Diethylene Glycol Monobutyl Ether (DEGBE) (CAS# 112-34-5)

(Synonyms: 2-(2-butoxyethoxy)ethanol; butyl carbitol; BUCB; Butoxy diethylene glycol; Butoxydiethylene glycol; Butoxydiglycol; Butoxyethoxyethanol; Butyl Ethyl Cellosolve; Butyl diglycol; Butyl digol; Butyl dioxitol; Caswell No. 125H; Diethylene glycol butyl ether; Diethylene glycol monobutyl ether; Diethylene glycol n-butyl ether; Diethylene gylcol monobutyl ether; Diglycol monobutyl ether; Dowanol DB; Ektasolve DB; Ethanol, 2,2'-oxybis-, monobutyl ether; Ethanol, 2-(2-butoxyethoxy)-; Glycol ether DB; Jeffersol DB; O-Butyl diethylene glycol; Poly-Solv DB).

Diethylene glycol monobutyl ether (DEGBE) 8-hour REL

Reference Exposure Level	**10 μg/m^3**
Critical effects	Hepatocyte vacuolization, and dose-dependent change in liver weight
Hazard Index target	Liver

1 Physical and Chemical Properties

Physical form	colorless liquid
Molecular Formula	C8-H18-O3
Structural Formula	CH_2-$(CH_2)_3$-O-CH_2-CH_2-O-CH_2-CH_2-OH
Molecular weight	162.23 g/mol
Density	0.9536 g/cm^3
Boiling point	230.4ºC
Melting point	-68.1ºC
Vapor pressure	2.19x10^{-2} mm Hg @ 25ºC (0.027 hPa)
Flash point	78ºC
Log K_{OW}	0.56
Solubility	soluble in ethanol, ethyl ether, acetone; soluble in benzene. miscible with oils and water
Conversion Factor	1 mg/L = 150.8 ppm; 1 mg/m^3 = 0.148 ppm; 1 ppm = 6.743 mg/m^3

2 Production, Use, and Exposure

DEGBE is produced by the reaction of ethylene oxide and n-butanol with an alkalic catalyst. The estimated production of diethylene glycol monobutyl ether (DEGBE) in 1991-1993 in the

European Union ranged from 20,000 to 80,000 tons. DEGBE was 24 to 25% of all butyl glycol ether production in the EU from 1994 (44,000 tons) (ECB 2000).

In pesticide products, DEGBE acts as an inert ingredient as a deactivator for formulation before the crop emerges from the soil and as a stabilizer. DEGBE is also a chemical intermediate for the synthesis of diethylene glycol monobutyl ether acetate, diethylene glycol dibutyl ether, and piperonyl acetate, and as a solvent in high baked enamels. Other applications of DEGBE are as a dispersant for vinyl chloride resins in organosols, a diluent for hydraulic brake fluids, and a mutual solvent for soap, oil, and water in household cleaners. The textile industry uses DEGBE as a wetting-out solution. DEGBE is also a solvent for nitrocellulose, oils, dyes, gums, soaps, and polymers. DEGBE is also used as coupling solvent in liquid cleaners, cutting fluids, and textile auxiliaries. In the printing industry, DEGBE applications include: solvent in lacquers, paints, and printing inks; high boiling point solvent to improve gloss and flow properties; and used as a solubilizer in mineral oil products (HSDB, 2008).

The greatest exposure potential exists for commercial workers and other consumers, most likely via inhalation or dermal contact, when coatings are applied to surfaces or when liquid products containing DEGBE are otherwise used manually, as may occur in the use of DEGBE-containing cleaners (Gibson et al., 1991). Inhalation is a potential route of exposure during use of metal working fluids and hot melt adhesives containing the substance. There are also concerns for anticipated general systemic or developmental effects as a consequence of repeated respiratory or dermal exposures. Fire extinguishing agents, paints, varnishes, aqueous paints, adhesives, polishing agents, stain removers, and detergents are all sources of exposure. Indirect exposure from the environment (soil, water, ambient air) may also occur.

3 Pharmacokinetics and Metabolism

Absorption, metabolism, and excretion were studied in male and female Sprague-Dawley rats given 200 and 2000 mg/kg bw of ^{14}C-DEGBE and 200 mg of 10% aqueous solution/kg bw for 24 hours. The ^{14}C was found both in the animals and urine. Dermal absorption was high but incomplete, and higher for females than males. Absorption through human skin in vitro from a cleaning product containing 4% DEGBE applied at 100%, 50%, and 1.5% dilutions were 0.98, 0.40, and 0.007 umol/cm^2/h, respectively (Procter and Gamble, 1985 as cited in (ECB, 2000). The absorption across human abdominal epidermis was measured. The acetate form was rapidly hydrolyzed by rat blood to DEGBE with a biological half-life of less than 3 minutes (Deisinger and Guest, 1989).

The major urinary metabolite of DEGBE is 2-(2-butoxyethanol) acetic acid identified and the glucuronide conjugate was present at levels of 5.2% to 8.2% of the urinary ^{14}C (ECB; 2000). 2-2(butoxyethoxy) acetic acid represented 61-80% of total urinary radioactivity. DEBGE was excreted by the urine following oral, dermal, or parenteral administration in rats (ECETOC, 2005).

4 Acute Toxicity

Acute mammalian toxicity data were summarized in the European Union Risk Assessment Report 2-(2-butoxyethoxy)ethanol. Institute for Health and Consumer Protection, European Chemicals Bureau. 1St Priority List Volume 2. 2000. Table adapted as follows: undiluted DEGBE for 8 hours was 0.035 mg/cm^2/h (Dugard et al., 1984 as cited in ECETOC, 2005).

The metabolism of diethylene glycol monobutyl ether acetate was studied in vitro and in vivo dermally in male Sprague-Dawley rats.

Table 4.1. Summary of Acute Studies for DEGBE

Route	**Species**	**Acute LD_{50}** **mg/kg bw**	**Reference**
Oral	Rat (fed)	9623	Eastman Kodak 1984, ECB, 2000; Krasavage and Terhaar, 1981 as cited in ECETOC. (2005)
Oral	Rat (fasted)	7292	Eastman Kodak 1984, ECB, 2000
Oral	Mouse (fed)	5526	Eastman Kodak 1984, ECB, 2000; Krasavage and Terhaar, 1981 as cited in ECETOC. (2005)
Oral	Mouse (fasted)	2406	Eastman Kodak 1984, ECB, 2000
Oral	Guinea pig	2000	Smyth et al. (1941) as cited in ECETOC. (2005)
Oral	Rabbit	2200	Boatman and Knak, 2001 as cited in ECETOC (2005)
Dermal	Rabbit	2764	Eastman Kodak 1984, ECB, 2000

5. Repeated Dose Toxicity

A summary of repeated dose toxicity studies with DEGBE was outlined in the European Union Risk Assessment Report 2-(2-butoxyethoxy)ethanol. Institute for Health and Consumer Protection, European Chemicals Bureau. 1St Priority List Volume 2. 2000. Table 5.1 was adapted as follows and only includes the inhalation toxicity, although information on oral and dermal toxicity were also provided:

Table 5.1. Summary of Inhalation Studies for DEGBE.

Inhalation Studies	NOAEL	LOAEL	Effects	References
Subacute, rat (5 wk, 6 hr/d, 5 d/wk; 0, 13, 39, 117 mg/m^3)	39 mg/m^3	117 mg/m^3	At high concentration, hepatocyte vacuolization consistent w/ fatty change and increased relative liver weight in females, decreased relative liver weight in males	Gushow et al., 1984
Subacute, rat (2 wk, 6 hr/d, 5 d/wk ; 100 and 350 mg/m^3 vapor, and 1000 mg/m^3) aerosol	< 100 mg/m^3	100 mg/m^3	At all concentrations, perivascular and peribronchial infiltrate, decreased spleen weights in males increased lung weight	BASF AG 1987
Subacute, female rat (2 wk, 6 hr/d, 5 d/wk; 350 mg/m^3)	< 350 mg/m^3	350 mg/m^3	At mid and high concentrations, decreased body weight gain; multifocal perivascular and peribronchial accumulation of granulocytes	BASF AG 1991
Semichronic, rat (90 d, 6 hr/d, 5 d/wk; 14.5, 43.5, and 105 mg/m^3)	105 mg/m^3		At all concentrations, no treatment-related effects.	BASF AG 1992

6. Other Toxicity

The teratogenicity of DGBE was evaluated using Wistar rats fed a diet containing DGBE on days 0 through 20 of pregnancy. The dietary concentrations were 0, 0.04, 0.2, and 1% of the daily intakes, which were 0, 25, 115, and 633 mg/kg, respectively (Ema et al., 1988). In the groups treated w/ DGBE, the maternal body weight gains were significantly reduced (Ema et al., 1988). No significant differences in pre-implantation losses, litter survival, and fetal or placental weights were observed (Ema et al., 1988).

7. Derivation of Interim Reference Exposure Levels (RELs)

Acute REL (1-hour exposure)

No studies of short-term exposure to DEGBE were located that were appropriate for the derivation of an acute REL. While an LC_{50} was reported, this value represents the upper limit for acute exposures that are compatible with survival without regard to protecting health. As such LC_{50} values are not the preferred basis for the derivation of an acute REL, which requires consideration of effects much less severe than lethality.

In the course of an 8-hour exposure, intermittent spikes in exposure levels are included in the time-weighted average addressed with the 8-hr REL. The values associated with 8-hr RELs are typically lower than allowed for acute 1-hr exposures, due to the longer exposure duration and possibility of recurring exposures. Therefore application of the 8-hr REL to exposure scenarios involving short-term peaks in concentration should be health protective in most cases.

Derivation of Interim 8-hour REL

Study	Gushow et al. 1984
Study population	F344 rats
Exposure method	Whole body inhalation
Exposure continuity	6 h/d, 5d/wk
Exposure duration	5 weeks (~ 25 exposures)
Critical effects	Hepatocyte vacuolization, dose-dependent change in liver weight
LOAEL	117 mg/m^3
NOAEL	39 mg/m^3
Time-adjusted exposure	$C^n * T = K$, $n = 1$
Extrapolated concentration	20.9 mg/m^3 (39 mg/m^3 * 6/8 * 5/7)
Human concentration adjustment	20.9 mg/m^3 (RGDR = 1 systemic)
LOAEL uncertainty factor (UF_L)	Not applicable
Subchronic uncertainty factor (UF_s)	10
Interspecies Uncertainty Factor	
Toxicokinetic (UF_{A-k})	2
Toxicodynamic (UF_{A-d})	√10
Intraspecies Uncertainty Factor	
Toxicokinetic (UF_{H-k})	10
Toxicodynamic (UF_{H-d})	√10
Cumulative uncertainty factor	2000
Reference Exposure Level	**10 μg/m^3**

The 8-hour Reference Exposure Level is a concentration at or below which adverse noncancer health effects would not be anticipated for repeated 8-hour exposures. This draft 8-hour REL is derived from a study by Gushow et al (1984), in female and male rats exposed by whole body inhalation 0, 13, 39, or 117 mg/m^3 DEGBE for 5 weeks at 6 hours per day for 5 days per week for an approximate total of 25 exposures. The time adjustment for the 8-hour REL used was 6

h/8 h * 5/7 days/week. A LOAEL uncertainty factor was unnecessary because both a LOAEL (117 mg/m^3) and a NOAEL (39 mg/m^3) was determined for the study.

Significant differences in toxicokinetics between rats and humans are not expected to be large so a value of 2 was used for the interspecies toxicokinetics UF. In the absence of data, a default toxicodynamic UF of √10 was applied. Uncertainty factors for intraspecies variability were 10 for toxicokinetics and √10 for toxicodynamics in the absence of specific data. The use of these default UF values in combination with a subchronic UF of 10 are expected to cover residual deficiencies in the database. The cumulative UF is therefore 200, which is divided by the time-adjusted NOAEL for a draft 8-hour reference exposure level of 10 μg/m^3.

8 References

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