SIDS INITIAL ASSESSMENT PROFILE

CAS No.	123-86-4
Chemical Name	n-butyl acetate
Structural Formula	CH_3-COO-CH_2-CH_2-CH_2-CH_3

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Data from n-butanol (BA) toxicity studies have been included in the assessment of butyl acetate (BAc). Data from n-butanol is useful when assessing the hazards associated with the systemic toxicity of n-butyl acetate (BAc) 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 due to metabolism of the acetate ester within barrier tissues. Since exposure to either BAc or BA results in systemic exposure to BA, systemic toxicity data from studies that administer BAc directly 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 acetate (BAc) exhibits low acute toxicity by the oral, dermal, and inhalation routes. The oral LD50 ranges from 3,200 mg/kg in rabbits to 14,130 mg/kg in rats. Dermal LD50 values range from >5,000 mg/kg to 17,600 mg/kg in rabbits. Inhalation LC50 values for vapour exposures were >8,000 ppm (38,320 mg/m^3) in well-controlled studies. Nose-only inhalation studies using atomizers to generate a mixture of aerosols and vapour yielded conflicting and nonreplicable data with deaths below 8,000 ppm in some instances. In these acute studies, the major sign of toxicity observed were depressed central nervous system function, which is documented to be well known to alcohols and esters of alcohols. BAc is not a dermal sensitizer or an eye or skin irritant. In repeat-dose inhalation toxicity studies, (9 days to 13 weeks), NOAELs of 500 ppm (2395 mg/m^3) and higher were observed in rats. Effects observed included decreased activity during exposure, decreases in motor activity immediately post-exposure, decreases in body weights and rate of weight gain, and degeneration of olfactory epithelium in the nose. Repeated exposures for 13-weeks to concentrations as high as 3000 ppm (1437 mg/m^3) did not find any evidence of cumulative neurotoxicity when motor activity, functional observational batteries, and scheduled controlled operant behaviour were assessed. Therefore, other than transient reversible sedation during exposure, BAc should not be considered a neurotoxicant. The degeneration of the olfactory epithelium within the nose is a common lesion in rats exposed by inhalation to acetate esters of short-chain alcohols due to the liberation of acetic acid in these cells from the hydrolysis of the ester linkage. Since rats are obligate nose-breathers, the delivered dose to this portion of the nose is higher in rats than humans and the significance of this lesion in human health is questionable. Pharmacokinetic studies have demonstrated an elimination half-life for BAc of 0.41 minutes in blood *in vivo* in rats. The rapid appearance of the n-butanol (BA) metabolite allows the use of studies conducted directly with BA to be used in hazard identification and assessment for BAc.

In the 13-week inhalation study using BAc, no effects on homogenisation-resistant sperm or spermatid head

counts collected from the testes and epididymides, respectively were observed. Developmental toxicity studies have been conducted in rats and rabbits exposed via inhalation to 1500 ppm (7185 mg/m^3) BAc. In rats, reduced fetal size was observed after exposure to BAc during gestation days 1-16 or 7-16 and decreased body weight was seen in dams exposed from GD 1-16. Therefore, the maternal and developmental LOAEC was determined to be 7185 mg/m^3 in rats. In rabbits, there was an increase in the incidence of "misaligned sternabra" and "retinal folds" in the group exposed from GD 1-19. A single increased incidence of a morphologic variation ("clear gallbladder") was also seen in this group of rabbits. A maternal NOAEC and developmental LOAEC of 7185 mg/m^3 were determined for rabbits. No teratogenicity was observed in rats or rabbits. These results indicate that BAc may result in developmental toxicity at high doses.

In vitro mutagenicity and chromosomal aberration studies indicate that BAc is not a genotoxicant. In addition, BA was negative in an *in vivo* mouse micronucleus study. Inhalation of 200 ppm (958 mg/m^3) BAc or higher has been reported to cause slight irritation to the throat of human subjects, while lower exposure concentrations were without effects. In humans, eye irritation occurs at levels > 1400 mg/m^3.

Environment

The available physicochemical data are adequate to describe the properties of n-butyl acetate (BAc).). Bac has a vapour pressure of 12-21 hPa at 20^{0}C, a water solubility of 14 g/l at 20^{0}C and a Log K_{ow} of 1.82. The photochemical removal of n-butyl acetate from the troposphere occurs at a slow rate with the total tropospheric lifetime of n-butyl acetate expected to be about 50 hours. BAc is readily biodegradable under aerobic conditions. However, the primary mode of removal from surface water is volatilisation. BAc is not persistent in the environment and is not likely to bioaccumulate in food webs. Based on fugacity-dependent modelling it is estimated that the majority of BAc released to the environment will partition into air (97.2 %), with a smaller amount in water (2.4%). The stability of BAc in water is pH dependent, at neutral pHs (7) the $T_{1/2}$ = 3.1 years at 20^{0}C and at higher pHs (8 and 9) the $T_{1/2}$ is shortened to 114 days and 11.4 days respectively. Based on acute aquatic toxicity data, the most sensitive species appears to be in fish (*Pimephales promelas*) which has a 96h LC50 of 18 mg/L. Terrestrial data are not available, but based on negligible soil release and low potential for bioaccumulation, adverse terrestrial outcomes are considered unlikely.

Exposure

Approximately 132,000 tonnes (290 million pounds) of BAc were manufactured in the USA in 1993, using a continuous, closed process. Environmental release from production facilities is low. BAc is used as a solvent in liquid formulation products, typically lacquers, solvent mixtures, inks, coatings, and adhesives. Application of these materials results in exposure via the dermal and inhalation routes, and release of BAc into the environment through volatilisation. Due to the physical-chemical properties of BAc, the material is not typically present as an aerosol. In regards to physical hazard, the chemical has a low flash point and a flammable range of 1.7 to 7.6% volume in air. Monitoring of lacquer spray booths (believed to represent a worst-case occupational exposure) provided breathing zone measurements of BAc in the 1-10 ppm (.21 – 2.1 mg/m^3) range. BAc is also a product of normal intermediary metabolism in mammals and a natural component of apple, potatoes, and nuts.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.