SIDS INITIAL ASSESSMENT PROFILE

CAS No.	71-36-3
Chemical Name	n-butyl alcohol
Structural Formula	CH_3-CH_2-CH_2-CH_2OH

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Data from butyl acetate (BAc) toxicity studies have been included in the assessment of n-butanol (BA). Data from BAc is useful when assessing the hazards associated with the systemic toxicity of BA exposure due to the rapid and complete hydrolysis of BAc to BA *in vivo*. Exposure to BAc via dermal, inhalation, and water or dietary administration results in the rapid appearance of BA in the systemic circulation. Since exposure to either BAc or BA results in systemic exposure to BA, systemic toxicity data from studies that administer BAc are useful in identifying hazards associated with BA exposure. Endpoints of BAc toxicity that are associated with direct contact-mediated effects (e.g. eye, skin, and respiratory tract irritation) cannot be extrapolated from BA data due to the difference in physical-chemical properties of the two materials.

Human Health

n-Butyl alcohol (BA) was only slightly toxic to experimental animals following acute oral, dermal, or inhalation exposure. The acute oral LD_{50} values for female rats ranged from 790 to 4360 mg/kg. Different strains of rat were used in each of four studies, which may account for the variability. Oral LD_{50} values for mice, rabbits, hamsters, dogs, and male rats all fell within the same range. The rat inhalation LC_0 of 8000 ppm (24000 mg/m^3) indicates very low inhalation toxicity (no lethality at 8000 ppm). The rabbit dermal LD_{50} was 3402 mg/kg, indicating that BA can penetrate the skin, but not very readily. Animal experiments and human experience indicate that BA is, at most, moderately irritating to the skin, but it is a severe eye irritant. These effects are most likely due to BA's localized defatting and drying characteristics. Although no animal data are available, human studies and experience show that BA is not likely to be a skin sensitizer. A recent *in vivo* toxicokinetics study confirmed the rapid metabolism of n-butyl acetate (BAc) to BA. Hydrolysis of BAc in blood and brain was estimated to be 99 percent complete within 2.7 minutes (elimination $t_{½}$ = 0.41 minute). Thus, organisms exposed to BAc can experience appreciable tissue concentrations of BA. In this way, the results of toxicity studies with BAc can be used as supplemental, surrogate data to provide information on the toxicity of BA. A thirteen-week, subchronic exposure to BAc, the metabolic precursor of BA, produced transient hypoactivity (during exposure only) at 1500 and 3000 ppm (7185 and 14370 mg/m^3) along with decreased body weight and food consumption, but no post exposure neurotoxicity even at 3000 ppm. A concurrent subchronic neurotoxicity study under the same exposure conditions showed no evidence of cumulative neurotoxicity based upon functional observational battery endpoints, quantitative motor activity, neuropathology and scheduled-controlled operant behavior endpoints. A no observable effect level (NOAEL) of 500 ppm (2395 mg/m^3) was reported for systemic effects in rats, and a NOAEL of 3000 ppm (14370 mg/m^3) was reported for post exposure neurotoxicity in rats. Several studies indicate that BA is not a reproductive toxicant. Female rats exposed to 6000 ppm (18000 mg/m^3) BA throughout gestation and male rats exposed to 6000 ppm (18000 mg/m^3) BA for six weeks prior to mating showed no effects on fertility or pregnancy rate. Male rats given BA at 533 mg/kg/day for 5 days had no testicular toxicity. BA produced only mild fetotoxicity and developmental

alterations at or near the maternally toxic (even lethal) dose of 8000 ppm (24000 mg/m^3) throughout gestation. An entire battery of negative *in vitro* tests and a negative *in vivo* micronucleus test indicate that BA is not genotoxic. The median odor threshold for BA (0.17 ppm) is well below the lowest nasal irritation threshold in humans (289 ppm), allowing warning of possible chemical exposure prior to nasal irritation occurring. Human studies are complicated by the odor characteristics of the material, as the odor threshold is well below the levels at which irritation is observed.

Environment

BA's vapor pressure is 0.56 kPa at 20^{0}C, water solubility is 77 g/L at 20^{0}C and a Log K_{ow} is 0.88. Based on level III fugacity modeling, BA will partition 83.5% in air, 5.9% in soil, 10.6% in water, <0.1% in suspended solids, and <0.1% in biota and in sediment. BA degrades in air by reaction with hydroxyl radicals, having a half-life in air of 1.2 to 2.3 days. The volatilization half-life for BA in water is estimated to be 2.4 hours for streams, 3.9 hours for rivers and 126 days for lakes. BA exhibits low toxicity to fish, amphibians and aquatic invertebrates, plants, algae, bacteria and protozoans. However, some algal species are sensitive to BA. Acute toxicity to aquatic life may occur at concentrations greater than 500 mg/l. BA is classified as "readily biodegradable" under aerobic conditions. The octanol:water partitioning coefficient (log K_{ow}) for BA ranges from 0.88 to 0.97, and the calculated bioconcentration factor (BCF) is 3. These data indicate that BA has a low potential to bioaccumulate. BA is expected to migrate readily through soil to groundwater and not to sorb to soil particles.

Exposure

BA is used primarily as an industrial intermediate in the production of ethers and butyl ether acetates, pharmaceuticals, polymers and plastics. BA is used to a lesser extent as a solvent, reactant/diluent and component in consumer (nail polish formulations, rubber cement and safety glass) and industrial products. Production in the US is estimated at 784,000 tonnes, 575,000 tonnes in Western Europe and 225,000 tonnes in Japan. In regards to physical hazards of the chemical, it has a flammable range of 1.4 – 11.2 volume % in air (14,000 – 112,000 ppm) and a flash point of 98^{0}F (37^{0}C). In the US, due to the physical chemical properties of BA, workplace exposure during manufacture and use as industrial intermediate is limited by closed processing. For the same reasons, exposure is not anticipated during the formulation of butyl alcohol into various products as a solvent. Inhalation and dermal exposure can occur during industrial and commercial application of products containing butyl alcohol, such as lacquers and other coatings. Use in consumer products is limited, but is a possible source of exposure. Releases to the environment are primarily from solvent use. Butyl alcohol occurs naturally in foods.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.