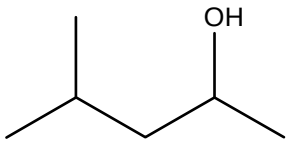
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	108-11-2
Chemical Name	4-Methylpentan-2-ol
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Justification

The metabolism and clearance of 4-methylpentan-2-ol (methyl isobutyl carbinol; MIBC) is rapid (Cmax and t½ approximately 30 min and 2 hr, respectively). MIBC is metabolized to 4-hydroxy-4-methyl-2-pentanone (HMP) through methyl isobutyl ketone (MIBK). Dosing with MIBC or MIBK results in similar internal exposure to MIBK and HMP and minimal exposure to MIBC. Thus, the data for MIBK and HMP adequately support the evaluation of MIBC systemic toxicity.

Human Health

Studies with experimental animals indicate that MIBC is of low toxicity by the oral, dermal and inhalation routes of exposure. MIBC has typical organic solvent effects in rats following acute inhalation exposures with anesthetic effects occurring at 10 mg/L (2360 ppm) and death following an 8-hour exposure to 8.4 mg/L (2000 ppm). The acute oral and dermal LD_{50} values for MIBC are 2260 - 2970 mg/kg and 2870 mg/kg, respectively.

In standard primary irritation studies, MIBC was slightly irritating to skin and moderately to severely irritating to the eye. Human volunteers exposed to MIBC vapors at 50 ppm experienced eye irritation in most subjects with nose and throat irritation experienced at higher concentrations. The maximum tolerable concentration was considered to be 25 ppm. A skin sensitization study in animals was negative and indicates that MIBC is not likely to be a sensitizer in humans.

Repeated dose studies with MIBC and its primary metabolites, MIBK and HMP, indicated that systemic toxicity is minimal. The NOAEC for subchronic inhalation exposure was 886 ppm (3.70 mg/L) for MIBC (6-weeks with rats) and 1000 ppm (4.09 mg/L) for MIBK (14-weeks with rats and mice). There were no organ-specific toxic effects for either chemical. The NOAEL for the ultimate metabolite, HMP, via gavage dosing for 45 days was 30 mg/kg/day for males (based on hyaline droplet nephropathy) and 100 mg/kg/day for females. The LOAEL for this study was 100 mg/kg/day for males and 300 mg/kg/day for females.

MIBC and HMP were not mutagenic to bacterial cells (bacterial reverse mutation assay) *in vitro* with or without metabolic activation. In a mammalian cell cytogenetic assay (rat liver cells), MIBC was negative with and without metabolic activation. HMP was negative in an *in vitro* chromosomal assay. Based on the negative results in the bacterial mutagenicity and mammalian cell cytogenetic assays with MIBC and bacterial mutagenicity and chromosomal aberration assays with HMP, MIBC is unlikely to be mutagenic in humans.

MIBC showed no effects on reproductive organs following 6 weeks of inhalation exposure to concentrations as high as 3.70 mg/L (886 ppm). MIBK showed no reproductive effects in a two-generation study with inhalation exposures

up to 8.18 mg/L (2000 ppm). Slight changes in reproductive performance (decreased fertility and implantations) and pup viability following high oral exposure to HMP (1000 mg/kg/day) in an OECD TG 422 study may have occurred in the presence of maternal toxicity (reduced weight gain, statistically significant changes in hematology, clinical biochemistry and relative organ weights; renal and hepatic histopathological lesions). No teratogenic effects were observed for rats or mice at MIBK inhalation concentrations as high as 3000 ppm (12.3 mg/L) and no fetal toxicity was observed without the presence of maternal toxicity; the NOAEC for maternal and fetal toxicity was 1000 ppm (4.09 mg/L) due to clinical signs of toxicity including neuromuscular effects (both species), and statistically significant changes in body weight, relative kidney weights and decreased food consumption (rats only) and increased liver weight (mice only), and decreased fetal body weight with evidence of delayed ossification. Based on the available animal data, MIBC is not expected to be a human reproductive or developmental toxicant.

Environment

The melting point of MIBC is – 90°C and the boiling point is 131.7°C. The vapor pressure is 4.97 hPa at 20°C. The water solubility of MIBC is 16.4 g/L (20°C) and density is 0.81 g/cm^3 at 25°C. The calculated log Kow is 1.68. MIBC is predicted to be photodegraded by reaction with hydroxyl radicals in the atmosphere with a half-life of approximately 10 hours (calculated). MIBC does not have hydrolyzable groups and therefore hydrolysis is not a degradation pathway. Distribution modeling using Mackay Level I indicated that partitioning will occur to air (37.8%), water (59.6%), and soil (2.5%) phases. Fugacity model Level III predicted greatest distribution (≥ 86%) to the primary compartment of release. When equal releases were assumed, the predicted distribution was: 3.6% (air), 45% (water), 51% (soil) and <1% (sediment). A low bioaccumulation potential is expected based on the partition coefficient and other physical/chemical parameters. MIBC is readily biodegradable attaining 94% degradation within 20 days and meeting the "10-day window".

The 96-hour LC_{50} for rainbow trout (*Oncorhynchus mykiss*) is 359 mg/L (measured), the 48-hour EC_{50} for *Daphnia magna* is 337 mg/L (measured) and the 96-hour EC_{50} value for growth rate of algae (*Pseudokirchneriella subcapitata*) is 334 mg/L (measured) and for biomass is 147 mg/L (measured) .

Exposure

The estimated total volume of MIBC production in North America in 1998 was 25,000 tonnes. MIBC is primarily used (~70%) in the production of lube oil additives. MIBC (~20% of the total production) is used as a flotation frother for treating copper ores and coal with usual concentrations less than 1000 ppm and in many cases in the hundreds of ppm range (100 - 600 ppm). The remaining production is primarily for its use as an additive to surface coatings as a solvent to maintain binder softness until the binder fuses.

The use as a solvent and as flotation frothers result in environmental releases at very low concentrations. Human exposure to MIBC is very limited based on its use patterns. With the exception of tar sand mining frothers, MIBC is used in closed systems and only catastrophic failure results in any appreciable exposure. In tar sand mining, exposure (in the ppm range) is typically limited to the equipment operators. MIBC used as an intermediate in the manufacture of lube oil additives is blended with other alcohols and reacted. Normally these reactors are closed systems and exposure is limited to upsets or catastrophic failure of the reactor. In its primary use as an intermediate for corrosion inhibitor production, significant residual MIBC is not anticipated. As noted above, in mining operations, low ppm vapor exposure may occur in operators. Minimal exposure to vapors from the use of MIBC as a solvent in coating applications may also occur. The ACGIH TLV-TWA for MIBC is 25 ppm (104 mg/m^3) and the TLV-STEL is 40 ppm (167 mg/m^3). The German MAK value is 25 ppm.
Based on its pattern of use, consumer exposure to MIBC is expected to be negligible. Environmental exposure to MIBC can occur during mining processes or through accidental release.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is currently a low priority for further work. The chemical possesses properties indicating a potential hazard for human health (eye irritation, narcosis at high inhalation concentrations) These hazards do not warrant further work as they are related to acute toxicity which may become evident only at high exposure levels. They should nevertheless be noted by chemical safety professionals and users.

Environment: The chemical is currently a low priority for further work due to its low hazard profile.