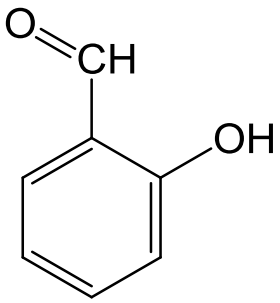
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	90-02-8
Chemical Name	2-Hydroxybenzaldehyde
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-chemical properties

2-Hydroxybenzaldehyde is a colourless oily liquid at standard temperature and pressure with almond like odour. Melting point and boiling point are -7 °C and 197 °C respectively. Vapour pressure is 75 Pa at 25 °C and partition coefficient between octanol and water (log K_{ow}) is 1.66 at pH 6.2 – 6.3. Water solubility is 4.9 g/L at 25 °C. As a dissociation constant (pK_a) in water is 8.28, 2-hydroxybenzaldehyde is partially dissociated in environmental water. However, the un-dissociated form is dominant between pH 6 and pH 8.

Human Health

After administration of a single oral dose of 400 mg/kg bw of 2-hydroxybenzaldehyde to a fasted rabbit, 75% of the dose was excreted as ether-soluble acids in urine within 24 hrs, indicating that this substance was well absorbed via the gastrointestinal tract. Urine analysis revealed that 27% and 3% of the dose was excreted as glucuronic acid and sulphate conjugates, respectively.

In an acute oral study conducted according to OECD TG 423, the approximate lethal dose in female rats was estimated to be 500 mg/kg bw. No deaths occurred at 300 mg/kg bw, and all (3/3) died at 2000 mg/kg bw. The substance caused decreased locomotor activity, deep respiration, diarrhea and a soiled perineal region in dead animals. No abnormality was found at necropsy. Reliable acute toxicity studies with dermal or inhalation exposure were not available.

In a skin irritation test conducted in accordance with OECD TG 404, undiluted 2-hydroxybenzaldehyde caused a very slight to well defined erythema and very slight to severe oedema after a 4-hour semi-occlusive application to the skin of rabbits. These changes remained for 7 days after application, and desquamation from the skin was found in some animals. Primary Irritation Index was calculated to be 2.54. Reliable studies on skin irritation in human are not available. No information was identified regarding the eye and respiratory tract irritancy of 2-hydroxybenzaldehyde.

With regard to skin sensitization, reliable data on animal studies are not available. In humans, some skin sensitization studies and case reports demonstrated positive reactions to 2-hydroxybenzaldehyde in patch tests conducted in patients with contact dermatitis. Therefore, 2-hydroxybenzaldehyde is considered to have a sensitizing potential in humans.

One study investigated repeated dose toxicity of 2-hydroxybenzaldehyde. This study was conducted according to the procedures of OECD TG 422, except for the limited haematological and clinical chemistry examination in

only male. The substance was administered via gavage to 12 rats/sex/dose at 0, 2.5, 10, 40 or 160 mg/kg bw/day for 49 days (starting from14 days before mating) in males and 41-46 days (starting from 14 days before mating to day 3 of lactation) in females. No treatment-related changes were found in the clinical signs, body weight, food consumption, and haematological and blood biochemical parameters. Increased absolute and relative liver weights and decreased absolute and relative ovary weights were observed in the female 160 mg/kg bw/day group. A decrease in the degree and incidence of cytoplasmic lipid droplets in the liver was observed in the males of the groups treated with 40 and 160 mg/kg bw/day and a slight increase in glycogen deposits in the liver was observed in females treated with 40 and 160 mg/kg bw/day. Based on effects on liver histopathology, the NOAEL for repeated dose oral toxicity was considered to be 10 mg/kg bw/day.

In an Ames test with multiple strains of *Salmonella typhimurium* and *Escherichia coli* [OECD TG 471 and 472], 2-hydroxybenzaldehyde was negative both with and without metabolic activation. An *in vitro* chromosome aberration test using cultured Chinese hamster lung (CHL/IU) cells [OECD TG 473] was positive with and without metabolic activation. However, an *in vivo* bone marrow micronucleus assay [OECD TG 474], in which 2-hydroxybenzaldehyde was administered orally to male rats at up to 400 mg/kg bw/day and to female rats at up to 200 mg/kg bw/day for 2 days, was negative. In this study, body weight was lowered at 400 mg/kg bw/day in males, but no dose-related change was found in the incidence of polychromatic erythrocytes. Doses were selected based on the results of the dose-finding study, in which deaths occurred at 800 mg/kg bw/day in males and 400 mg/kg bw/day and above in females. Based on these results, 2-hydroxybenzaldehyde is considered non genotoxic *in vivo*.

No data are available for the carcinogenicity of 2-hydroxybenzaldehyde.

In a combined repeated dose toxicity study with the reproductive/developmental toxicity screening test in rats [the modified OECD TG 422, repeated-dose portion described above], 2-hydroxybenzaldehyde was administered orally via gavage to 12 animals/sex/dose at 0, 2.5, 10, 40 or 160 mg/kg bw/day for 49 days (starting from 14 days before mating) in males and 41-46 days (starting from 14 days before mating to day 3 of lactation through mating and pregnancy period) in females. No adverse effects on reproductive parameters (i.e. estrous cycle, copulation index, precoital interval, fertility and gestation index, gestation length, and the number of corpora lutea and implantations) were observed up to the highest dose tested; however, two dams at 160 mg/kg bw/day had undeveloped nipples and all pups of the two dams died. At the end of the administration period, there was a decrease in absolute and relative weight of the right ovary at 160 mg/kg bw/day. Based on the effect on nipple development and the ovary weight, the NOAEL for reproductive toxicity was considered to be 160 mg/kg bw/day for males and 40 mg/kg bw/day for females. As for the developmental effects, trends of decreases (not significant) in newborn viability index on postnatal day 4 were observed at 160 mg/kg bw/day. This change was attributed to deaths of all pups from the two dams with undeveloped nipple. Two litters from two of the twelve dams died between postnatal day 0 and day4. No dose-related changes were observed in any group for the number of stillborn and live born, delivery index, live birth index, sex ratio and external and necropsy findings of pups on postnatal day 4. Therefore, a plausible explanation for the pup death from the two dams is mainly due to a failure of lactation caused by physically undeveloped nipple. The NOAEL on developmental effects was considered to be 160 mg/kg bw/day in this study.

2-Hydroxybenzaldehyde may present a hazard to human health (skin irritation, skin sensitization, repeated dose toxicity and reproductive toxicity). Adequate screening level data are available to characterize the human health hazard for the purposes of the OECD HPV Chemicals Programme.

Environment

In the atmosphere, 2-hydroxybenzaldehyde is expected to be degraded by hydroxyl radicals. A calculated half-life time of 0.38 days is obtained by AOPWIN (version 1.92) for the indirect photo-oxidation by reaction with hydroxyl radicals in air.

2-Hydroxybenzaldehyde is not hydrolysed due to the lack of hydrolysable functional groups. A hydrolysis test according to OECD test guideline 111 showed that 2-hydroxybenzaldehyde was stable in water at pH 4, pH 7 and pH 9 at 50 °C for five days.

An OECD test guideline 301C test was conducted with 2-hydroxybenzaldehyde with activated sludge for four weeks. The concentration of the test substance was 100 mg/L and the concentration of the activated sludge was 30 mg/L as suspended solid matters. The test result showed 2 % degradation by BOD. However,

2-hydroxybenzaldehyde was not detected in the test system and whole amount of the chemical was converted to 2-hydroxybenzoic acid (salicylic acid) after the cultivation period.

After the main test, an additional biodegradation test with 2-hydroxybenzaldehyde was conducted under the condition of OECD test guideline 302C without measurement of BOD. The concentration of 2-hydroxybenzaldehyde was 30 mg/L and the concentration of activated sludge was 100 mg/L as suspended solid matters. After four weeks cultivation period, neither 2-hydroxybenzaldehyde nor 2-hydroxybenzoic acid was detected in the test system, which means 2-hydroxybenzaldehye was biodegraded. Based on the results of algae test and other available eco-toxicity tests, it is likely that 2-hydroxybenzaldehyde may be toxic to microbial inoculums used in the test-guideline 301 C at relatively high concentration of 100 mg/L.

An independent biodegradation study with 2-hydroxybenzoic acid with an equivalent protocol with OECD test-guideline 301C showed 88.1 % degradation by BOD after two weeks.

BIOWIN estimation (version 4.10) predicts that 2-hydroxybenzaldehye is classified as ready biodegradable. Based on the weight of evidence consideration, 2-hydroxybenzaldehyde is considered to be biodegradable.

No information was available on the bio-concentration of 2-hydroxybenzaldehyde. Using an octanol-water partition coefficient (log K_{ow}) of 1.66, a bio-concentration factor of 5.8 was calculated with BCFBAF (version 3.00). This chemical is not expected to bioaccumulate.

Fugacity level III calculations show that 2-hydroxybenzaldehyde is mainly distributed to the soil compartment (69.2 %) and the water compartment (29.8 %) if equally and continuously released to the air, soil and water. These results have to be treated with caution because partial dissociation of the substance is possible under particular environmental conditions (pKa = 8.28). A Henry's law constant of 0.178 Pa.m3/mole at 25 °C suggests that volatilization of 2-hydroxybenzaldehyde from water is slow. A soil adsorption coefficient of log K_{oc} = 1.8 indicates 2-hydroxybenzaldehyde has low adsorption to soil and sediment.

The following acute toxicity test results have been determined for aquatic species;

Fish [*Oryzias latipes* OECD-TG 203]:	96 h LC50 = 1.6 mg/L (measured)
[*Pimephales promelas*]	96 h LC50 = 2.3 mg/L (measured)
Daphnid [*Daphnia magna* OECD-TG 202]:	48 h EC50 = 2.6 mg/L (measured)
Algae[*Pseudokirchneriella subcapitata* OECD-TG 201]:	72 h ErC50 = 4.8 mg/L (measured, growth rate)
	72 h EbC50 = 1.6 mg/L (measured, biomass)

The following chronic toxicity test results have been determined for aquatic species:

Daphnid [*Daphnia magna* OECD-TG 211]:	21 d LOEC = 0.23 mg/L (measured)
	21 d NOEC = 0.13 mg/L (measured)
Algae[*Pseudokirchneriella subcapitata OECD-TG 201*]:	72 h NOErC = 0.55 mg/L (measured; growth rate)
	72 h NOEbC = 0.55 mg/L (measured; biomass)

2-Hydroxybenzaldehyde possesses properties indicating a hazard for the environment (acute aquatic toxicity values between 1 and 10 mg/L for fish, invertebrate and algae, and chronic toxicity values less than 1mg/L for invertebrate and algae). This chemical is considered biodegradable and is not expected to bioaccumulate. Adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD HPV Chemicals Programme.

Exposure

Production volume and/or import volume of hydroxybenzaldehyde in Japan (sponsor country) was between 100 and 1,000 tonnes in fiscal year 2007. This figure includes amounts of 2-hydroxybenzaldehyde, 3-hydroxybenzaldehyde and 4-hydroxybenzaldehyde. Production and/or import volume of 2-hydroxybenzaldehyde in the United States was less than 500,000 pounds (227 tonnes) during 2006 according to Inventory Updated Reporting. Production volume in the world was not available.

According to the Japanese pollution release transfer register system, 19 kg of 2-hydroxybenzaldehyde were released in the air compartment and 2 kg of 2-hydroxybenzaldehyde were released to the public water body in the

fiscal year of 2008. Release to the soil compartment was not reported. Based on this reporting results, environmental release of 2-hydroxybenzaldehyde from manufacturing and processing sites is thought to be not significant.

2-Hydroxybenzaldehyde is produced from phenol, chloroform and alkali according to Reimer-Tieman reaction. 2-Hydroxybenzaldehyde is used in perfume, coumarin synthesis and as an intermediate for pharmaceutical products and pesticides. This chemical is also used as an auxiliary fumigant, flavour ingredient in foods, medical chemicals, reagent in analytical chemistry, and gasoline additive.

Occupational exposure to 2-hydroxybenzaldhyde through inhalation of vapor and via the dermal route is anticipated from its physical properties. No OEL's for 2-hydroxybenzaldehyde are established.

As 2-hydroxybenzaldehyde is used as an ingredient of perfume, a flavour ingredient in foods and gasoline additive, consumer exposure is anticipated. Daily intakes of 2-hydroxybenzaldehyde as a food flavouring agent were estimated to be 1.6 μg/kg bw/day in Europe and 0.3 μg/kg bw/day in the United States. The Joint FAO/WHO Expert Committee on Food Additives evaluated that no safety concern of 2-hydroxybenzaldehyde as a food flavouring agent would be expected at current estimated levels of intakes. No other information on the consumer exposure is obtained.