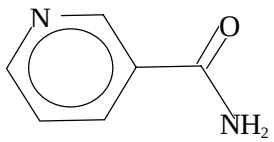
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	98-92-0
Chemical Name	3-Pyridinecarboxamide (nicotinamide)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Nicotinamide is a vitamin, an essential constituent for the synthesis of pyridine coenzymes in mammalian systems. The substance can be synthetised directly in the body from the aminoacid tryptophan. In humans exogeneous nicotinamide is easily absorbed from the gastro-intestinal tract. In other species it may be deamidated to nicotinic acid by intestinal micro-organisms before entering the systemic circulation. The substance can be incorporated into NAD(P) either directly or after deamidation or metabolised and excreted in urine. The primary metabolite in both humans and rats is N-methylnicotinamide.

The acute toxicity of nicotinamide after oral administration or dermal application is very low: oral LD_{50} 3-7 g/kg bw in rodents and dermal LD_{50} >2000 mg/kg bw in rabbits. Skin irritation studies indicate that nicotinamide has no potential to irritate the skin. Nicotinamide is an eye irritant. Evidence from human exposure indicates that nicotinamide is not a skin sensitiser.

In a 4-week oral toxicity study male rats dosed with 215 and 1000 mg/kg bw showed a significant decrease in body weight gain and food consumption during part of the treatment period. Liver weight was increased accompanied histopathologically by mild liver centrilobular hypertrophy in all treated animals. These effects were considered to be an adaptive response to nicotinamide treatment. In females at the high dose group extramedullary haematopoiesis was reported. The NOAEL derived from this study is 215 mg/kg bw. In this study no effects on male and female gonads were found.

A developmental toxicity test was performed in rats with nicotinic acid, which has a similar physiological function as nicotinamide and comparable kinetics as nicotinamide in rats. The NOAEL for maternal toxicity derived from this study was 200 mg/kg bw/d based on effects on body weight (equivalent to 198 mg/kg bw/d for nicotinamide). The NOAEL on reproduction toxicity and developmental toxicity is 200 mg/kg bw/d (equivalent to 198 mg/kg bw/d nicotinamide) based on the significantly decreased placental and pup body weight (males only). No teratogenic effects were observed.

Nicotinamide is considered not mutagenic in bacterial strains. No chromosomal effects in mammalian cells were reported. In an *in vivo* micronucleus test no clastogenic effects were seen. Thus nicotinamide is not mutagenic.

In humans nausea with or without vomiting was the main effect after acute exposure and generally seen after doses in excess of 5 g/day. No persisting effects were reported.

Environment

Nicotinamide is a solid with a vapour pressure of 31.4 hPa (at 25ºC), a water solubility of 691-1000 g/L and a Log

K_{ow} of -0.38 (at 22°C). It has a calculated half-life for photo-oxidation of 2.23 days in the atmosphere. Nicotinamide will partition primarily to water (Mackay level III modelling). No hydrolysis is expected based on the stability of the amide bond. Nicotinamide is readily biodegradable (100% within one week). Based on the log K_{ow} nicotinamide is not expected to bioaccumulate (calculated BCF 3.162). It has a low potential for sorption to soil (predicted log Koc 0.97).

The 96-hour LC_{50} in fish for nicotinamide is >1000 mg/L The 24-hour EC_{50} for daphnia is >1000 mg/L. In a test with algae (*Scenedesmus subspicatus*, 72-hours exposure) virtually no growth was seen during the first 24 hours. The 72-hour E_bC_{50} and E_rC_{50} were >1000 mg/L. The EC_{10} for the inhibition of micro-organisms is 4235 mg/L.

Exposure

Nicotinamide can be found as a dietary supplement in food and feed and in cosmetics. Consumers may be exposed to nicotinamide by the oral and dermal routes of exposure. There is a potential for occupational exposure through inhalation and skin contact.

There is potential exposure for the aquatic compartment arising from the production and processing of nicotinamide.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemical is currently of low priority for further work based on a low hazard potential. However it is noted that the substance is an eye irritant.