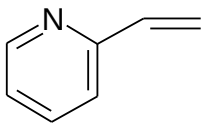
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	100-69-6
Chemical Name	2-Vinylpyridine
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-chemical properties

2-Vinylpyridine is colourless liquid with unpleasant, nauseating odour at standard temperature. Measured melting point and boiling point are below - 100 °C and 161.7 °C respectively. Vapour pressure at 25 °C extrapolated from the experimental value is 4.56 x 10^{-1} kPa. Measured partition coefficient between octanol and water (log K_{ow}) is 1.54 and measured water solubility is 26.7 g/L at 20 °C. Measured dissociation constant of pKa = 5.06 shows that 2-vinylpyridine exists primarily as its neutral species in the environment at pH values between 6 and 9.

Human Health

No specific studies were found on the absorption, distribution, metabolism, or excretion of 2-vinylpyridine in mammals. However, deaths occurred in acute oral and dermal toxicity tests. Therefore, 2-vinylpyridine is considered to be absorbed readily from the gastrointestinal tract and through the skin.

Dermal LD_{50} of 2-vinylpyridine was 640 mg/kg bw in rabbits and 0.16 mL/kg (160 mg/kg bw) in guinea pigs. Oral LD_{50} in rats ranged between >50 and <300 mg/kg bw (OECD TG423), and clinical signs of toxicity included excessive salivation, soft feces, reddening of legs and auricles, soiling of perioral and perianal regions, tachypnea, prostration, weakness, tremors, vasodilatation, and anorexia. According to secondary information, inhalation exposure of 2-vinylpyridine in humans caused systemic signs including headache, nausea, nervousness, and anorexia.

In rabbits, undiluted 2-vinylpyridine caused severe eye irritation and skin corrosion. In guinea pigs, it caused severe skin irritation. According to secondary information, 2-vinylpyridine caused skin, eye and respiratory tract irritation in humans.

In a mouse local lymph node assay similar to OECD TG 429, 2-vinylpyridine was sensitizing. In a study providing only limited information, moderate sensitization was found in guinea pigs. Two case reports indicated that 2-vinylpyridine may induce skin sensitization in humans.

The repeated dose oral toxicity of 2-vinylpyridine has been investigated in four reliable studies in rats and is particularly well demonstrated in 28- and 92-day studies. Due to the corrosive nature of the substance, the NOAEL and/or LOAEL of each repeated dose study were separately assessed for local and systemic effects.

A 28-day study was conducted in accordance with Japanese guidelines for repeated dose toxicity tests in mammalian species under GLP compliance. The substance was administered by gavage to 5 or 10 animals/sex/dose at 0 (vehicle, corn oil), 12.5, 50, and 200 mg/kg bw/day 7 days/week for 4 weeks with a 14-day recovery period in rats. Five animals/sex from the 0 and 200 mg/kg dose groups were categorized as recovery groups. No deaths were observed in either sex. Salivation in both sexes and decreases in body weight and food consumption in males were observed at 200 mg/kg bw/day. Relative testis weights increased in males receiving 200 mg/kg bw/day. Absolute and relative spleen weights decreased and relative liver weights increased in females receiving 200 mg/kg bw/day. Squamous hyperplasia and submucosal edema in the forestomach were observed in both sexes receiving 50 and 200 mg/kg bw/day, along with thickening of the mucosa at the higher

dose. Submucosal edema and/or erosion in the glandular stomach were also observed in females receiving 50 or 200 mg/kg bw/day. On the basis of the toxicological effects on the stomach, the NOAEL of local and systemic effects for this 28-day repeated dose oral toxicity study was estimated to be 12.5 mg/kg bw/day for both sexes in rats.

A 92-day study was conducted in accordance with the EPA OPPS 870.31000 (90-day oral toxicity in rodents) guideline under GLP compliance. 2-Vinylpyridine in corn oil suspension was administered to rats (30 animals/sex/group) by gavage at doses of 0, 20, 60, or 180 mg/kg bw/day (5 days/week for 92 days). Convulsions and sialorrhea were observed in the 180 mg/kg bw/day dose group. Clinical chemistry showed dose-dependent decreases in mean AST values (60 and 180 mg/kg bw/day) that were accompanied by an increase in relative liver weights. Relative kidney weights increased in males at ≥20 mg/kg bw/day and in females at 180 mg/kg bw/day. Hyperkeratosis and acanthosis of the gastric epithelium increased in a dose-dependent manner from 20 mg/kg bw/day. On the basis of increased relative kidney weights in males and histopathological changes in the gastric epithelium at 20 mg/kg bw/day, the LOAELs of both local and systemic effects for this 92-day study were estimated to be 20 mg/kg bw/day.

On the basis of these results from all available studies, the overall NOAEL for local and systemic effects for repeated oral dose toxicity was estimated to be 12.5 mg/kg bw/day.

In a bacterial reverse mutation assay (Ames test) with multiple strains of *Salmonella typhimurium* and *Escherichia coli* (OECD TG 471 and 472 and Japanese guidelines for screening mutagenicity testing of chemicals), 2-vinylpyridine showed clear mutagenic responses in *Escherichia coli* with exogenous metabolic activation, although no mutagenicity to *Salmonella typhimurium* was observed with or without exogenous metabolic activation. In three other studies with *Salmonella typhimurium* strains, mutagenicity was only observed in the presence of exogenous reductive metabolic activation. In addition, an *in vitro* chromosomal aberration test (OECD TG 473) showed positive results both with and without metabolic activation. No *in vivo* data were identified. On the basis of these results, 2-vinylpyridine is considered to be genotoxic *in vitro*.

No adequate carcinogenicity studies were identified.

In a reproduction/developmental toxicity screening test, rats (12 animals/sex/dose) were orally administered 2-vinylpyridine by gavage at a dose of 0, 20, 50, or 125 mg/kg bw/day (OECD TG 421; GLP). The compound was administered to males for 42 days from day 14 before mating to the day before sacrifice and to females from day 14 before mating and throughout mating and pregnancy to day 3 of lactation (maximum 47 days in total). Parental general toxicities (hyperplasia and hyperkeratosis of the squamous epithelium in the forestomach) were observed at 20 mg/kg bw/day and more. In the 125 mg/kg bw/day group, nine females died or were euthanized between days 22 of gestation and day 1 of lactation due to prolonged parturition. The remaining three females at the high dose were euthanized between day 1 and day 4 of lactation, following total litter loss. Significant decreased bodyweight gain was observed during gestation and on day 0 of lactation and persistent diestrus was observed in 2 females, and an irregular estradiol cycle was observed in 1 female in the 125 mg/kg bw/day dose group. Abnormal lactation and cannibalism was observed at 125 mg/kg bw/day. Although changes in spermatogenesis in male were observed at 125 mg/kg bw/day, fertility index was not significantly affected. In the 50 mg/kg bw/day, one female was euthanized due to dystocia and one female was euthanized following total litter loss on day 0 of lactation. In the dam with dystocia all pups were still-born. The pup deaths observed between day 0 and day 4 of lactation in the 2 top doses suggest a developmental effect. Body weights in pups were lower than the control animals at days 1 and 4 of lactation at 20 and 50 mg/kg bw/day, respectively. No morphological abnormalities associated with 2-vinylpyridine administration were found in any pup. On the basis of the dystocia at 50 mg/kg bw/day, the NOAEL for reproductive toxicity was estimated to be 20 mg/kg bw/day. On the basis of decreased body weights in pups in all treatment groups, the LOAEL for developmental toxicity was estimated to be 20 mg/kg bw/day in rats, the lowest dose tested.

2-Vinylpyridine possesses properties indicating a hazard for human health (acute oral and dermal toxicity, skin/eye/respiratory tract irritation, skin sensitization, repeated dose toxicity, *in vitro* genotoxicity, and reproductive/developmental toxicity). Adequate screening level data are available to characterize human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

In the atmosphere, 2-vinylpyridine is expected to be degraded by hydroxyl radicals. A calculated half-life time of 0.40 days is obtained by AOPWIN (version 1.92a) for the indirect photo-oxidation by reaction with hydroxyl radicals in air.

2-Vinylpyridine is not hydrolysed due to the lack of hydrolysable functional groups. A hydrolysis test according to OECD test guideline 111 showed no hydrolysis of 2-vinylpyridine in water at pH 4, 7 and 9 in 50 °C after five days.

An OECD test guideline 301C study was conducted with 2-vinylpyridine 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 0 % degradation by BOD. According to the result, 2-vinylpyridine is considered to be not-readily biodegradable.

No experimental information was available on the bio-concentration on 2-vinylpyridine. Using an octanol-water partition coefficient (log Kow) of 1.54, a bio-concentration factor of 4.82 was calculated with BCFBAF (version 3.01). This chemical is not expected to bioaccumulate.

Fugacity level III calculations show that 2-vinylpyridine is mainly distributed to the soil compartment (73.7 %) and water compartment (25.6 %) if equally and continuously released to the air, soil and water. A Henry's law constant of 1.80 $Pa.m^3$/mole at 25 °C suggests that 2-vinylpyridine is moderately volatile from water. A soil adsorption coefficient of Log K_{oc} = 2.34 indicates 2-vinylpyridine has low adsorption to soil and sediment.

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

Fish [*Oryzias latipes*]: 96 h LC_{50} = 6.5 mg/L (nominal; all measured concentrations were within 20% of the nominal, semistatic), OECD TG 203

Daphnid [*Daphnia magna*]: 48 h EC_{50} = 9.5 mg/L (measured, static), OECD TG 202

Algae[*Pseudokirchneriella subcapitata*]: 72 h ErC_{50} = 62 mg/L (measured, growth rate, static) , OECD TG 201

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

Daphnid [*Daphnia magna*]: 21 d LOEC = 1.8 mg/L (measured, semistatic) , OECD TG 211

21 d LOEC(reproduction) < or = 0.22 mg/L (measured, semistatic, based on the total number of juveniles per parent animal at the start of the test) , OECD TG 211

21 d NOEC(reproduction) = 0.90 mg/L (measured, semistatic, based on the total number of juveniles per parent animal alive at the end of the test), OECD TG 211

21 d NOEC(reproduction) < 0.22 mg/L (measured, semistatic, based on the total number of juveniles per parent animal at the start of the test) , OECD TG 211

Algae[*Pseudokirchneriella subcapitata*]: 72 h NOErC = 27 mg/L (measured; growth rate, static) , OECD TG 201

2-Vinylpyridine possesses properties indicating a hazard for the environment (acute aquatic toxicity values between 1 and 100 mg/L for fish, invertebrate and algae and chronic toxicity below 1 mg/L for invertebrate). This chemical is considered not readily biodegradable and has a low potential for bioaccumulation. Adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

Production and/or import volume of 2-vinylpyridine in Japan (sponsor country) was reported to be 958, 673 and 871 tonnes/year in fiscal years 2005, 2006 and 2007, respectively. Production and/or import volume of 2-vinylpyridine in the United States was between 1 million and 10 million pounds (454 - 4,540 tonnes) during 2006 according to Inventory Updated Reporting. Production volume in the world is not available.

2-Vinylpyridine is produced by treatment of 2-methylpyridine with aqueous formaldehyde, followed by dehydration of the resulting intermediate alcohol.

2-Vinylpyridine is used as a raw material for resins used in adhesive for car tire cords, pharmaceuticals and surfactant in Japan. 2-Vinylpyridine is also used as a monomer for producing polyvinylpyridine polymers and used in synthetic rubbers, photographic film, and ion-exchange resins, as well as pharmaceuticals.

In a nation-wide environmental survey of chemicals conducted by Japanese Ministry of Environment in fiscal year 2004, 2-vinylpyridine was detected in environmental air in one place with the level of 6.2 – 18 ng/m^3.

According to the Japanese PRTR (Pollution Release and Transfer Register) system, reported amounts of 2-vinylpyridine released into air and public water are 0.25 tonnes and 0.94 tonnes respectively in fiscal year 2009. Reported amounts of 2-vinylpyridine transferred to off-site was 2.7 tonnes and no transfer to the sewage treatment plant was reported.

Taking into account the situation mentioned above, environmental exposure of 2-vinylpyridine is expected to be low.

2-Vinylpyridine is processed to synthetic rubber in closed system in Japan and no significant release during processing is expected. Although this chemical is produced in a closed system, occupational exposure through inhalation of vapour and the dermal route is anticipated when a worker handles this chemical directly.

As 2-vinylpyridine is used as a raw material or an intermediate, no significant consumer exposure to this chemical is anticipated. A study reported that trace amounts of 2-vinylpyridine was detected from cigarette smoke.