SIDS INITIAL ASSESSMENT PROFILE

CAS No.	107-13-1
Chemical Name	Acrylonitrile
Structural Formula	CH_2=CH-CN

CONCLUSIONS AND RECOMMENDATIONS

Environment

Acrylonitrile is toxic for aquatic organisms and is not readily biodegradable. Ready biodegradability can however be assumed in the industrial setting where dedicated industrial biotreatment plants and acclimated microorganisms are used. A number of PEC/PNEC ratios for emissions to the aquatic environment were above 1. There is some concern about coastal sites which do not have waste water treatment plants and which release effluent directly into marine estuaries or the open sea. More information on the dilution at point of outflow has been requested.

Human Health

Acrylonitrile is acutely toxic to humans by inhalation, in contact with skin and if swallowed. It is also a severe eye irritant and may cause sensitization by skin contact. Repeat dose toxicity studies in animals have shown treatment-related changes in the gastrointestinal tract, central nervous system and adrenal gland. There are occasional reports of liver and kidney damage. It is a rodent carcinogen, tumours being observed in the brain, Zymbal gland, gastrointestinal tract and mammary gland. Detailed, recent epidemiological studies do not however provide evidence of human carcinogenicity. Acrylonitrile is an *in vitro* mutagen, indicating that the mechanism of carcinogenicity may be genotoxic. This is not however supported by the results of *in vivo* mutagenicity studies. It is concluded that there is a need for active management of the identified risk and further consideration of the risk management measures currently being applied in relation to workers, consumers and the population exposed via the environment.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

World production of acrylonitrile in 1985 exceeded 3,000,000 tonnes per annum. Estimated world capacity in 1991 was 4,200,000 tonnes per annum, while world demand in 1993 was 3,846,000 tonnes. Current production volume in the EU is in excess of 1,250,000 tonnes per annum, US production is approximately 1,500,000 tones per annum, Japan produces approximately 600,000 tonnes per annum, and the rest of the world accounts for the balance. In 1996, approximately 53% of the total EU production of acrylonitrile was used in production of fibres, 20% in production of ABS and SAN resins and 27% for other uses.

Acrylonitrile does not occur naturally in the terrestrial environment, although it has been detected in interstellar space. Anthropogenic acrylonitrile can potentially be released to the environment during (1) synthesis of the monomer, (2) polymer production, (3) end product usage. Release of acrylonitrile may also occur as a result of (4) combustion of hydrocarbon fuels and (5) cigarette smoking. The major compartments of release are water and air. There is rapid photodegradation of acrylonitrile, while in the aquatic environment acrylonitrile, while not readily biodegradable based on available information, degrades rapidly in wastewater treatment plants following acclimation, and also degrades, although at a slower rate, if released directly into the marine or freshwater environment. PECs for the aquatic environment for production of acrylonitrile and further processing to polymers, acrylamide and adiponitrile have been calculated using the approach outlined in the EU TGD: PEClocal, water (production) = 0.003 - 0.03 mg/L; PEClocal, water (processing site) = 0.003 - 1.18 mg/L.

The data set for acrylonitrile includes a wide range of information on short and long term toxicity in fish, Daphnia and other aquatic invertebrates. Acrylonitrile is moderately toxic to fish, with 96-hour LC_{50} for fresh water fish generally lying in the range of 10 - 20 mg/l (nominal). A recent short term study in the saltwater species *Cyprinodon variegatus*, carried out in full compliance with current protocols, reported a 96-hour LC50 of 8.6 mg/l. The lowest 48 hour EC50 for Daphnia was 7.6 mg/l. The fish early life stage toxicity test in *Pimephales promelas*, using flow-through conditions, provided a LOEC/NOEC of 0.34 mg/l, while a 30 day flow through test in mature fish of the same species provided a long-term LC50 of 2.6 mg/l. If the value of 0.34 mg/l is taken as a LOEC, a NOEC may be derived by application of safety factor of 2, giving a NOEC of 0.17 mg/l. Applying an assessment factor of 10 to the NOEC derived from the fish early life stage toxicity test gives a PNEC of 17 µg/l. For micro-organisms, the lowest EC50 for specific bacterial populations were in the range 1 - 10 mg/l. The conservative value of 1 mg/l has been assumed for NOEC in newly exposed populations and applying a factor of 10 to this derives a PNEC of 100 µg/l.

For the majority of the 43 sites involved in the production and further processing of acrylonitrile in the European Union, the derived PEC/PNEC ratios for the aquatic environment including sediment, for soil and for the atmospheric compartment for these sites are below 1. In the case of 4 sites the PEC:PNEC ratios for the aquatic environment lie between 1.3 and 3.8, however a default dilution factor of 10 was used in the assessment of these sites. Given the dilution factors applying at other sites where information has been provided, it is concluded that these sites present little risk to the local environment. Three sites located in coastal positions have PEC:PNEC ratios of greater than 1, do not have waste water treatment plants and the levels of acrylonitrile in effluent are relatively high compared with the majority of other sites. It is concluded that such sites, releasing directly to the marine environment with little or no pre-treatment of effluent, are of some concern and further information on dilution at the point of outflow is needed.

It is considered that there is no potential for dermal exposure to acrylonitrile during production under normal working conditions, as closed systems are used. Methods for sampling and taking measurements are devised in such a way that exposure via this route should not occur. For processing, again the risk or potential for dermal exposure to acrylonitrile is low to negligible to low based on confirmed good occupational hygiene practice, and given that the systems used in processing are partially closed. In addition local exhaust ventilation and the strictly monitored use of personal protective equipment is applied. However for the purposes of this report and in particular with regard to the area of risk characterisation a very worst case scenario for dermal deposition is assumed i.e. between 0.0 and 0.1 mg/cm2/ day.

For consumers, the available data suggest that exposure via either the oral or dermal route of exposure is very low, based on the level of residual acrylonitrile monomer present in consumer products and the amount of this monomer that can be released to give exposure to the consumer.

It can also be concluded that people living close to or in the surroundings of acrylonitrile production or processing plants are exposed to low to negligible levels of acrylonitrile in the air.

Acrylonitrile is acutely toxic to humans, causing irritation of the eyes and nose, weakness, laboured breathing, dizziness, impaired judgement, cyanosis, nausea, and convulsions following accidental exposure to high levels. Neuropathological effects have been reported at high doses. The main toxic effects seen in animals include respiratory changes, cyanosis, convulsions and death. Reported LD50s in a number of species range from 24 - 186 mg/kg, it is also acutely toxic via inhalation and via dermal exposure and is a skin irritant. Acrylonitrile is already classified in accordance with EU criteria for all these end-points. Additional data presented in this risk assessment additional supports classification in the EU system as a respiratory irritant (R37), a severe eye irritant (R41) (Risk of serious damage to eyes) and as a skin sensitiser (R43).

In animals repeated exposure to acrylonitrile results in damage to the gastrointestinal tract, central nervous system and adrenal gland. There are occasional reports of liver and kidney damage. The respiratory tract is also affected following inhalation exposure, based on histopathological changes in the nasal turbinates of rats in the Quast et al.,(1980) two year study. A LO(A)EL of 20 ppm was established in the study, treatment-related nasal changes being evident at this exposure level, and this was used as a starting point in the risk assessment in relation to inhalation

exposure. A No Adverse Effect Level (NAEL) of 4 ppm for the inhalation route was been derived from the LO(A)EL of 20 ppm, by application of a safety factor of 5. In relation to oral administration of acrylonitrile, the N(A)OEL is estimated to be 3 ppm (0.25 mg/kg/day) in drinking water, based on the information from the Biodynamics study (1980) study in rats which showed systemic toxicity, probably attributable to metabolic release of cyanide.

The results of a range of mutagenicity and genotoxicity tests indicate that acrylonitrile interacts only weakly with DNA and that the DNA-active compound is the metabolite epoxide cyanoethylene oxide, CEO. The negative results obtained in *in vivo* genotoxicity tests with acrylonitrile may be due to metabolism of CEO by glutathione and by (in man) epoxide hydrolase to produce non-DNA-reactive species. This metabolic detoxification of the epoxide may not occur *in vitro*.

Acrylonitrile is classified in the EU as carcinogenic (Category 2. R45), based on the results of studies in the rat following either oral (drinking water or gavage) administration or via inhalation. The common target organs identified were the central nervous system (brain and spinal cord), zymbal gland, gastrointestinal tract (tongue, non-glandular stomach and small intestine) and mammary gland. A linear dose:response relationship for the incidence of astrocytomas was observed in both in the inhalation and the drinking water studies. On the basis of the animal carcinogenicity and positive *in vitro* mutagenicity data acrylonitrile is considered to be a genotoxic carcinogen, although a non-genotoxic mechanism of carcinogenicity has also been suggested. Recent detailed epidemiological studies do not however provide evidence of human carcinogenicity, and IARC in 1998 re-categorised acrylonitrile from category 2a to category 2b, based mainly on the new epidemiological evidence.

In relation to reproductive toxicity, at 65 mg/kg via the oral route embryotoxicity and foetotoxicity occurred in the presence of maternal toxicity, but there was also evidence of an effect on foetal development. Given the maternal toxicity, the developmental effects seen may not indicate a true teratogenic hazard. Inhalation of 80 ppm acrylonitrile also caused developmental effects, while foetotoxicity was observed at exposure levels as low as 25 ppm, a exposure level which was again maternally toxic. Although acrylonitrile has been reported to damage the testes of rats, no effects on fertility were seen in a 3-generation fertility study.

It is concluded that the carcinogenicity of acrylonitrile remains of concern, given its carcinogenicity in rodents and positive *in vitro* mutagenicity data. It is considered however that the legislative requirements and the consequent controls which operate in the industry are sufficient in imposing pressures to drive down exposures to significantly below the OEL of 2 ppm, as supported from recent measured data from industry.

Consumer exposure and indirect exposure via the environment are theoretically possible, but considered to be very low. However, due to its carcinogenicity, there is a need for further consideration of risk management measures.

NATURE OF FURTHER WORK RECOMMENDED

Information on dilution at the point of outflow for specific coastal sites.

There is a need for active management of the identified risk which arises as a concern regarding carcinogenicity, and a need for further consideration of risk management measures currently being applied in relation to workers, consumers and the population exposed via the environment.