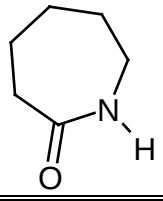
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	105-60-2
Chemical Name	ε-caprolactam
Structural Formula	

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The LD50 for the rat after oral application is 1475-1876 mg/kg bw. After inhalation of the substance as an aerosol by rats, the LC50 is 8.16 mg/l/4h. The LD50 for rats after dermal application is >2000 mg/kg bw. Main symptoms following exposure are clonic convulsions (oral), and irregular respiration (inhalation). Key effect following inhalation exposure to Caprolactam in humans and rats is irritation (skin, eyes, respiratory tract). Caprolactam was not sensitising in a guinea pig maximisation test and in a Buehler test with guinea pigs. The observed dermal effects in the study were regarded to be due to irritation. However, there are very few cases of sensitization in humans (see below).

Caprolactam given by feed (up to 1333 mg/kg bw) to rats in a 90-day study caused a species and sex-specific effect on the kidney of the male rat (hyaline-droplet-related nephropathy), which is supposed to be of no relevance for other species, including humans (NOEL 33 mg/kg bw). Furthermore there are no lesions in the kidney in two 2-year carcinogenicity bioassays.

A 13 week-inhalation study with caprolactam (aerosol, MMAD 3 um) resulted in local nasoturbinal and laryngeal tissue changes and transient clinical signs in all treated rats. There is no NOEC from this study. These effects have been interpreted as an adaptive response by the authors. However, recovery from these effects was not complete after 4 weeks. Keratinization of the metaplastic epithelium in the larynx (reversible within 4 week recovery) was observed in the highest dose group indicating a NOAEC for local effects in the upper respiratory tract, of 70 mg/m^3 (14 mg/kg bw./day;). Systemic toxic effects also with respect to ophthalmology and neurobehaviour were not observed, NOAEC 243 mg/m^3 (49 mg/kg bw./day). Caprolactam showed neither mutagenic nor clastogenic potential with respect to most of the different genetic endpoints tested. Positive results in *in vitro* cytogenetic tests are observed only with high concentrations tested (> 10 mM). However, several tests in vitro and in vivo show induction of mitotic recombination. The relevance of this effect remains unclear, especially taking into account the negative results in rats and mice carcinogenicity bioassays. Caprolactam was not carcinogenic in two 2 year oral studies in rats and mice when tested up to 7500 ppm and 15000 ppm by feed (750 and 2143 mg/kg bw/day.).

No adverse effect to reproductive organs was found in a three-generation feeding study with rats (feed: 1000-10 000 ppm=83-833 mg/kg bw; NOAEL parental: 417 mg/kg bw, NOAEL F1/F2/F3 generation: 83 mg/kg bw, NOAEL fertility: 833 mg/kg bw. Maternal as well as fetal effects are reduced body weight gain. Developmental studies

performed in rats and rabbits with doses of caprolactam that were non-detrimental to the parental animals showed no evidence of a fetotoxic effect. Observed effect again is reduced maternal and fetal body weight gain. Teratogenicity from the gavage application of caprolactam was not observed in rats and rabbits (rats: NOAEL maternal toxicity: not established; NOAEL teratogenicity: 1000 mg/kg bw; NOAEL fetotoxicity 500 mg/kg bw; rabbit: NOAEL maternal toxicity: 50 mg/kg bw; NOAEL teratogenicity: 250 mg/kg bw; NOAEL fetotoxicity 50 mg/kg bw). According to the data from rats and mice, Caprolactam appears to be absorbed rapidly. Excretion is also rapid and predominantly via the urine, mainly in metabolized form with only a small portion of unchanged substance.

In humans, irritation of the skin and the mucous membranes were reported. No signs of irritation was observed at 33 mg/m^3 for Caprolactam vapor. The irritation threshold was reported to be at 56 mg/m^3 and an irritation effect was noted at 61mg/m^3 for vapor. There is no information on severity of irritating effects by dust compared to vapors, however, effects seem to be more severe in dry air. Caprolactam fume at 68 mg/m^3 is irritating to the skin .In some rare cases allergic contact dermatitis, resp. Positive patch-test reactions were reported. Disturbance of the menstrual function and an increased number of toxicosis, premature delivery and post-natal hemorrhages were reported in female employees in the processing industry, where exposure to other compounds was also possible (no evaluation possible).

Environment

The distribution of the substance between the compartments air, biota, sediment, soil and water was calculated according to Mackay Level I. The main compartment is water 99,98%.

The low vapour pressure (0.13 Pa at 20 °C) and complete water solubility (4560 g/l at 20 °C) of caprolactam suggest that volatilization from water and soil surfaces would not be an important fate process. The substance has no considerable potential for bio- and geoaccumulation (log P_{OW} = 0.12, measured). It is readily biodegradable (OECD 301 C 82% after 14 days). The hydrolysis rate is extremely slow ($t_{1/2}$ > 1 year). The photodegradation rate is fast under environmental conditions (50% after 4.9 hours).

The following aquatic effects are available:

Salmo gairdneri LC_{50} (96 h) = >500<1000 mg/l
Daphnia magna EC_{50} (48 h) > 500 mg/l; 2430 mg/l
Scenedesmus subspicatus EC_{50} (72 h) = 130 mg/l; *Selenastrum capricornutum* 4550 mg/l
Pseudomonas putida EC_{50} (17 h) = 4200 mg/l

From the effect value for the most sensitive species, *Scenedesmus subspicatus*, a PNECaqua of 130 µg/l was derived by applying an assessment factor of 1000. This factor is justified as only short-term effect values are available.

No data are available on terrestrial organisms.

Exposure

The production volume of this chemical in EU was 500,000 –1,000,000 t in 1999. More than 1,000,000 tonnes are produced in Asia and 500,000 – 1,000,000 tonnes in North America. The substance is used as an intermediate (non-disperse use) in chemical industry to produce polyamides. Currently 73% of the polyamide is being used for fibre-based applications (carpets and clothing), while the remainder 27% is used for the production of engineering plastics (gear wheels, drive systems, intermediates into Nylon-6). SIAM was informed that exposure to workers is adequately controlled in the industry of the sponsor countries (Germany, Japan and the USA).

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.