# SIDS INITIAL ASSESSMENT PROFILE

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| **CAS No.** | 78-83-1 |
| **Chemical Name** | Isobutanol |
| **Structural Formula** | $(CH_3)_2$-CH-$CH_2OH$ |

## SUMMARY CONCLUSIONS OF THE SIAR

### Category/Analogue Rationale

The acute aquatic plant (green algae) toxicity data on isobutanol (IBOH) was supported/addressed-using data from the structural analog, n-butanol (CAS No. 71-36-3).

### Human Health

Isobutanol is rapidly absorbed following inhalation and oral exposures. Isobutanol is rapidly metabolised to isobutyraldehyde and isobutyric acid in rodents and humans.

This chemical has low acute toxicity by all routes. The oral $LD_{50}$ in male rats is >2830 mg/kg bw and in female rats was 3350 mg/kg bw. Dermal $LD_{50}$ in male rabbits was >2000 mg/kg bw and 2460 mg/kg bw in female rabbits. Inhalation $LC_{50}$ values for vapor exposures were >6,000 ppm (18,120 mg/m$^3$) in male and female rats. Isobutanol is a slight to moderate skin irritant and a severe eye irritant.

Repeated exposures to moderate to high concentrations of isobutanol are well tolerated in rats. In a 90-day inhalation study, rats were exposed to isobutanol at 0, 250, 1,000, or 2,500 ppm (760, 3,030 or 7,580 mg/m$^3$). 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 1,000 ppm (3,030 mg/m$^3$) based on increases in erythrocyte count, hemoglobin, and hematocrit measures in the female rats. Based on the definitive measures of neurotoxicity (FOB, motor activity, histopathology), the NOAEL for neurotoxicity was 2,500 ppm (7,580 mg/m$^3$). A 13-week oral gavage study was conducted with isobutanol with dose levels of 0, 100, 316, and 1,000 mg/kg bw/day. Hypoactivity, ataxia and salivation were noted in the 1,000 mg/kg bw/day dose groups. Hypoactivity and ataxia were resolved by the 4$^{th}$ week of the study. In addition, slight decreases in body weight gain and feed consumption were noted in the first two weeks of the 13-week study in the 1,000 mg/kg bw/day dose group. The NOAEL was 316 mg/kg bw/day.

Several *in vitro* mutagenicity studies indicate that isobutanol 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 2500 ppm (7,580 mg/m$^3$)) did not cause any parental systemic, reproductive, or neonatal toxicity when administered for two generations via whole-body exposure. The NOEL for reproductive and neonatal toxicity was 2,500 ppm (7,580 mg/m$^3$). No adverse developmental effects were noted in rats or rabbits exposed by inhalation to 10,000 mg/m$^3$ isobutanol during gestation. The NOAEL for developmental toxicity was 10,000 mg/m$^3$.

**Environment**

The available physicochemical data are adequate to describe the properties of isobutanol. Isobutanol has a vapor pressure of 13.9 hPa (10.43 mmHg) at $25^0$C, a water solubility of 85 g/l at $25^0$C and a log $K_{ow}$ of 0.79. The melting and boiling points for isobutanol are approximately -108° and 108° C, respectively. The photochemical removal of isobutanol as mediated by hydroxyl radicals occurs with a calculated half-life of 1.55 days. Isobutanol is readily biodegradable under aerobic conditions. Isobutanol volatilises moderately from moving rivers, but less so from quiescent lakes and other surface water bodies (calculated volatilization half-lives of 43 hours from a river and 23 days from a lake). Isobutanol 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 isobutanol released to the environment will partition into water (51.6%) and soil (43.5%), with a smaller amount in air (4.85%).

Acute fish and aquatic invertebrate toxicity data are available for isobutanol. Data from the structure analog n-butanol have been used to support/address the acute aquatic plant endpoint. A flow-through test with fathead minnows (*Pimephales promelas*) reported a 96-hour $LC_{50}$ of 1430 mg/L. Static tests were conducted using three water column-dwelling invertebrate species (*Daphnia magna, D. pulex, Ceriodaphnia reticulata*) according to ASTM procedures. Forty-eight hour $EC_{50}$ values of 1300 (96% CI 1200-1400), 1100 (950-1200), and 1200 (1100-1300) mg/L were reported for the three species, respectively. Since no reliable data are available for describing the toxicity of isobutanol to algae, the results of a test on the structurally analogous substance, n-butanol, are presented. The test with *Selenastrum capricornutum* determined a 96-hour EC50 of 225 mg/l.

**Exposure**

Isobutanol is manufactured at 16 plant sites in the United States and about 35-40 companies or sites worldwide. Production in the United States was reported to be in the range of 100 – 500 million pounds (45-227 thousand metric tons) in 1998. Worldwide production capacity outside the U.S. is about 402 thousand metric tons. The largest uses of IBOH are as follows: production of isobutyl acetate and other chemicals; use as a direct solvent and as an intermediate in the production of lubricant additives. Use as a direct solvent in coatings, lacquers, primers, and adhesives offers the most potential source of human exposure, since some of these applications are open processes, and isobutanol solvent may be released to ambient air through evaporation as the coating or lacquer dries. Consumers may use some of these products. Human exposure to isobutanol may occur in the work place during manufacture, formulation into products or in various industrial applications, such as working with coatings containing isobutanol as solvent. Such exposures can occur through inhalation and dermal contact. Workplace exposure limits have been established for isobutyl alcohol in most OECD countries. Consumers are exposed when working with consumer products, such as coatings, that contain isobutanol, and through ingestion of foods and beverages that contain naturally occurring isobutanol. Consumers may also be exposed to environmental concentrations of isobutanol in the air or water. Almost all human beings are exposed daily to low concentrations of isobutanol from natural sources, such as in foods and from fermentation of carbohydrates. Exposures to artificial sources also occur, primarily in the vicinities of plants that manufacture, process or use isobutanol in many applications.

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

**Human Health:** Isobutanol possesses properties indicating a hazard for human health (dermal and eye irritation). These hazards do not warrant further work as they are related to reversible, transient effects that may become evident only at high exposure levels. They should nevertheless be noted by chemical safety professionals and users.

**Environment:** Isobutanol is currently of low priority for further work due to its low hazard profile.