SIDS INITIAL ASSESSMENT PROFILE

CAS Nos.	7631-99-4 7757-79-1 no CASRN 6484-52-2 15245-12-2 no CASRN 15978-77-5
Chemical Names	Nitrate category: sodium nitrate potassium nitrate potassium sodium nitrate ammonium nitrate calcium nitrate fertilizer calcium ammonium nitrate (CAN) nitrogen solutions (UAN)
Structural Formula	$NaNO_3$ KNO_3 $NaNO_3/(KNO_3)_x$ NH_4NO_3 $Ca(NH_4)_x(NO_3)_y$ $(NH_4NO_3)_z$ /$CaCO_3$ and/or $CaMg(CO_3)_2$ CH_4N_2O and $H_4N_2O_3$ blend

SUMMARY CONCLUSIONS OF THE SIAR

Category/Analogue Rationale

The nitrate category for fertilizer materials includes sodium nitrate (CAS No: 7631-99-4), potassium nitrate (CAS No: 7757-79-1), potassium sodium nitrate (CAS No: not available), ammonium nitrate (CAS No: 6484-52-2), 'nitric acid, ammonium calcium salt' (calcium nitrate fertilizer: CAS No: 15245-12-2), calcium ammonium nitrate (CAN: CAS No: not available) and nitrogen solutions (UAN; urea ammonium nitrate: CAS No: 15978-77-5).

The nitrate category members are all inorganic salts which are solid under ambient conditions (except UAN, which is a solution). Volatility of inorganic salts should be considered insignificant; any measurable vapor pressure is due to decomposition and release of ammonia gas from some ammonium containing category members (ammonium nitrate, calcium nitrate fertilizer, calcium ammonium nitrate and UAN). The nitrate salts are soluble in water and dissociate into the nitrate ion and the corresponding cations in biological fluids and aquatic environments. Based on similar environmental fate, ecotoxicological and toxicological properties, these nitrate compounds can be considered part of the same category.

Read-across is used for SIDS data gaps using data from other nitrate category members. The salts in the nitrate category will dissociate directly into nitrate ion and the corresponding cations, i.e. sodium, potassium and calcium. The cations are not expected to play a significant toxicological role at low doses. Data for urea and ammonium nitrate are also used as read-across for any data gaps.

Urea (CAS No. 57-13-6) has been presented in the OECD HPV Chemicals Programme and the dossier is published on the UNEP website (http://www.chem.unep.ch/irptc/sids/oecdsids/sidspub.html). Urea data are provided in the context of the UAN category member. Data on the toxicity of the ammonium ion/*un-ionized* ammonia equilibrium in aqueous environments are available from the Ammonia category which was also previously presented in the OECD HPV Chemicals Programme, Ammonia Category (http://cs3-

hq.oecd.org/scripts/hpv/).

Human Health

After uptake into biological systems, the salts in the nitrate category will dissociate directly into nitrate ion and the corresponding cations, i.e. sodium, potassium and calcium. The cations will enter the body electrolyte pool, and are not expected to play a significant toxicological role at low doses. Animal studies indicated that after intestinal absorption, ammonium ions are converted to urea in the liver, and subsequently excreted in urine (within 6 hours). After ingestion of nitrate, it will be partly reduced to nitrite in the saliva in the mouth (and the gastro-intestinal tract) in humans and nitrite is less efficiently absorbed in the rat than in humans. In humans most of ingested nitrate is excreted via the urine (65-75%). ADME data were not available for sodium nitrate or ammonium nitrate.

The acute oral LD_{50} values range from 2,680 mg/kg bw for sodium nitrate (rabbit), 1,900 mg/kg bw for potassium nitrate (rabbit), and >2,000 mg/kg bw for potassium sodium nitrate, as well as for UAN (rat). No adverse clinical effects were observed. Reliable data were not available for the acute oral toxicity of ammonium nitrate. No acute oral study is available for calcium nitrate fertilizer. Dermal LD_{50} values for potassium nitrate and ammonium nitrate were >5,000 mg/kg bw in rats. No signs of toxicity were observed. Potassium nitrate is fatal to humans at an oral dose of 214-500 mg/kg bw.

No reliable data were available on irritation and the sensitisation potential of the nitrates in animals or humans.

In a six-week dietary study with sodium nitrate, there was a slight or moderate reduced weight gain in rats at 5,000 or 10,000 mg/kg bw/day and at autopsy the abnormal colour of the blood and spleen due to methaemoglobin was marked in these same animals. In an OECD TG 422 study, rats were exposed to 0, 250, 750 and 1,500 mg/kg bw/day potassium nitrate via the oral route for 28 days. The NOAEL was 1,500 mg/kg bw/d based on the absence of adverse effects. Administration of sodium nitrate (0 and 4,000 mg/L) to rats in a drinking water study resulted in a LOAEL of 4,000 mg/L based on a decrease of vitamin E levels as well as an increased incidence of pulmonary lesions. A NOAEL was not established in this study.

Potassium nitrate and ammonium nitrate were not genotoxic *in vitro* in either bacterial or mammalian cell systems. Sodium nitrate was negative in an Ames test with and without metabolic activation and negative in *in vitro* micronucleus and chromosome aberration tests with mammalian human lymphocyte cells. The nitrate category members are not considered genotoxic *in vitro*.

Nitrates taken up in food may be implicated in the formation of N-nitroso compounds that are known mutagens and/or carcinogens. Sodium nitrate was found to promote urinary bladder cancer in rats after induction with N-butyl-N-(4-hydroxybutyl)-nitrosamine. However, no data indicating carcinogenicity of nitrate category members were available. No positive relationship has been found between cancer incidence and nitrate intake in several epidemiological studies.

In an OECD TG 422 reproductive/developmental toxicity screening study, rats were exposed to 1, 250, 750 and 1,500 mg/kg bw/day potassium nitrate. The NOAEL for reproduction and developmental toxicity was 1,500 mg/kg bw/d based on the absence of adverse effects. Potassium nitrate was given by gavage during gestation at doses up to 400 mg/kg (mice), up to 280 mg/kg (hamsters), up to 1980 mg/kg (rats) and up to 206 mg/kg (rabbits). No adverse effects of potassium nitrate were reported on nidation, maternal or fetal survival, or incidence of soft or skeletal tissue abnormalities. In a reproductive study in guinea pigs given potassium nitrate at concentrations of 300, 2,500, 10,000, and 30,000 ppm up to 204 days, the NOAEL for maternal reproductive toxicity was 10,000 ppm. In a two-generation rabbit study, sodium nitrate at dose levels of 0, 8, 250 or 500 mg/L in drinking water had no effect on the number of pregnancies, litter size or pup weights. Sodium nitrate was given by gavage during gestation at doses up to 400 mg/kg for groups of mice and hamsters and up to 250 mg/kg for groups of rats and rabbits. No effects of sodium nitrate were reported on nidation, maternal or fetal survival, or incidence of soft or skeletal tissue abnormalities. Sodium nitrate did not induce abnormalities of sperm heads in mice treated for three days but following 14 days of treatment with sodium nitrate, sex chromosomal univalency and abnormal sperm-head frequency were significantly higher in mice. However, statistically significant reductions in fertility and litter size were not observed. Based on the available data, members of the nitrate category are not considered reproductive or developmental toxicants.

Members of the ammonia category, as previously discussed in the OECD HPV Chemicals Programme, are not considered reproductive or developmental toxicants.

Environment

All nitrate compounds in this category, except UAN (liquid), are solid under ambient conditions, very soluble in water and dissociate upon release into water. The melting points of the category members range from 169.6 to 334 ^{o}C. The category members decompose upon heating at temperatures greater than 210 ^{o}C. The vapor pressure of the nitrate category members is negligible for the inorganic salts and for UAN. In addition, in an aqueous environment the chemical behavior of ammonium nitrate is pH-dependent. Nitrate is denitrified by micro-organisms to nitrogen and nitrous oxide. Nitrates are not expected to bioaccumulate based on the fact that they are salts that dissociate in aqueous environments. Nitrate can be taken up by plants or denitrified again to yield nitrogen and nitrous oxide gas. As nitrates are biodegradable and very soluble in water, they are not expected to bioaccumulate in aquatic organisms. However, nitrates can have indirect and long-term effects on ecosystems, e.g. eutrophication. Nitrite may accumulate in plant tissue. Ammonium nitrate is capable of undergoing detonation if heated under confinement.

The ammonia/ammonium ion will exist in equilibrium depending on the pH. Under many environmental conditions (pH 5 to 8), the predominant form will be NH4+. At pH 9 the ratio of ammonia to ammonium ion (NH3/NH4+), should approach unity; at higher pHs, the proportion of NH3 should increase. As pH decreases, the concentration of ammonium ion increases with respect to decreases of unionized ammonia concentrations. However, the toxicity of the unionized ammonia is considered several orders of magnitude greater than the more abundant ammonium ion.

The 96-hour LC_{50} values for fish (*Lepomis macrochirus* and *Oncorhynchus mykiss*) were greater than 100 mg/L (nominal) for all category members. For urea, the 96-hour LC_{50} was > 9100 mg/L in *Barilius barna*. For sodium nitrate and potassium nitrate the 48-hour EC_{50} values for *Daphnia magna* were 490 and 3,581 (analytical not specified) mg/L, respectively. For ammonium nitrate, the 7-day EC_3 for algae was 83 mg/L. Studies in several algal species (*Gyrosigma spencerii, Navicula spp, and Nitzschia spp.*) with potassium nitrate indicate that the 7 or 10 d EC_{50} was> 1700 mg/L. In a cell multiplication inhibition test, the toxicity threshold for urea for *Scenedesmus quadricauda* for 192 hours was > 10,000 mg/L; the toxicity threshold for Green algae (*Scenedesmus quadricauda*) for 192 hours was > 10,000 mg urea/L. Based on the available data, members of the nitrate category are not considered toxic to aquatic organisms.

Exposure

Ammonium nitrate is predominantly produced in Europe and the USA (ca. 14,000 ktonnes). Calcium ammonium nitrate is produced mainly in Europe (ca. 10,000 ktonnes) whereas nitrogen solution is mainly produced in the USA (ca.10,000 ktonnes). Calcium nitrate fertilizer, sodium nitrate, potassium nitrate and potassium sodium nitrate are produced in substantially lower volumes (< 7,500 ktonnes). The substances are mainly used as fertilizers.

Occupational exposure may occur in general during production, transport and processing of the substances. Field exposure to workers is possible during use as a fertilizer. The dermal and inhalation routes will be the most important routes of exposure. In the United States, the Occupational Safety and Health Administration (OSHA) has set permissible exposure limits (PEL) of 15 mg/m^3 (as total dust); PEL (as respirable fraction) = 5 mg/m^3 (8 hour Time Weighted Average). The OSHA PEL for particulates not otherwise regulated applies to all fertilizer dusts.

Consumer exposure may occur when using fertilizers. In the USA, sodium nitrate is also used as a direct and indirect food additive and is regulated by the Food and Drug Administration. Consumer exposure to potassium nitrate may also occur from its use in toothpaste and to ammonium nitrate from its use in inks and adhesives. Ammonium nitrate is also used in explosive materials such as fireworks. In the USA, the water quality criterion for nitrate in water is 10 mg/L. Sodium nitrate, potassium nitrate, ammonium nitrate and nitric acid, ammonium calcium salt are also used as inert materials in pesticide formulations.

Environmental exposure is mainly limited to soil and water after fertilizer use.

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

Human Health: The chemicals in this category are of low priority for further work for human health due to their low hazard profile.

Note: It is recommended that the use of the chemicals as fertilizers be taken into account when assessing the exposure of nitrate and nitrite through drinking water.

Environment: The chemicals in this category are of low priority for further work for the environment due to their low hazard profile.