Social Europe

Recommendation from the Scientific Committee on Occupational Exposure Limits for 2-(2-Butoxyethoxy)ethanol

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8 hour TWA: 10 ppm (67.5 mg/m^3)
STEL 15 ppm (101.2 mg/m^3)

Additional classification:

This document is based on Risk Assessment Report 2-(2-Butoxyethoxy)ethanol (European Commission, EUR 18998 EN, 2000).

Substance Identity and Properties:

2-(2-Butoxyethoxy)ethanol $C_8 H_{28} O_3$

Classification R36

Synonyms DEGBE, diethylene glycol butyl ether, butyl diglycol

EINECS No 203-961-6

EEC No 603-096-00-8

CAS No 112-34-5

Mwt: 162.23

Conversion factor (20°C, 101 kPa): 6.75 mg/m^3 = 1 ppm

2-(2-Butoxyethoxy)ethanol (DEGBE) is a liquid. It is miscible with water (log Pow = 0.56). Mpt is -68°C, bpt 228-234°C at 1013 hPa, vapour pressure 0.027 hPa at 20°C.

1. Occurrence and Use

DEGBE is used as a solvent in paints, dyes, inks, detergents and cleaners. It is also used as an intermediate and as a component of fire extinguisher foam and hydraulic fluids.

2. Health Significance

Rats were occlusively exposed via the skin to 200 or 2000 mg/kg bw ^{14}C-DEGBE for 24 hours. In the low dose group 30 to 54% of the DEGBE was absorbed, in the high dose group 3 to 19%. Dermal absorption rates varied between 0.25 and 1.46 mg/cm^2/h. The major urinary metabolite was 2-(2-butoxyethoxy)acetic acid with up to 80% of urinary radioactivity and 5 – 8% as the glucuronic acid conjugate, indicating oxidative metabolism of the terminal primary alcohol group to the aldehyde and then the acid (Boatman et al. 1993). There are no data on metabolism in humans. In vitro, a dermal absorption rate of 0.033 mg/cm^2/h was determined for human epidermis (Dugard et al. 1984).

Acute toxicity is low with oral LD_{50} in rats from 7292 to 9623 mg/kg bw and dermal LD_{50} for rabbits of 2764 mg/kg bw (Eastman Kodak 1984a,b). When exposed to a saturated atmosphere of DEGBE for 7 h, none of the 7 rats died. A saturated atmosphere is estimated to contain about 18 ml DEGBE/m^3 (120 mg/m^3) (Patty 1994). However, according to the vapour pressure data given above, at 20°C the saturated vapour concentration should be around 26 ml/m^3.

DEGBE is not irritating to the skin (Southwood 1987), but irritates the eye (Ballantyne 1984).

Undiluted DEGBE is not sensitising in the maximisation test with guinea pigs (Basketter 1985). One case of positive skin reaction to DEGBE in a human patch test has been published (Berlin et al. 1995). No indications of the purity of the test materials were given by the authors. A positive patch test was also reported with the acetate, which is rapidly hydrolysed to DEGBE (Dawson et al 1989). No allergic reactions were found in 202 construction painters in contact with water-based paints possibly including DEGBE when patch-tested with DEGBE (Fischer et al. 1995).

In a 2-week study with exposure of male and female rats to 100 mg/m^3 (vapour), 350 mg/m^3 and 1000 mg/m^3 (aerosols), perivascular and peribronchial infiltrates as well as decreased spleen weight were seen from 100 mg/m^3. From 350 mg/m^3, increased lung weight in males was observed (BASF 1987, 1991).

In a second 2-week-study with exposure of female rats to 350 mg/m^3, decreased body weight gain and multifocal perivascular and peribronchial accumulation of granulocytes were seen (BASF 1991).

Another subacute study with exposure of rats to 13, 39 or 117 mg/m^3, 6 h/d, 5 d/w for 5 weeks yielded a NOEL of 39 mg/m^3. At 117 mg/m^3, vacuolisation and fatty hepatic changes and increased relative liver weight in females were seen. In males, on the other hand, relative liver weight was decreased (Gushow et al. 1984). The findings of the study are doubtful because hepatic fatty changes were also seen in control animals and the liver weight changes are opposite in the two sexes.

In a 90-day-study with whole-body vapour exposure of rats to 13, 40 or 94 mg/m^3, 6 h/d, 5 d/w, no treatment-related effects were seen at 94 mg/m^3, which is the highest vapour concentration achievable at room temperature (BASF 1992). Higher concentrations lead to aerosol formation, which might explain the lung effects seen in the subacute studies

(BASF 1987, BASF 1991) with aerosols. The lung effects in the subacute study with 100 mg/m^3 (vapour) (BASF 1987) were not observed in the subchronic study. The results of the 90-day study, however, are preferred over the subacute results due to the longer duration, which is more relevant for chronic work-place exposure. Thus, the NOEL for lung effects is 94 mg/m^3.

Rats were gavaged with doses of 51-65, 254-327 or 1270-1630 mg/kg bw, 5 d/w for 90 days. From the lowest dose, a dose-related decrease in WBC and lymphocytes in females and a dose-related increase in creatinine in males was seen. 30 and 60%, respectively, of the female and male animals died in the mid-dose group, whereas about 90% of the animals in the high-dose group died (Hobson et al. 1987). The effects seen are not typical for glycol ethers and are therefore considered unreliable; this study is not taken into account for setting an OEL.

Dermal doses up to 2000 mg/kg bw occlusively applied to rats for 6 h/d, 5 d/w for 13 weeks did not induce systemic effects, including neurotoxicity. From 200 mg/kg bw, erythema at the application site was seen with concentration-dependent incidence. The highest dose caused scab formation (Beyrouty et al. 1993; Auletta et al. 1993).

DEGBE did not show genotoxicity in vitro in the Salmonella mutagenicity test, in the chromosomal aberration test in CHO cells, in the UDS test with rat hepatocytes, in the mouse lymphoma assay, or in the HPRT test in CHO cells. In D. melanogaster it did not induce sex-linked recessive lethality and in the bone marrow of mice no micronuclei were formed after single oral doses of up to 3300 mg/kg bw (European Commission 1998).

There are no data available on carcinogenicity.

In a one-generation study, rats were gavaged with 250, 500 or 1000 mg/kg bw. The NOEL for the F0 animals was 1000 mg/kg bw. In this dose group, the number of live-born pups was slightly but not significantly reduced and the body weight gain of the pups was decreased during later stages of lactation (Nolen et al. 1985).

With occlusive dermal application of 2000 mg/kg bw, 6 h/d, 5 d/w, no effects on fertility parameters in F0 and F1 animals were seen in a one-generation study in rats (Auletta et al. 1993).

The NOEL for toxicity for fertility is > 1000 mg/kg bw by gavage and > 2000 mg/kg bw by dermal application.

14 to 16 rats per group were fed 25, 115 or 633 mg/kg bw from day 0 to day 20 of gestation. In every dose group, the weight gain of the dams was reduced, though not dose-related. The only effect was an non-significantly reduced number of implantations in the high dose group (Ema et al. 1988). This might be considered as a treatment-related effect since a small reduction in the number of live-born pups was also seen in the one-generation study of Nolen et al. (1985) with rats.

Mice were gavaged with 500 and 2050 mg/kg bw on days 6 to 13 of gestation. Apart from 25% maternal death in the high dose group, no effects were seen; however, fetal malformations were not investigated microscopically (Hardin et al. 1987).

Rabbits were exposed non-occlusively to 100, 300 or 1000 mg/kg bw for 4 h/d from day 8 to 19 of gestation. There were no indications of developmental effects at any of the dose levels tested. The two higher levels produced skin irritation (Nolen et al. 1985).

In a study with s.c. injection of 119, 239, 478 or 716 mg/kg bw in rats, the NOAEL for embryotoxicity and fetotoxicity was 478 mg/kg bw. The higher dose resulted in a decrease in fetal weight and delayed ossification. The maternal NOEL was 239 mg/kg bw. Reduced body weight gain occurred at the higher doses, with transient hemoglobinuria at 716 mg/kg bw (Wilson 1983). The fetotoxic effects might be explained by the maternal toxicity observed.

From the studies of Ema et al. (1988) and Nolen et al. (1985) with rats, it can be concluded that the NOEL for developmental toxicity is about 500 mg/kg bw.

Recommendation

The systemic toxicity of DEGBE is low. The NOEL in 90-day dermal studies is 2000 mg/kg bw. The NOEL for reproductive toxicity is 500 mg/kg bw. The critical effect is local irritation of the lung seen with concentrations that lead to the formation of aerosols, i.e. with concentrations > 100 mg/m^3. In a 90-day inhalation study, the NOEL was 94 mg/m^3 (15 ml/m^3), leading to inflammatory reactions. No interspecies factor is to be used, because the critical effect is local irritation, which should not differ much between species. Local irritation mainly depends on the concentration and not on time. Therefore, the OEL for DEGBE is set at 10 ppm (67,5 mg/m^3). The corresponding body weight dose is 9.7 mg/kg (67,5 mg/m^3 x 10 m^3 / 70 kg bw) assuming 100% absorption. To avoid irritation due to aerosols of DEGBE, a STEL is set at 15 ppm (101,2 mg/m^3).

According to the in vitro data with human epidermis, one-hour contact of both forearms (2000 cm^2) would lead to an uptake of 1 mg/kg bw. assuming 70 kg bw. Although there is skin penetration, the low systemic toxicity after repeated dermal application does not warrant a skin notation. There is one positive patch test with DEGBE and one with its acetate ester, which is rapidly hydrolysed to DEGBE. This information is not sufficient for designation as a sensitiser.

At the levels recommended, no measurement difficulties are foreseen.

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