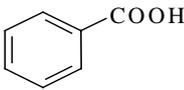
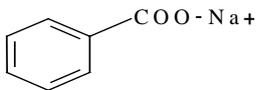
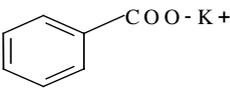
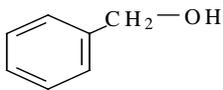


SIDS INITIAL ASSESSMENT PROFILE**Benzoates Category**

| | | | | |
|---------------------------|---|---|--|---|
| CAS No. | 65-85-0 | 532-32-1 | 582-25-2 | 100-51-6 |
| Chemical Name | Benzoic acid | Sodium benzoate | Potassium benzoate | Benzyl alcohol |
| Structural Formula |  |  |  |  |

RECOMMENDATIONS

The chemicals are currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

The benzyl alcohol, benzoic acid and its sodium and potassium salt can be considered as a single category regarding human health, as they are all rapidly metabolised and excreted via a common pathway within 24hrs. Systemic toxic effects of similar nature (e.g. liver kidney) were observed. However with the benzoic acid and its salts at higher doses than the benzyl alcohol. For environmental effects the category is less clear, however all are readily biodegradable, non-bioaccumulative and acute toxicity values are similar. For human health all exposure routes are possible, despite benzoic acid and its salts are solids and benzyl alcohol is a liquid. For workers it will mainly be by inhalation and by skin, whereas for consumers it will mainly be oral and dermal.

Human Health

The compounds exhibit low acute toxicity as for the oral and dermal route the LD50 values are > 2000 mg/kg bw except for benzyl alcohol that needs to be considered as harmful by oral route in view of an oral LD50 of 1610 mg/kg bw. The 4 hrs inhalation exposure of benzyl alcohol or benzoic acid at 4 and 12 mg/l as aerosol/dust respectively gave no mortality, showing low acute toxicity by inhalation for these compounds.

Benzoic acid and benzyl alcohol are slightly irritating to the skin, while sodium benzoate was not skin irritating. No data are available for potassium benzoate but it is also expected not to be skin irritating. Benzoic acid and benzyl alcohol are irritating to the eye and sodium benzoate was only slightly irritating to the eye. No data are available for potassium benzoate but it is expected also to be only slightly irritating to the eye.

The available studies for benzoic acid gave no indication for a sensitizing effect in animals, however occasionally very low positive reactions were recorded with humans (dermatological patients) in patch test. The same occurs for sodium benzoate. It has been suggested that the very low positive reactions are a non-immunologic contact urticaria. Benzyl alcohol gave positive and negative results in animals. Benzyl alcohol also demonstrated a maximum incidence of sensitization of only 1% in human patch

testing. Over several decades no sensitization with these compounds has been seen among workers. For benzoic acid repeated dose oral toxicity studies give a NOAEL of 800 mg/kg/day. For the salts values > 1000 mg/kg/day are obtained. At higher doses increased mortality, reduced weight gain, liver and kidney effects were observed.

For benzyl alcohol the long-term studies indicate a NOAEL \geq 400 mg/kg bw/d for rats and \geq 200 mg/kg bw/d for mice. At higher doses effects on bodyweights, lesions in the brains, thymus, skeletal muscle and kidney were observed. It should be taken into account that administration in these studies was by gavage route, at which saturation of metabolic pathways is likely to occur. It can be concluded that benzoic acid and its salts exhibit very low repeated dose toxicity. Benzyl alcohol exhibits low repeated dose toxicity.

All chemicals showed no mutagenic activity in *in vitro* Ames tests. Various results were obtained with other *in vitro* genotoxicity assays. Sodium benzoate and benzyl alcohol showed no genotoxicity *in vivo*. While some mixed and/or equivocal *in vitro* chromosomal/chromatid responses have been observed, no genotoxicity was observed in the *in vivo* cytogenetic, micronucleus, or other assays. The weight of the evidence of the *in vitro* and *in vivo* genotoxicity data indicates that these chemicals are not mutagenic or clastogenic. They also are not carcinogenic in long-term carcinogenicity studies.

In a 4-generation study with benzoic acid no effects on reproduction were seen (NOAEL > 750 mg/kg). No compound related effects on reproductive organs (gross and histopathology examination) could be found in the (sub) chronic studies in rats and mice with benzyl acetate, benzyl alcohol, benzaldehyde, sodium benzoate and supports a non-reprotoxic potential of these compounds. In addition, data from reprotoxicity studies on benzyl acetate (NOAEL >2000 mg/kg bw/d; rats and mice) and benzaldehyde (tested only up to 5 mg/kg bw; rats) support the non-reprotoxicity of benzyl alcohol and benzoic acid and its salts.

In rats for sodium benzoate dosed via food during the entire gestation developmental effects occurred only in the presence of marked maternal toxicity (reduced food intake and decreased body weight) (NOAEL = 1400 mg/kg bw). NOEL: 300 mg/kg bw (hamsters); 250 mg/kg bw (rabbits); 175 mg/kg bw (CD-1 mice). For hamster, rabbit and mice no higher doses (all by gavage) were tested and no maternal toxicity was observed. For benzyl alcohol: NOAEL= 550 mg/kg bw (gavage; CD-1 mice). LOAEL = 750 mg/kg bw (gavage mice). In this study maternal toxicity was observed e.g. increased mortality, reduced body weight and clinical toxicology. Benzyl acetate: NOEL = 500 mg/kg bw (gavage rats). No maternal toxicity was observed.

Environment

From the data (fish, daphnia, algae, bacteria) it is obvious that neutralization of the pH greatly reduces (up to one order of magnitude) the acute toxicity of benzoic acid. This is also supported by the lower toxicity observed with the sodium benzoate. Under environmental relevant conditions therefore the acute toxicity of benzoic acid, sodium benzoate and potassium benzoate for all four trophic levels is > 100 mg/l. Under environmental relevant conditions the acute toxicity of benzyl alcohol for fish, daphnia and bacteria is > 100mg/l. For algae, an EC 50 3hrs of 95 mg/l is reported. Under environmental relevant conditions, benzoic acid and its salts have very low acute toxicity, whereas benzyl alcohol has low to moderate acute toxicity.

Exposure

Worldwide production capacity of benzoic acid is estimated at 700 kt. The major outlet (75%) for benzoic acid is as a chemical intermediate in the production of phenol, which in turn is mainly used to produce caprolactam. The next largest outlet is as a feedstock for sodium benzoate (10%) and chemical synthesis of plasticizers (5%).

Worldwide production capacity of sodium benzoate is estimated at 100 kt. The major outlet for sodium benzoate is as preservative in food and beverages (60%). Second most important market is cooling liquids (10%). The main function of sodium benzoate in most applications is as preservative.

Worldwide production capacity of potassium benzoate is estimated at 7Kt. It is used as a preservative in nonalcoholic beverages.

Worldwide production capacity of benzyl alcohol is estimated at 50 kt. Major use for benzyl alcohol is as curing agent in epoxy coatings (30%), where it becomes chemically bounded after reaction. Other important uses include the use as a solvent in low concentrations in waterborne coatings (10%) and use in paint strippers (10%) and chemical intermediate for synthesis for benzyl esters that are used in the flavor and fragrance industry (10%). The use in paint strippers is limited to uses in industrial settings.

Benzyl alcohol, benzoic acid and its sodium and potassium salt are decades also used in pharmaceuticals, cosmetics and/or food. Consumer exposure in these specific applications are controlled by the fact that, for all these applications, specific regulatory frameworks (regional and/or national) with authorization/approval procedures and specific advisory bodies exist (*inter alia*: the US FDA, WHO JECFA, EU SCF, etc), including, on a regular basis, reevaluation of approvals, hazardous properties and factual exposures. According to information from products registers, uses that are not specifically regulated include uses of the substances in different kinds of products e.g. paints, varnishes solvents, cleaning and washing agents, photochemicals and antifreeze agents.

Benzoic acid is a white solid, with a solubility in water of 2.9 g/l and with a vapour pressure of 0.0011 hPa at 20 °C. The log octanol/water partition coefficient was measured to 1.88; the Henry coefficient = 0.0046-0.022 Pa*m³/mol; and the pKa = 4.2. Sodium benzoate and potassium benzoate are white solids, with solubility in water of 556 g/l and with a vapour pressure of <0.0011 hPa at 20 °C. The log octanol/water partition coefficient were measured to -2.269. Benzyl alcohol is a colorless liquid, with a solubility in water of 40 g/l and with a vapour pressure of 0.13 hPa at 20°C. The log octanol/water partition coefficient was measured to 1.1.

The distribution modeling according to Mackay Level III indicates soil and water to be the favored compartments for the chemicals. However, physical chemical properties and use patterns indicate water to be the main compartment for these substances. None are expected to hydrolyze. All are readily biodegradable. None has bioaccumulative potential.

NATURE OF FURTHER WORK RECOMMENDED

Regarding all the information provided, the substances have low priority for further work.