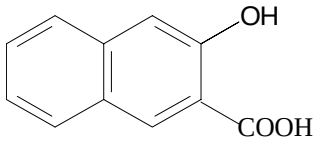
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	92-70-6
Chemical Name	3-Hydroxy-2-naphthoic acid
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The acute oral LD50 of 3-Hydroxy-2-naphthoic acid in rats was 823-1040 mg/kg bw. Clinical signs included reduced activity, accelerated breathing, closure of eyes, and diarrhoea. Gastro-intestinal irritation and dark or mottled livers were seen in the animals that had died during the studies.

A 10% solution of 3-Hydroxy-2-naphthoic acid (approx. 2000 mg/kg bw) was lethal to guinea pigs when applied dermally for 24 hours under occlusive conditions.

Moistened 3-Hydroxy-2-naphthoic acid was slightly irritating to the skin of rabbits in a test performed in accordance with OECD TG 404. Skin necroses and subcutaneous hemorrhages were observed in guinea pigs after occlusive exposures for 24 hours to the 10-12% solutions in mixtures of acetone and olive oil or corn oil. It caused serious damage to the eyes of rabbits (corneal vascularization/opacity) in tests performed in accordance with OECD TG 405. It may also have caused skin and upper respiratory tract irritation in workers.

3-Hydroxy-2-naphthoic acid has skin sensitisation potential.

After repeated administration to rats by the oral route for 28 days, there were indications of a possible effect on the adrenals in females at dose levels of 60 mg/kg bw/day and above. The only effects observed in males were a significantly reduced serum phosphate level and increased levels of bilirubin in serum and urine at a dose level of 300 mg/kg bw/day. The same findings, and, in addition, increased liver weights were reported for females at 300 mg/kg bw/day. NOEL (male): 60 mg/kg bw/day; NOEL (female): 12 mg/kg bw/day.

Poorly documented studies in rats involving repeated administration by the inhalation route gave indications of an effect on the kidneys (kidney necroses were reported after 10-days inhalation of 100 mg/m3).

3-Hydroxy-2-naphthoic acid was judged non- mutagenic in three Ames bacterial tests in Salmonella typhimurium and Escherichia coli strains, but it caused chromosomal damage in V79 hamster cells in vitro (only in the absence, but not in the presence of metabolic activation). No clastogenic activity, and no toxicity was observed in vivo in bone marrow cells of hamsters, dosed with the maximum recommended dose of 2000 mg/kg bw, suspended in starch mucilage. Due to severe limitations (only 50 metaphases were examined per animal and there was no indication that the target tissue was reached by the chemical), the available in vivo study is not sufficient to assess whether the in vitro mutagenic activity is reproduced in vivo.

3-Hydroxy-2-naphthoic acid was tested for its reproductive toxicity in a one-generation study according to OECD TG 415. The administration of the test substance had no adverse effect on the reproductive abilities of the parental

generation. At a dose level of 200 mg/kg bw/day, the body weight of the offspring was decreased. Growth retardation and malformations (brachyury, kinked tail) were observed in the offspring of few litters at a maternally toxic dose (200 mg/kg bw/day). No Effect Level (NOEL) for reproductive toxicity: 200 mg/kg bw/day (highest tested dose); NOEL for toxicity to the offspring: 50mg/kg bw/day. The NOEL for systemic toxicity in males was 12.5 mg/kg bw/day (forestomach lesions at 50 mg/kg bw/day). The NOEL for systemic toxicity in females was 50 mg/kg bw/day (reduced body weight gain, forestomach lesions at 200 mg/kg bw/day).

Environment

3-Hydroxy-2-naphthoic acid has a calculated water solubility of 474 mg/l, a calculated vapor pressure of < 1.4 Pa and calculated log Kow values in the range of 3.4 – 3.59. The calculated data available are estimated for the undissociated acid. As 3-Hydroxy-2-naphthoic acid has a pKa-value of 2.8, under environmental relevant pH conditions the substance is completely dissociated. That means that the physico-chemical properties that are derived for the undissociated acid are not valid for the ionized substance.

The environmental distribution of the substance cannot be estimated with a fugacity model as the available physico-chemical properties were determined for the undissociated acid and not for the dissociated form that is present under environmental relevant pH conditions. However, as both volatilisation and adsorption are not expected for the dissociated substance, it can be assumed that the hydrosphere is the main target compartment for 3-hydroxy-2-naphthoic acid. This is confirmed by a Mackay I model run for the sodium salt.
3-Hydroxy-2-naphthoic acid is not readily biodegradable as was shown in a test according to OECD 301 C (1.3 % after 14 days). In a Zahn-Wellens test (OECD 302 B) with adapted inoculum the chemical was inherently biodegradable (85 % after 21 days). In a 42d bioaccumulation study with Cyprinus carpio BCF values of < 0.5 resp. < 4 were found for 3-hydroxy-2-naphthoic acid concentrations of 1 mg/l and 0.1 mg/l. Therefore, 3-hydroxy-2-naphthoic acid has no potential for bioaccumulation.

For 3-hydroxy-2-naphthoic acid there are short-term tests with fish, daphnids and algae available. In addition, a long-term test with *Daphnia magna* was performed. The following effect values were found:

Brachydanio rerio: 96h-LC_{50} = 68mg/l, *Daphnia magna*: 48h-EC_{50} = 32.9 mg/l, *Pseudokirchneriella subcapitata*: 72h-E_rC_{50} = 65.3 mg/l, 72h-EbC50=26.1 mg/l; 72h-NOEC = 6.8 mg/l; *Daphnia magna*: 21d-NOEC = 10.4 mg/l.

With an assessment factor of 50 a PNECaqua of 136 µg/l was derived from the lowest available NOEC of 6.8 mg/l found for green algae.

Exposure

In the EU the production and import volume is in the range of 10,000 to 50,000 t/a. The worldwide production capacity for 3-hydroxy-2-naphthoic acid is reported to 30,000 t/a . 3-Hydroxy-2-naphthoic acid is mainly used as intermediate for the production of dyes and pigments. Further uses are as intermediate for insecticides and pharmaceuticals.

Occupational exposure may occur during production and processing of 3-hydroxy-2-naphthoic acid, mainly via the dermal route. Workplace measurements are available from one European production plant, ranging up to 1.23 mg/m^3 (mean value: 0.35 mg/m^3). No exposure information is available with regard to processing sites.

3-Hydroxy-2-naphthoic acid is a chemical intermediate for the production of dyes and pigments, which may also be used for pharmaceutical applications. A product containing 100% 3-Hydroxy-2-naphthoic acid is listed in the Swiss Product Register (2002) for industrial use (product category: developer/paints/dyes/laquers). No information on consumer products containing 3-Hydroxy-2-naphthoic acid was located in the Danish, Swedish and Swiss Product Registers (2002) and for Germany.

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

Human Health: The chemical is a candidate for further work, because 3-Hydroxy-2-naphthoic acid was a potent in vitro clastogen in an assay without metabolic activation. Due to severe limitations of the available in vivo chromosomal aberration study (only 50 metaphases were examined per animal and there was no indication that the target tissue was reached by the chemical), it is not possible to finally assess whether the in vitro mutagenic activity is reproduced in vivo. A standard in vivo test (mouse bone marrow chromosome aberration test (OECD TG 475) or an erythrocyte micronucleus test (OECD TG 474)) should therefore be performed as post-SIDS work. It is noted that the chemical is a skin irritant, can cause serious damage to the eye, is a skin sensitiser and there are indications of a teratogenic potential.

Environment: The chemical possesses properties indicating a hazard for the environment. Based on data presented by the Sponsor Country (that reports that the only known use of the chemical in two OECD countries is as an intermediate, and relating to an unknown fraction of the global production volume), exposure to the environment is anticipated to be low, and therefore, this chemical is of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.