SIDS INITIAL ASSESSMENT PROFILE

CAS No.	110-63-4
Chemical Name	1,4-Butanediol
Structural Formula	$HO\text{-}CH_2CH_2CH_2CH_2\text{-}OH$

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Acute lethal toxicity of 1,4-butanediol is low via all administration routes. Major toxicity by oral administration is respiratory failure and catalepsy. This chemical is a slight irritant to the skin, eyes and respiratory tract, but not a skin sensitizer. As 1,4-butanediol is rapidly absorbed and metabolized to gamma-hydroxybutyric acid in animals and humans, neurotoxic effect of 1,4-butanediol such as depression of central nervous system is considered to be caused by the metabolite, gamma-hydroxybutyric acid. 1,4-Butanediol seems to show a competitive inhibition of alcohol dehydrogenase and increase the toxic effect of alcohol.

In an OECD combined repeat dose and reproductive/developmental screening toxicity test (OECD TG 422), rats were administered by gavage at doses of 200, 400 and 800 mg/kg/day for 45 days in males and from 14 days before mating to day 3 of lactation in females. Neurobehavioral toxicity (i.e. hyperactivity and coma after hypoactivity and recumbency) and pathological changes (diffuse transitional epithelial hyperplasia and fibrosis in the lamina propria of the urinary bladder) were observed. The transient hyperactivity only just after administration was observed at the lowest dose of 200 mg/kg/day. This neurotoxicity in dams was also observed in developmental toxicity study of mice at doses of 300 and 600 mg/kg/day by gavage during gestational days 6-15 but not at 100 mg/kg/day. This study was conducted by NTP test guideline under GLP. Therefore NOAEL of 100 mg/kg/day for oral repeated toxicity is sufficiently reliable.

In a 2 week inhalation rat study at 1.1 g/m^3 (6 hours/day, 5 days/week), no changes including neurotoxicity were observed. Therefore, 1.1 g/m^3 was considered to be inhalation NOAEL. Repeated intraperitoneal administration induced narcotic effect at more than 500 mg/kg/day, but NOAEL was not established.

From repeated dose studies, it is evident that critical effect is neurotoxicity. However, the nature of the data does not allow for the identification of the dose-response and NOAEL for this effect.

As for reproductive toxicity, a reduction in fetal body weight of rats was observed in the above OECD combined repeat dose and reproductive/developmental screening toxicity test (OECD TG 422) but this effect was considered to be secondary to maternal toxicity. NOAEL for reproductive toxicity is the highest dose of 800 mg/kg/day. In the developmental toxicity study of mice at 100, 300 and 600 mg/kg/day described above, the only definitive expression of developmental toxicity was a reduction in average fetal body weight at doses of 300 and 600 mg/kg/day (92% and 83% of control weight, respectively). However, this effect against foetal development was considered to be secondary to maternal toxicity. No teratogenicity was observed at any doses. Thus, 600 mg/kg/day is the developmental NOAEL. Genotoxicity of this chemical may be negative because of neither bacterial mutation in *S.*

Typhimurium TA100, TA98, TA1535, TA1537, and *E.coli* WP2 *uvr*A with and without metabolic activation (OECD TG 471 and 472), nor chromosomal aberration *in vitro* in CHL/IU cells with or without metabolic activation system OECD TG (473).

Environment

1,4-Butanediol is a liquid at 20 °C, and this chemical is classified as a readily biodegradable chemical (OECD 301C: 100 % after 14-day). Bioconcentration factor may be low judging from a low P_{ow} value (0.50 at 25 °C).

The lowest acute and chronic toxicity data were 14d LC50 (>100 mg/l) of fish (Medaka; *O. latipes*) and 21d NOEC (> 85 mg/l) of *Daphnia magna*, respectively. Assessment factor of 100 was used to chronic toxicity data to determine PNEC, because chronic toxicity data for fish were not available. Thus, PNEC of this chemical is >0.85 mg/l. Toxicity of this chemical to aquatic organisms is low, because all toxicity data are higher than 85 mg/l.

Exposure

The production volume of this chemical was 29,717 tones in 1993 in Japan. This chemical is used as an intermediate for resins and/or solvents in closed system, and not included in consumer products of Sponsor county. The potential environmental distribution of this chemical obtained from a generic fugacity model (Mackey level III) shows that this chemical will be distributed mostly in water (99.6 %) and partly in sediment (0.4%) when it is discharged into water. The route of occupational exposure is inhalation and skin with a limited numbers of workers. As for consumer use, this chemical is used as an ingredient in deodorants in European countries, and marketed as dietary supplement in US.

NATURE OF FURTHER WORK RECOMMENDED

Human health

Further exposure information should be collected in each member country**.**