SIDS INITIAL ASSESSMENT PROFILE

CAS Nos.	7697-37-2
Chemical Names	Nitric acid
Structural Formula	HNO_3

SUMMARY CONCLUSIONS OF THE SIAR

Supporting Chemical Rationale

The nitrate salts, sodium nitrate (CAS No. 7631-99-4) , potassium nitrate (CAS No. 7757-79-1) and ammonium nitrate (CAS No. 6484-52-2), are used as supporting chemicals to assess toxicity of nitric acid. The nitrates category was presented and agreed upon at SIAM 25. Nitric acid is a strong acid with a pKa of -1.4. The toxicological effect of nitric acid is related to severe corrosive effects at the point of contact. Nitric acid almost completely (93% at 0.1 M) ionizes into the nitrate ion NO_3^- and the hydronium ion H_3O^+ under environmental conditions. Many aquatic and mammalian toxicity tests with nitric acid are precluded due to its pH effects. The nitrate salts are soluble in water and dissociate into the nitrate ion and the corresponding cations in biological fluids and aquatic environments. The cations sodium, potassium and ammonia are not expected to play a significant toxicological role at low doses. Therefore, the data from these salts are used as read across to fill data gaps in this assessment.

Human Health

In rats, the 4-hr LC_{lo} for red fuming nitric acid (RFNA) was $\leq$ 8 ppm (~21 mg/m^3). Widespread inflammation of the upper respiratory tract, rhinitis, trachetitis and pneumonitis were seen in the rats sacrificed shortly following exposure. Respiratory inflammation subsided in animals examined several weeks following cessation of exposure. The 30-minute LC_{50} values for RFNA and white fuming nitric acid (WFNA) were 310 and 334 ppm (~799 and 861 mg/m^3), respectively. Deaths were due to pulmonary edema. Burns were noted on the skin of animals exposed to high concentrations of WFNA. Following ingestion, humans exhibited ulceration of all tissues and membranes with which the acid came into contact. Acute inhalation of nitric acid has been shown to result in respiratory distress and fatal pulmonary edema. Nitric acid is highly corrosive to skin and eyes of animals and humans due to its strong acidic nature. Acid aerosols are known to irritate the respiratory tract and may induce bronchoconstriction, and pulmonary edema at high vapor concentrations.

Repeated-dose toxicity studies were not available for nitric acid, but have been conducted with supporting compounds potassium nitrate; ammonium nitrate; and sodium nitrate. These data are applicable to nitric acid due to the ready dissociation of nitric acid and the nitrate salts to the nitrate ion (NO_3^-) and the corresponding cations. In a combined repeated-dose/reproductive/developmental toxicity screening study, rats were administered potassium nitrate by oral gavage at 0, 250, 750 and 1,500 mg/kg bw/day for 28 days during the pre-mating period. No effect was observed on body weight, food consumption, functional observational battery, and motor activity parameters. Slight increases in levels of blood urea nitrogen (males and females) at 750 and 1,500 mg/kg bw/day and phosphates (males) at 1,500 mg/kg bw/day were not considered clinically relevant due to the absence of other indicators of renal dysfunction. The NOAEL was 1,500 mg/kg bw/day, the highest dose tested. Administration of sodium nitrate in the drinking water to rats for 14 months resulted in a LOAEL of 4,000 mg/L (ca. 200 mg/kg bw/day)

based on a decrease of plasma vitamin E and an increase in the incidence of pulmonary lesions. No effects were observed after inhalation exposure of rats and guinea pigs to ammonium nitrate for two to four weeks; the NOAEL was 1 mg/m^3/day.

Nitric acid was not mutagenic in an *in vitro* bacterial system (Ames test) in the presence and absence of metabolic activation. Additional studies on nitric acid were not available. Potassium nitrate and ammonium nitrate (supporting chemicals) were not genotoxic *in vitro* in either bacterial or mammalian cell systems. Sodium nitrate (supporting chemical) was negative in an Ames test with and without metabolic activation and *in vitro* micronucleus test and chromosome aberration tests with mammalian human lymphocyte cells. Therefore, nitric acid (evaluated as NO_3^- in several of these tests) is not expected to be genotoxic. However, the H+ ion may react with the surfaces that it contacts.

In the combined repeated-dose/reproductive/developmental toxicity screening study described above, male rats were dosed by oral gavage with potassium nitrate at 0, 250, 750 or 1500 mg/kg bw/day for 28 days and females for 14 days prior to mating, during mating and gestation, and through day 4 of lactation. No treatment-related effects were seen on mating performance, fertility, gestation length, gestation index, litter size, offspring survival, sex ratio or offspring body weights. There were no gross pathological effects in offspring. The NOAEL for reproductive toxicity was 1,500 mg/kg bw/day, the highest dose tested. Sodium nitrate did not induce abnormalities of sperm heads in mice dosed by oral gavage at 600 or 1,200 mg/kg bw/day for three days, but following 14 days of treatment sex chromosomal univalency and abnormal sperm-head frequency were significantly higher in males. However, statistically significant reductions in fertility and litter size were not observed. Nitric acid is not expected to result in reproductive toxicity.

Environment

Nitric acid is produced as an aqueous solution with a concentration of 42 – 99%. The melting point of nitric acid is -41.6°C and the boiling point is 83°C at 1013 hPa. The vapor pressure is 84.1 hPa at 25°C. Nitric acid is considered miscible with water. The pKa of nitric acid is -1.4, and therefore, in water, nitric acid readily dissociates to its respective ions (H^+; NO_3^-) under environmental conditions. A log K_{ow} value for an inorganic compound such as nitric acid is not relevant.

Photodegradation and distribution modeling for nitric acid was not conducted. Nitric acid dissociates in water; therefore, a standard hydrolysis study is not relevant. Standard biodegradation tests are not applicable to inorganic substances. Bioaccumulation is not anticipated for inorganic compounds that are miscible with water such as nitric acid.

LC_{50} value for nitric acid toxicity to fish was 72 mg/L (nominal) at pH of 3.25- 3.5, pH 3.7 and pH 4.0. LC_{50} values for fish toxicity were greater than 100 mg/L (nominal) for the supporting substances. The observed toxicity was considered a result of pH effects (acidity), as opposed to any intrinsic toxicity. EC_{50} values for daphnia toxicity were not available for nitric acid. For supporting substances sodium nitrate, potassium nitrate and ammonium nitrate, EC_{50} values for daphnia toxicity range from 490 (nominal) – 3,581 mg/L (measured or nominal unknown). Data on acute toxicity to aquatic plants were not available for nitric acid. For the supporting substance ammonium nitrate, the 7-day EC_3 for algae was 83 mg/L (measured or nominal unknown). For the supporting substance potassium nitrate, data from testing with lower forms of algae (*Gyrosigma spencerii, Navicula spp*. and *Nitzschia spp*.) indicate EC_{50} values >1,700 mg/L (measured).

Exposure

Nitric acid is predominantly produced in Europe (ca. 16,500 ktonnes or 36 billion pounds) and the USA (ca. 6,700 ktonnes or 15 billion pounds). Nitric acid is used in the manufacture of fertilizers, dye intermediates and explosives, metallurgy (e.g., steel pickling), photo-engraving, etching steel, ore flotation, in the synthesis of urethanes and rubber chemicals, and reprocessing of spent nuclear fuel.

Nitric acid is produced in closed reactor vessels (hard piped). Occupational exposure may occur during manufacturing (coupling/decoupling of pipelines). However, due to the corrosive nature of nitric acid, strict safety precautions are applicable. The dermal and inhalation routes will be the most important routes of exposure.

The U.S. Occupational Safety and Health Administration established a permissible exposure limit (averaged over 8 hours) of 2 ppm for nitric acid.

In consumer applications, nitric acid is used as an acidifier in some pharmaceuticals. It is a cauterizing agent (for warts) in veterinary applications. Consumer exposure is expected to be minimal.

In 2005, US manufacturers reported that 12.86 million pounds (ca 5833 tonnes) were released to air, surface water as well as landfills, underground injection, or other disposal options. Some of this total is contained and will result in minimal exposure but some releases may result in exposure.

NOx are precursors to the formation of nitric acid, which is one component of acid rain, and thus nitric acid may be deposited on water, soil and vegetation.

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

Human Health: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for human health (corrosivity to skin and eyes, acute toxicity to the respiratory tract). Based on data presented by the Sponsor country, risk management measures are being applied (occupational exposure limits). Consumer exposures are expected to be minimal. Countries may desire to check their own risk management measures to find out whether there is a need for additional measures.

Environment: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for the environment (acute toxicity to aquatic organisms between 1 and 100 mg/L). However the hazard does not warrant further work as it is related to pH effects.