SIDS INITIAL ASSESSMENT PROFILE

CAS Nos.	17855-14-0 7778-80-5 7778-18-9
Chemical Names	Sulfate category: potassium magnesium sulfate calcium sulfate potassium sulfate
Structural Formula	$K_2Mg(SO_4)_2$ K_2SO_4 $CaSO_4$

SUMMARY CONCLUSIONS OF THE SIAR

Category/Analogue Rationale

The sulfate category consists of the inorganic salts; potassium magnesium sulfate, potassium sulfate and calcium sulfate. In biological fluids and aquatic environments, the soluble portion of each category member completely dissociates into the sulfate ion (SO_4^{2-}) and the corresponding cations; potassium (K^+), magnesium (Mg^{2+}) and calcium (Ca^{2+}) at neutral pH. Based on similar physicochemical, ecotoxicological and toxicological properties, these sulfate compounds can be considered part of the same category. Available data for calcium sulfate, dihydrate (CAS No. 10101-41-4), the hydrated form of the category member, and previously presented in the OECD HPV program, is used as read-across to fill data gaps for the category members.

Human Health

Upon uptake into biological systems the inorganic salts in the sulfate category will dissociate into the sulfate ion and the corresponding cations. Potassium, magnesium and calcium will enter the body electrolyte pool, and are not expected to play a significant toxicological role except at extremely high doses. Sulfate is an important macronutrient for the normal function of cells and is the fourth most abundant anion in human plasma (300 µM). Sulfate is absorbed from the intestine by an active transport system. All cells have sulfate transporters for the influx/efflux of sulfate. Sulfate is also used for detoxification of compounds to sulfate esters, which can be excreted in the urine. Sulfate is eliminated by the kidney and levels are regulated by the kidney through a reabsorption mechanism.

The acute oral LD_{50} values for potassium magnesium sulfate is>2,000 mg/kg bw (OECD TG 423/425).No adverse clinical signs were observed. Although only reliability 4 studies were available for calcium sulfate and potassium sulfate, reported LD_{50}s for these substances were consistent with that reported for potassium magnesium sulfate. No reliable acute dermal or inhalation toxicity data in animals are available. There are no reliable skin/eye irritation or sensitization studies for the sulfates. The category/analogue, calcium sulfate dihydrate is not a skin irritant or a skin sensitizer in experiments performed to OECD TG 404 and 406, respectively. Dust of anhydrous calcium sulfate has an irritant effect on the respiratory tract and eyes in humans in occupational settings, which may be related to its dessicant properties. The irritating effects of anhydrous calcium sulfate cannot be applied to the category as a whole.

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In a combined repeated-dose/reproductive/developmental toxicity screening study (OECD TG 422) rats were treated with 0, 50, 750 and 1,500 mg/kg bw/day potassium sulfate by oral gavage for 28 days. The NOAEL was 1,500 mg/kg bw/day based on the absence of treatment related adverse effects at the highest dose tested. In a combined repeated-dose/reproductive/developmental screening study (OECD TG 422), rats were treated by oral gavage with 0, 100, 300 and 1000 mg/kg bw/day of the category analogue calcium sulfate, dihydrate. Male rats showed changes in clinical chemistry (decreased levels of total protein, albumin, blood urea nitrogen, and creatinine) at 300 mg/kg bw/day. Female rats showed no treatment related effects at the highest dose tested. The overall NOAEL was 100 mg/kg bw/day. As the clinical chemistry effects observed were only seen for calcium sulfate and not for potassium sulfate the effects can be ascribed to the calcium ion. No repeated-dose studies for calcium sulphate and potassium magnesium sulphate are available.

Potassium sulfate and calcium sulfate were negative with and without metabolic activation in Ames tests (OECD TG 471) and *in vitro* chromosomal aberrations tests (OECD TG 473). No *in vitro* genotoxicity studies were available for potassium magnesium sulphate. Calcium sulfate dihydrate tested negative in the micronucleus test *in vivo* up to the test concentration of 5000 mg/kg bw (OECD TG 474). The members of the sulfate category are not considered to be mutagenic or genotoxic. No reliable data are available for carcinogenicity.

In a reproductive/developmental toxicity screening study (OECD TG 422), rats were treated with 0, 50, 750 and 1500 mg/kg bw/day potassium sulfate by oral gavage. The NOAEL for reproduction and developmental toxicity was 1,500 mg/kg bw/day based on the absence of treatment related adverse effects at the highest dose tested. In a reproductive/developmental toxicity screening study (OECD TG 422) with calcium sulfate dihydrate, rats treated up to 1000 mg/kg bw/day by oral gavage showed no treatment-related effects on reproduction and development. The NOAEL for reproductive and developmental toxicity was 1000 mg/kg bw/day. Based on the available data, members of the sulfates category are not expected to be reproductive or developmental toxicants.

Environment

The sulfate category members are solid compounds with melting points ranging from 972 to 1450ºC and a relative density ranging from 2.31 to 2.97. Physico-chemical properties such as partition coefficient are not applicable for inorganic salts. Vapor pressure for these inorganic salts is expected to be negligible. All substances from the sulfate category are soluble in water (2.09-240 g/L) and dissociate upon release into aqueous environments. The pKa of sulfuric acid describes the behavior of the sulfate ion in aqueous solution; the equilibrium hydrogen sulfate/sulfate is 1.92 at 25 ^{o}C, which indicates that the sulfate dianion is present at pH 7. The cations are not expected to play a significant toxicological role at low doses.

Any sulfate released into the environment will be distributed between water and soil. Sulfate is constantly replenished by means of the sulfur cycle (sulfate/sulfide oxidation and reduction), and is ubiquitous in the environment because of the abundance of sulfur on earth. Terrestrial evaporite minerals and the ocean are the largest reservoirs of planetary sulfate. The fate and behavior of sulfates, such as bioaccumulation, are also closely related to the sulfur cycle in air, soil and water. Living organisms assimilate sulfate and reduce it to organic sulfur, an essential constituent of some amino acids and polysaccharides. The reduction of sulfate by sulfate-reducing bacteria may produce hydrogen sulfide under anaerobic conditions.
LC_{50} values for the sulfate salts ranged from >63.6 mg/L for potassium magnesium sulfate to 3,550 mg/L for potassium sulfate for fish toxicity (*Oncorhynchus mykiss, Pimephales promelas* and *Lepomis macrochirus*) and >100 mg/L for calcium sulfate dihydrate to >1970 mg/L for calcium sulfate for aquatic invertebrates (*Daphnia magna* and *Ceriodaphnia dubia*). For calcium sulfate dihydrate a growth rate EC_{50} for algae (*Pseudokirchneriella subcapitata*) of >100 mg/L was reported.

Exposure

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According to the latest figures (2004) the production volume for the sulfate category was estimated to be approximately 6,100 ktonnes for Japan and the Nordic countries. Worldwide production of potassium sulfate in 2006 was 5.12 Mtonnes. Potassium magnesium sulfate and potassium sulfate are mainly used as fertilizers. In 2005-2006, 149,892 tonnes of potassium magnesium sulfate were consumed in the United States. Calcium sulfate (identified as phosphogypsum) is used as a fertilizer. Purified calcium sulfate is also used in construction materials, as filler in paint, paper and toothpaste, and as a food additive (to coagulate soy milk, production of tofu, as a nutrient, dietary supplement, yeast food, dough conditioner, firming agent, and sequestrant).

Occupational exposure may occur in general during production, transport and processing of the substances. Field exposure of 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 has set permissible exposure limits (PEL) of 15 mg/m^3 (as total dust) and 5 mg/m^3 PEL (as respirable fraction) (8 hour Time Weighted Average). Consumer exposure may occur when using fertilizers. In the Sponsor country, calcium sulfate and potassium sulfate are used as food additives and are generally recognized as safe (GRAS) by the Food and Drug Administration.

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

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

Human health: The chemicals are currently of low priority for further work. The chemicals do not possess hazards for human health with the exception of irritation caused by anhydrous calcium sulfate. This hazard does not warrant further work as it is related to transient effects. It should nevertheless be noted by chemical safety professionals and users.

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

It is recommended that the use of the chemicals as fertilizers be taken into account when assessing environmental exposure.

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