SIDS INITIAL ASSESSMENT PROFILE

CAS No.	110-19-0
Chemical Name	Isobutyl Acetate
Structural Formula	CH_3-COO-CH_2-(CH_3)CH-CH_3

SUMMARY CONCLUSIONS OF THE SIAR

Based on the rapid and complete hydrolysis of isobutyl acetate to isobutanol, *in vivo* data from isobutanol is useful when assessing the hazards associated with the systemic toxicity of isobutyl acetate exposure. Exposure to isobutyl acetate via dermal, inhalation, and water or dietary administration results in the rapid appearance of isobutanol in the systemic circulation due to metabolism of the acetate ester within barrier tissues. Since exposure to either isobutyl acetate or isobutanol results in systemic exposure to isobutanol, systemic toxicity data from studies that administer isobutanol directly are useful in identifying hazards associated with isobutyl acetate exposure. Endpoints of isobutyl acetate toxicity that are associated with direct contact-mediated effects (e.g. eye, skin, and respiratory tract irritation) cannot be extrapolated from isobutanol data due to the difference in physical-chemical properties of the two materials.

For acute aquatic toxicity, database of isobutyl acetate was supported using data from structural analogs, alleviating the need for additional testing on isobutyl acetate. Data from propyl acetate (CAS# 109-60-4), n-butyl acetate (CAS# 123-86-4), and 2-ethylhexyl acetate (CAS# 103-09-3) were used. These analogs have molecular backbones ranging from C3 to C8.

Human Health

This chemical has low acute toxicity by all routes. The oral LD_{50} ranges from 4,763 mg/kg bw in rabbits to 15,000 mg/kg bw in rats. Dermal LD_{50} values range from >5,000 mg/kg bw to >17,400 mg/kg bw in rabbits. Inhalation LC_{lo} values for vapor exposures were 38,000 mg/m^3 (8,000 ppm) with an LC_{100} of 99,750 mg/m^3 (21,000 ppm).

Isobutyl acetate is a moderate eye and skin irritant but not a dermal sensitizer. Inhalation of 200 ppm (950 mg/m^3) isobutyl acetate or higher has been reported to cause strong irritation to the throat of human subjects, while lower exposure concentrations were without effects. Repeated inhalation exposures would likely exacerbate the irritative effects.

Repeated exposures to moderate to high concentrations of isobutanol by the inhalation and oral routes of exposure are well tolerated in rats. In a 90-day inhalation study, rats were exposed to isobutanol at 0, 758, 3030, and 7575 mg/m^3 (0, 250, 1000, and 2500 ppm). A reduced response to an external stimulus was noted in the exposed animals only during the exposure period. Repeated exposures did not exacerbate these transient effects. There was no evidence of neurotoxicity based on functional observational battery (FOB), quantitative motor activity, neuropathy and scheduled-controlled operant behavior endpoints. The NOAEL was 3030 mg/m^3 or 1000 ppm based on increases in erythrocyte count, hemoglobin, and hematocrit measures in female rats. The NOAEL for neurotoxicity was 7575 mg/m^3 or 2500 ppm. A 13-week oral gavage study was conducted with isobutanol with dose levels of 0, 100, 316, and 1000 mg/kg bw/day. Hypoactivity and ataxia were noted in the 1000 mg/kg bw/day dose groups after dosing. In addition slight decreases in body weight gain and feed consumption was noted in the first two weeks of the 13-week study in the 1000 mg/kg bw/day dose group. The 100 and 316 mg/kg bw/day dose groups

were unaffected. The use of toxicity data from a metabolic series has been used in previous SIDS documents (e.g. n-butyl acetate and n-butanol, ethyl acetate, and ethanol) to provide toxicity information for related members.

An *In vitro* mutagenicity study indicates that isobutyl acetate is not a genotoxicant. In addition, isobutanol was negative in an *in vivo* mouse micronucleus study.

An inhalation two-generation reproductive toxicity study conducted with isobutanol (up to 7575 mg/m^3 or 2500 ppm) did not cause any parental systemic, reproductive, or neonatal toxicity when administered for two generations via whole-body exposure. No adverse developmental effects were noted in rats or rabbits exposed to 10,000 mg/m^3 (10 mg/L) isobutanol during gestation days 6-15 (rats) or 7 –19 (rabbits).

Environment

The available physicochemical data are adequate to describe the properties of isobutyl acetate. Isobutyl acetate has a vapor pressure of 18 hPa at 20^{0}C, a water solubility of 6 g/l at 20^{0}C and a Log K_{ow} of 1.78 (assumed at 25^{0}C). The photochemical removal of isobutyl acetate as mediated by hydroxyl radicals occurs with calculated half lives of about 1.9-2.3 days.

Isobutyl acetate is readily biodegradable under aerobic conditions. Isobutyl acetate volatilises easily from moving rivers, but volatilises only moderately from quiescent lakes and other surface water bodies (calculated volatilization half-lives of 2.9 hours from a river and 5.08 days from a lake). Isobutyl acetate is not persistent in the environment and is not likely to bioaccumulate in food webs.

Based on Level III distribution modelling it is estimated that the majority of isobutyl acetate released to the environment will partition into water (42.7%) and soil (44.9%), with a smaller amount in air (12.3%). The stability of isobutyl acetate in water is pH dependent, at neutral pHs (7) the $T_{1/2}$ = 3.3 years at 20^{0}C and at higher pHs (8) the $T_{1/2}$ is shortened to 122 days.

Aquatic toxicity data are available for isobutyl acetate. However, since the duration of the isobutyl acetate studies was either shorter or longer than current OECD guidelines and because of uncertainties in study details, data for analogous compounds are presented. The analogous compounds used were propyl acetate (CAS# 109-60-4), n-butyl acetate (CAS# 123-86-4), and 2-ethylhexyl acetate (CAS# 103-09-3). For propyl acetate, a flow-through test was conducted using fathead minnows (*Pimephales promelas*) and reported a 96-h LC50 of 60 mg/L. For n-butyl acetate, a flow-through test was conducted with fathead minnows and reported a 96-h LC50 of 18 mg/L. For 2-ethylhexyl acetate, a static-renewal test (daily renewals) with rainbow trout (*Oncorhynchus mykiss*) was conducted using the water accommodated fraction (WAF) method for compounds that are difficult to solubilize in water. A 96-h LC50 of 8.27 mg/L was reported. For 2-ethylhexyl acetate, a test with *Daphnia magna* was conducted using the WAF method, reporting a 48-h EC50 of 22.9 mg/L. Also using 2-ethylhexyl acetate, test with the green alga *Selenastrum capricornutum* was conducted using the WAF method, reporting a 72-h EC50 of >21.9 mg/L. Terrestrial data are not available, but based on low potential for bioaccumulation and the low hazard indicated by the mammalian toxicity data adverse effects on terrestrial mammals are not expected.

Exposure

Approximately 74,000 tonnes (163 million pounds) of isobutyl acetate was manufactured in the world in 2001, in continuous, closed processes. Environmental release from production facilities is low. Isobutyl acetate is used as a solvent in liquid formulation products, typically coatings, thinners, sealants, adhesives, printing inks, and cleaners. Application of these materials results in exposure via the dermal and inhalation routes, and release of isobutyl acetate into the environment through volatilisation. Due to the physical-chemical properties of isobutyl acetate, 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 1.3 to 10.5% volume in air. Isobutyl acetate is also a natural component of nectarines, bananas, apples, and other fruits as well as milk.

RECOMMENDATION

Isobutyl Acetate is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses properties indicating a hazard for human health (dermal, respiratory, and eye irritation) and the environment. Although these hazards do not warrant further work, as they are related to transient effects or acute toxicity which may become evident only at high exposure levels, they should nevertheless be noted by chemical safety professionals and users.