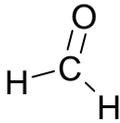


SIDS INITIAL ASSESSMENT PROFILE

CAS No.	50-00-0
Chemical Name	Formaldehyde
Structural Formula	

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR**Human Health**

Formaldehyde had acute effects in mammals: LD₅₀ (rat, oral) 600 – 800 mg/kg b.w., LC₅₀ (rat, inhalation, 4 h) 578 mg/m³ (480 ppm). Inhalation of high concentrations (> 120 mg/m³) of formaldehyde caused hypersalivation, acute dyspnea, vomiting, muscular spasms, convulsions and finally deaths. Histopathology examination showed respiratory tract irritation, bronchioalveolar constriction and lung oedema. Formaldehyde was irritating to the eyes, and aqueous solutions of formaldehyde (0.1% to 20%) were irritating to the skin of rabbits. Formaldehyde was sensitising in the guinea pig maximisation test and the local lymph node assay with mice. On the other hand, specially designed studies (IgE tests, cytokine secretion profiles of lymph node cells) did not reveal evidence of respiratory sensitisation in mice.

In humans, transient and reversible sensory irritation of the eyes and respiratory tract has been observed in clinical studies and epidemiological surveys. Odour threshold for most people ranges between 0.5 and 1 ppm. In general, eye irritation, the most sensitive endpoint, is associated with airborne concentrations beginning in the range of 0.3 to 0.5 ppm. Eye irritation does not become significant until about 1 ppm, and rapidly subsides. Moderate to severe eye, nose and throat irritation occurs at 2 to 3 ppm. Sensory irritation has also been reported at lower exposure levels, but is then difficult to distinguish from background. Most studies show no effect on lung function in either asthmatics or non-asthmatics. Formaldehyde causes skin irritation and has corrosive properties when ingested. In some individuals, contact dermatitis may occur at challenge concentrations as low as 30 ppm.

Formaldehyde is a highly reactive gas that is absorbed quickly at the point of contact and is also produced by endogenous metabolism. It is rapidly metabolised, such that exposure to high concentrations (up to 15 ppm in rats) does not result in increased blood concentrations. Repeated formaldehyde exposure caused toxic effects only in the tissues of direct contact after inhalation, oral or dermal exposure characterised by local cytotoxic destruction and subsequent repair of the damage. The typical locations of lesions in experimental animals were the nose after inhalation, the stomach after oral administration and the skin after dermal application. The nature of the lesions depended on the inherent abilities of the tissues involved to respond to the noxious event and on the local concentration of the substance. Atrophy and necrosis as well as hyper- and metaplasia of epithelia may occur. The most sensitive No Observed Adverse Effect Levels (NOAELs) for morphological lesions were between 1 and 2 ppm for inhalation exposure and about 260 mg/l in drinking water.

Formaldehyde is weakly genotoxic and was able to induce gene mutations and chromosomal aberrations in

mammalian cells. DNA-protein crosslinks are a sensitive measure of DNA modification by formaldehyde. However, the genotoxic effects were limited to those cells, which are in direct contact with formaldehyde, and no effects could be observed in distant-site tissues. In conclusion, formaldehyde is a direct acting locally effective mutagen.

Chronic inhalation of concentrations of 10 ppm and higher led to clear increases in nasal tumour incidence in rats. Most of the nasal tumours were squamous cell carcinomas. Marked non-neoplastic pathological lesions of the nasal epithelium accompanied them. No increased incidence of tumours was found in other organs after inhalation, and administration routes other than inhalation did not result in local or systemic tumour formation. The damage of nasal tissue played a crucial role in the tumour induction process, since nasal cancer was only found at concentrations inducing epithelial degeneration and increased cell proliferation. Thus the stimulation of cell proliferation seems to be an important prerequisite for tumour development. Although formaldehyde exhibits some genotoxic activity, the correlation between cytotoxicity, cell proliferation and the induction of nasal cancer in rats provides a convincing scientific basis for aetiology of the carcinogenic response to be cytotoxicity driven. In contrast to that, no significant numbers of tumours were seen in mice and Syrian hamsters following chronic exposure to concentrations up to 14.3 or 30 ppm, respectively. These clear species differences appeared to be related, in part, to the local dosimetry and disposition of formaldehyde in nasal tissues. Species differences in nasal anatomy and respiratory physiology may have a profound effect on susceptibility to formaldehyde-induced nasal tumours.

In epidemiological studies in occupationally exposed human populations, there is limited evidence of a causal association between formaldehyde exposure and nasal tumours. Taking into account the extensive information on its mode of action, formaldehyde is not likely to be a potent carcinogen to humans under low exposure conditions.

There are no indications of a specific toxicity of formaldehyde to foetal development and no effects on reproductive organs were observed after chronic oral administration of formaldehyde to male and female rats. Amounts of formaldehyde which produce marked toxic effects at the portal of entry, do not lead to an appreciable systemic dose and thus do not produce systemic toxicity. This is consistent with formaldehyde's high reactivity with many cellular nucleophiles and its rapid metabolic degradation.

Environment

Formaldehyde is a colourless gas with pungent odour, soluble in water forming methylene glycol and low molecular mass poly(oxymethylene)glycols $\text{HO}(\text{CH}_2\text{O})_n\text{H}$ ($n = 1-8$). It has a measured vapour pressure of 5185 hPa at 25°C.

The favourite target compartment for formaldehyde is water as indicated by Mackay Level I calculation (water: 99% equilibrium distribution). In air, formaldehyde is expected to be indirectly photodegraded, with a half life of 1.71 d. The substance is readily biodegradable. Hydrolysis is not expected under environmental conditions. However in water formaldehyde undergoes essentially complete hydration to yield the gem-diol, methylene glycol. The log P_{ow} was measured to 0.35 at 20 °C. Hence bioaccumulation is unlikely to occur.

The lowest valid effect value of 5.8 mg/l was found for *Daphnia pulex* (48h- EC_{50}). For fish the lowest effect value of 6.7 mg/l (96h- LC_{50}) was found for *Morone saxatilis* (marine). For freshwater fish the lowest effect value (96h- $\text{LC}_{50} = 24.8$ mg/l) was found for *Ictalurus melas*. For the green alga *Scenedesmus subspicatus* a 24h- EC_{50} of 14.7 mg/l and a 24h- EC_{10} of 3.6 mg/l is available for the endpoint oxygen production and consumption. Applying an assessment factor of 1000 according to EU Risk Assessment procedure to the lowest valid effect value, a $\text{PNEC}_{\text{aqua}}$ of 5.8 µg/l can be derived.

Exposure

Formaldehyde is ubiquitously present in the environment as a result of natural processes and from man-made sources. The major source of atmospheric formaldehyde is the photochemical oxidation and incomplete combustion of hydrocarbons. The global production of formaldehyde in 1999 is estimated to be 5 – 6 million tons. The substance is mainly used as an intermediate in the chemical industry for the production of condensed resins for the wood, paper and textile processing industries and in the synthesis of methylene dianiline (MDA), diphenylmethane diisocyanate (MDI), hexamethylenetetraamine (HTMA), trimethylol propane, neopentylglycol, pentaerythritol and acetylenic agents. Aqueous solutions of formaldehyde are employed as germicides, bactericides and fungicides. The use of

formaldehyde as biocide and in other applications is estimated to be 1.5 % of the total production, i.e. 75 000 to 90 000 t/a related to the worldwide production amount. Formaldehyde is used as a preservative in a large number of consumer products, such cosmetics and household cleaning agents. Tobacco smoke as well as urea-formaldehyde foam insulation and formaldehyde-containing disinfectants are all important sources of formaldehyde exposure. Releases into the environment are likely to occur during production and processing as intermediate as well as from use of products containing the substance. For almost all sites there is no information available about releases into the waste water from production and processing. In Canada, about 1424 t were released into the environment from industrial sites in 1997, from which about 20 t/a were releases to surface waters by 4 sites. The US TRI gives industrial releases of formaldehyde for 1999 with about 6,000 t/a to air and about 175 t/a to surface waters. From the direct use of the substance as e.g. biocide it can be assumed that a very high amount is released into the environment. With an amount of 75 000 to 90 000 t/a worldwide this is a significant pollution source. It can be estimated that formaldehyde contained in consumer products, like cleaning agents is released completely into the wastewater. In addition, reported use of formaldehyde in fish farming and in animal husbandry may lead to a significant environmental exposure.

NATURE OF FURTHER WORK RECOMMENDED

Environment: The substance is a candidate for further work. No information is available about releases into surface water from production and processing sites. In addition, it can be assumed that from the use of 1.5 % of the worldwide production volume (5 to 6 Mio t/a) as biocide and in other applications i.e. 75 000 – 90 000 t/a a high amount of formaldehyde is released into the environment (e.g. from fish and livestock farming). Product register information shows that formaldehyde is contained in a large number of consumer products, like cleaning agents, detergents, soaps etc. For these applications it can be estimated that the whole amount is released into the waste water. Due to the low PNECaqua of 5.8 µg/l a risk to the aquatic environment cannot be excluded. Therefore, an exposure assessment is recommended.

Human Health: No recommendation for further work, because all SIDS endpoints are adequately covered and because exposure is controlled in occupational settings.