THRESHOLD LIMIT VALUE IS INTENDED FOR USE IN THE PRACTICE OF INDUSTRIAL HYGIENE AS A GUIDELINE OR RECOMMENDATION IN THE CONTROL OF POTENTIAL HEALTH HAZARDS.

entry date: DEC 1991 effective date: 1989

title: THRESHOLD LIMIT VALUES
 original : ACGIH*, AMERICAN CONFERENCE OF GOVERNMENT INDUSTRIAL HYGIENISTS, , , 11 , 1989
 amendment: ACGIH*, AMERICAN CONFERENCE OF GOVERNMENT INDUSTRIAL HYGIENISTS, , , 11 , 1991

file: 17.01 LEGAL rn : 1345130
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : 2-n-Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : USA type : REG

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|subject|specification|descriptor|
|-----+-----+-----|
| MONIT |           |   RQR   |
|-----+-----+-----|
  
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; Summary - THIS IS A CHEMICAL OR MIXTURE FOR WHICH REPORTING IS CURRENTLY REQUIRED UNDER THE TOXIC SUBSTANCE CONTROL ACT HEALTH AND SAFETY STUDIES SECTION 2607D. PERSONS WHO CURRENTLY MANUFACTURE OR PROCESS CHEMICAL SUBSTANCES OR MIXTURES FOR COMMERCIAL PURPOSES, THOSE WHO PROPOSE TO DO SO, AND THOSE WHO ARE NOT CURRENTLY INVOLVED WITH A LISTED CHEMICAL BUT WHO MANUFACTURED OR PROCESSED IT OR PROPOSED TO DO SO ANY TIME DURING THE TEN YEAR PERIOD PRIOR TO THE TIME IT BECAME LISTED MUST SUBMIT TO THE ADMINISTRATOR OF THE U.S. EPA STUDIES OR LISTS OF HEALTH AND SAFETY STUDIES CONDUCTED ON THIS SUBSTANCE FOR EVALUATION.

entry date: OCT 1991 effective date: 1986

title: HEALTH AND SAFETY DATA REPORTING RULES SECTION 8(D)
 original : FEREAC, FEDERAL REGISTER, 51 , , 32726 , 1986
 amendment: CFRUS*, CODE OF FEDERAL REGULATIONS, 40 , 716 , 120 , 1990

file: 17.01 LEGAL rn : 1407014
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : Ethylene glycol monobutyl ether

cas no :111-76-2 rtecs no :KJ8575000
 area : EEC type : REG

subject	specification	descriptor
FOOD		RQR
FOOD		MXL
FOOD		RSTR

THE SUBSTANCE MAY BE USED FOR THE MANUFACTURE OF REGENERATED CELLULOSE FILM WHICH IS INTENDED TO OR DOES COME INTO CONTACT WITH FOODSTUFFS UNDER THE CONDITIONS LAID DOWN. THE SUBSTANCE MAY BE USED AS COATING SOLVENT IN COATED REGENERATED CELLULOSE FILM. NOT MORE THAN 50 MG OF COATING/DM2 OF FILM ON THE SIDE IN CONTACT WITH FOODSTUFFS IS ALLOWED. THE TOTAL QUANTITY OF SOLVENTS MAY NOT EXCEED 0.6 MG/DM2 IN THE UNCOATED REGENERATED CELLULOSE FILM, INCLUSIVE OF THE COATING ON THE SIDE IN CONTACT WITH FOODSTUFFS.

file: 17.01 LEGAL rn : 1407014
 systematic name:Ethanol, 2-butoxy-
 common name :Ethylene glycol monobutyl ether
 reported name :Ethylene glycol monobutyl ether
 cas no :111-76-2 rtecs no :KJ8575000
 entry date: AUG 1995 effective date: 01JAN1994

title: COMMISSION DIRECTIVE OF 15 MARCH 1993 RELATING TO MATERIALS AND ARTICLES MADE OF REGENERATED CELLULOSE FILM INTENDED TO COME INTO CONTACT WITH FOODSTUFFS (93/10/EEC).
 original : OJEC**, OFFICIAL JOURNAL OF THE EUROPEAN COMMUNITIES, L93 , , 27 , 1993
 amendment: OJEC**, OFFICIAL JOURNAL OF THE EUROPEAN COMMUNITIES, L310 , , 41 , 1993

file: 17.01 LEGAL rn : 1470439
 !!! WARNING - not original IRPTC record - WARNING !!!
 systematic name:Ethanol, 2-butoxy-
 common name :Ethylene glycol monobutyl ether
 reported name :2-Butoxyethanol
 cas no :111-76-2 rtecs no :KJ8575000
 area : EEC type : REG

subject	specification	descriptor
MANUF	INDST	CLASS
IMPRT	INDST	CLASS

The substance is included in a list of existing substances produced or imported within the Community in quantities exceeding 1000 tonnes per year. - A system of data reporting by any manufacturer who has produced or any importer who has imported the substance, as such or in a preparation, in quantities exceeding 10 tonnes per year is established.
 entry date: AUG 1999 effective date: 04JUN1993

title: Council Regulation (EEC) No 793/93 of 23 March 1993 on the

evaluation and control of the risks of existing substances
 original : OJECFC, Official Journal of the European Communities, L84 , ,
 1 , 1993

file: 17.01 LEGAL rn : 1477556
 !!! WARNING - not original IRPTC record - WARNING !!!
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : 2-Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : EEC type : REG

subject	specification	descriptor
CLASS		CLASS
LABEL		RQR
PACK		RQR

Classification: Xn; R20/21/22. Xi: Irritant; R36/38. - Labelling: Xn:
 Harmful. Risk phrases (R): 20/21/22-36/38. Harmful by inhalation, in
 contact with skin and if swallowed (R20/21/22). - Irritating to eyes and
 skin (R36/38). Safety advice phrases (S): (2-)36/37-46. (Keep out of the
 reach of children (S2).) - Wear suitable protective clothing and gloves
 (S36/37). - If swallowed, seek medical advice immediately and show this
 container or label (S46).
 entry date: OCT 2001 effective date: 24AUG2001

title: Council Directive of 27 June 1967 on the approximation of the
 laws, regulations and administrative provisions relating to the
 classification, packaging and labelling of dangerous substances
 (67/548/EEC)
 original : OJECFC, Official Journal of the European Communities, 196 , ,
 1 , 1967
 amendment: OJECFC, Official Journal of the European Communities, L225 ,
 , 1 , 2001

file: 17.01 LEGAL rn : 1861014
 !!! WARNING - not original IRPTC record - WARNING !!!
 systematic name: Ethanol, 2-butoxy-
 common name : Ethylene glycol monobutyl ether
 reported name : 2-Butoxyethanol
 cas no : 111-76-2 rtecs no : KJ8575000
 area : WHO type : REC

subject	specification	descriptor
AIR	AMBI	MTC

Average ambient air concentration: 0.1 - 15 ug/m3. Health endpoint:
 haematotoxicity in rats; no observed adverse effect level (NOAEL): 242
 mg/m3; uncertainty factor: 10; tolerable concentration: 13100 ug/m3;
 averaging time: 1 week.
 entry date: JAN 2001

title: Guidelines for Air Quality

original : WHOAI*, Guidelines for Air Quality, WHO, Geneva, , , , 2000

