SIDS INITIAL ASSESSMENT PROFILE

CAS No.	79-06-1
Chemical Name	Acrylamide
Structural Formula	$CH_2 = CH - CONH_2$

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The human health effects database meets the requirements for the SIDS data package. Few significant human data are available so this assessment of the hazardous properties of acrylamide is based mainly on animal data.

Acrylamide has been comprehensively studied in animals. It is rapidly and extensively absorbed by oral and dermal routes and presumably also by the inhalation route.

At sufficient doses, toxicity may occur following a single ingestion or contact to the skin. For acute toxicity oral LD50 values of 175 and 203 mg/kg in the rat, 107 and 203 mg/kg in the mouse, and a rabbit and Guinea pig value in the range 150-180 mg/kg are available. The principle effects prior to death are severe clinical effects related to neurotoxicity. Severe effects on spermatid development was also observed in mice. A rabbit dermal LD50 value of 1148 mg/kg is available, but no LC50 values are available. However, as it is presumed that acrylamide would be well absorbed by the inhalation route, it could also be presumed that toxicity may occur following inhalation at sufficiently high concentrations.

No signs of skin irritation were observed in a well-conducted study in rabbits. Case reports and workplace surveys have demonstrated skin effects usually attributable to occupational exposure to aqueous solutions of acrylamide. However, based on human experience it appears that acrylamide is a skin irritant. Information on eye irritation is available from a well-conducted animal study. Acrylamide was clearly irritating to the eyes, producing corneal opacity and iridial reactions. The animal data provide clear evidence that acrylamide is a skin sensitiser.

Human evidence from case reports and workplace surveys demonstrate neuropathological effects, principally peripheral neuropathy, following exposure to acrylamide. Exposures are considered likely to be a combination of inhalation and dermal. One case report of accidental oral ingestion, which was likely to have involved repeated rather than single exposure, also demonstrated neuropathic effects.

For oral exposure, most of the information in animals related to neurotoxicity and provide supporting evidence for the effects observed in humans. In rodent studies, histopathological examination of tissues in a 2-year rat chronic study where acrylamide was administered in the drinking water, gave a clear no observed adverse effect level (NOAEL) for neurotoxicity of 0.5 mg/kg/day, with only slight peripheral nerve lesions in the absence of any clinical signs of toxicity seen at 2 mg/kg/day. These observations were consistent with 90-day rat studies and studies in mice of shorter duration, which demonstrated similar effects at slightly higher exposure levels.

No firm conclusions could be drawn from the available animal studies using the dermal route of exposure; however the effects are predicted to be similar by this route.

Acrylamide was negative in standard bacterial assays but clearly a direct-acting clastogen in mammalian cells *in vitro*, producing chromosome aberrations and polyploidy. Supporting evidence for *in vitro* clastogenicity was also evident in mammalian cell gene mutation assays. There is a large body of evidence clearly demonstrating acrylamide is mutagenic *in vivo*. Positive results were observed in the bone marrow micronucleus test and metaphase analysis, mouse mammalian spot test and a mouse transgenic assay. In the case of germ cells, acrylamide has been demonstrated to induce heritable mutations. Positive results have been obtained in a number of different germ cell assays; chromosome aberrations, micronucleus assays, UDS, dominant lethal assays, heritable translocation, and specific locus assays. Thus, acrylamide is genotoxic *in vivo* to both somatic and germ cells.

For carcinogenicity, two well conducted studies are available in male and females F344 rats, where they received aqueous acrylamide in drinking water for up to 2 years. In both studies there were increases in a number of benign and malignant tumours in a variety of organs, some of which showed a possible relationship with disturbed endocrine function. There is inconclusive evidence from both studies that acrylamide may induce neoplastic neural lesions; tumours were observed in the brain and spinal cord of both sexes, but were not statistically significant and did not show a clear dose-response. The results of both studies clearly demonstrate that acrylamide is carcinogenic in animals. Given the genotoxicity profile of acrylamide, genotoxic activity cannot be conclusively discounted from contributing to tumour formation.

Fertility data are available from studies in rats and mice using the oral route of exposure. Overall, there is sufficient evidence to conclude that acrylamide impairs male fertility in rats and mice (reduction in the number of pregnant dams). In some studies it was possible to identify NOAELs; no effects on fertility in rats were observed in a 2-generation reproduction study in which males and females of each generation received 5 mg/kg/day for 10-11 weeks. No clear effects on fertility were seen in a continuous breeding study in mice exposed to about 9 mg/kg/day acrylamide for up to 27 weeks.

Data on developmental toxicity are available in rats and mice using the oral route of exposure. In the absence of marked maternal toxicity there was no evidence of selective developmental toxicity in rats or mice.

Studies in rats attempted to investigate whether acrylamide could induce toxicity in pups during lactation. However, the dose level used induced significant effects in dams and on lactation. Thus, no conclusions could be drawn with respect to acrylamide-specific effects mediated via breast milk.

Environment

The environmental effects database meets the requirements for the SIDS data package. Short term aquatic toxicity data are available for fish, invertebrates and algae (all from validated sources) and micro-organisms (not valid). The lowest 96-hour LC_{50} reported for fish is 100 mg/l (*Lepomis macrochirus*); the lowest 48-hour EC_{50} for invertebrates is 98 mg/l (*Daphnia magna*); and the lowest 72-hour EC_{50} for algal growth inhibition is 33.85 mg/l (*Selenastrum capricornutum*) (based upon a 72-hour EC_{50} of 67.7 mg/l for a 50% acrylamide solution). In addition there are two valid long-term toxicity results: a 28-day NOEC of 2.04 mg/l (based upon mortality) for the saltwater shrimp *Mysidopsis bahia*; and a 72-hour NOEC of 16 mg/l (growth inhibition) for *Selenastrum capricornutum*. An aquatic PNEC of 20.4 µg/l can be derived by applying a factor of 100 to the lowest long term NOEC from species representing two trophic levels (i.e. invertebrates and algae) where the most sensitive species group in the long term studies is not the most sensitive in the acute studies.

For the terrestrial compartment the only available data are for plants. Acrylamide shows a slight toxic effect to plant growth at concentrations of 10 mg acrylamide/kg soil. An EC_{50} of 220 mg/l (based upon root elongation) is reported for plant seedlings. As the EC_{50} is a short term toxicity test an assessment factor of 1000 (in accordance with EU guidance) may be applied giving a PNEC for terrestrial species of 220 µg/l. This calculation is based on only one terrestrial toxicity result. Due to the partitioning behaviour of acrylamide, the PNEC for the aquatic compartment (20 µg/l) can also be used directly as an alternative PNEC for terrestrial organisms (as a soil pore water concentration)

using the equilibrium partitioning method.

Exposure

Total European Union (EU) production is 80,000-100,000 tonnes/year (~1995). It is used to make polyacrylamides, with a residual monomer content of <0.1% w/w. About 80-90% of polyacrylamide is used in waste water treatment, paper and pulp processing, and mineral processing. Other uses of the polymer include crude oil production, cosmetic additives (such as soap, shaving foam, and hair gels), and soil and sand stabilisation. Acrylamide can also be used in the formulation of grouting agents for sewer line sealing and manhole sealing (and also structural water control and geotechnical applications). About 0.1% of the acrylamide produced in the EU may also be sold directly for on-site preparation of polyacrylamide electrophoresis gels in research establishments, universities and hospitals.

Acrylamide is a powder (normally supplied as a 30-60% w/w aqueous solution) with a vapour pressure of 0.9 Pa at 25 °C, a water solubility of 2,155 g/l at 30 °C and a log octanol-water partition coefficient (log K_{OW}) of ~ -1.0. It does not polymerise significantly at temperatures up to its melting point (~84°C) in the absence of light. However, above its melting point it can polymerise rapidly and exothermically. Hydrolysis and photolysis in water are environmentally insignificant but it is considered readily biodegradable meeting the 10-day test window. The log K_{OW} value implies a low bioaccumulation potential in aquatic species (confirmed by fish bioconcentration factors (BCFs) of 0.26 - 2.53) and low adsorption to soils and sediments. The substance chiefly partitions to water.

In workers, there may be potential for inhalation from exposure to acrylamide or polyacrylamide dust, vapour from sublimation of the solid or vapour from liquid forms. Dermal exposures may occur where workers come into contact with splashes of solid or liquid forms, or from contact with condensed vapour. In consumers, there is potential for dermal exposure, primarily from cosmetic products. There may be potential for oral intake of acrylamide due to contamination of drinking water.

NATURE OF FURTHER WORK RECOMMENDED

Sufficient information exists to address hazard classification for all SIDS endpoints and for other non-SIDS endpoints. However, the chemical is a candidate for further work as follows:

- National or regional exposure information gathering and risk assessment may need to be considered.
- A regional risk assessment has been carried out for Europe indicating concern in particular for grouting applications. The US has conducted a risk and exposure assessment for grouting applications to support possible restrictions on this use.
- In addition, various workers continue to generate data for this substance (especially, in the field of the mechanisms for carcinogenicity) and new data may need to be reviewed on a periodic basis.