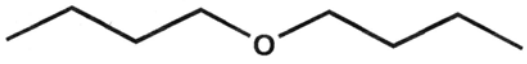
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	142-96-1
Chemical Name	Dibutyl ether
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

No experimental data are available regarding the toxicokinetic behavior, and metabolism of dibutyl ether. The appearance of systemic toxicity after oral and inhalative exposure shows the bioavailability of dibutyl ether via these routes.

Dibutyl ether is of low acute toxicity after inhalative (approximate 4-hour LC_{50} rat: 21 600 mg/m³ (4000 ppm)), dermal (LD_{50} rabbit: 7741 mg/kg bw (10.08 ml/kg bw)) and oral exposure (oral LD_{50} rat: 7400 mg/kg bw). Dibutyl ether has no pronounced narcotic potential.

Dibutyl ether is only very slightly irritating to the skin and the eyes of rabbits, as determined in GLP studies performed in accordance with OECD TG 404 and 405, respectively. All symptoms of irritation were completely reversible within 96 and 48 hours, respectively. In humans, a 15 minutes exposure towards 200 ppm (corresponding to 1066 mg/m³) dibutyl ether was reported to be sensory irritating to the eyes and the nose, but not to the throat. In a 28-day inhalation GLP study, performed according to standard guidelines, dibutyl ether at concentrations of up to and including 1500 mg/m³ was not irritating to the respiratory tract of rats. There are no indications of sensitizing properties of dibutyl ether.

No target organ appeared up to and including the highest tested concentration of 1500 mg/m³ in a 28-day inhalation study in rats, performed under GLP according to OECD TG 412 with test concentrations of 0, 150, 500, and 1500 mg dibutyl ether/m³. The repeated exposure to 1500 mg dibutyl ether/m³ caused only a temporary body weight loss in females during the first exposure week. After the first week of exposure and during the 14-day recovery period, growth of high-dose females was comparable to the control group. The treated male rats showed changes in testes, epididymides, liver and brain weights in the low- and mid-dose groups that were not confirmed by data of the high-dose group of 1500 mg/m^3. Therefore the findings regarding the low- and mid-dose groups were considered as fortuitous and thus the no observed adverse effect level (NOAEL) was 1500 mg/m^3. The temporary effect on body weight seen in female rats is not considered to be a serious adverse effect, and the high-concentration level of 1500 mg/m³ can be regarded as a minimum observed adverse effect level in female rats. Due to the absence of treatment-related changes, the next lower level tested, viz. 500 mg/m³, was considered to be the NOAEL in females.

In vitro, dibutyl ether was neither mutagenic in a bacterial test system (two Ames tests, each performed according to OECD TG 471 (1983)) nor clastogenic in a mammalian test system (chromosomal aberration GLP test according to OECD TG 473 on human peripheral lymphocytes).

There was no data available concerning carcinogenicity.

No specific studies have been performed on the toxicity of dibutyl ether to reproduction. Organ weight determinations and gross and histopathological examinations in a 28-day study revealed no pathological change in reproductive organs (testes, epididymides, prostate, seminal vesicles, coagulating glands, ovaries, uterus, vagina, and mammary glands) when dibutyl ether was administered by inhalation to male and female rats at concentration levels up to and including 1500 mg/m³. No histopathological effects or weight changes were found in testes and

epididymides of rats treated orally with up to 200 mg/kg bw/day for four weeks in a study specifically designed to detect effects on male reproductive organs. In the latter study, clear testicular effects were produced in a concurrent group of animals treated with 1,6-dimethoxy hexane. This gives confidence that the study was sensitive enough to detect relevant adverse effects on the male reproductive organs, although the duration of treatment was relatively short (4 weeks). In the prenatal developmental toxicity study which is described below, there were no indications on adverse effects on female reproductive organs at doses up to and including 1000 mg/kg bw/day. The data set regarding female fertility is limited and therefore no firm conclusions can be drawn.
In a GLP study performed in accordance with OECD TG 414 on rats with oral administration of dibutyl ether from the 6th to the 19th day of pregnancy, developmental effects (fetal weight reduction, skeletal retardations in form of missing or incomplete ossification of the hyoid, caudal vertebral bodies and 5th metacarpalia, and soft tissue variations in form of dilatation of the 4th cerebral ventricle) were found at the maternally toxic dose level of 1000 mg/kg bw. There was no test item-related increase in the incidence of fetal malformations, or external or skeletal variations. Signs of maternal toxicity at 1000 mg/kg bw/day were piloerection, a reduction in body weight and food intake and an increase in water consumption, absolute and relative liver weights, and plasma aspartate aminotransferase activity. Necropsy revealed no test item-related pathological changes in reproductive organs. Under the conditions of this study the NOAEL for maternal toxicity and developmental toxicity was 300 mg/kg bw/day

Environment

Dibutyl ether has a melting point of - 95.2 °C, a boiling point of 142 °C at 1013 hPa, a water solubility of 113 mg/l, and a vapor pressure of 4.6 hPa at 20 °C. The experimental log K_{OW} is 3.35.

Dibutyl ether is not readily biodegradable under standard test conditions (OECD TG 301 D: 5 % in 28 days, test according to OECD TG 301 C 3 - 4 % in 28 days). However, naturally occurring bacteria enriched in the laboratory as mono-species cultures were used as inoculum and were able to biodegrade dibutyl ether very well, as seen with an aerobic *Gordonia terrae* strain adapted to ethyl t-butyl ether and selected from activated sludge or several *Rhodococcus sp.* and *Terrabacter sp.* strains isolated from various environmental samples like activated sludge, river water, or contaminated soils. In the atmosphere dibutyl ether is expected to undergo rapid indirect photodegradation by the reaction with photochemically produced hydroxyl radicals with a calculated half-life of 15.6 hours. Dibutyl ether does not hydrolyze under environmental conditions. However, dibutyl ether will be degraded in water under favorable environmental conditions (summer, midday) by reaction with OH radicals with calculated half-lives in the range of hours to days. According to a Mackay Fugacity Model Level I calculation dibutyl ether is mainly distributed to air (> 97 %). A high volatility from water to air is also indicated by the calculated values for the Henrys´ law constant (0.00362 - 0.00472 atm m^3/mole). A half-life of 3.5 hours (= 0.15 days) for volatilization of dibutyl ether from river water to air and of 110 hours (= 4.6 days) for volatilization from lake water to air was calculated by EPIWIN v3.12. According to a Mackay Fugacity Model Level III calculation the residence time of dibutyl ether attributable to reaction only is below 28 days when released into air, water, or soil (100 % release into air: < 1 day, 100 % release into water: 25.5 days, 100 % release into soil: 24.4 days, 33.3 % release into air, water and soil: 16.3 days). Measured bioconcentration factors (BCF) in the range of 47 to 83 and 30 to 114 determined in laboratory tests on fish (*Cyprinus carpio*) and the calculated BCF of 76 are indicating a low bioaccumulation potential.

For the aquatic toxicity of dibutyl ether reliable experimental results (based on nominal concentrations) from tests with fish, *Daphnia*, and algae are available. The lowest valid test results were as following:

Oryzias latipes:	48 h-LC_{50} = 31 mg/l
Daphnia magna:	48 h-EC_{50} = 26 mg/l
Microcystis aeruginosa:	8 d-EC_{50} > 50 mg/l (biomass at test end)
	(This test measured an EC_1 with a non standard organism.)

No valid study with a standard algae species is available. Based on a QSAR calculation the 96 h-EC_{50} for dibutyl ether is 3.43 mg/l for the green algae *Pseudokirchneriella subcapitata* (formerly *Selenastrum capricornutum*).
In an activated sludge respiration inhibition test a 30 min-EC_{50} > 1000 mg/l was obtained. For protozoa, the lowest toxicity value was determined for *Uronema parduczi* (20 h-EC_5 > 40 mg/l).
The most sensitive species was *Daphnia magna* with a 48 h-EC_{50} of 26 mg/l. Applying an assessment factor of 1000 according to the EU Technical Guidance Document, a $PNEC_{aqua}$ of 26 µg/l is obtained.

Exposure

The reporting consortium knows about production sites for dibutyl ether in Germany, United Kingdom, the USA,

Japan, and the P.R. of China. The production volumes in Germany and in the USA are both approximately 1000 to 2000 tonnes per year. In Japan, this chemical is produced by at least three manufactures with an annual production volume of 450 tonnes in 2000. No information is available about the world-wide production volume and the world-wide traded volumes.

Dibutyl ether is used as a technical solvent for e.g. fats, oils, organic acids, alkaloids, natural and synthetic resins and as solvent for Grignard syntheses. It is also used as an extractant. Furthermore it is a constituent of catalysts for (co-) polymerization. Recently it has been added to the register of flavoring substance used in or on foodstuffs in the European Union. However, such an application is not known to the reporting consortium.

Releases into the environment may occur during production and processing of the substance. However at the only German production site the release into the environment is minimal under normal conditions, on account of its production and handling in closed systems by the manufacturer. At filling and decanting, state of the art exposure control measures (charcoal absorber) are installed to prevent any releases into the environment and exposures during production are below the detection limit of 2 mg/m³. Also production wastes are minimal because of recovery measures and controlled combustion. During its use in downstream products, e. g. as ingredient in industrial special cleaners (degreasers) or as technical solvent in fats, natural, and synthetic resins releases into the environment and occupational exposure may be higher than those from production, however, quantitative information is not available.

Dibutyl ether is not commonly used in consumer products. Only one single consumer product each is listed in publicly accessible European and US product registers: a degreaser containing 5 % dibutyl ether and a special cleaner, respectively. If dibutyl ether is used as flavoring substance in or on foodstuffs, consumer exposure could occur. However, this kind of application of dibutyl ether is not known to the reporting consortium.

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

Human Health: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for human health (slightly irritating to eyes and upper respiratory system). These hazards do not warrant further work as they are related to reversible, transient effects. They should nevertheless be noted by chemical safety professionals and users.

Environment: The chemical is currently of low priority for further work. The chemical has properties indicating a hazard for the environment (acute aquatic EC_{50}/LC_{50} values between 1 and 100 mg/l). However the chemical is of low priority for further work for the environment because of its fugacity, its fast photodegradation in the atmosphere, and its limited potential for bioaccumulation.