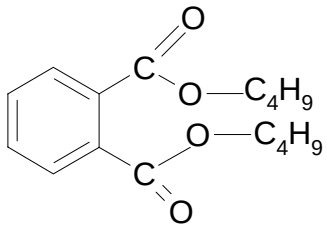
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	84-74-2
Chemical Name	Dibutylphthalate
Structural Formula	

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Dibutylphthalate is rapidly absorbed, orally up to more than 90%. After 48 hours .63-90% % is excreted in the urine. The dermal absorption is around 20% in rats. Data on absorption after inhalation are not available. Dibutylphthalate has a low toxicity after oral, dermal and inhalation exposure. Oral LD50 for the rat is $\geq$ 6300 mg/kg b.w. The dermal LD50 is > 20000 mg/kg bw for the rabbit. The 4 h LC50 inhalation for the rat is $\geq$ 15.68 mg/l. Dibutylphthalate is not irritating to the skin or eye and is not a skin sensitiser. Several studies are available for repeated dose toxicity. In a 3 month dietary study effects on haematology and clinical chemistry combined with liver effects and increased relative kidney weight were observed at $\geq$ 752 mg/kg bw. A NOAEL of 152 mg/kg bw was the lowest of the repeated dose toxicity studies. Neurofunctional tests did not show abnormalities. In studies with rats with special attention to testicular effects the LOAEL was 250 mg/kg b.w. In an inhalation study of 28-days duration in rats, no systemic effects including neurotoxic effects were observed up to and including the highest exposure concentration of 509 mg DBP/m^3. At all exposure concentrations (1.18, 5.57, 49.3 and 509 mg/m^3) adverse local (histopathological) effects in the upper respiratory tract were observed, but no signs of inflammation. In addition, at the highest exposure concentration of 509 mg/m^3 red crust formation at the snouts was observed after cessation of daily exposure (recovered within 18 hours) in a maximum of 4/10 animals at a maximum duration from day 13-27. It is concluded that 509 mg/m^3, the highest concentration tested, is a NOAEC for systemic effects including neurotoxic effects. The lowest exposure concentration of 1.18 mg/m^3 is a LOAEC for local effects in the upper respiratory tract.

Based on *in vitro* as well as *in vivo* genotoxicity studies and taking into consideration the non-genotoxic properties of other phthalate esters, dibutylphthalate can be considered a non-genotoxic substance.

Dibutyl phthalate is considered a reproductive toxicant; causing embryotoxicity and impaired fertility. Several studies on reproductive organs have been performed. In a one- and two-generation study, embryotoxicity such as effects on pup weight (both studies), growth of pups during entire lactation (first generation study) and number of live pups per litter (second generation study) were observed. In the first generation study after 7 weeks post weaning testicular effects, including histopathological effects

were observed at 500 mg/kg bw and some maternal toxicity. A NOAEL from this study was 50 mg/kg bw. The two-generation was performed with a continuous breeding protocol including improved sensitive endpoints (such as sperm parameters, estrous cycle characterization and detailed testicular histopathology) and with exposure of both male and female animals. The protocol of this study was supposed to adequately identify compounds with endocrine activity. In this study embryotoxic and testicular effect were observed at the lowest dose tested 52 mg/kg b.w. without maternal toxicity. Including all reproduction studies (the other studies showing similar effects at higher doses) a NOAEL of 50 mg/kg b.w. was derived. Developmental studies in rats with exposure during gestation or during gestation and lactation had delayed preputial separation and reproductive tract malformations in male offspring at oral dose-levels at $\geq$ 250 mg/kg bw. Maternal toxicity was seen at doses $\geq$ 500 mg/kg b.w. At the lowest oral dose-level of 100 mg/kg b.w. studied in developmental studies in rats, still delayed preputial separation in male progeny was seen. A NOAEL could not be derived for these studies. In some special *in vitro* studies DBP showed weak estrogenic activity. These effects were not confirmed in *in vivo* studies. Therefore the relevance of the estrogenic effects observed *in vitro* for the *in vivo* estrogenic toxicity of DBP is questionable. The results of a recent assay indicate an anti-androgenic activity of DBP. However, in contrast with classical anti-androgens DBP required dosing immediately following weaning for the induction of weight changes in male reproductive organs.

Environment

Both short-term and long-term dibutylphthalate toxicity data are available for aquatic organisms. There are also a number of studies with bacteria and protozoa's. Short term LC50-values for fish range from 0.35-7.3 mg/l. The NOEC for fish is based on *Oncorhynchus mykiss*: 100 µg/l. *Daphnia magna* EC50 values and other aquatic invertebrates range from 0.76 – 17mg/l. NOEC aquatic invertebrates range from 0.1- 1.05 mg/l. EC50 for algae range from 1.2-9 mg/l. NOEC algae range from 0.2-2.8 mg/l. For *Tetrahymena pyriformis* the EC50 was 2.2 mg/l, a NOEC Of > 10 mg/l for *Pseudomonas* was derived. For the terrestrial environment a NOEC of 200 mg/kg soil was derived for *Zea mays*. For the atmospheric compartment several studies on plants were available. Cabbage was found to be the most sensitive species. A NOEC could not be derived from a study on *Brassica*; the EC100 was 11.8 ug/m^3.

Exposure

In the EU dibutylphthalate is mainly used as a plasticiser in resins and polymers such as polyvinyl chloride. It is further used in printing inks, adhesives, sealants/grouting agents, nitrocellulose paint, film coating and glass fibres. The ubiquity of dibutylphthalate in consumer products is demonstrated by its wide usage in cosmetics: a perfume solvent and fixative, a suspension agent for solids in aerosols, a lubricant for aerosol valves, and antifoamer, a skin emollient and a plasticiser in nail polish and fingernail elongators. The total EU production volume for 1998 was estimated to be 26,000.

Identity and Physico-chemical properties

Dibutylphthalate is a oily liquid substance with a low vapour pressure (9.7 x 10^{-5} hPa, 25°C), low solubility in water (10 mg/l, 20°C) and log Kow of 4.57. Dibutylphthalate hydrolyses at pH 9 (50°C) with a half-life of 65.8 hours and is stable at pH4 and 7. The DT50 of dibutylphthalate in the atmosphere is estimated to be 1.8 days. Dibutylphathalate is considered as ready biodegradable. Henry's Law constants (0.27 Pa.m3/mol) indicate that DBP is distributed in air, water and soil. The bioaccumulation of the parent compound in fish is low. The experimental BCF value is 1.8, although 14C-based BCF is 2125 and is several orders of magnitude higher.

NATURE OF FURTHER WORK RECOMMENDED

There is a need for further information and further consideration of exposure and risk assessment for the environment and human health.

The substance has been agreed in the European Union Risk assessment program under Regulation EC. (No.) 793/93. The EU risk assessment concludes that for environment more information is needed on potential risks of dibutylphthalate on plants. For the occupational exposure, there is a need for limiting the risks for aerosol forming activities and adverse local effect due to repeated inhalation exposure cannot be excluded in all occupational exposure scenarios