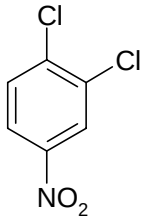
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	99-54-7
Chemical Name	1,2-Dichloro-4-nitrobenzene
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

1,2-Dichloro-4-nitrobenzene is absorbed from the gastro-intestinal tract and although there are some species differences in experimental animals from the available data it can be concluded that 1,2-dichloro-4-nitrobenzene is excreted mainly via urine in the form of the mercapturic acid derivate N-acetyl-S-(2-chloro-4-nitrophenyl)-L-cysteine. Data on humans were not identified in the available literature.

There are no valid acute inhalation studies available. Based on the results of the acute dermal toxicity study with rats the LD50 is > 2000 mg/kg bw. From studies with rabbits no LD50 could be derived, the lowest Lethal Dose Level (LDLo) was 950 mg/kg bw. The acute oral toxicity in rats ranges from 625 to 950 mg/kg bw. 1,2-Dichloro-4-nitrobenzene causes the formation of methaemoglobin. Predominant signs of intoxication were lethargy, increasing weakness, collapse and coma.

1,2-Dichloro-4-nitrobenzene gave no skin irritation effects when tested for 4 hours under semiocclusive conditions according to OECD TG 404 and showed slightly irritating effects, which disappeared within 72 hours under occlusive conditions according to the method of Federal Register 38 No. 187. 1,2-Dichloro-4-nitrobenzene is slightly irritating to the eyes when tested according to OECD TG 405. 1,2-Dichloro-4-nitrobenzene was not found to induce dermal sensitization when tested according to OECD TG 406. In addition, 1,2-dichloro-4-nitrobenzene was not found to induce dermal sensitization in humans in a limited study.

The main targets identified in animal studies after repeated oral administration as well as after inhalation exposure are the haematological system and in addition the kidneys after oral application and the liver after inhalation. From a 28-day oral study performed according to OECD TG 407 a NOAEL of 4 mg/kg bw/day was derived. The NOAEL following subchronic inhalation exposure study of limited validity (limited documentation) was 0.4 mg/m³ (4 hours per day).

Changes in haematological parameters (e.g. methaemoglobinaemia, Heinz bodies) are the main target in the only available report on exposure of workers. As these findings relate to mixed exposures they cannot be clearly attributed to 1,2-dichloro-4-nitrobenzene, but would be plausible, because they were also observed in animal experiments. In the recent open literature reports of human poisoning could not be identified.

1,2-Dichloro-4-nitrobenzene exhibits mutagenic activity in *Salmonella typhimurium* but not in the HPRT test in Chinese Hamster Ovary (CHO) cells. 1,2-Dichloro-4-nitrobenzene induced chromosomal aberrations in V79 cells

with metabolic activation only at the highest concentration, which was cytotoxic. In insects (*Drosophila melanogaster*) 1,2-dichloro-4-nitrobenzene revealed no mutagenic activity in the SLRL-test after application over 3 days with slight increased toxicity, but revealed mutagenic activity following a single i.p. injection of a clearly toxic dose. 1,2-Dichloro-4-nitrobenzene showed no clastogenic activity *in vivo* in a chromosomal aberrations test with rats. Overall in non-toxic doses, there was no evidence for genotoxicity *in vivo* under the conditions tested.

Studies dealing specifically with toxicity to reproduction were not identified. The subacute study with 1,2-dichloro-4-nitrobenzene yielded no damage of the reproductive organs in rats despite clear systemic toxicity up to the maximum tolerated dose of 100 mg/kg bw.

1,2-Dichloro-4-nitrobenzene commercial grade (85% 1,2-dichloro-4-nitrobenzene and 15% 1,2-dichloro-3-nitrobenzene) caused effects on development at maternally toxic doses probably due to methaemoglobinaemia in dams and foetuses. A significant dose-response trend for variations (dilated ureters) was seen in the foetuses of the >= 30 mg/kg bw/day-groups and significant reduced body weight gain of dams at dose levels of 30 mg/kg bw/day on gd 6-10 with an even stronger effect at 100 mg/kg bw/day. Thus, 10 mg/kg bw/day was determined as the NOAEL for maternal and developmental toxicity.

Environment

1,2-Dichloro-4-nitrobenzene is a yellow substance with a melting point of 43 °C, a boiling point of 255 °C, a flash point of 155 °C, and an ignition temperature of 420 °C. With a density of 1.56 g/cm³ at 15 °C and 1.487 g/cm³ at 50 °C 1.2-dichloro-4-nitrobenzene is heavier than water. The substance is slightly soluble in water with 121 mg/l at 20 °C. The vapour pressure was determined to be 2 Pa at 25 °C. A log Kow of 3.04 at 25 °C was experimentally determined.

With regard to its chemical structure 1,2-dichloro-4-nitrobenzene is not expected to hydrolyse under environmental conditions. According to the Mackay level I fugacity model, the main target compartments for 1,2-dichloro-4-nitrobenzene are air (48 %) and water (44 %). The measured Henry's law constant of 0.82 $Pa*m^3*mol^{-1}$ indicates that the compound has a low to moderate potential for volatilization from surface waters.

In the atmosphere slow photodegradation takes place by reaction with photochemically produced OH radicals. The atmospheric half-life is calculated to be 321 days with an atmospheric concentration of 0.5×10^6 hydroxyl radicals/cm^3 as a 24 h average. 1,2-Dichloro-4-nitrobenzene will undergo direct photolysis in air due to absorbance of environmental UV light, however, the respective half-life is not known. In water, no photolysis will occur to a significant extent.

1,2-Dichloro-4-nitrobenzene is not readily biodegradable (Manometric respirometry test: biodegradation < 10 % after 21 days based on BOD; OECD TG 301 C biodegradation 0 % within 28 days, presumably due to inhibition of inoculum). 1,2-Dichloro-4-nitrobenzene is biodegradable by adapted microorganisms under aerobic conditions and by non-adapted inocula under anaerobic conditions (primary degradation). Sewage from adapted wastewater treatment plants has significant potential to primary degrade 1,2-dichloro-4-nitrobenzene (Test method "Simulation of an industrial waste water treatment plant": after 3 days 100 %).

Bioconcentration factors determined for fish were in the range of 26 – 65. A measured Koc (Koc = 417) for sediment suggests the substance to have a medium geoaccumulation potential.

Concerning the acute toxicity of 1.2-dichloro-4-nitrobenzene towards aquatic species reliable experimental results of tests with fish, *Daphnia*, and algae are available. The acute toxicity determined for fish (*Leuciscus idus*) was of 3.1 mg/l (48 h LC_{50}) [DIN 38412 L15] and *Daphnia* (*Daphnia magna*) of 3 mg/l (24 h-EC_{50}) [DIN 38412 L11]. In the growth inhibition test with algae (*Scenedesmus obliquus)* the value 5.8 mg/l was achieved after 48 h (48 h-ErC_{50}) [OECD TG 201]. For the algae *Chlorella fusca* a value of 0.32 mg/l was found after 24 h (24 h-ErC50).
In a chronic (21 d) study with *Daphnia magna* a NOEC of 0.025 mg/l was determined for the most sensitive endpoint reproduction rate. An E_rC_{10} > 0.1 mg/l was reported for the algae *Scenedesmus subspicatus* after 48 hours
For terrestrial organisms the lowest measured 6d-EC_{50} for was 27 mg/l for the plant *Phaseolus aureus.*
Applying an assessment factor of 50 to the lowest available chronic value of 25 µg/l (21d reproduction in *D. magna*),

a $PNEC_{aqua}$ of 0.5 µg/l is obtained.

Exposure

About 36,800 tonnes of 1,2-dichloro-4-nitrobenzene were produced worldwide (excluding Eastern Europe) in 2001. 1,2-Dichloro-4-nitrobenzene is a basic chemical for the synthesis of intermediates which are further processed to herbicides, bactericides, and dyestuffs. A direct use of 1,2-dichloro-4-nitrobenzene is not known in the Sponsor country. 1,2-Dichloro-4-nitrobenzene is not contained in products registered in the Danish, Finnish, Norwegian, Swedish and Swiss Product Registers.

In the Sponsor country, 1,2-dichloro-4-nitrobenzene is manufactured and processed in closed systems. From this site the effluent concentrations was below the detection limit of 2 µg/l.
In Gemany in 1999, the 90-percentile of the 1,2-dichloro-4-nitrobenzene concentrations in the River Rhine was < 0.5 µg/l and in the River Danube < 0.02 µg/l. For the River Elbe the maximum was < 0.02 µg/l.
A non-quantifiable contamination of the terrestrial compartment by 1,2-dichloro-4-nitrobenzene might result from the application of herbicides manufactured from 3,4-dichloroaniline. This assumption is based on the observation that during the biodegradation of such herbicides 3,4-dichloroaniline is formed that in trace amounts may be oxidized biotically or abiotically to 1,2-dichloro-4-nitrobenzene. However, a significant exposure of the terrestrial compartment by this source is not expected.

Exposure is well controlled in occupational settings of the main producer in the Sponsor country and the exposure of workers is well below the workplace guidance value (ARW) of 1 mg/m^3 for 1,2-dichloro-4-nitrobenzene recommended by the German Association of the Chemical Industry (VCI).
The levels of 3,4-dichloro-aniline-adducts in blood and of 3,4-dichloro-aniline in urine of manufacturing and processing plants workers were never higher than 5 % of the tolerance values (no health effect for worker in case that value is not exceeded).

Based on the very low emissions of 1,2-dichloro-4-nitrobenzene into air and water by the manufacturing and processing plants in the Sponsor country, on the very low environmental concentrations, and on the low bioaccumulation potential, a significant indirect exposure of the general public via the environment or via the food chain is not expected.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical possesses properties indicating a hazard for human health (principally haematological toxicity, and developmental toxicity, probably linked to methemoglobinemia) and the environment. Based on data presented by the Sponsor country, exposure to the environment is anticipated to be low, exposure is controlled in occupational settings, and exposure of consumers is not known to occur. Therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.