SIDS INITIAL ASSESSMENT PROFILE

CAS No.	62-53-3
Chemical Name	Aniline
Structural Formula	Ø-NH ₂

RECOMMENDATIONS

The chemical is a candidate for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Aniline is absorbed through the skin and the lungs with formation of methaemoglobin leading to cyanosis as main toxic effect. Acute intoxication of humans with aniline/aniline vapours is reported frequently. The average lethal inhalation dose for humans is reported to be 25 mg/l air or 0.35-1.43 g/kg body weight.

The acute toxicity of aniline in experiments to rats and rabbits is moderate: In rats oral LD50-values of 442 and 930 mg/kg bw in males and of 780 mg/kg bw in females were determined. Inhalation LC50 values in rats are different depending on the kind of exposure: head-only exposure 3.3 mg/l/4 hours and whole-body exposure 1.86 mg/l/4 hours. Acute dermal toxicity of aniline is characterized by LD50 values of 1540 mg/kg bw for rabbits and 1290 mg/kg bw for guinea pigs. Cats, however, react much more sensitive, with a dermal LD50 of 254 mg/kg bw and death following oral application of approximately 50-100 mg/kg.

Aniline causes weak irritation to the skin but long lasting severe irritation with pannus formation to the eyes of rabbits. Aniline has no local corrosive properties, but causes mild to moderate skin sensitization in guinea pigs. In humans aniline causes contact allergy, often associated with para-group cross reactivity.

Repeated aniline administration to rats has been shown to damage erythrocytes followed by haemolytic anaemia, cyanosis and methaemoglobinemia. Corresponding effects were haemosiderin deposits in the spleen, kidneys and liver as well as increased erythropoeitic activity in the bone marrow and spleen. Congestion of the red pulp sinuses, increased spleen weight, excessive fibrosis and fatty metamorphosis of splenic stroma and chronic capsulitis were demonstrated. Adverse effects of minor relevance were also reported in the adrenals (cortical hyperplasia) and ovaries (reduced organ weights).

Aniline shows positive results in mammalian cell cultures with respect to chromosomal effects, sister chromatid exchanges and possibly for gene mutations. In general, stronger effects are induced in the presence of an exogenous metabolic activation system than in the absence. *In vivo*, aniline is an inducer of micronuclei in mouse and rat bone marrow cells. The mutagenicity *in vitro* and *in vivo* of aniline is supported by *in vivo* studies showing DNA strand breaks and DNA adduct formation in different organs.

Aniline is carcinogenic in rats, however, no clear tumor response could be associated with aniline exposure to humans. Taking into account positive *in vivo* genotoxicity tests and metabolic information a carcinogenic hazard cannot be excluded.

Concerning reproductive toxicity (fertility), data from animal studies (sperm-morphology, repeated exposure) did not give evidence of an impairment of parameters related to male fertility. The significance of incidental findings

concerning female sex organs (ovaries, uterus) for reproductive capacity and/or performance was not further evaluated. The available developmental studies did not give evidence for a specific embryotoxic, fetotoxic or teratogenic potential of aniline. As far some effects on fetuses and on postnatal development were observed, these findings were associated with dose levels resulting in maternal toxicity over an extended period.

Environment

Aniline has a log Kow of 0.9, a water solubility of 35 g/l and a vapour pressure of 0.4 hPa. With a Henry's law constant in the range of 0.1-0.2 Pa.m³.mol⁻¹, the substance is not expected to be volatile from aqueous solution.

Aniline does not undergo hydrolysis. Aniline is readily biodegradable in treatment plants and in the hydrosphere. In surface water photolysis occurs to but this degradation mechanism is of minor importance compared to biodegradation. In soils and sediments, aniline reacts with humic acids. This reaction product is immobile and only slowly degraded (half-life of 350 days). In the atmosphere, the substance is readily removed by reaction with OH-radicals, with a half-life of 3.2 h.

In agricultural soils, aniline is formed by biodegradation of plant protection agents. Within some days, aniline forms covalent bonds with soil organic matter. The reaction product is extremely slowly biodegraded and accumulates in soils when the agents are periodically applied.

In a bioaccumulation study with fish a BCF of 2.6 was found. Because aniline forms covalent bounds with the organic matter, the substance may accumulate in sediment and soils. Therefore, bioaccumulation via the route sediment/soil – sediment/soil-dwelling organisms – bird or mammal may occur.

For aniline short- and long-term tests with fish, daphnids and algae are available. Daphnids are the most sensitive species to aniline in short- and long-term tests. For *Daphnia pulex* a 48h-EC₅₀ of 0.1 mg/l was found. For *Daphnia magna* the 21d-NOECs from three reproduction tests are in the range of 4 µg/l to 24 µg/l. From these data an average value of 15 µg/l can be calculated. With an assessment factor of 10 a PNECaqua of 1.5 µg/l can be derived. There are no data available on effects on benthic and terrestrial organisms for the reaction product of aniline with organic matter. For aniline two 14d-EC50 for *Lactuca sativa* of 33 mg/kg and 56 mg/kg were found.

Exposure

In the European Union, 500,000 t aniline (1990) were produced by hydrogenation of nitrobenzene. Aniline is exclusively used as an intermediate in chemical industry for the synthesis of 4,4'-methylenedianiline (71%), dyes, caoutchouc chemicals, pesticides, pharmaceuticals, fibres and others. During production and processing, aniline is released via waste water into the hydrosphere and into the atmosphere. Further releases in both compartments are expected during processing of caoutchouc chemicals, and from coal and oil industry. In Europe, consumer exposure is unlikely to occur.

NATURE OF FURTHER WORK RECOMMENDED

There is a need for further information and further consideration of exposure and risk assessment. Depending on review by national and regional authorities risk reduction measures may need to be reviewed.

- missing emission data into atmosphere and hydrosphere for several aniline production and processing sites have to be completed;
- emissions into atmosphere by the caoutchouc industry have to be clarified;
- effect tests with terrestrial and benthic organisms with pre-incubated soil and sediment should be conducted;
- a nitrification inhibition test with domestic and industrial sludge should be conducted;
- depending on emission data into atmosphere the conduction of plant fumigation test should be considered;
- genotoxic effects of aniline in combination with its carcinogenic properties causes concern for human health.

This substance is under discussion in the European Union Risk Assessment Program under Regulation EEC/793/93.