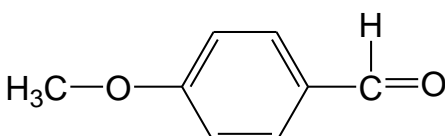


SIDS INITIAL ASSESSMENT PROFILE

CAS No.	123-11-5
Chemical Name	<i>p</i> -Methoxybenzaldehyde
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR**Physical-chemical properties**

p-Methoxybenzaldehyde is a colourless to pale yellow liquid with sweet odour of hawthorn. Melting point and boiling point are 0 °C and 248 °C respectively. Water solubility and vapour pressure are 4.4 g/L at 25 °C(measured) and 4 Pa at 25 °C respectively. Partition coefficient between octanol and water (Log K_{ow}) is 1.76 (measured). Estimated Log K_{oc} is 1.37.

Human Health

As for the metabolism, available experimental data suggest that *p*-methoxybenzaldehyde is demethylated to a small extent and the aldehyde group is oxidized to the acid. The resulting metabolite anisic acid would be conjugated with glucuronic acid and/or glycine, and excreted in the urine. Although there is no other experimental data on the toxicokinetics of *p*-methoxybenzaldehyde, the physicochemical properties and the reproduction/developmental toxicity screening test via oral gavage suggest that this substance could be absorbed via the gastrointestinal tract.

In an acute toxicity study (OECD TG 401) of *p*-methoxybenzaldehyde in rats, the oral LD₅₀ value was considered to be more than 2,000 mg/kg bw in both sexes. At the lethal doses, there were dyspnea, apathy, abnormal position, staggering gait, atonia, arthrogryposis, tremor, skin redness, ruffled fur and poor general state. Based on a inhalation test, the inhalation LC₅₀ value was considered to be more than 0.32 mg/L (vapour) in rats for both sexes. During exposure, snout wiping and attempts to escape were observed. No reliable acute dermal studies are available for *p*-methoxybenzaldehyde.

A human patch test (190 subjects as total) of *p*-methoxybenzaldehyde was negative. A dermal irritation study in 3 rabbits (similar to Federal Register 38 No. 187, § 1500.41) showed that the substance was slightly irritating after application for 4 hours under occlusive conditions, but the effects were fully reversible within 8 days for 2 of 3 animals. *p*-Methoxybenzaldehyde was slightly irritating in the eye irritation assay in 3 rabbits (similar to Federal Register 38 No.187, §1500.41), but the effects were fully reversible within 72 h. *p*-Methoxybenzaldehyde is considered to be non irritating to the skin and eye.

In a maximisation test on 25 male volunteers, 10 % *p*-methoxybenzaldehyde was not sensitizing. The result of animal experiments performed according to the OECD TG 429 and EPA OPPTS 870.2600 was also negative. *p*-Methoxybenzaldehyde is considered to be non sensitizer to the skin.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422), rats were given *p*-methoxybenzaldehyde by gavage at 0, 20, 100 or 500 mg/kg bw/day. Males were dosed for 42 days from 14 days before mating and females were dosed from 14 days before mating to day 4 of lactation throughout the mating and pregnancy period. No animals died in any group. Temporary salivation after administration was observed in males and females in the 500 mg/kg bw group. Body weight tended to be increased in males in the 500 mg/kg bw group and females in the 100 and 500 mg/kg bw groups. Decrease in platelets was observed in males in 500 mg/kg bw group and in females in the 100 and 500 mg/kg bw groups. Hyperplasia of squamous epithelium was detected in males and females given 100 or 500 mg/kg bw. In the 500 mg/kg bw group, the liver weight was increased in males and females. Histologically, centrilobular hypertrophy or hepatocytes was detected in these animals. On biochemical analysis, the A/G ratio, GOT activity and inorganic phosphorus concentration were found to be increased in males in the 500 mg/kg bw group. Therefore,

the NOAEL for repeated dose oral toxicity was considered to be 20 mg/kg bw/day in both sexes

p-Methoxybenzaldehyde did not induce gene mutations in bacterial *in vitro* tests (OECD TG 471) or chromosomal aberrations in non-bacterial *in vitro* tests (OECD TG 473). The test substance showed positive results in *in vitro* studies using the mouse lymphoma and the induction of SCE in the *in vitro* study using human lymphocytes at non-cytotoxic doses. Equivocal results exist concerning genotoxicity based on *in vitro* reports and QSAR predictions, suggesting some concerns for genotoxicity of *p*-methoxybenzaldehyde. No valid *in vivo* genotoxicity study of *p*-methoxybenzaldehyde is available for clarification of the positive results reported *in vitro*. However, an *in vivo* micronucleus test on the closely related structural analogue, i.e. 4-ethoxybenzaldehyde, was negative up to the maximum tolerated dose in mice. Based on the available data, *p*-methoxybenzaldehyde was not considered to raise a health concern about *in vivo* genotoxicity.

There is no reliable information on carcinogenicity either for *p*-methoxybenzaldehyde or for 4-ethoxybenzaldehyde.

In the combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422), the rats were given *p*-methoxybenzaldehyde by gavage at 0, 20, 100, or 500 mg/kg bw/day for 42 days beginning 14 days before mating in males, and from 14 days before mating to day 4 of lactation throughout the mating and pregnancy period in females. In the 500 mg/kg bw group, the number of non-pregnant females was increased although all pairs copulated. The fertility index was also reduced, and the number of pups, the delivery index and the number of live pups on lactation day 0 and 4 were lower than in the controls at 500 mg/kgbw/day. Therefore, the NOAEL for reproductive and developmental toxicity in rats was considered to be 100 mg/kg bw/day.

***p*-Methoxybenzaldehyde possesses properties indicating a hazard for human health (repeated dose, reproductive and/or developmental toxicity). Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD HPV Chemicals Programme.**

Environment

p-Methoxybenzaldehyde is stable in water: a hydrolysis test according to OECD Guideline 111 showed no hydrolysis at pH 4, 7 and 9 at 50 °C for five days. Using AOPWin (version 1.91), a calculated half-life time of 5.2 hours is obtained for the indirect photo-oxidation of *p*-methoxybenzaldehyde by reaction with hydroxyl radicals in air.

A test result with activated sludge shows 99 % degradation by BOD after two weeks cultivation period according to OECD Guideline 301C. A test result according to OECD Guideline 301E with activated sludge shows 97 % of biodegradability after 7 days. These results show that *p*-Methoxybenzaldehyde is readily biodegradable. A bio-concentration factor (BCF) of 4.5 was obtained by BCFWin using a log K_{ow} of 1.76, showing a limited potential for bioaccumulation of *p*-methoxybenzaldehyde.

Fugacity level III calculations with EPISuite show that *p*-methoxybenzaldehyde is mainly distributed to the water compartment (34.3 %) and the soil compartment (64.5 %) with negligible amounts in air and sediment compartments if equally and continuously released to the air, soil and water. A Henry's law constant of 7.94×10^{-7} atm.m³/mole at 25 °C suggests that volatilization of *p*-methoxybenzaldehyde from the water phase is expected to be low.

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

Fish [<i>Oryzias latipes</i>]:	96 h LC ₅₀ = 40 mg/L (measured)
Invertebrate [<i>Daphnia magna</i>]:	48 h EC ₅₀ = 45 mg/L (measured)
Algae [<i>Pseudokirchneriella subcapitata</i>]:	72 h ErC ₅₀ = 61 mg/L (measured; growth rate)
	72 h EbC ₅₀ = 59 mg/L (measured; biomass)

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

Invertebrate [<i>Daphnia magna</i>]:	21 d NOEC = 0.71 mg/L (measured)
Algae [<i>Pseudokirchneriella subcapitata</i>]:	72 h NOEC = 0.65 mg/L (measured; growth rate)
	72 h NOEC = 0.65 mg/L (measured; biomass)

***p*-Methoxybenzaldehyde possesses properties presenting a hazard for the environment (acute aquatic toxicity values between 10 and 100 mg/L for fish, invertebrate and algae, and chronic toxicity lower than 1 mg/L for invertebrate and algae) however the substance is readily biodegradable and has low bioaccumulation potential. Adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD HPV Chemicals Programme.**

Exposure

Production and import volume of *p*-methoxybenzaldehyde in the sponsor country was 100 ton – 1000 ton in 2007. Production and import volume in USA was 1 – 10 million pounds (454 ton – 4540 ton) in 2006 according to IUR information. In Germany, production volume of 500 – 3000 ton/year was reported. According to SPIN database, total volume of the use of *p*-methoxybenzaldehyde in the Nordic countries was less than 1 ton in 2007. Worldwide production volume of *p*-methoxybenzaldehyde was not available. *p*-Methoxybenzaldehyde is produced by methylation of the raw material *p*-cresol followed by further oxidation. Another method of the production is from oxidation of anethole with either chromic acid or sulphuric acid.

p-Methoxybenzaldehyde is used as a fragrance compound for soaps, shampoos and toiletry products, an intermediate of pharmaceutical products and a surface treatment agent for metalizing plating process in the sponsor country. *p*-Methoxybenzaldehyde is also used as a flavoring in food and beverages as this chemical is designated as a food additive in the sponsor country. According to SPIN database, the main use patterns in the Nordic countries in 2007 are odour agents, cleaning/washing agents and industry perfumes.

p-Methoxybenzaldehyde may be released to the waste water during the manufacturing and packing process. However, waste water is treated in the waste water treatment plant with activated sludge before it is released to the environment in the sponsor country. As *p*-methoxybenzaldehyde is readily biodegradable, production and packaging are unlikely to lead to environment exposure. However, as *p*-methoxybenzaldehyde has a number of dispersive uses such as components in soaps, shampoos and toiletry products, emissions to the environment from some downstream uses are possible.

p-Methoxybenzaldehyde is a naturally occurring substance as it is a metabolic product of fungal organisms. Therefore, human and non-human organisms will be naturally exposed with non-quantifiable amount of this substance.

Occupational exposure to this chemical through inhalation of mist or vapor is possible. Dermal exposure is also possible, but effect of dermal exposure may be small.

p-Methoxybenzaldehyde may be contained in food and beverage as this chemical is allowed to use as a food additives in the sponsor country. Therefore, consumer exposure through consumer products and foods/beverages is expected. No other information on the consumer exposure in the sponsor country is available.