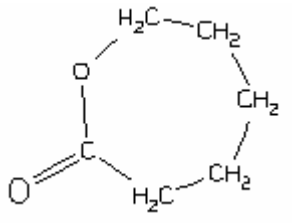
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	502-44-3
Chemical Name	ε-Caprolactone
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

After absorption of ε-caprolactone, the substance will be hydrolyzed rapidly in stomach and blood resulting in the formation of 6-hydroxyhexanoic acid. This hydrolysis product is water soluble and expected to be distributed throughout the body and excreted rapidly, principally through the urine.

ε-Caprolactone exhibits low acute toxicity by all potentially relevant routes of exposure. The acute oral LD_{50} for rats was 4290 mg/kg, while the acute dermal LD_{50} in rabbits was 6400 mg/kg body weight. The primary symptoms following a single high exposure are skin erythema (dermal) as well as apathy and effects on motor coordination and respiration (oral). ε-Caprolactone is considered not-irritating to skin and irritating to eyes.

In a 9-day inhalation study in which ε-caprolactone was administered at a concentration of 45 ppm (213 mg/m^3), no treatment-related effects were found. Therefore the 45 ppm level can be considered a NOAEL. A 90-day inhalation study with ε-caprolactone at concentrations of 15 ppm (71 mg/m^3) and 45 ppm (213 mg/m^3) resulted in perinasal and periocular encrustation and eyelid swelling in the males of the 45 ppm group. As no other treatment related effects were found, this level is considered the lowest observed adverse effect level (LOAEL). The 15 ppm level is considered the NOAEL. ε-Caprolactone given by drinking water to rats at levels of 500, 2000 and 5000 ppm in a 14-day study did not result in any treatment-related clinical signs of toxicity, clinical pathology findings, organ weight changes, necropsy observations or histopathological findings. ε-Caprolactone affected food and water consumption (low palatability) as well as body weight gain at the level of 5000 ppm only. The NOAEL was 2000 ppm, which is equivalent with a dose 152 and 184 mg/kg bw for males and females, respectively.

Bacterial and mammalian *in vitro* mutagenicity tests gave in general negative results. *In vivo*, ε-caprolactone was negative in the mouse micronucleus assay.

No studies are available with regard to reproduction and developmental toxicity of ε-caprolactone. However, a well conducted 90-day inhalation repeated dose study showed no macroscopic and histopathological changes on reproductive organs and also other systemic effects were not found during this study. The lack of systemic effects can be explained by the rapid hydrolysis in stomach and blood, resulting in the formation of 6-hydroxyhexanoic acid. Analogues of 6-hydroxyhexanoic acid show no evidence of reproductive or developmental toxicity. For this reason there is no indication for a reprotoxic concern. This is supported by the toxicological profile of structurally similar lactones, where also no organ specific toxicity was observed in long term studies (with up to 2-year exposure).

Environment

ε-Caprolactone is a colourless liquid with a melting point of -1.3 °C and a boiling point of 237 °C. The substance is miscible with water in all proportions and the calculated log Kow (octanol-water partition coefficient) is 0.68. The vapour pressure of ε-caprolactone is 0.81 Pa.

Based on the Mackay model (level III) ε-caprolactone is expected to partition almost exclusively to the aquatic compartment (> 99.9 %). In water ε-caprolactone is hydrolysed to 6-hydroxyhexanoic acid. At 20 degrees Celsius the half-life at pH values of 4, 7 and 9 was 16, 53 and 2.2 days, respectively. 6-Hydroxyhexanoic acid (CAS 1191-25-9) is not listed on the European Inventory of Existing Commercial Substances (EINECS). Ecotoxicity data of this hydrolysis product were not found. However, based on structural comparison the ecotoxicological properties of this substance are expected to be similar to hexanoic acid and adipic acid. ε-Caprolactone is readily biodegradable according to an OECD 301 B guideline study. It is anticipated that ε-caprolactone will not bioaccumulate based on its low octanol-water partition coefficient and rapid degradation in the environment.

Aquatic ecotoxicity tests, which were done according to GLP and standard guidelines, are available for 4 different species encompassing the 3 trophic levels and microorganisms. A 72 hour toxicity test with algae (*Scenedesmus subspicatus*) revealed an EC_{50} and NOEC value of 1217 and 256 mg/l, respectively (based on biomass). Based on the specific growth rate (μ), the EC_{50} (72 h) was calculated to be 2616 mg/l. Water fleas (*Daphnia magna*) appeared to be more sensitive than algae. An acute test with an exposure period of 48 hours resulted in EC_{50} and NOEC values of 204 and 124 mg/l, respectively. For guppy (*Poecilia reticulata*) a steep concentration-response relatonship was observed. A toxicity test with a duration of 96 hours with this fish species revealed an LC_{50} and NOEC value of 295 and 250 mg/l, respectively. However for bacteria (*Pseudomonas putida*) a large difference between the EC_{50} (1260 mg/l) and NOEC (32 mg/l) was found. During this test the bacteria were exposed for 16 hours. Neither chronic aquatic toxicity tests nor terrestrial toxicity tests are available for ε-caprolactone.

Exposure

In 2003, the estimated world-wide production of ε-caprolactone was 40,000 – 60,000 tonnes. In recent years the world-wide production was growing slowly (<5 % per year). The production occurs at four sites located in the USA (two sites), Japan and the United Kingdom.

About 50 % of the quantity produced is used on site for the production of polymers (polycaprolactones). The remaining 50 % is sold to customers (downstream users). The total number of downstream users is less than 1000. ε-Caprolactone is used by downstream users to modify resins and polymers in order to enhance the performance of the end-products. The majority is used for the modification of acrylic resins and polyesters, but it is also used for modification of epoxy resins and polyurethanes. A small quantity of ε-caprolactone (< 1 %) is used as reactive diluent and as a solvent (e.g. for vinyl resins).

During production and processing, inhalation of vapours and direct skin contact are potentially relevant exposure scenarios. However, inhalation exposures to vapours of ε-caprolactone at ambient temperature are likely to be limited due to its low volatility. Based on the information available to the consortium members, ε-caprolactone is not used in consumer products.

Releases into the environment may occur during production and processing of ε-caprolactone. A release of ε-caprolactone to the environment could potentially also occur via use and disposal of polycaprolactone because polycaprolactone may be (bio)degraded to ε-caprolactone, 6-hydroxyhexanoic acid and oligomers.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical possesses properties indicating a hazard for human health (eye irritation). This hazard does not warrant further work as it relates to reversible effects. This should nevertheless be noted by chemical safety professionals and users.

Environment: The chemical is currently of low priority for further work because of its low hazard potential.