FOREWORD INTRODUCTION

Sodium sulfate

CAS N°: 7757-82-6

SIDS Initial Assessment Report

For

SIAM 20

Paris, France, 19 – 22 April 2005

1.	**Chemical Name:**	Sodium sulfate
2.	**CAS Number:**	7757-82-6
3.	**Sponsor Country:**	Slovak Republic Contact Point: Centre for Chemical Substances and Preparations, Bratislava Contact Person: Peter Rusnak, Ph.D. Director
	Co-sponsor Country:	Czech Republic Contact Point: Ministry of Environment Contact Person: Karel Bláha, Ph.D. Director Department of Environmental Risks Prague
4.	**Shared Partnership with:**	Sodium Sulfate Producers Association (SSPA)* and TOSOH
5.	**Roles/Responsibilities of the Partners:**	
•	Name of industry sponsor /consortium	Sodium Sulfate Producers Association (SSPA)
•	Process used	Documents were drafted by the consortium, then peer reviewed by sponsor countries experts
6.	**Sponsorship History**	
•	How was the chemical or category brought into the OECD HPV Chemicals Programme?	Nominated by ICCA in the framework of the ICCA HPV program
7.	**Review Process Prior to the SIAM:**	Two drafts were reviewed by the Slovakian/Czech authorities; third draft subject to review by OECD membership
8.	**Quality check process:**	Data was reviewed against the OECD criteria as described in the SIDS manual. These criteria were used to select data for extraction into the SIDS dossier. Original data was sought wherever possible. Originally reported work was deemed reliable if sufficient information was reported (according to the manual) to judge it robust. Reviews were only judged reliable if reported

by reputable organisations/authorities or if partners had been directly involved in their production

9. Date of Submission: Deadline for circulation: 21 January 2005

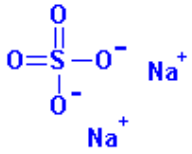
10. Date of last Update: 13 January 2005

11. Comments:

*

The HPV dossier on Sodium sulphate was sponsored by the European Sodium sulphate Producers Association (SSPA). At the time of writing the dossier, members were:	
Adisseo France	FRANCE
Akzo Nobel Nederland NV	THE NETHERLANDS
Alkim Alkali Kimya A.S.	TURKEY
Cordenka	GERMANY
Crimidesa	SPAIN
Elementis Chromium	UNITED KINGDOM
FMC Foret SA	SPAIN
Lenzing AG	AUSTRIA
Minera de Santa Marta	SPAIN
Perstorp AB	SWEDEN
Säteri Oy	FINLAND
Sulquisa	SPAIN
Tessenderlo Chemie SA	BELGIUM
Co Sponsored by:	
TOSOH CORPORATION	Japan

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7757-82-6
Chemical Name	Sodium sulfate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Sulfate (and sodium) ions are important constituents of the mammalian body and of natural foodstuffs and there is a considerable daily turnover of both ions (several grams/day expressed as sodium sulfate). Near-complete absorption of dietary sulfates may occur at low concentration, depending on the counter-ion, but absorption capacity can be saturated at higher artificial dosages resulting in cathartic effects. Absorption through skin can probably be ignored since sodium sulfate is fully ionised in solution. One source suggests that very high levels of sulfate in urine may occur due to absorption from dust inhalation. At dietary levels, excretion is mainly in the urine. Sulfates are found in all body cells, with highest concentrations in connective tissues, bone and cartilage. Sulfates play a role in several important metabolic pathways, including those involved in detoxification processes.

The acute toxicity (LD_{50}) of sodium sulfate has not been reliably established but is probably far in excess of 5000 mg/kg. In an inhalation study with an aerosol, no adverse effects were found at 10 mg/m^3. Also human data indicate a very low acute toxicity of sodium sulfate. Human clinical experience indicates that very high oral doses of sodium sulfate, 300 mg/kg bw up to 20 grams for an adult, are well tolerated, except from (intentionally) causing severe diarrhoea. WHO/FAO did not set an ADI for sodium sulfate. There is no data on acute dermal toxicity, but this is probably of no concern because of total ionisation in solution.

Sodium sulfate is not irritating to the skin and slightly irritating to the eyes. Respiratory irritation has never been reported. Based on wide practical experience with sodium sulfate, in combination with the natural occurrence of sulfate in the body, sensitising effects are highly unlikely.

No suitable dermal and inhalation repeated-dose toxicity studies are available. Valid oral repeated dose toxicity studies with 21, 28 and 35 day studies in hens and pigs are available. Toxicity was confined to changes in bodyweight, water and feed intake and diarrhoea. These changes occurred only at very high doses of sodium sulfate. In ruminants, high concentrations of sulfate in food may result in the formation of toxic amounts of sulfites by bacterial reduction the rumen, leading to poly-encephalomalacia. The available data do not allow the derivation of a NOAEL. Based on available consumer data, a daily dose of around 25 mg/kg/day is well tolerated by humans.

There are no data on *in vitro* and *in vivo* genotoxicity, apart from a negative Ames test. There is no valid oral carcinogenicity study. Limited data from experimental studies support the notion that a substance that is abundantly present in and essential to the body is unlikely to be carcinogenic.

Limited data of poor validity did not provide an indication of toxicity to reproduction.

There are considerable data gaps and the data that are available are not all of standard quality or from animals commonly used for toxicity testing. Nevertheless the weight of evidence, combined with previous assessments of both the sodium ion and sulfic ions lead to the conclusion that the identified data gaps need not necessarily be filled.

Environment

Sodium sulphate is a solid inorganic salt well soluble in water (161-190 g/l at 20 ºC) with a melting point of 884 ºC and density of 2.7 g/cm^3. In water solutions it is fully dissociated to sodium and sulfate ions.

In water sodium sulfate completely dissociates into sodium and sulfate ions. The ions cannot hydrolyse. In anaerobic environments sulfate is biologically reduced to (hydrogen) sulphide by sulfate reducing bacteria, or incorporated into living organisms as source of sulphur, and thereby included in the sulphur cycle. Sodium sulfate is not reactive in aqueous solution at room temperature. Sodium sulfate will completely dissolve, ionise and distribute across the entire planetary "aquasphere". Some sulfates may eventually be deposited, the majority of sulfates participate in the sulphur cycle in which natural and industrial sodium sulfate are not distinguishable

The BCF of sodium sulfate is very low and therefore significant bioconcentration is not expected. Sodium and sulfate ions are essential to all living organisms and their intracellular and extracellular concentrations are actively regulated. However some plants (e.g. corn and *Kochia Scoparia*), are capable of accumulating sulfate to concentrations that are potentially toxic to ruminants.

Algae were shown to be the most sensitive to sodium sulfate; EC_{50} 120h = 1,900 mg/l. For invertebrates *(Daphnia magna)* the EC_{50} 48h = 4,580 mg/l and fish appeared to be the least sensitive with a LC_{50} 96h = 7,960 mg/l for *Pimephales promelas*. Activated sludge showed a very low sensitivity to sodium sulfate. There was no effect up to 8 g/l. Sodium sulfate is not very toxic to terrestrial plants. *Picea banksiana* was the most sensitive species, an effect was seen at 1.4 g/l. Sediment dwelling organisms were not very sensitive either, with an LC_{50} 96h = 660 mg/l for *Trycorythus sp*. Overall it can be concluded that sodium sulfate has no acute adverse effect on aquatic and sediment dwelling organisms. Toxicity to terrestrial plants is also low.

No data were found for long term toxicity. The acute studies all show a toxicity of sodium sulfate higher than 100 mg/l, no bioaccumulation is expected, therefore it can be considered that no further chronic studies are required.

Exposure

Production: production of sodium sulfate is 4.6 million tonnes/year (1999), of which approximately 50% a by-product of the chemical industry and the remainder is extracted from natural deposits.
Use: The main uses are manufacturing of glass and detergents. Other users are from a wide range of industries, including dyeing technology, electrochemical metal treatment, (animal) feeds, pharmaceuticals, textile, semi-conductors, intermediates, agriculture.
Release: Releases to water come from natural sources as well as from detergents and nearly all industrial sources listed above.
Occupational exposure: Exposure to sodium sulfate-containing dusts or aerosols is possible
Consumer products: Exposure to sodium sulfate occurs via drinking water and through naturally occurring or added amounts in foodstuffs. The maximum acceptable concentration for drinking water is 200 – 500 mg/l sulfate, and is based on taste rather than toxicity.

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

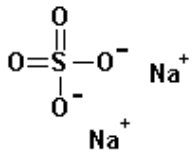
The chemical is of low priority for further work due to its low hazard profile.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 7757-82-6
IUPAC Name: Sodium sulfate
Molecular Formula: Na_2SO_4
Structural Formula:



Molecular Weight: 142.04
Synonyms: Sulfuric acid , disodium salt
Sodium sulfate anhydrous

Sodium sulfate may also occur in hydrated form, usually the hepta- or decahydrate (Glauber's salt)

1.2 Purity/Impurities/Additives

Purity: above 99.5 %. The nature and amounts of impurities are dependent on the production process used., which are quite numerous and may include recycling of waste sulfuric acid from a multiude of industrial processes. Therefore the impurities cannot be specified.

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Reference	Comment
Physical state	Solid		
Melting point	884 °C	Ullmann, 1979 and Handbook of chemistry and Physics, 1997/1998	
Boiling point	Decomposition occurs above 884°C.	Ullmann, 2004	
Density	2.7 g/cm^3 at 20 °C 2.7 g/cm^3 at 25 °C	Ullmann, 1979 Chemiekaarten, 2000	
Vapour pressure	No data		expected to be extremely low
Water solubility	161 g/l at 20 °C 430 g/l at 100 °C	Handbook of chemistry and Physics, 1997/1998 Chapmann & Hall, 1992	
Partition coefficient n-octanol/water (log value)	-3	Chemiekaarten, 2000	
Henry's law constant	No data		The substance is an inorganic salt and it will dissociate in water, therefore it is not of importance.

Sodium sulfate occurs in nature as mineral salts (e.g. thenardite also known as salt cake, and mirabilite also known as Glauber's salt) and is present in almost all fresh and salt waters. Sodium sulfate exists as white crystals or powder, is odourless and has a bitter saline taste.

1.4 Category Justification

A category is not proposed[1]

[1] Although most of the data presented in this monograph are probably applicable to sulfate ions in general, 4 irrespective of the source, care should be taken in extrapolating to other substances. The physico-chemical properties and the toxicity of other sulphate containing compounds will to a large extent be dependent on the counter-ion (e.g. metals other than sodium or organic compounds) and should be assessed separately.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Estimated world-wide production of sodium sulfate was 4.6 million tons in 1999 (U.S. Geological Survey, 2000). The production in the USA is approximately 20% of the world production and in Western Europe this amounts to 35 %. The total production is for approximately 50% a by-product of the chemical industry and the remainder is being extracted from natural deposits.

The main users of sodium sulfate are manufacturers of glass and detergents. Tonnages of sodium sulfate going to detergents (SSPA, 2003) are as follows:
- World total, 1,058,000 Tons,
- Europe, 652,000 Tons (ca. 62 % of world).

These data are valid only for SSPA members. It is difficult to acquire data on glass production and from producers that are not a member of the CEFIC Sodium Sulfate Production Association.

The average concentration of sodium sulfate in detergents (SSPA, 2003) based on a representative sample of 50 commercial detergents, powders and tablets collected in 10 different EU countries (including Eastern) was 20.8 % with a range of 0.0 % to 56.7 %.

Other users are from a wide range of industries, including dyeing technology, electrochemical metal treatment, (animal) feeds, pharmaceuticals, textile, semi-conductors, intermediates, agriculture.

2.2. Environmental Exposure and Fate.

In anaerobic environments sulfate is biologically reduced to (hydrogen)sulfide by sulfate reducing bacteria, or incorporated into living organisms as source of sulfur. Sodium sulfate is not reactive in aqueous solution at room temperature. In moist air sodium sulfate will take up water (hygroscopic) to form hydrates. Sodium sulfate is also soluble in glycerol, but insoluble in alcohol. Sodium sulfate has no oxidising properties, is not explosive and is non-flammable.

2.2.1. Sources of Environmental Exposure

Mineral deposits of sodium sulfate occur naturally around the world. The deposit results from evaporation of inland seas and terminal lakes. Sulfate is a major anion in natural fresh and salt waters and drinking water. The occurrence is mainly due to natural causes, but also to use of sodium sulfate in washing detergents, discharge of industry, mining activities and runoff from fertilized agricultural lands.

Sulfate (sulfur) is an essential nutrient for plants and concentrations of at least 0.5 mg/l in irrigation water are required to prevent detrimental effects on growth.

2.2.2. Photodegradation

There are no data available because no photodegradation can be reasonably expected, based on the character of the substance.

2.2.3. Stability in Water

In water sodium sulfate completely dissociates into sodium and sulfate ions. The ions cannot hydrolyze

2.2.4. Transport between Environmental Compartments

There are no data available on transport between environmental compartments. However, it can be estimated that due to low vapour pressure there is no transfer to or via the atmosphere and that given the very low log Kow (-3 (Chemiekaarten, 2000) and -4.38 (EPI-Suite, 2000)), sodium sulfate is not expected to sorb to sewage sludge or sediments. Some sodium sulfate may be expected in soil due to agricultural use and via irrigation water from rivers.

2.2.5. Biodegradation

Sodium sulfate may be used as an electron acceptor in anaerobic sulfate reduction by sulfate reducing bacteria. Sulfate is converted to (hydrogen)sulfide (Greben, *et al.,* 2000 and Henry *et al.,* 2000).

In the presence of organic substances sodium sulfate is reduced as described in the following reactions:

Sugar: $C_{12}H_{22}O_{11} + 5\ H_2O + 4\ SO_4^{2-} \rightarrow 4\ CO_2 + 8\ H_2 + 4\ HS^- + 8\ HCO_3^- + 4\ H^+$

$8\ H_2 + 2\ SO_4^{2-} + 2\ H^+ \rightarrow 2\ HS^- + 8\ H_2O$

$C_{12}H_{22}O_{11} + 8\ H_2SO_4 \rightarrow 8\ S + 12\ H_2CO_3 + 7\ H_2O$

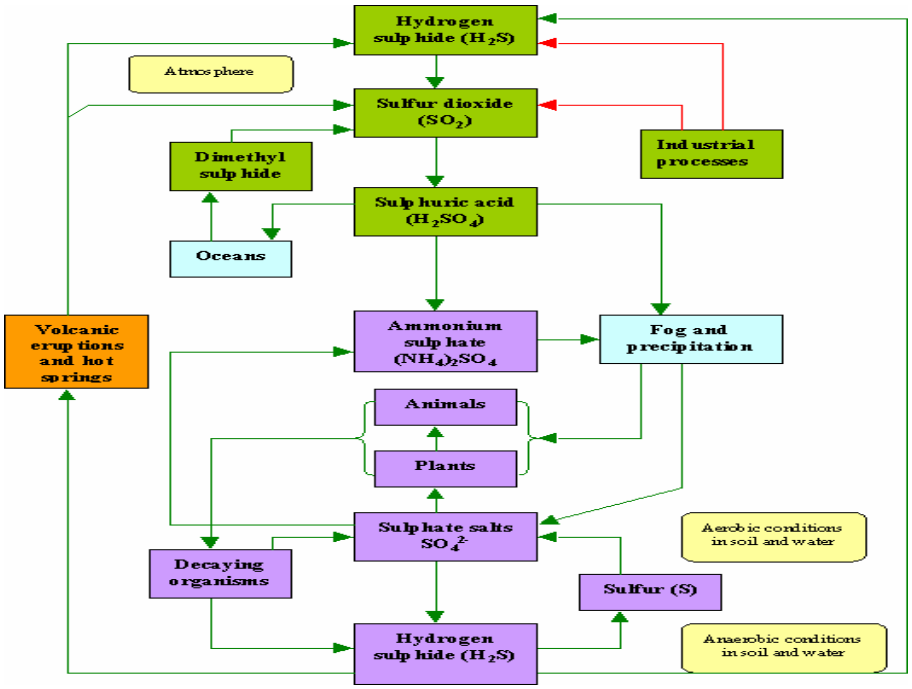
Ethanol: $2\ C_2H_5OH + 3\ SO_4^{2-} \rightarrow 3\ HS^- + 3\ HCO_3^- + 3\ H_2O + CO_2$

$C_2H_5OH + H_2SO_4 \rightarrow 2\ S + 2\ H_2CO_3 + 3\ H_2O$

The sulfur cycle (College of Biological sciences, 2003):

- Assimilative sulfate reduction: sulfate (SO_4^{2-}) is reduced to organic sulfhydryl groups (R-SH) by plants, fungi and various prokaryotes.
- Desulfuration: organic molecules containing sulfur can be desulfurated, producing hydrogen sulfide gas (H_2S).
- Oxidation of hydrogen sulfide produces elemental sulfur (S^o). This reaction is done by the photosynthetic green and purple sulfur bacteria and some chemolithotrophs.
- Further oxidation of elemental sulfur by sulfur oxidizers produces sulfate.
- Dissimilative sulfur reduction: elemental sulfur can be reduced to hydrogen sulfide.
- Dissimilative sulfate reduction: sulfate reducers generate hydrogen sulfide from sulfate.

A schematic representation of the sulfur cycle (http://www.lenntech.com/sulfur-cycle.htm):



2.2.6. Bioaccumulation

Bioconcentration of sodium sulfate was predicted using the EPI-Suite program (2000). The predicted BCF is 0.5, which is very low and does not suggest any concern with respect to bioaccumulation. Sodium and sulfate ions are essential to all living organisms and their intracellular and extracellular concentrations are actively regulated. Some plants (e.g. corn and *Kochia Scoparia*), are capable of accumulating sulfate to concentrations that are potentially toxic to ruminants. (Gould, 1991)

2.2.7. Other Information on Environmental Fate

The following sulfate concentrations in rivers were found on an internet page of United States Environment Program (2001). In the last 100 years sulfate concentrations have greatly increased in some North American rivers because of increased industrial and agricultural activities. In the Volga river the concentration has increased as well due to human activities, from 50 mg/L (natural background) to 60 mg/L since the 1950's. In the Ob river basin of Siberia no significant changes could be observed. The sulfate ion concentration is highly variable in surface waters where it is linked to sulfur-bearing minerals. Sulfate concentrations range from 2 to 30 mg/l for most rivers and lakes in British Columbia. However, some lakes in the Cariboo region and in Richter pass near Osoyoos have particularly high natural sulfate levels of the thousands of mg/l (Ministry of water, land and air protection, British Columbia, Canada, 2000). Most freshwaters contain at least a few parts per million of sulfate, but 20 to 50 ppm or more are common in the eastern United States and most of Europe. Seawater contains levels of about 2700 ppm (Hitchcock, 1975).

Sea salt aerosols are produced in large quantities but do not appear to be a significant source of atmospheric sulfate, except near the place where they are produced due to the fact that they are too

large to remain in the air. Hitchcock (1975) also states that levels of sulfate in air samples in plumes from fossil fuel power-generating plants decline very rapidly with distance from the source even when atmospheric conditions produce minimal dispersion of the plume.

The author measured the following concentrations in the air in North-east America:

- Non-urban sites: 4.9-8.6 μg/m^3
- Coastal urban sites in New York: 8.1-11.3 μg/m^3
- Other coastal sites: 10.7-12.2 μg/m^3
- Inland New York cities: 6.0-10.3 μg/m^3

Urbanisation does not appear to influence the sulfate levels in North-east America. Most of the sulfate observed in the non-urban sites appears to be of local origin.

Hydrogen sulfide derived from the energy metabolism of bacterial sulfate reducers is the principal source of the 100 to 200 million ton of sulfur annually contributed to the global atmosphere.

Since sodium sulfate is soluble in water it is expected to infiltrate the soil. Most of the ions will migrate downwards through the soil with the penetrating water, for it does not interact with soil given the very low log K_{ow}. Sodium sulfate may run off with surface water when the soil is saturated with moisture e.g. after a rainfall (Environment Canada, 1985).

2.3. Human Exposure

2.3.1. Occupational Exposure

Sodium sulfate can exist as dust (by-product) during manufacturing of various chemicals. Occupational exposure to sodium sulfate is likely by dermal contact and inhalation of the dust

The occupational exposure limit value (OEL) is determined at 10 mg/m^3 (UK) for an 8 hour exposure

2.3.2.Consumer Exposure

Exposure to sodium sulfate occurs via drinking water and through naturally occurring amounts in foodstuffs. In drinking water (wells) concentrations up to 2 g/l were measured in the USA. The taste threshold for sodium sulfate is 250 – 900 mg/l. The maximum acceptable concentration for drinking water is 200 – 500 mg/l sulfate, and is based on taste (Ministry of Environment, Lands and Parks Province of British Columbia, Canada, 2000).

No data on the sulfate content of foodstuffs were found; however, according to WHO, sulfates are used as additives in the food industry and the estimated average daily intake of sulfate in food in the USA is 453 mg/person, based on data on food consumption and reported usage of sulfates as additives (WHO, 2003). An Acceptable Daily Intake for sodium sulfate has not been established.

Potential exposure to consumers also occurs from the use of detergents.

WHO/FAO did not set an ADI for sodium sulfate, since they consider this to be a substance of no concern. This was re-confirmed in the joint WHO/FAO meeting of June 2001.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Sulfate is a normal constituent of the blood and is a normal metabolite of sulfur-containing amino acids, and excess sulfate is excreted in the urine. Daily sulfate excretion is reported to be 0.20 to 0.25 mmol/kg bw/day and higher in children (Health Canada, 1994).

In humans, absorption of small amounts of sulfate from the gut occurs rapidly and almost completely. In a study with 8 volunteers, small amounts (60-80 μCi) of radioactive sulfate-35 (^{35}S) were administered orally or intravenously. Plasma equilibrium was reached within 60 to 105 and 60 to 90 minutes respectively, and in both cases 80% or more of the administered amount of radioactivity was recovered in the urine within 24 hours (Bauer *et al,* 1976). In contrast, absorption studies with very large amounts of sodium sulfate (18.1 gram as decahydrate = 8 g as Na2SO4) demonstrated incomplete absorption (53% urinary recovery of sulfate in 72 hours), which was associated with severe diarrhea (Cocchetto and Levy , 1981). When the same amount was given in four fractions over several hours, urinary recovery was 62% in 72 hours and no or only mild diarrhea occurred. Similar results were obtained with magnesium sulfate, although absorption seems to be less complete and more erratic, thus leading to more adverse effects (Morris and Levy, 1983). Apparently, the capacity of intestinal transport mechanism for sulfates can be exceeded. In a human volunteer study described 3.1.2 (Heizer 1999) , 40-80% of a single dose of 63 mg/kg of sodium sulfate was resorbed and excreted in urine. Effects of saturation of absorption could not be detected over a dose range of 21-63 mg/kg/day in the range-finding part of this study.

After absorption free sulfate ions rapidly distribute over the extracellular space, the apparent volume of distribution being ~ 20% of the body volume. The serum concentration of sulfate in humans ranges between 1.4 and 4.8 mg/100 mL, with a mean of about 3.1 mg/100 mL. Excretion is mainly in urine. The renal clearance is approximately one third of the glomerular filtration rate, indication tubular re-absorption. However, the total free sulfate excretion rate is not dependent on urine flow rate. Organically bound sulfate may follow different excretion patterns. (Cocchetto and Levi, 1981).

About 800 mg of elemental sulfur are eliminated daily through the urine of humans, compared with 140 mg in the faeces. (ICRP, 1984) Some 85% of urinary sulfur is present as inorganic sulfates and a further 10% as organic sulfates, whereas the remainder is excreted as conjugated alkyl sulfates (Diem, 1972).

Similar data are available from experimental animals: In a study on male wistar rats using ^{35}S labeled Na2SO4, rapid and almost complete absorption occurred. When the radioactively labeled material was added to a large amount of unlabeled sodium sulfate and subsequently orally administered, the plasma peak occurred at the same time, but the amount of radioactivity decreased as the dose of unlabeled sulfate increased. This indicates that there is a saturation of the absorption mechanism (Krijgsheld, 1979). In male adult Wistar rats, approximately 73% of dietary calcium or magnesium sulfate salts was absorbed, although absorption was partly dependent on other dietary elements (Health Canada, 1994).

Since disturbances in sulfate metabolism are possibly associated with only one rare form of inherited dwarfism, this area is largely unexplored. Therefore, no attempts have been made to fully describe sulfate metabolism. Sulfate incorporation has been observed with such biologically important compounds as chondroitin, fibrinogen, l-tyrosine derivatives, bilirubin, and steroids. A

number of amino acids contain sulfur and take part in the sulfate cycle. Hydrolytic (sulfatase) activity has been demonstrated in liver, kidney, pancreas, serum, and urine. Sulfates play an important role in sulfoconjugation processes, which are of great importance in a variety of detoxification/excretion processes (Percy, 1964).

In ruminants, excess amounts of sodium sulfate in feed may result in considerable toxicity due to formation of sulfides through bacterial action in the rumen (see section 3.1.5.)

Conclusion: relatively large amounts of sodium sulpfate are normally taken up by the gut from food and drinking water through a saturatable mechanism. Absorbed sodium and sulfate ions circulate freely throughout the entire body and form part of a large intra- and extracellular sodiun and sulfate pool respectively. Sulfates are normally incorporated in a great variety of body compounds and as such essential to life.

3.1.2 Acute Toxicity

The acute toxicity studies conducted with sodium sulfate that could be checked are summarised in the following tables.

Studies in Animals

Oral

Table 2 Acute oral toxicity studies with sodium sulfate

Ref. (year)	Species, strain	Protocol	Administration	Endpoint	Value (mg/kg)
Okahara, (1963)	Mouse	non-standard	oral (?)	LD_{50}	5989 mg/kg bw
Henkel, unpublished	rat	unknown	Oral	LD_{50}	> 10.000 mg/kg bw

Only one LD50 value appears to have been reported in the open literature (in Japanese) (Okahara, 1963). A summary report from Henkel (Henkel, unpublished) stated oral administration of 2-5 ml of a solution in water (concentration not given) to 10 rats (mean body weight 270 gram), with an observation period of 8 days. No symptoms were observed and the LD50 was given as > 10 g/kg. Other data quoted in previous editions of IUCLID could not be found.

Dermal

No valid data are available on the acute dermal toxicity for sodium sulfate. Given the complete dissociation in solution, penetration through the intact skin is not to be expected.

Inhalation

Table 3 Acute inhalation toxicity studies with animals exposed to sodium sulfate

Ref. (year)	Species (strain)	Protocol	Source of mists	Exposure Time	Particle size (MMAD, µm)	Endpoint
Last *et al.* (1980)	Rat (Sprague –Dawley)	non-standard protocol	particle aerosol	72 h	1.15	LOEC> 10 mg/m^3

No standard inhalation studies with Na2SO4 are available. There is one study (Last *et al*, 1980) in which rats were exposed to 10 mg/m3 of Na_2SO_4 as a dry particle aerosol in air with 50% humidity (particle size 1.15 µm Mean Mass Aerodynamic Diameter;, σ_g = 2.5) for 72 hours. These six male rats served as negative controls for rats exposed to various concentrations of sodium sulfite and sodium hydroxymethane sulfonate. Clinical effects were not reported. Compared to the filtered-air control group, no significant changes in various inflammation-related lung tissue parameters, determined post-mortem, were found (DNA, RNA, protein, wet-to-dry weight ratio, glycoprotein secretion in trachea explants).

In a study discussed in more detail in section 3.1.4, effects on serum liver cholinesterase concentration, blood coagulation time, brain irritability and spermatogenesis were claimed after 8 hours exposure to 60 mg/ m^3 Na2SO4 as well as after longer exposures to lower concentrations but these results were considered implausible (Denisov, 1989)

Studies in Humans

Oral

There is one fully controlled study on the effects of sodium sulfate in humans (Heizer 1997). In a range-finding study, four healthy volunteers received controlled amounts of drinking water with stepwise increasing concentrations of sulfate, up to 1200 mg/l of sulfate, over six consecutive two-day periods. The calculated dose of sodium sulfate was 0, 21, 31.5, 42, 52,5 and 63 mg/kg/day. Apart from a faster stool passage, no abnormalities were found. In a subsequent two-day studys en volunteers received of 0 mg on the first and 63 mg sodium sulfate on the second day. A clinically insignificant increase in stool volume, decrease in stool consistency and passage time was noted, but no change in stool frequency or diarrhea.

In another study (US-EPA 1999, Backer L, abstract only) volunteers received bottled water containing 0 to 1200 mg/ l of sulfate for three days and plain water on twos days before and one day after the sulfate exposure. Atually received dose was calculated from returned bottles. There was no effect on bowel movements at any concentration and sulfate dose, although not reported, was stated not be a predictor for diarrhea. . In another abstract of a case-control study (US-EPA,1999, no relationship between sulfate levels and diarrhea was found in infants receiving tap water with sulfate concentrations below 500 mg/l.

Sulfate concentrations above 600 mg/l (equivalent to more than 875 mg/l of sodium sulfate) in well water, used to prepare infant formula was described as a cause of diarrhea without any other sign or symptom of disease in three infants (Chien 1967). The estimated daily dose would have been around 70- 100 mg/kg/day. Although the clinical cause and effect relationship is absolutely clear in these three cases, the number of cases versus the population at risk (i.e. infants with similar oral exposure) is unknown and a dose-effect relationship or threshold concentration cannot be established from three cases. Nevertheless, the author's recommendation not to use water with more than 400 mg of sulfates is in line with WHO standards.

In clinical practice sodium sulfate, alone or with magnesium sulfate, was used as a laxative to induce rapid emptying of the gut, in doses of 300 mg/kg up to 20 grams maximum for an adult. The laxative action is ascribed to fecal fluid retention caused by the hygroscopic action of unresorbed sodium sulfate in the large intestine (Gilman *et al*, 1980). Use of sodium sulfate has been gradually abandoned and the substance has been replaced by other laxatives because of the uncontrollable watery diarrhea and accompanying abdominal cramping it tends to produce.

Other Routes of Exposure

An isotonic (3.89%) solution of sodium sulfate decahydrate, administered intravenously, was used as an antihypercalcemic (Remington, 1980). This practice is considered obsolete.

Conclusion

Only limited data on the acute toxicity of sodium sulfate are available. However, in view of the large body pool of sulfate anions and the high body turnover, the acute toxicity of sulfates must be low, as long as the counter-ion is not toxic. . The laxative effect of oral ingestion is well known and was used medicinally. High dosages given in medical practice with the purpose of inducing diarrhoea were usually accompanied by severe abdominal cramps. Apart from that, no side effects are mentioned in the medical literature."

3.1.3. Irritation

Skin Irritation

Studies in Animals

Table 4 Skin irritation testing with sodium sulfate

Ref. (year)	Species, Test Type	Protocol	Doses	Result
Bayer AG (1991)	Rabbit, Skin irritation test on intact skin	OECD 404, "Acute Dermal Irritation/ Corrosion"	500 mg, Occlusive	Not irritating

Sodium sulfate appears not to be irritating to the skin in rabbit. The study was performed under GLP, and according to international well-accepted guidelines. Endpoint determination was based on the DRAIZE scoring system. The exposure period was 4 hours, under occlusion, and the result was scored after 14 days (Bayer, 1991 unpublished).

Studies in humans

No reports on acute studies in humans are available. Skin problems were not found in a group of 119 workers with long-term exposure to sodium sulfate (see 3.1.4; Kelada & Euinton, 1978)

A human repeated insult skin sensitisation test (see 3.1.4.) was performed with a bath salt allegedly containing 80.8% sodium sulfate on 61 human volunteers, mainly females of all ages. It this test, te test substance was applied under semi-occlusion in a concentration of 1.25%, 8 times for 24 hours and once for 48 hours and induced mild irritation only once in one volunteer.However, the validity of this report could not be assessed (CTFA 1976) Another , unavailable CTFA report (1985) is quoted elsewhere as stating that a 10% solution of sodium sulfate under occlusion for 24 hours produced mild irritation in one out of 19 volunteers.

Eye Irritation

Studies in Animals

Table 5 Eye irritation testing with sodium sulfate

Ref. (year)	Species, Test type	Protocol	Doses	Result
Bayer AG, (1991)	Rabbit, Eye Irritation test	OECD Guideline 405, "Eye Irritation"	90 mg, pulverized	Slightly irritating

Sodium sulfate appears to be slightly irritating to the eye in rabbit. The study was performed under GLP, and according to international well-accepted guidelines. Endpoint determination was based on the DRAIZE scoring system. Sodium sulfate had no adverse effect on the iris and cornea. The substance was instilled into the conjunctival sac of the eye. The positive effects were primarily based on the conjuctivea (redness) observed in the test. The effects were reversible within 7 days. (Bayer, 1991 unpublished).

Conclusion : Sodium sulfate was not a skin irritant in a well conducted study. It is a slight eye irritant with redness of the conjunctiva observed. The redness was reversible within 7 days.

Respiratory Tract Irritation

Studies in Animals

In the acute inhalation toxicity test with 72 hours of exposure described in 3.1.2 (Last *et al*, 1980), no signs of irritation of the respiratory tract were described.

In an experiment set up to determine the difference in inhalatory effects of various sulfur oxide species which occur in ambient air, 5 male rabbits were exposed for one hour to aerosols containing an actual mass concentration of 1800-1950 μg/m^3 sodium sulfate particles. Mean mass aerodynamic diameter of the aerosol particles was 0.4 μm (σ_g =1.6). Animals served as their own controls through sham exposures. Mucociliary clearance served as an indication of pulmonary irritation. This was determined by means of retention measurements of previously inhaled radioactively labeled microspheres. No effects on mucociliary clearance were found. Since similar exposures with acid sulfates (H2SO4, NH4HSO4) resulted in significant increase in retention time, i.e. lowering of the clearance, whereas (NH4)2SO4 also had no effect, the conclusion is that any irritative effects are not caused by the sulfate ion but by the hydrogen sulfate ion (Schlessinger, 1984)

Studies in humans

An abstract only is available of a study describing the effects of 10 minute inhalation of sodium sulfate aerosols with a mass median aerodynamic diameter of 0.5 μm in concentrations of 2 and 3 3 mg/m^3 on asthmatic and normal adults., with sodium chloride aerosols of the same size as controls. Two out of 5 asthmatics showed an immediate but not dose-dependent drop in FEV_1,but group mean values of respiratory resistance, FEV_1 and VC were comparable up to 60 minutes post-exposure. In a second series, 6 asthmatics and 6 normal adults were followed for 3 hours after 10-minute inhalation of 3 mg/m^3 and no differences were found in the same volume/flow parameters nor in various diffusion capacity parameters (Sackner et al, 1979)

Symptoms indicating local upper respiratory tract irritation were observed in the study by Kelada and Euinton (1978). Workers from natural sodium sulfate mines developed symptoms such as nasal irritation and runny noses (see section 3.1.5).

Conclusion: It is unlikely that short-term inhalation of respirable sodium sulfate particles cause pulmonary irritation.

3.1.4. Sensitisation

Skin and inhalation

Studies in Animals

No valid study was identified for skin sensitisation potential with sodium sulfate.

Studies in Humans

An incomplete report is available on a repeated insult patch test in human volunteers with 10 different cosmetic products, among them bath salt crystals allegedly containing 80.8% sodium sulfate, tested in a concentration of 1.25% under semi-occlusion on 61 human volunteers, mainly females of all ages. The conclusion of the report is that the substance did not demonstrate any potential for inducing allergic sensitization. The validity of this report could not be assessed. (CTFA, 1976)

Sodium sulphate is unlikely to cause allergy, since the body contains large amounts of sulfate (~0.33 mmol/L in serum and about 50 times higher concentration intracellularly) as well as large amounts of sodium ions. Various metal sulfates (e.g. nickel sulfate, cobalt sulfate) are used as standard allergens in routine skin allergy testing, but positive reactions are related to the metal ion, not to the sulfate, as can be deduced from the definitely non-allergenic zinc sulfate (ECETOC, 1999).

Based on the above, it may be concluded that sodium sulfate is not an allergen in humans, and that animal testing for sensitisation potential would not provide any information relevant for hazard identification and risk assessment.

Conclusion

Despite the absence of formal study results, it can be concluded, based on the natural intra- and extracellular occurrence of the substance, that sensitisation to sodium sulfate is highly unlikely

3.1.5. Repeated Dose Toxicity

Studies in Animals

Oral

Validated (reliability 1 or 2) repeated dose toxicity studies with sodium sulfate are summarised in the Table 6. Two reliable non-standard repeated dose toxicity studies were reported. A non-standard. Non-GLP study feeding study in rats was reported and given reliability 2. An invalid carcinogenicity study is reported here since it has (very) limited reliability as a repeated dose study Two veterinary clinical studies are also described which provide valuable clinical observations and could also be given a reliability 2 despite deficiencies with respect to control groups. The reported clinical effects are so severe that they may safely be assumed absent from any control group. Two more studies assigned validity 3 are mentioned in the text but not included in table 6.

Table: 6: Repeated dose toxicity studies with sodium sulfate

Ref. (year)	Species (strain, sex)	Duration, frequency	Administration	Doses	End-point	Value (unit)/ results
Blunck & Crowther (1975)	Rat, Sprague-Dawley, 5 / Male	27 and 44 weeks, daily	In food	0.84 % in diet, 320-400 mg/kg/day	Mortality, tumours , body weight, food and water consumption	NOAEL ~320-400 mg/kg/day
Moinuddinand Wing-Tsit Lee	Rat, 24, male Sprague-Dawley	4 weeks, daily	In food	0.0; ~0.01%ww; Incremental 0.125,0.250, 0.5, 1% 2% (estimated 2000 mg /kg/d)	Food & water consumption, body weight gain, food conversion efficiency, urine production, diarrhoea, blood hemoglobin & white blood count, serum alkaline phosphatase, inorganic phosphate, gross organ pathology	NOAEL 2000 mg/kg/d
Adams *et al.* (1975)	Hen (48 White Leghorn	4 weeks, daily	Drinking water	Concentrations : 250-23328 mg/l Calculated doses per group of 6 hens: 34 mg/kg/d; 45 mg/kg/d 120 mg/kg/d 210 mg/kg/d 550 mg/kg/d 1670 mg/kg/d 4900 mg/kg/d 1650 mg/kg/d	$LC_{100;}$ Body weight, Histopathology, Food and water consumption, Egg production	23328 mg /l at 4,000 mg/l depressed feed consumption and egg production. Increase in water consumption was observed at 4,000 mg/l.

Table: 6: Repeated dose toxicity studies with sodium sulfate (continued)

Ref. (year)	Species (strain, sex)	Duration, frequency	Administration	Doses	End-point	Value (unit)/ results
Veen-huizen *et al.* (1992)	Pig (415, weaned)	28 days, daily	Drinking water	54-1800 mg/l (water consumption/animal & body weights not given)	Body weight, food-water consumption, gastro-intestinal infections	Increased prevalence of diarrhea was a trend as sulfate concentration increased. A non-significant trend in increased water intake was observed with increasing sulfate. No differences in feed intake were observed between various sulfate concentrations. Body weight increased at 600 mg/l and higher.
Gould (1991)	Cattle (9 young steers)	21 days, daily	In food	0.8 % Na-sulfate (0.36% sulfur)	Neurological symptoms, histopathological brain damage, Sulfide formation in rumen	Five out of nine animals developed symptoms and signs of polioencephalomalacia (PEM), onset correlating well with formation of sulfide in rumen
Niles *et al* (2002)	Cattle (15 heifers)	35 days	In food	3860 ppm, 5540 ppm and 7010 ppm of sulfur	Neurological symptoms, histopathological brain damage, Sulfide formation in rumen	All low-dose animals microscopic signs of PEM, all others macroscopic signs of PEM. Onset of symptoms correlated well with formation of sulfide in rumen.

In the study by Blunck and Crowther (1975), also described under Carcinogenicity, two groups of 5 male rats were fed 2% sodium sulfate in the diet for 27 and 44 weeks respectively. No adverse effects were detected with respect to the limited number of endpoints reported from this study. Obviously, group size is too limited to draw firm conclusions bit a tentative NOAEL of >= 320 mg.kg may be deduced. .

In a non-standard non-GLP 4 week repeated dose study comparing the effects of Mg SO_4, Mn SO_4 and Na_2 SO_4, rats were fed an artificial diet enhanced with minimal amounts of MgS04 and MnSO4 but not Na_2SO4; the pure sulfates were added on a mmole/kg food basis. At the top dose, the food contained around 2% of the respective sulfates (calculated to be around 2000 mg/kg/d). While the Mn SO_4 and Mg SO_4-exposed rats showed various functional and even gross pathological aberrations at the top dose, the Na_2SO_4 -exposed rats were comparable to to the controls in every aspect (see table) except slight diarrhoea in one animal for a few days (Moinuddin & Wing-tstit Lee, 1960). Thus the NOAEL from this study is 2000 mg/kg/day

In the studies of Adams et al (1975) and Veenhuizen et al (1992) the test animals were exposed to sodium sulfate in the drinking water which was available on a daily basis. The primary end-points were food and water intake, body weight (occurrence of diarrhoea) and clinical signs of dehydration. In the study (Adams *et al., 1975)* with 48 hens, small and not clearly dose-related effects on food consumption and egg production were observed at concentrations up to and including 4,000 mg/l of sodium sulfate, compared to two weeks of pre-test observations (calculated dose ~ 550 mg/kg/d of sodium sulfate). Water consumption was strongly increased at concentrations of 4000, 5832 mg/l and 16000 mg/l and dramatically decreased at the top level of 23328 mg/l. At 5832 mg/l a serious decline in egg production and decrease of food consumption was observed. At this concentration, the calculated dose was about 1670 mg/kg/d due to increased water consumption. No mortality was observed at 16.000 mg/l (4900 mg/kg/d) but 100 % mortality was observed at 23328 mg/l (only 1644 mg/kg/d due to strongly reduced water consumption) . Necropsy of hens receiving 23340 mg/l sodium sulfate and above showed extreme emaciation and visceral urate deposits. Microscopic examination of kidney tissues showed urate accumulation of individual glomeruli and tubules losing cellular detail in animals receiving 5832 mg/l or more Examinations of other organs were not reported. The above data seem to indicate that the mortality in the top dose was due more to dehydration because of inpalatable drinking water than to the dose of sodium sulfate.

In the study with 415 weaned pigs (Veenhuizen 1992) diarrhoea was observed with increasing test concentrations. No significant effects were observed in feed and water intake at the tested concentrations. Body weight gain was observed at 600 mg/l or higher. Weight gain to feed ratios for all treatments were not different. Isolates of E-coli were found in 14% of the pigs, from 1 pig rotavirus was isolated. No pigs were exposed to transmissible gastroenteritis virus. None of the treatments had an adverse effect on nursery pig performance. During the study one pig died at a concentration of 600 mg/l. Daily doses could not be calculated in the absence of body weigh and water consumption data; percentages only were given.

Another oral study (Upton, 1976) with rats (exposure 6 weeks) indicated that daily dietary supplementation (1-2%) with sodium sulfate did not significantly affect food/water intake and live-weight gain of rats. In an oral chicken study (Sibblad, 1976) effects on weight gain were reported with increasing sodium sulfate in the drinking water (1-5%). The exposure period was 11 days, and no mortality was observed.

In a study with 9 young Holstein steers, a concentrate diet containing 0.8 % sodium sulfate (total sulfur content approximately 0.36%) was given during 21 days. 3 controls were given the same diet without added sodium sulfate (total sulfur or sulfate content not reported). Five out of nine test animals vs. no controls developed clinically manifest poli-encephalomalacia (PEM) as well as

macroscopically visible and histologically recognisable cerebral lesions (brain histology of not-affected animals not reported). The onset of the disease correlated well with increasing concentrations of sulfide in the rumen. Thiamine concentrations in serum (another alleged cause of PEM) were not significantly affected. (Gould *et al.,* 1991)Similar disease due to high sulfur content of food was allegedly also reported earlier in sheep

In another study three groups of young heifers (5 heifers per group) were fed diets with 3860 ppm, 5540 ppm and 7010 ppm of sulfur respectively during 5 weeks. Sulfur concentrations were reached by adding sodium sulfate to the desired level. Microscopic signs of PEM were seen in all four low-dose animals, macroscopic signs in 4/5 medium-dose and 4/5 high-dose animals. Clinical signs of PEM were seen in all animals. Onset of PEM correlated highly with sulfide concentrations in rumen. Other potential causes of PEM were excluded. (Niles *et al*, 2002).

Dermal

No data have been found with respect to repeated dermal toxicity

Combined Inhalation/ oral exposure

An inhalation study on rats was found describing inhalation exposures of 8, 12, 44, 90 and 720 hours duration to Na_2 SO_4 concentrations of 60.45, 40.05, 18.03, 11.06 and 3 mg/m3 respectively, with concurrent exposure to sodium sulfate in drinking water at a concentration of 500 mg/l. (estimated dose at the lowest level / longest duration 60 mg/kg/day orally and 1.8 mg/kg/d by inhalation). Small but statistically significant effects were claimed at all concentrations on serum liver cholinesterase concentration (first appearing at 6, 12, 44, 90 and 720 hours respectively), prolongation of blood coagulation time (first appearing at 4, 8, 30, 64 and 510 hours respectively) and brain irritability as measured by "summated threshold potential", (first appearing at 4, 8, 24, 45 and 288 hours respectively), and these effects were stated to be worse at end-of exposure (no data provided). (Denisov *et al*, 1989). Depression of spermatogenesis (presumably at end-of-exposure), was also at all concentrations and all effects were stated to be completely reversible within one month post-exposure (size of recovery groups not given). No abnormalities were observed in number of erythrocytes and leucocytes, total haemoglobin, meth- and sulfhaemoglobin, blood histamine, presence of Heinz-Ehrlich bodies brain cholinesterase, number of sulfhydryl groups, basic phosphatase activity in blood serum and content of ascorbic acid in the adrenals.

However, the documentation of this study is insufficient, some of the results are clearly artificially constructed and incredible and the effects are biologically implausible (see below)

“Similar effects were described in a follow-up 90-day study (Denisov and, Tkachev, 1990) in which rats were exposed to 1 mg/m3 sodium sulfate, or 0.1 and 1 mg/m3 of sodium sulfite or 1 mg/m3 of an unspecified mixture of both, together with 500 mg/l in drinking water, i.e an estimated dose of 60 mg/kg/d orally and 0.6 mg/kg/day by inhalation. Apart from the neuro-physiological and biochemical parameters described above, body weight was also depressed, relative liver weight was decreased, histopathological evidence of serious lung damage and testicular damage was described. Effects were similar for sulfites, sulfates and the mixture, but more severe and earlier for the sulfites. Again, the description of the experiment is insufficient and no actual data are presented. The biological plausibility of such relatively severe effects at such low concentrations, from a compound normally abundantly present in drinking water and food is very much in doubt. There is no reason why a simple, non-reactive and freely circulating ion like sulfate would exert systemic effects when absorbed through the lungs at a fraction of the amount absorbed from the gastro-intestinal tract. These findings also strongly contrast with all other available data.

A possible explanation of the findings from these two studies, if accepted at face value, is contamination of the dust used for the inhalation studies with heavy metals, e.g. cadmium. Spent

sulfuric acid commonly contains heavy metals, so pre-refinery sodium sulfate made from such recycled material may well be contaminated.. In the absence of any analytical data, this cannot be verified.

Studies in Humans

Oral/dermal

No information found.

Inhalation

The effects of long-term inhalation of sodium sulfate dust were determined in a cross-sectional study among 119 male workers from natural sodium sulfate mines (Kelada and Euinton, 1978). Age of the subjects ranged from 17 to 58, exposure duration from two months to 31 years (no control group, study outcomes compared with "normal values", source not given). Dust exposures ranged from less than 5 mg/m3 to 150 mg/m3 during specific tasks (sampling method, strategy, number, frequency and timespan of sampling not given). General medical screening, lung function tests, blood pressure, skin condition, gastro-intestinal functioning, serum sodium, calcium, potassium chloride and sulfate content were all within normal ranges (i.e. presumably as found in the general population). Mean urinary excretion of inorganic sulfate exceeded 2.2 g/liter in all workers and thirty percent of the workers excreted more than 3 g of inorganic sulfate per day, indicating massive uptake from recent exposure. The only subjective symptom indicated by the workers was nasal irritation and runny noses on exposure to dust.

An internal comparison between workers from this group with less than 10 years of exposure (n=77, mean age 28.0 +-10, mean exposure duration 3.1 $\pm$ 2.8 years) with those with more than 10 years exposure (n=42, mean age 45.5 $\pm$ 8.8, mean exposure duration 19.9 $\pm$ 3.6 years) did not show any differences that could not be explained by normal ageing processes There are differences between the group with longer and the group with shorter exposure, but these differences appear to be normal for the respective ages and are therefore attributed to the substantial age difference between groups rather than to exposure to sodium sulfate.No abnormalities were detected that could be explained by exposure to sodium sulfate. (The possibility of a "healthy worker effect" was not addressed in this study).

The study by Denisov and Tkachev (1990) also mentions exposure concentrations in working atmosphere. Shift averages of 88 mg/m3 are given, yet there is no mention of any clinical or biochemical effects on the workers.

Conclusion: A clear NOAEL cannot be derived from the available data. Tentatively a chronic NOAEL of >= 320 mg/kg/day may be deduced from a 27 / 44 week study and a sub-chronic NOAEL of 2000 mg/kg from a 28 day study in rats. Ruminating animals are at risk at much lower levels because of the potential formation of sulfide in the rumen. Since this substance has no discernable systemic toxicity, the tentative chronic NOAEL of >= 320 mg/kg in rats would seem to provide a reasonable margin of safety compared to the estimated daily intake of 453 mg/person/day or around 6.5 to 7.5 mg/kg/day (see 2.3.2)

3.1.6. Mutagenicity

In vitro studies

Table 7 Genetic toxicity in vitro with sodium sulfate

Ref. (year)	Species, Test type	Protocol	Doses	Result
Bayer AG, (1988)	*S. Typhimurium*, Ames test	Salmonella/ Microsome test	312-5000 µg with and without activation	Negative

Sodium sulfate has been shown to be without effect in the Ames test using various strains of *S. typhimurium* (TA1535, TA1537, TA100, TA98) both with and without S9 activation in a GLP standardised test.

In a paper describing cytogenicity studies with sodium bisulfite in human cultured lymphocytes, Meng and Zhang (1992) state that sodium sulfate did not increase the frequencies of chromosomal aberrations, sister chromatid exchanges or micronuclei , nor did it cause changes in mitotic index or cell cycle at concentrations ranging from 5 x 10-5 to 5 x 10-3 M. However, no data are shown and it is not clear from the study description how, when and why these determinations were made. Therefore this study is assigned reliability 4.

Based on the natural intra- and extracellular occurrence of the substance it can be concluded that sodium sulfate is highly unlikely to be mutagenic

3.1.7. Carcinogenicity

Valid standard carcinogenicity studies with sodium sulfate are not available. The carcinogenicity studies listed in Table 8 and described below are those involving the longest exposure to sodium sulfate. Their power to detect any carcinogenic potential that sodium sulfate might possess is extremely low

Table 8 Carcinogenicity studies with sodium sulfate

Ref. (year)	Test Type, Species, Strain	Duration, Frequency	Animal/group	Dose	Result
Blunck & Crowther (1975)	Carcinogenicity, Rat, Sprague-Dawley	27 and 44 weeks, daily	5 / Male	0.84 % in diet, 320-400 mg/kg/day	No mortality, no tumors
Toth (1987)	Carcinogenicity, Swiss albino mice	26 weeks, weekly	50 male, 50 female	31 µg in 0.01 ml sodium chloride (0.9%) per g body weight, s.c. injected	Tumor of subcutis and/or skin in 1% of the female and 4% in male.(normal for this strain in this lab)

In the study of Blunck and Crowther animals were fed an additional 0.84% sodium sulfate in the diet. Because of protocolled food restrictions, the actual additional dose could be calculated and was around 320-400 mg/kg /day. These animals served as controls for animals in which the enhancing effect was studied of the same amount of sodium sulfate on the carcinogenicity of various azo dyes. No carcinogenic effects (tumors) were observed in these control animals. No significant differences in overall body weight gain were observed during the study. Liver weight was not changed. No

evidence of hyperplastic and/or dysplastic change, and no cholangiofibrosis or mild cirrhosis was observed as compared to controls. In addition, no changes in the water or food intake was reported. In the experimental animals fed additional sodium sulfate together with carcinogenic azo dyes, the latency period of tumor development appeared to be reduced, supporting the hypothesis that sulfotransferase plays an important role in the activation of azo dyes.

In a study with mice (Toth, 1987), animals S.C. injected with 31 µg in 0.01 ml of saline per gram body weight (31 mg/kg bw) during 26 weeks served as controls for animals injected with a carcinogenic substance, 4-HMBD. The tumor incidences of the subcutis and skin and of tumors in other organs in the sodium sulfate injected animals were in the normal range observed in the historical untreated control Swiss mice in the same test laboratory.

Conclusion

The limited available data do not allow firm conclusions with respect to carcinogenicity of sodium sulfate. However, they do not contradict the notion that a substance that is abundantly present in and essential to the body, is unlikely to be carcinogenic.

3.1.8. Toxicity for Reproduction

Studies in Animals

Effects on Fertility

One study was found with reliability 4 (Non-standard protocol, non-GLP, insufficient data for assessment, in which 10 female mice per group were exposed to sulfate in the drinking water onwards from one week prior to mating with untreated males. Sodium sulfate concentrations in drinking water were 0 mg/l (distilled water control), 0 mg/l (Na control), .924 mg/l, 1848 mg/l, 3696 mg/l and 7.392 mg/l with sodium concentrations in the Na control and all sodium sulfate groups made identical by addition of $NaHCO_3$ as required.water concentrations correspond to calculated doses of around 140, 280, 560 and 1120 mg/kg/d. Dams with litters from each group were re-bred immediately after weaning. No effects on maternal weight gain, lactational performance, litter size, pup survival and weaning weight at maximum treatment levels over 2 parities were found. However, since it is stated in the paper that only animals with two subsequent litters were involved in the analysis, i.e. ultimately 4 animals/group, and full data on reproductive succes are not given, the effects on fertility cannot be properly assessed. (Andres & Cline, 1989).

The available data on fertility are quite limited but in view of the fact that the substance is abundantly occurring in the body, toxicity for reproduction is unlikely.

Developmental Toxicity

Table 9 Developmental toxicity/teratogenicity studies with sodium sulfate

Ref. (year)	Species, Strain	Protocol	Administration	Exposure time, frequency	Doses	Results
Arcuri & Gautieri (1973)	Mouse, CF-1	Other	SC, single injection	Day 8 or 9 of gestation, single dose	60 mg/kg bw	Increased maternal weight gain, normal litters/ litter size, statistically significant increase in delayed ossifications no other abnormalities,
Seidenberg et al (1986)	Mouse, ICR/SIM	other	gavage	day 8-12	2800 mg/kg bw	no maternal mortality, normal litters/litter size, 100% survival, no visible abnormalities (no necropsy) Increased litter weight on day 1 pn, normal on day 3

Two studies of limited validity were found in the literature. In the study of Arcuri and Gautieri, (1973), which was aimed at documenting teratogenic effects of morhine sulfate, atropine sulfate and physostigmine sulfate, sodium sulfate served as anion control, with sodium chloride as negative control. The study was well documented, with various endpoints (clinical observations, maternal weight ratio, uterine lef/righ horn fetal ratio and resorption ration, fetal weight, sex ratio, skeletal abnormalities, ,soft tissue abnormalities, more specifically exencephaly, cryptorchid test and axial skeletal fusions, but covered only the 8-9 day period of gestation for exposure and the dose of 60 mg/kg was relatively small. There was a statistically significant increase in skeletal abnormalities, described as delayed ossification in the phalanges, sternebrae and skull. Such variations are quite common in tests with rodents and, in the absence of skeletal malformations, generally not regarded as indicative of developmental toxicity. No abnormalities for any of the other end-points were reported.

In another study (Seidenberg *et al.,* 1986) the developmental effects of sodium sulfate in the mouse were examined as part of a validation effort of a developmental screening test. The test substance was administered (2800 mg/kg/day) by gavage on gestation days 8 through 12. No mortality, an unchanged average weight gain, and normal number of litters and neonates/litter were found. A 100 % perinatal survival was found, with an increased postnatal weight at day 1, normal weight at day 3 in the absence of externally visible abnormalities. In a later paper (Seidenberg *et al*, 1987) that summarised the results of this validation test, the outcome of the screening test was considered positive for sodium sulfate, based solely on the increased postnatal weight on day 1 post-partum. However, the significance of such an effect, in the absence of any other effect, is unclear and the reasons for taking this as a positive result are not given

In a summary report (Paterson *et al.*, 1979) the effects of various concentrations of sulfate in drinking water were described on the pregnancy and lactation of sows and gilts (primiparous sows), 58 in total, divided in three groups. Sodium sulfate in drinking water was given in concentrations of 320, 1820 and 3320 mg/l respectively from 30 days post-breeding through 28 days of lactation (body weights and water consumption not given). No effects were found on gestation and lactation in terms of weight gain during gestation, number or weight of piglets at birth or development during lactation. 41 of the newborn piglets, equally representing all treatment groups, were taken from the litters. These newborns were split in three groups and were raised for 28 days on a 18% protein diet plus drinking water containing either 3000 mg/l added sulfate from sodium sulfate, 3000 mg/l

sulfate from magnesium/sodium sulfate or no sulfate added; no differences in development were found between the groups. The study is of not assignable validity.

Studies in Humans

No data.

Conclusion

The limited available data give no indication that sodium sulfate is toxic for reproduction. With regard to the natural occurrence of the substance in the body, developmental toxicity is very unlikely.

3.2 Initial Assessment for Human Health

Sodium sulfate is not known to have acute oral effects other than laxative effects, caused by its hygroscopy. It is not irritating to the skin and is a slight eye irritant. The substance is unlikely to be sensitiser. Oral repeated dose toxicity is limited to diarrhoea and subsequent dehydration at dosages far higher than the normal daily intake from food and water. Ruminant animals may develop serious brain disorders from high sulfate content in food and water due to formation of sulfides in the rumen but this is not relevant to humans. Limited inhalation data from humans do not indicate serious concerns with respect to acute or chronic dust inhalation. There is limited data on reproduction which give not indication that sodium sulfate is toxic for reproduction. There is no valid data on carcinogenicity. However, given the natural occurrence in the body of this substance which is essential to life, carcinogenicity and toxicity for reproduction is not an issue.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute toxicity

Effects in fish

Three studies were reliable with restrictions as the studies were not performed according to standardised guidelines, but were performed using an adequate scientific methodology and described with enough details (see table 10). No studies were performed under GLP. All three tests were performed in reconstituted water. In two tests a concentration range of the test substance and determination of test parameters are described. The study with *Pimephales promelas* was performed according to EPA guideline with determination of test substance concentrations (ion-chromatography). During two studies (with *Lepomis macrochirus*, Trama (1954) and *Pimephales promelas*, Mount *et al.* (1997)) the critical confounding factors pH and oxygen were within acceptable ranges, while in the third study (with *Lepomis macrochirus*, Patrick *et al.* (1968)) these parameters were not indicated. The acute toxicity for fish is very low, with LC_{50} values far above 1,000 mg/l for both species, *Lepomis macrochirus* and *Pimephales promelas*.

Table 10 Validated data (validity 1 or 2) on acute toxicity to fish.

	Ref. (year)	Species	Method/ Protocol	Results
Acute/ prolonged toxicity to fish	Trama (1954)	*Lepomis macrochirus*	Concentration range in reconstituted water	LC_{50} 96h = 13,500 mg/l; LC_0 = 8,700 mg/l.
	Patrick *et al.* (1968)	*Lepomis macrochirus*	96 hours test, based on Cairns *et al.* (1964)	LC_{50} 96h = 13,500 mg/l
	Mount *et al.* (1997)	*Pimephales promelas*	96 hours test, based on EPA/600/4-90/ 027 (1991) guideline.	LC_{50} 96h = 7,960 mg/l

Effects in aquatic invertebrates

Only one reference describing a *Daphnia magna* test in 48 hours (Mount *et al.,* 1997) was assigned validity 2. This test was not performed under GLP, but was performed according to EPA guideline, with determination of test substance (ion-chromatography), and details on test performance and statistics.

As indicated the toxicity of sodium sulfate for *Daphnia* is very low, with an EC_{50} value far above 1000 mg/l.

Table 11 Validated data (validity 2) on acute toxicity to aquatic invertebrates.

	Ref. (year)	Species	Method/Protocol	Results
Acute toxicity to aquatic invertebrates	Mount *et al.* (1997)	*Daphnia magna*	48 hours test, based on EPA/600/4-90/ 027 (1991) guideline.	EC_{50} 48h = 4,580 mg/l; EC_{50} 24 h = 6,290 mg/l.

Effects in aquatic plants / algae

The only valid study was a 120-hour growth test with *Nitzschia linearis* (Patrick *et al.,* 1968). It was classified as valid with restrictions, as a different species was used and a greater test duration than recommended in the OECD-guidelines. An EC_{50} value of 1,900 mg/l was calculated.

Table 12 Validated data (validity 2) on acute toxicity to aquatic plants.

	Ref. (year)	Species	Method/Protocol	Results
Acute toxicity to aquatic plants	Patrick *et al.* (1968)	*Nitzschia linearis*	120 hours test, based on Cairns *et al.* (1964)	EC_{50} 120h = 1,900 mg/l

Effects in sediment dwelling organisms

There are four studies found with sediment dwelling organisms (*Lymnea* and Polychaeta) of which the publications are not available. There was one study found that was considered valid with restrictions. It was an acute semi static test with *Trycorythus sp.* performed in river water (Goetsch and Palmer, 1997). The method used was not a standard method but it was described in detail and considered appropriate. The EC_{50} values for *Lymnea sp*. and *Lymnea sp.* eggs are 799 and 3,553 mg/l respectively. The toxicity for the marine worm *Ophryotrocha labronica* was determined at 5.4 mg/l (Saliba and Ahsanullah, 1973), which deviates enormously from the effects to other

invertebrates. As the original publication(s) are not available, conclusions on the sensitivity of soil dwelling organisms cannot be drawn.

Three studies on mosquito and mosquito larvae (*Culex sp*.) were found (Dowden, 1961; Dowden and Bennet, 1965), two were not available and one was documented insufficiently. The toxicity data of these tests indicate that the toxicity of sodium sulfate for these terrestrial organisms is low (EC_{50} values of > 1000 mg/l for both adults and larvae).

Chronic Toxicity

No data were found in the literature search for long term toxicity.

Toxicity to Microorganisms

Four studies on activated sludge bacteria, motile protozoa and stalked ciliates were reliable with restrictions as the studies were not performed according to standardised guidelines, but were described with enough details. There was no effect on the microorganisms up to approximately 8 g/l (Tokuz & Eckenfelder (1979), Tokuz (1986), Gilli & Comune (1980)). Two studies on the toxicity to *Pseudomonas fluorescens and Pseudomonas putida* were found but were not available.

Table 13 Validated data (validity 1 or 2) on acute toxicity to microorganisms.

	Ref. (year)	**Species**	**Method/Protocol**	**Results**
Acute toxicity to micro-organisms	Tokuz & Eckenfelder (1979), Tokuz (1986)	Bacteria in activated sludge	37 days test with increasing concentration	NOEC ca. 26 g/l
	Tokuz & Eckenfelder (1979), Tokuz (1986)	Motile protozoa in activated sludge	37 days test with increasing concentration	NOEC ca. 26 g/l
	Tokuz & Eckenfelder (1979), Tokuz (1986)	Stalked ciliates in activated sludge	37 days test with increasing concentration	NOEC ca. 8 g/l
	Gilli & Comune (1980)	Activated sludge	ca. 40 days test with increasing concentration	NOEC ca. 30 g/l

With respect to the high NOEC values sodium sulfate is not expected to be hazardous for activated sludge.

4.2 Terrestrial Effects

Effects in soil dwelling biota

There are no data available

Table 14 Validated data (validity 2) on acute toxicity to sediment dwelling organisms.

	Ref. (year)	Species	Method/Protocol	Results
Acute toxicity to sediment dwelling organisms	Goetsch and Palmer (1997)	*Trycorythus sp.*	96 hours semi static test in river water	LC_{50} 96h = 0.66 g/l

Effects in terrestrial plants

There were six studies found on terrestrial plants. Three (Navarro, *et al.*, 2002; Banet, *et al.*, 1996; Egan and Ungar, 1998) were considered invalid because it was not clear at what concentrations significant effects occurred. In two of these studies the test concentration was expressed in osmotic potential and it is not clear what the equivalent sodium sulfate concentration is. Three studies were valid with restrictions. The methods were not standardised, but described in detail. *Pinus banksiana* appeared to be the most sensitive to sodium sulfate and the roots appeared to be the most sensitive part of the plant. Root length and the number of lateral roots were affected at 10 mM (1.4 g/l) (Croser, *et al.,* 2001).

Table 15 Validated data (validity 1 or 2) on toxicity to terrestrial plants

	Ref. (year)	Species	Method/Protocol	Results
Toxicity to terrestrial plants	Croser, *et al.* (2001)	*Picea glauca*	Test with seeds in sand	Emergence: decrease in 20 mM and higher Survival: decrease in 50 mM and higher Root length: reduction in 20 mM and higher Lateral roots: decrease in 50 mM and higher Leaf necrosis: in 50 mM and higher Fresh weight: reduced in 50 mM and higher Photosynthesis: not changed
	Croser, *et al.* (2001)	*Pinus banksiana*	Test with seeds in sand	Emergence: decrease in 20 mM and higher Survival: decrease in 50 mM and higher Root length: reduction in 10 mM and higher Shoot length: reduced in 50 mM and higher Lateral roots: decrease in 10 mM and higher Leaf necrosis: in 50 mM and higher Fresh weight: reduced in 50 mM and higher PHOTOSYNTHESIS: NOT CHANGED
	Croser, *et al.* (2001)	*Picea mariana*	TEST WITH SEEDS IN SAND	Emergence: decrease in 100 mM and higher Survival: decrease in 100 mM and higher Shoot length: reduced in 50 mM and higher Root length: reduction in 20 mM and higher Lateral roots: decrease in 50 mM and higher Leaf necrosis: no necrosis Fresh weight: reduced in 50 mM and higher Photosynthesis: not changed

4.3 Other Environmental Effects

No data on other environmental effects are available.

4.4 Initial Assessment for the Environment

For short term toxicity many studies were performed, but most were not considered reliable. There were no studies with reliability 1, but for every SIDS endpoint at least one study was found which was valid with restrictions. Algae were shown to be the most sensitive to sodium sulfate; EC_{50} 120h = 1,900 mg/l. For invertebrates *(Daphnia magna)* the EC_{50} 48h = 4,580 mg/l and fish appeared to be the least sensitive with a LC_{50} 96h = 7,960 mg/l for *Pimephales promelas*.

Activated sludge showed a very low sensitivity to sodium sulfate. There was no effect on the stalked ciliates in the activated sludge up to 8 g/l, the bacteria and motile protozoa showed no effect up to 26 g/l.

Sodium sulfate is not very toxic to terrestrial plants. *Picea banksiana* was the most sensitive species. The roots appeared to be the most sensitive part of the plant and showed effects at 1.4 g/l. Sediment dwelling organisms were not very sensitive either, with an LC_{50} 96h = 660 mg/l for *Trycorythus sp*.

Overall it can be concluded that sodium sulfate has no acute adverse effect on aquatic and sediment dwelling organisms. For terrestrial plants it is not very toxic either.

Sulfate can be reduced anaerobically by sulfate reducing bacteria to sulfide, but will not be aerobically degraded.

No data were found in the literature search for long term toxicity. The acute studies all show LC50s and EC50s for sodium sulfate that are substantially higher than the EU (European Union, 1967) and GHS (United Nations, 2003) threshold for classification as dangerous for the environment (100 mg/l). The calculated BCF is 0.5, which means that no bioaccumulation is expected. From these results it can be considered that no further chronic studies are required.

5 RECOMMENDATIONS

Because of low toxicity to humans and the environment, the chemical is of low priority for further work.

6 REFERENCES

References cited in SIAR:

Adams, A.W., Cunningham, F.E., Munger, L.L. (1975). Some effects on layers of sodium sulfate and magnesium sulfate in their drinking water. Poultry Sci. 54(3):707-714.

Andres, C.J. and Cline, T.R. (1989). Influence of Sulfate in Drinking Water on Mouse Reproduction during two Parities. J. Anim. Sci. 67:1313-1317.

Arcuri, P. and Gautieri, F. J. (1973). Morphine-induced fetal malformations. 3. Possible mechanisms of action. Pharmaceut. Sci. 62(10): 1626-1634.

Banet, G., Wininger, S., Badani, H., Ben–Dor, B., Friedman and Y., Kapulnik, Y. (1996). Toxic and osmotic effects of salinity on growth and nodulation of Medicago sativa. Symbiosis. 21:209-222.

Bauer, J.H. (1976). Oral administration of radioactive sulfate to measure extracellular fluid space in man. J. Appl. Physiol. 40(4):648-650.

Bayer, A.G. (1988). Salmonella/Microsome test to evaluate for point mutagenic effects. Unpublished report. Study no. T9027163, Report no. 16839, Wuppertal, Germany.

Bayer, A.G. (1991). Study for skin and eye irritation/corrosion in rabbits. Unpublished report. Study no. T7039997, Report no. 20338, Wuppertal, Germany.

Blunck, J.M. and Crowther, C.E. (1975). Enhancement of azo dye carcinogenesis by dietary sodium sulphate. Europ. J. Cancer. 11(1): 23-31.

CFTA (1976). Allergic contact sensitization test (Test No. <intentionally blanked-out>.003-76) on Bubble Bath 60082-C containing 80.8% Sodium Sulfate. Unpublished report. Study no. <intentionally blanked-out>.003-76, Report no. Not stated.

Chapmann and Hall (1992). Dictionary of Inorganic Compounds. Vol.3.

Chemiekaarten (2000). pp. 921, C–0979, The Netherlands.

Chein, L., Robertson, H., Gerrard, J.W. (1968). Infantile gastroenteritis due to water with high sulfate content Canadian Medical Association Journal 99: 102-104.

Cocchetto, D.M. and Levy, G. (1981). Absorption of orally administered sodium sulfate in humans. J. Pharm. Sci. 70(3):331-333.

College of Biological Sciences. Lecture 23: The Sulfur Cycle. Available: http://www.biosci.ohiostate.edu/~mgonzalez/Micro521/23.html. [Accessed: 22-09-2005]

Croser, C., Renault, S., Franklin, J. and Zwiazek, J. (2001). The effect of salinity on the emergence and seedling growth of Picea mariana, Picea glauca and Pinus bankciana. Environmental pollution. 115(1):9-16.

Denisov, Y.N. and Tkachev, P.G. (1989). Hygienic characteristics of small doses of sodium sulfate after its inhalation. Gigiena i sanitaria. 4:69-71.

Denisov, Y.N., and Tkachev, P.G. (1990). Health aspects of sodium salts of sulfurous and sulfuric acids as environmental pollutants. Gigiena i sanitariia. 9:11-13.

Diem, K. (ed.) (1972). Documenta Geigy scientific tables. 6th edition. J.R. Geigy S.A., Basle, Switzerland. 533 pp.

Dowden, B.F. (1961). Cumulative toxicities of some inorganic salts to Daphnia

maena as determined by median tolerance limits. Proc. La. Acad. Sci. 23:77-85.

Dowden, B.F. and Bennett H.J. (1965). Toxicity of selected chemicals to certain

animals. J. Water Pollut. Control Fed. 37(9):1308-1316.

ECETOC (1999). Skin and respiratory sensitisers: Reference chemical data bank. ISSN 0773-8072-77. ECETOC, Brussels.

Egan, T.P. and Ungar, I.A. (1998) Effect of different salts of sodium and potassium on the growth of Atriplex prostrata (Chenopodiaceae). Journal of plant nutrition, 21(10):2193–2205.

Environment Canada (1985) Tech Info for Problem Spills: Sodium sulfate.

EPI Suite (2000). U.S. Environmental Protection Agency.

EU Dangerous Substances Directive 67/548/EEC, Annex VI.

Gilli, G. And Comune, P.M. (1980). Effetti della salinità su sistemi biologici. Inquinamento 22(100):31-35

Gilman, A.G., Goodman, L.S., Gilman, A. (eds). (1980). Goodman and Gilman's The Pharmalogical Basis of Therapeutics. 6th ed. New York: Macmillan Publishing Co. Inc. p.1005.

Goetsch, P.A. and Palmer, C.G. (1997). Salinity tolerance of selected macroinvertebrates of the Sabie river, Kruger national park, South Africa. Arch. Environ. Contam. Toxicol. 32:32-41.

Gould, D.H., McAllister, M.M., Savage, J.C., Hamar, D.W. (1991). High sulfide, concentrations in rumen fluid associated with nutritionally induced polioencephalomalacia in calves. Am. J. Vet. Res.51(7):1164-1169.

Greben, H.A., Maree, J.P., Mnqanqeni, S. (2000). Comparison between sucrose, ethanol and methanol as carbon and energy source for biological sulphate reduction. Water Science and Technol. 41(12):247-253.

Handbook of chemistry and Physics (1997-1998). 78th ed. CRC press, pp. 4-87.

Hawley, G.G. (1981). The Condensed Chemical Dictionary, 10th ed. New York, Van Nostrand Reinhold Co. USA.

Health Canada, November 1987 (updated September 1994), Sulphate. Avialable: http://www.hc-sc.gc.ca/. [Accessed 09-22-2005]

Heizer, W.D., Sandler, R.S., Seal, E., Murray, S.C., Busby, M.G., Schliebe, B.G., Pusek, S.N. (1997). Intestinal effects of sulfate in drinking water on normal human subjects. Digestive Diseases and Sciences 42(5):1055-1061.

Henkel (1971). Orientierende toxizität. Unpulished

Henry, J.G. and Prasad, D., (2000). Anaerobic treatment of landfill leachate by sulphate reduction. Water Science and Tecnol. 41(3):239-246.

Hitchcock, D.R. (1975). Biogenic contribution to atmospheric sulfate levels. Water's interface with energy, air and solids: proceedings of the second national conference on complete water-reuse, Chicago, Illinois, May 4-8, 1975. pp 291-310.

ICRP (1984). International Commission on Radiological Protection: Report no. 23: Report of the Task Group on Reference Man. Pergamon Press, Oxford, UK.

Kelada, F. and Euinton, L.E. (1978). Health effects of long term exposure to sodium sulfate dust. J. Occup. Med. 20(12):812-814.

Krijgsheld, K.R., Frankena, H., Scholtens, E., Zweens, J. and Mulder, G.J. (1979). Absorption, serum levels and urinary excretion of inorganic sulfate after oral administration of sodium sulfate in the conscious rat. Biochim. Biophys. Acta, 586(3):492-500.

Last, J.A. Purnendu, K.D., Ethinson, J.R. (1980). Inhalation Toxicology of Sodium Sulfite Aerosol in Rats. Toxicol. Appl. Pharmacol. 55:229-234.

Laury, N.A. (1927). Hydrochloric acid and sodium sulfate. American Chemical Society. Monograph series 36. Chemical catalog Co, USA.

Lenntech Water treatment & air purification Holding B.V. (2003) Lenntech: Sulfur cycle. Available: http://www.lenntech.com/sulfur-cycle.htm. [Accessed 2003].

Meng, Z.Q. and Zhang, L.Z. (1992). Cytogenetic damage induced in human lymphocytes by sodium bisulfite. Mutation Research. 298:63-69

Merck 12ed (1996). pp. 1483, Merck&Co, NJ, USA.

Ministry of water, land and air protection (2000). Ambient water quality guidelines for sulfate. Overview report. British Columbia, Canada. Available:

http://wlapwww.gov.bc.ca/wat/wq/BCguidelines/sulphate.html [Accessed 09-22-2005]

Moinuddin, J.F., Wing-Tsit Lee, H. (1960). Alimentary, blood and the other changes due to feeding MnSO4, MgSO4 and Na2SO4. American Journal of Physiology. 199(1): 77-83.

Morris, M.E. and Levy, G. (1983). Serum concentration and renal excretion by normal adults of inorganic sulfate after acetaminophen, ascorbic acid, or sodium sulfate. Clin. Pharmacol. Ther. 33(4):529-536.

Mount, D.R., Gulley, D.D., Hockett, J.R., Garrison, T.D., Evans, J.M. (1997). Statistical models to predict the toxicity of major ions to Ceriodaphnia dubia, Daphnia magna, and fathead minnows (Pimephales promelas). Environ. Toxicol. Chem. 16(10):2009-2019.

Navarro, J.M., Garrido, C., Carvajal, M and Martinez, V. (2002). Yield and fruit quality of pepper plants under sulphate and chloride salinity. Journal of Horticulture and Biotechnology. 77(1):52–57.

Niles, G.A. , Morgan, S., Edwards, W.C. , Lalman, D. (2002). Effects of Dietary Sulfur Concentrations on Incidence and Pathology of Polioencephalomalicia in Beef Calves. Vet. Human Toxicol. 44(2):70-72.

Okahara. (1963). Food Hygiene Journal (Shokuhin Eiseigaku Zassi) 4:15.

Paterson, D.W., Whalstrom, R.C., Libal, G.W. Olson, O.E. (1979). Effects of sulfate in water on reproduction in swine and young pig performance. J.Anim. Sci. 49(S1):105.

Patrick, R.J., Cairns, J., Scheier, A. (1968). The relative sensitivity of diatoms, snails, and fish to twenty common constituents of industrial wastes. The Progressive Fish-Culturist. 30(3):137-140.

Percy, A.K. and Yaffe, S.J. (1964). Sulfate metabolism during mammalian development. Pediatrics. 33(6):965-974.

Research Triangle Inst. (1998). Toxicological profile for sulfur trioxide and sulfuric acid. U.S. Department of Commerce, National Technical information Service.

Remington's pharmaceutical sciences (1980).16th ed. Easton, Pennsylvania: Mack publishing co.

Sackner, M.A., Ford, D. Kim, C. (1979). Effect of brief exposure to high concentrations of sodium chloride and sodium **sulfate** aerosols with mass median aerodynamic diameter of 0.5 μm on pulmonary function of normal and asthmatic adults. American Review of Respiratory Disease. 119(4):.233.

Saliba, L.J. and Ahsanullah, M. (1973). Acclimation and Tolerance of Artemia salina and Ophryotrocha labronica to Copper Sulphate. M. Mar.Biol. 23(4):297–302.

Schlessinger, R.B. (1984). Comparative irritant potency of inhalated sulfate aerosols–Effects on bronchial mucociliary clearance. Environ. Res. 34(2):268-279.

Seidenberg, J.M., Anderson, D.G., Becker, R.A. (1986). Validation of an in vivo developmental toxicity screen in the mouse. Teratogenesis, Carcinogenesis and Mutagenesis. 6:361-374.

Seidenberg, J.M. and Becker, R.A. (1987). A summary of the results of 55 chemicals screened for developmental toxicity in mice. Teratogenesis, Carcinogenesis, mutagenesis. 7:17-28.

Sibblad, I.R. and Cave, N.A. (1976). The responses of chicks to ammonium, calcium, magnseium, potassium and sodium sulphates and to ammonium and potassium carbonates. Poult. Sci. 55:2209–2213.

SSPA (2003) Internal report.

Tokuz, R.Y. and Eckenfelder, W.W. (1979). The effect of inorganic salts on the activated sludge process performance. Water Res. 13(1):99-104.

Tokuz, R.Y. (1986). The effect of high salinity on activated sludge effluent quality. Curr. Pract. Environ. Sci. Eng. 2:143-154.

Toth, B. (1987). Cancer Induction by the sulfate form of 4-(Hydroxymethyl)-benzenediazonium ion of Agaricus bisporus. In Vivo 1:39-42.

Trama, F.B. (1954). The acute toxicity of some common salts of sodium potassium and calcium to the common Bluegill. (Lepomis Macrochirus Rafinesque). Proc. Acad. Nat. Sci. Philadelphia. 106: 185-205.

Ullmann's Encyclopedia of Industrial Chemistry (2004). 7th ed. John Wiley & Sons, Inc.

United Nations (2003). The Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

United States Environment Program. Global Environmental Monitoring System. Freshwater Quality Program (GEMS)."Salts and Salinization of Surface Waters". Available: http://www.gemswater.org/atlas-gwq/salts-e.html. [Accessed 09-22-2005]

US-EPA (1999). Health effects from exposure to sulfate in Drinking water Workshop CDC protocol #1779; Office of Water 4607; EPA 815-R-99-002.

Upton, P.K. and L'Estrange, J.L. (1976). Effects of high intakes of dietary sodium sulphate and sodium chloride on voluntary food intake of rats. Proc. Nutr. Soc. 20A–21A.

U.S. Geological Survey (2000). Mineral Commodity Summaries. February 2000.

Veenhuizen, M.F., Shurson, G.C., Kohler, E.M. (1992). Effect of concentration and source of sulfate on nursery pig performance and health. JAVMA. 201(8):1203-1208.

WHO (2003). Sulfate in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality. Geneva, World Health Organization (WHO/SDE/WSH/03.04/114).

References checked but not used

Bird, P.R. (1972). Sulfur metabolism and excretion studies in ruminants. Secretion of sulfur and nitrogen in sheep pancreatic and bile fluids.Aust. J. Biol. Sci. 25:817.

Dziewiatkowski, D.D. (1962). Intracellular synthesis of chondroitin sulfate. J. Cell Biol. 13: 359.

Dziewiatkowski, D.D. (1951). Isolation of chondroitin sulfate-35S from articular cartilage of rats. J. Biol. Chem. 189:187.

Dziewiatkowski, D.D. (1970). Sulfur in animal nutrition. In: Proceedings of a Symposium on Sulfur in Nutrition. D.H. Muth and J.E. Oldfield (eds.). Ari Publishing Co., Westport, CT.

Kristensen P. (1993). Inorganic acid aerosols. Arbete och Halsa, 1, 7-54.

Laidlaw, J.C. and Young, L. (1953). A study of ethereal sulfate formation in vitro using radioactive sulfate. Biochem. J., 54:142.

Mulder, G.J. (ed.). (1981). Sulphation of drugs and related compounds.CRC Press, Boca Raton, FL.

Mulder, G.J. and Kevelmans, K. (1978). The metabolism of inorganic sulfate in the isolated perfused rat liver. Effect of sulfate concentration on the rate of sulphation by phenolsulphotransferase. Biochem. J., 176: 959.

Murer, H. (1988). Transport of sulfate and phosphate in small intestine and renal proximal tubule: methods and basic properties. Comp. Biochem. Physiol. 90A:749.

Rosner G. (1994) Fraunhofer-Institut fur Toxikologie und aerosolforschung.

Whiting, S.J. and Cole, D.E. (1986) Effect of dietary anion composition on acid-induced hypercalciuria in the adult rat. J. Nutr., 116: 388.

I U C L I D

D a t a S e t

Existing Chemical	ID: 7757-82-6
CAS No.	7757-82-6
EINECS Name	sodium sulphate
EC No.	231-820-9
TSCA Name	Sulfuric acid disodium salt
Molecular Formula	H2O4S.2Na

Producer Related Part	
Company:	Akzo Nobel Salt and Basic Chemical Division
Creation date:	06-SEP-2001
Substance Related Part	
Company:	Akzo Nobel Salt and Basic Chemical Division
Creation date:	06-SEP-2001
Memo:	OECD HPV Chemical Programme, SIDS DOssier, approved at SIAM 20 (19-22 April 2005)

Printing date:	07-AUG-2006
Revision date:	
Date of last Update:	07-AUG-2006

Number of Pages:	123

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 Applicant and Company Information

24-OCT-2001

1.0.2 Location of Production Site, Importer or Formulator

1.0.3 Identity of Recipients

1.0.4 Details on Category/Template

1.1.0 Substance Identification

IUPAC Name: sodium sulfate
Mol. Formula: Na2SO4
Mol. Weight: 142.04
Petrol Class: other

22-JUN-2005

1.1.1 General Substance Information

Purity type: other
Substance type: inorganic
Physical status: solid
Purity: > 99.5

Source: United States Pharmacopeial (2000)
31-OCT-2001

1.1.2 Spectra

1.2 Synonyms and Tradenames

Alcan recovered Cryolite

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Bisodium sulfate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Dibasic sodium sulfate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Dinatriumsulfat

Source: Henkel KGaA Duesseldorf
01-NOV-2001

Disodio monosolfato

Source: Luigi Stoppani SpA Milano
30-OCT-2001

Disodium monosulfate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Disodium sulfate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Disodium sulphate

Source: Akzo Nobel Chemicals, Amersfoort
Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

E 514

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Kemsol

Source: Henkel KGaA Duesseldorf
01-NOV-2001

Na-sulfat

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Natrii sulfas

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Natrium sulfuricum

Source: SYNTANA Handelsges. Muhlheim-Ruhr
30-OCT-2001

natriumsulfaatti

Source: Sateri Oy Valkeakoski
30-OCT-2001

Natriumsulfat rein

Source: Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
Faserwerk Kelheim GmbH Kelheim
30-OCT-2001

Natriumsulfate wasserfrei

Source: Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
Faserwerk Kelheim GmbH Kelheim
30-OCT-2001

Ningunoso

Source: CRIMIDESA Madrid
01-NOV-2001

Sal disodica del acido sulfurico

Source: FMC FORET SA Barcelona
30-OCT-2001

Salt cake

Source: Courtaulds Fibres Limited Grimsby
Henkel KGaA Duesseldorf
Occidental Chemical Corporation Niagara Falls, NY 14302-0728
30-OCT-2001

saureregualator E 514

Source: Henkel KGaA Duesseldorf
01-NOV-2001

Schwefelsaure, di-Na-Salz

Source: Henkel KGaA Duesseldorf
30-OCT-2001

Schwefelsaure-Natriumsalz

Source: MERCK Darmstadt
30-OCT-2001

Sodium sulfate (anydyrous)

Source: Amway Europe Zaventem
30-OCT-2001

Sodium sulphate anhydrous

Source: Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
30-OCT-2001

Solfato di sodio

Source: Laporte Italia SPA Divisione SILO Torino
30-OCT-2001

Sulfate de Sodium

Source: Produits Chimiques de Loos Loos
30-OCT-2001

Sulfato de sodio anidro

Source: Industrias Lever Portugesa LDA. Sacavem; ECB - Existing Chenicals Ispra (VA); Henkel KGgA Dueseldorf
01-NOV-2001

Sulfato sodico

Source: FMC FORET SA Barcelona
01-NOV-2001

Sulfato sodico anhidro

Source: S.A. Sulquisa Bilbao
30-OCT-2001

Sulfuric acid, disodium salt

Source: Henkel KGaA Duesseldorf
Henkel Hellas S.A. Atalanti
Novo Nordisk A/S Bagsvaerd
30-OCT-2001

Thenardite

Source: Chemie GmbH Bitterfeld-Wolfen Wolfen
30-OCT-2001

Trona

Source: Chemie GmbH Bitterfeld-Wolfen Wolfen
01-NOV-2001

1.3 Impurities

1.4 Additives

1.5 Total Quantity

Quantity: ca. 4600000 tonnes produced in 1999

22-SEP-2005 (100)

Quantity: ca. 4928000 tonnes produced in 1991

22-SEP-2005 (94)

1.6.1 Labelling

30-OCT-2001

1.6.2 Classification

Classified: no classification required (no dangerous properties)

30-OCT-2001

1.6.3 Packaging

1.7 Use Pattern

Type: industrial
Category: Agricultural industry

30-OCT-2001

Type: industrial
Category: Basic industry: basic chemicals

30-OCT-2001

Type: industrial
Category: Chemical industry: used in synthesis

30-OCT-2001

Type: industrial
Category: Metal extraction, refining and processing of metals

30-OCT-2001

Type: industrial
Category: Paints, lacquers and varnishes industry

30-OCT-2001

Type: industrial
Category: Paper, pulp and board industry

30-OCT-2001

Type: industrial
Category: Personal and domestic use

30-OCT-2001

Type: industrial
Category: Public domain

30-OCT-2001

Type: industrial
Category: Textile processing industry

30-OCT-2001

Type: industrial
Category: other: Detergent industry

30-OCT-2001

Type: industrial
Category: other: Glassindustry

30-OCT-2001

Type: use
Category: Cleaning/washing agents and disinfectants

30-OCT-2001

Type: use
Category: Conductive agents

30-OCT-2001

Type: use
Category: Fillers

30-OCT-2001

Type: use
Category: Food/foodstuff additives

30-OCT-2001

Type: use
Category: Intermediates

30-OCT-2001

Type: use
Category: Laboratory chemicals

30-OCT-2001

Type: use
Category: Pesticides

30-OCT-2001

Type: use
Category: Pharmaceuticals

30-OCT-2001

Type: use
Category: Process regulators

30-OCT-2001

Type: use
Category: Semiconductors

30-OCT-2001

1.7.1 Detailed Use Pattern

1.7.2 Methods of Manufacture

1.8 Regulatory Measures

01-NOV-2001

1.8.1 Occupational Exposure Limit Values

Type of limit: MAC (NL)

Remark: not determined
Reliability: (4) not assignable
no data available
22-SEP-2005 (24)

Type of limit: OES (UK)

Remark: O.E.L. : 10 mg/m3 8hr. TWA total inhalable dust.
O.E.L. : 5 mg/m3 8hr. TWA total respirable dust.
Reliability: (4) not assignable
Original reference not available
22-SEP-2005 (75)

1.8.2 Acceptable Residues Levels

1.8.3 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 0 (generally not water polluting)

22-SEP-2005 (19)

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 0 (generally not water polluting)

22-SEP-2005 (2)

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 0 (generally not water polluting)

19-JUN-2003 (18)

1.8.4 Major Accident Hazards

1.8.5 Air Pollution

1.8.6 Listings e.g. Chemical Inventories

1.9.1 Degradation/Transformation Products

1.9.2 Components

1.10 Source of Exposure

Source of exposure: Human: exposure by production
Exposure to the: Substance

Remark: Sodium sulfate in solution is a by product from the manufacture of Sodium Dichromate.
The solution, after separation of the minimal Sodium Dichromate content, is evaporated to saturation.The resultant crystals of Sodium sulfate are separated from solution by centrifuge prior to drying.
22-SEP-2005 (17)

1.11 Additional Remarks

Memo: Clinical use as laxative

Remark: Sodium sulfate, recommended dose:
300 mg/kg up to 20 grams maximum for an adult.
Probable mode of action: fluid retention caused by the hygroscopic action of unresorbed sodium sulfate in the large intestine.
Reliability: (4) not assignable
textbook reference
13-JAN-2005 (41)

Memo: Drinking Water Quality Standards

Remark: Sulfate Maximum Acceptable Concentration: 200 mg/l
Sulfate Maximum Allowable Concentration : 250 mg/l
01-NOV-2001 (74)

Memo: Drinking Water Quality Standards

Remark: The taste threshold concentrations for sodium sulfate is 250 - 900 mg/l.
16-NOV-2001 (3)

Memo: Drinking Water Quality for Poultry

Remark: Sulfate : Level considered average : 125 mg/l
Sulfate : MAC : 250 mg/l
22-JUN-2005 (88)

Memo: Ground water Quality Standards for Drinking water purposes

Remark: Sulphate Maximum Acceptable Concentration: 200 mg/l
Sulphate Maximum Allowable Concentration : 250 mg/l
01-NOV-2001 (74)

Memo: Secondary Maximum Contaminant Level

Remark: SMCL value : 250 mg/l Sulfate
01-NOV-2001 (76)

Memo: Speciation of urinary sulfur

Remark: 85% of urinary sulfur as s inorganic sulfates
10% as organic sulfates,
5% as conjugated alkyl sulfates
Reliability: (4) not assignable

textbook reference
13-JAN-2005 (31)

Memo: Sulfate elimination

Remark: Daily elimination of sulfate in human urine: ~ 800 mg as elemental sulfur are
Daily elimination of sulfate in human feces: : ~ 140 mg
Reliability: (4) not assignable
textbook reference
13-JAN-2005 (57)

Memo: Water Quality Guidelines for Sulfate

Remark: Drinking water (Aesthetics) : 500 mg/l dissolved sulfate
Freshwater Aquatic Life : 100 mg/l sulfate maximum concentration, 50 mg/l sulfate Alert level.
22-JUN-2005 (3)

1.12 Last Literature Search

1.13 Reviews

2.1 Melting Point

Value: = 800 degree C

Reliability: (2) valid with restrictions
Results from handbook
01-NOV-2001 (67)

Value: = 884 degree C

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available.
However, there is no need to perform such studies because:
- Exisiting data are available from at least 3 different sources from which the results are not conflicting.
07-NOV-2001 (101)

Value: ca. 884 degree C

Reliability: (2) valid with restrictions
Results from handbook
Flag: Critical study for SIDS endpoint
31-OCT-2001 (47)

Value: ca. 888 degree C

Reliability: (2) valid with restrictions
Results from handbook
07-NOV-2001 (49)

2.2 Boiling Point

Value:
Decomposition: yes

Test substance: as prescribed by 1.1 - 1.4

Result: Decomposes at temperatures above melting point (884 degree C).
Reliability: (2) valid with restrictions
Results from handbook
Flag: Critical study for SIDS endpoint
01-DEC-2004 (102)

Value: ca. 103.5 degree C

Remark: Determined in a saturated solution
Reliability: (2) valid with restrictions
Results from handbook
16-NOV-2001 (63)

Value: > 1700 degree C

Reliability: (2) valid with restrictions
Results from handbook
31-OCT-2001 (24)

2.3 Density

Type: relative density
Value: = 2.7 g/cm³ at 20 degree C

Reliability: (2) valid with restrictions
Results from handbook
Flag: Critical study for SIDS endpoint
13-JUN-2003 (101)

Type: relative density
Value: = 2.7 g/cm³ at 25 degree C

Reliability: (2) valid with restrictions
Results from handbook
13-JUN-2003 (24)

Type: relative density
Value: = 2.671 g/cm³

Reliability: (2) valid with restrictions
Results from handbook
13-JUN-2003 (49)

Type: relative density
Value: ca. 2.7 g/cm³

Reliability: (2) valid with restrictions
Results from handbook
31-OCT-2001 (47)

2.3.1 Granulometry

2.4 Vapour Pressure

Remark: The melting point is 800-888 degree C. therefore, the vapour pressure will be extremely low.
13-JUN-2003

2.5 Partition Coefficient

Partition Coeff.: octanol-water
log Pow: = -4.38

Method: other (calculated)

Reliability: (2) valid with restrictions

Result calculated with computer program
01-SEP-2003 (38)

Partition Coeff.: octanol-water
log Pow: = -3

Method: other (calculated)

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
19-JUN-2003 (24)

2.6.1 Solubility in different media

Solubility in: Water
Value: = 190 g/l at 20 degree C

Reliability: (2) valid with restrictions
Results from handbook
31-OCT-2001 (101)

Solubility in: Water
Value: ca. 430 g/l at 100 degree C

Reliability: (2) valid with restrictions
Results from handbook
07-NOV-2001 (23)

Solubility in: Water
Value: ca. 195 g/l at 20 degree C

Reliability: (4) not assignable
Results from handbook
16-JUN-2003 (63)

Solubility in: Water
Value: ca. 162 g/l at 20 degree C

Reliability: (2) valid with restrictions
Results from handbook
07-NOV-2001 (24)

Solubility in: Water
Value: ca. 161 g/l at 20 degree C

Reliability: (2) valid with restrictions
Results from handbook
15-NOV-2004 (47)

Solubility in: other: Glycerol

Remark: Sodium sulfate is soluble in glycerol

Reliability: (4) not assignable
Secondary literature. Reference not available.
16-JUN-2003 (67)

Solubility in: other: Alcohol

Remark: sodium sulfate is not soluble in alcohol
Reliability: (4) not assignable
Secondary literature. Reference not available.
16-JUN-2003 (67)

2.6.2 Surface Tension

2.7 Flash Point

2.8 Auto Flammability

2.9 Flammability

Result: non flammable

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
31-OCT-2001 (24)

2.10 Explosive Properties

Result: not explosive

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
31-OCT-2001 (24)

2.11 Oxidizing Properties

Result: no oxidizing properties

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
23-NOV-2001 (24)

2.12 Dissociation Constant

2.13 Viscosity

Value: = 2.481 mPa s (dynamic) at 20 degree C

Result: 22% solution

Test substance: as prescribed by 1.1 - 1.4

Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
02-DEC-2004 (48)

2.14 Additional Remarks

Memo: Data refer to dehydrated Na2SO4

Source: Enichem S.p.A Milan
Henkel S.p.A Duesseldorf
16-NOV-2001

3.1.1 Photodegradation

3.1.2 Stability in Water

Type: abiotic

Remark: Na2SO4 dissociates in water completely in sodium and sulfate ions. The ions cannot hydrolyze and therefore it is not scientifically necessary to perform a hydrolysis study.
Reliability: (2) valid with restrictions
Studies performed according to appropriate guidelines and GLP are not available. Data obtained from handbook.
22-SEP-2005 (47)

3.1.3 Stability in Soil

3.2.1 Monitoring Data (Environment)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. 3 - 30 mg/l

Remark: Sulfate concentrations measured in Canadian Lakes, British Columbia, Canada.
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
22-SEP-2005 (58)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. .001 - 3 g/l

Remark: Sulfate concentrations measured in rivers in Western Canada, British Columbia, Canada
Reliability: (4) not assignable
Reference not available
22-SEP-2005 (37)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. 2 - 30 mg/l

Remark: Sulfate concentrations measured in the Liard river, British Columbia, Canada
Reliability: (4) not assignable
Reference not available
22-SEP-2005 (15)

Type of measurement: background concentration
Medium: surface water
Concentration: > .4 - g/l

Remark: Sulfate concentration measured in the Great Plains shales, USA.
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific

principles, acceptable for assessment
22-SEP-2005 (103)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. 10 - mg/l

Remark: Sulfate concentration measured in the Ob River, Siberia, USSR.
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
22-SEP-2005 (103)

Type of measurement: background concentration
Medium: surface water
Concentration: ca. 50 - 60 mg/l

Remark: Sulfate concentrations measured in the Volga river, USSR.
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
22-SEP-2005 (103)

Type of measurement: background concentration
Medium: drinking water
Concentration: ca. .006 - 1.6 g/l

Remark: Sulfate concentrations measured at swine farms in Ohio, USA
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
26-SEP-2005 (107)

Type of measurement: background concentration
Medium: drinking water
Concentration: ca. 1 - 2 g/l

Remark: Sulfate concentrations measured in drinking water wells in North and South Dakota, USA
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment
22-SEP-2005 (69)

Medium: air

Result: North America:
· Non urban sites: 4.9-8.6 µg/m3
· Coastal urban sites in New York: 8.1-11.3 µg/m3
· Other coastal sites: 10.7-12.2 µg/m3
· Inland New York cities: 6.0-10.3 µg/m3
Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment.
22-SEP-2005 (54)

3.2.2 Field Studies

01-NOV-2001

3.3.1 Transport between Environmental Compartments

3.3.2 Distribution

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic

Remark: It is not possible to have aerobic biodegratation of sulfate.
13-JUN-2003

Type: anaerobic
Inoculum: anaerobic sludge
Result: other: see freetext

Method: other: see freetext
Year: 2000
Test substance: as prescribed by 1.1 - 1.4

Result: Sulfate was reduced according to the following reactions:
- Sugar:
$C_{12}H_{22}O_{11} + 5 H_2O + 4 SO_4^{2-} \rightarrow 4 CO_2 + 8 H_2 + 4 HS^- + 8 HCO_3^- + 4 H^+$
$8 H_2 + 2 SO_4^{2-} + 2 H^+ \rightarrow 2 HS^- + 8 H_2O$
$C_{12}H_{22}O_{11} + 8 H_2SO_4 \rightarrow 8 S + 12 H_2CO_3 + 7 H_2O$
- Ethanol:
$2 C_2H_5OH + 3 SO_4^{2-} \rightarrow 3 HS^- + 3 HCO_3^- + 3 H_2O + CO_2$
$C_2H_5OH + H_2SO_4 \rightarrow 2 S + 2 H_2CO_3 + 3 H_2O$
Test condition: - Inoculum: Anaerobic sludge obtained from the local municipal sewage treatment plant.
- Concentrations of test chemicals: $CaSO_4$ and COD (sugar and technical ethanol) both 1500 mg/l
- Temperature: 21 degree C
- Analytical determinations: All concentrations, alkalinity and pH were measured according to standard analytical procedures (APHA, 1985).
Reliability: (2) valid with restrictions
No guideline study, but includes detailed information on used method and endpoints.
22-SEP-2005 (46)

Type: anaerobic

Remark: Na_2SO_4 may be used as an electron acceptor in anaerobic sulfate reduction by sulfate reducing bacteria. Sulfate is converted to (hydrogen)sulfide.

Reliability: (3) invalid
Test is not applicable, but it gives some results about sulfate reduction.

22-SEP-2005 (53)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

BCF: = .5

Method: other: calculated

Remark: This result is calculated on the basis of log Kow = -2.20 from Sulfuric acid, because it cannot be calculated for Sodium. It is not expected that the value will be different for Sodium sulfate.

Reliability: (2) valid with restrictions
Result calculated with computer program

22-SEP-2005 (38)

3.8 Additional Remarks

Memo: BIOGENIC CONTRIBUTION

Remark: Study on the biogenic contribution to atmospheric levels of sulfate. study performed in the USA.
Results:
Hydrogen sulfide derived from the energy metabolism of bacterial sulfate reducers is the principal source of the 100 to 200 million ton of sulfur annually contributed to the global atmosphere.
Most of the sulfate observed in the nonurban sites appears to be of local origin in the north-east of the USA.
Urbanization does not appear to influence the sulfate levels in the north-east of the USA.

Reliability: (2) valid with restrictions
Study well documented, meets generally accepted scientific principles, acceptable for assessment

22-JUN-2005 (54)

Memo: PLANT NUTRIENTS

Remark: Sulfate concentrations of less than 0.5 mg/l in water is detrimental for plant growth, as sulfur is an essential element in living organisms.

Reliability: (4) not assignable
Reference not available

11-JUL-2003 (3)

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 12500 - 13000
Limit Test: no

Method: other: see freetext, method based on Doudoroff et al (1951). Bio-assays methods for the evaluation of acute toxicity of industrial wastes to fish. Sewage and Industrial Wastes, 23, (11):1380-1397.
Year: 1959
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Doudoroff et al (1951). Tests performed in standardized test medium. Test parameters pH, oxygen and temperature not reported. Concentration ranges not known. Study performed to evaluate differences between three size ranges of fish.
STATISTICAL METHODS: not described.
METHOD OF CALCULATION: not described
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: not described
- Effect data (Mortality):
TLm small size fish : 13000 mg/l
TLm medium size fish : 12750 mg/l
TLm large size fish : 12500 mg/l
- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described
Test condition: TEST ORGANISMS
- Strain: Raf.
- Supplier: Pennsylvanian Fish Commission, Pennsylvania, USA
- Wild caught: no
- Age/size/weight/loading:
size small : 3.88 cm - 0.96 gram
size medium : 6.09 cm - 2.80 gram
size large : 14.24 cm - 54.26 gram
- Feeding: cooked shrimp
- Pretreatment: not described
- Feeding during test: no
STABILITY OF THE TEST CHEMICAL SOLUTIONS: not described
REFERENCE SUBSTANCE: no
DILUTION WATER
- Source: artificial
- Aeration: artificial aeration
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- TSS: not described
- pH: not described
- Oxygen content: 5 - 9 ppm
- Conductance: not described
- Holding water: artificial
TEST SYSTEM
- Test type: static

- Concentrations: not described
- Dosing rate: singlefold
- Renewal of test solution: no
- Exposure vessel type: glass jarrs
- Number of replicates, fish per replicate: 1, 5-10
- Test temperature: 19 - 21 degree C
- Dissolved oxygen: 5 - 9 ppm
- pH: not described
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described

DURATION OF THE TEST: 96 hours

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (21)

Type: static
Species: Poecilia latipinna (Fish, estuary)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 15996 -
Limit Test: no

Method: other: see freetext, method based on Freeman, L. "A standardized method for determining toxicity of pure compounds to fish", Sewage and Industrial wastes, 25, 7, 845 (1953)
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
96 hours static test. Test parameters were monitored, but not reported.
METHOD OF CALCULATION: not described
Median Tolerance Limit (TLm), not reported. Only up to 48 hours a TLm was determined.
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Mortality):

24 hours LC50 : 20040 mg/l

- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain: not described
- Supplier: Local pet shop
- Wild caught: no
- Age/size/weight/loading: not described
- Feeding: not described
- Pretreatment: not described
- Feeding during test: no

DILUTION WATER
- Source: reconstituted water
- Aeration: yes
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- TSS: not described
- pH: not described

- Oxygen content: not described
- Conductance: not described
- Holding water: reconsituted water
TEST SYSTEM
- Test type: static
- Concentrations: geometric series, not known
- Dosing rate: not described
- Renewal of test solution: no
- Exposure vessel type: not described
- Number of replicates, fish per replicate: 1, 10
- Test temperature: not described
- Dissolved oxygen: not described
- pH: not described
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described
DURATION OF THE TEST: 48 hours
TEST PARAMETER: Mortality

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (34)

Type: static
Species: Morone saxatilis (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring:
LC50: ca. 56000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Mortality):
24 hours LC50 : 450 mg/l
48 hours LC50 : 220 mg/l
72 hours LC50 : 110 mg/l
- Concentration / response curve: not determined
- Effect concentration vs. test substance solubility: not determined
- Other effects: not determined
RESULTS: CONTROL
- Number/percentage of animals showing adverse effects: not determined
- Nature of adverse effects: not determined

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (56)

Type: static
Species: Gambusia affinis (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 120 -
Limit Test: no

Method: other: see freetext
Year: 1980
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
96 hours static test. Test parameters were monitored, but

not reported.
METHOD OF CALCULATION:
LC50, method not described.

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain:
- Supplier: Local fish market
- Wild caught: no
- Age/size/weight/loading: not described/15-18 cm/5-10 gram/50 - 100 gram
- Feeding: oil cake
- Pretreatment: no
- Feeding during test: no

DILUTION WATER
- Source: obtained from upper lake of Bhopal
- Aeration: yes
- Alkalinity: 95.0 CaCO3
- Hardness: 84.0 mg CaCO3
- Salinity: not described
- TOC: not described
- TSS: Total dissolved solids : 160 mg/l
- pH: 8.3
- Oxygen content: 7.9 mg/l
- Conductance: not described
- Holding water: Upper lake of Bhopal

TEST SYSTEM
- Test type: static
- Concentrations: not described
- Dosing rate: not described
- Renewal of test solution: no
- Exposure vessel type: glass 40 liter
- Number of replicates, fish per replicate: 2, 10
- Test temperature: 30 degree C
- Dissolved oxygen: > 6.0 mg/l
- pH: not described
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described

DURATION OF THE TEST: 96 hours
TEST PARAMETER: Mortality

Reliability: (3) invalid
Test was performed in natural dilution water with relative high content of dissolved solids and sulfate. Effects of these solids are not known. pH and oxygen concentrations during test were not reported. This is a significant methodological deficiency, which makes documentation insufficient for assessment.

26-SEP-2005 (81)

Type: static
Species: Gambusia affinis (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 16500 -
Limit Test: no

Method: other: see freetext

Year:	1957
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED: Test was run in singlefold with 5 concentrations with turbid natural water (high concentration suspended solids) as test medium. METHOD OF CALCULATION: Median tolerance limit (TLm) was calculated based on dose-effect plot on log-paper.
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: nominal - Effect data (Mortality): 24 hours LC50 : 24000 mg/l 48 hours LC50 : 17500 mg/l 6 days LC50 : 10000 mg/l - Concentration / response curve: not described - Effect concentration vs. test substance solubility: not described - Other effects: possible adverse effects of high turbidity of test medium
Test condition:	TEST ORGANISMS - Wild caught: Stillwater Creek, Oklahoma, USA - Age/size/weight/loading: adult female - Feeding: Plancton/detritus, artificial food - Pretreatment: Tetramycin in holding tanks to prevent tail-rot - Feeding during test: no DILUTION WATER - Source: obtained from local farm ponds - Aeration: artificial aeration - Alkalinity: low < 100 ppm - Hardness: not described - Salinity: not described - TOC: not described - TSS: 650 mg/l (initial) and < 25 mg/l (final) - pH: 7.8 - 8.3 - Oxygen content: not described - Conductance: not described - Holding water: local farm ponds TEST SYSTEM - Test type: static - Concentrations: geometric series between 1000 and 56000 mg/l - Dosing rate: single-fold - Renewal of test solution: no - Exposure vessel type: pyrex cylindrical 15 liter vessel - Number of replicates, fish per replicate: 1, 10 - Test temperature: 22 - 25 degree C - Dissolved oxygen: not described - pH: 7.0 - 8.8 - Adjustment of pH: no - Intensity of irradiation: not described - Photoperiod: not described TEST PARAMETER : Mortality DURATION OF THE TEST: 6 days
Reliability:	(3) invalid The dilution water was turbid, which may have influenced the test result. Although sodium sulfate does not adsorb substantially on to soil particles, effects of turbidity can

not be excluded. Oxygen concentrations during test are not reported. This means that documentation is insufficient for assessment.

26-SEP-2005 (109)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 8700 -
LC50: = 13500 -
Limit Test: no

Method: other: see freetext
Year: 1954
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
Test performed in duplicate with five concentrations. Main testparameters determined during test. Defined dilution water used.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: Median tolerance limit determined using estimation from log dose-response plot.
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described
Test condition: TEST ORGANISMS
- Strain: Raf.
- Supplier: private supplier Maryland, USA
- Wild caught: no
- Age/size/weight/loading: size 5 - 9 cm, weight 1 - 9 gram , on average 2.5 g/l
- Feeding: cooked shrimp
- Pretreatment: not described
- Feeding during test: no
DILUTION WATER
- Source: reconsituted water (Chu 14 modified)
- Aeration: yes
- Alkalinity: 36.8 - 37.0 mg/l ppm CaCO3
- Hardness: 37.4 - 40.6 mg/l ppm CaCO3
- Salinity: not described
- TOC: not described
- TSS: not described
- pH: 7.3 - 8.7
- Oxygen content: 4.4 - 8.9 ppm
- Conductance: 1.43x10-4 - 1.73x10-4 mhos 20 degree C
- Holding water: reconstituted water
TEST SYSTEM
- Test type: static
- Concentrations: 8700, 10000, 11500, 13500, 14000, 14500 mg/l
- Dosing rate: singlefold
- Renewal of test solution: no
- Exposure vessel type: Pyrex jarrs
- Number of replicates, fish per replicate: 2, 10
- Test temperature: 19 - 21 degree C

- Dissolved oxygen: 4.4 - 8.9 mg/l
- Alkalinity: 44 - 56 mg/l ppm CaCO3
- Hardness: 35 - 62 mg/l ppm CaCO3
- pH: 7.1 - 9.2
- Adjustment of pH: no
- Conductance: 60x10-4 -143x10-4
- Intensity of irradiation: not described
- Photoperiod: not described

DURATION OF THE TEST: 96 hours
TEST PARAMETER: Mortality

Reliability: (2) valid with restrictions
Although not all test criteria were met, results are reliable for assessment. Study with enough details.
Loading is not according to the guidelines, but because of aeration during the test this is not considered as having an impact on the test.
The low oxygen content (4.4 mg/l) had no impact on the fish considering the percentage of survival and oxygen content in the replicate.

26-SEP-2005 (98)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 13500 -
Limit Test: no

Method: other: see freetext, based on Cairns, J. et al, The effects of alkyl benzene sulfonate on aquatic organisms. Industrial Water and Wastes Journal, vol.9, no.1:22-28.
Year: 1968
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
static 96 hours test in reconstituted water.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described
- Reference substance: Potassium dichromate, TLm = 113 mg/l

Test condition: TEST ORGANISMS
- Strain: not described
- Supplier: not described
- Wild caught: not described
- Age/size/weight/loading: not described
- Feeding: not described
- Pretreatment: not described
- Feeding during test: no

DILUTION WATER
- Source: reconstituted water
- Aeration: yes
- Alkalinity: not described
- Hardness: not described
- Salinity: not described

- TOC: not described
- TSS: not described
- pH: not described
- Oxygen content: 5 - 9 ppm
- Conductance: not described
- Holding water: reconsituted water

TEST SYSTEM

- Test type: static
- Concentrations: geometric series, not known
- Dosing rate: not described
- Renewal of test solution: no
- Exposure vessel type: 18 liter vessels
- Number of replicates, fish per replicate: not described
- Test temperature: 16 - 20 degree C
- Dissolved oxygen: 5 - 9 ppm
- pH: not described
- Adjustment of pH:not described
- Intensity of irradiation: not described
- Photoperiod: not described

DURATION OF THE TEST: 96 hours
TEST PARAMETER: Mortality

Reliability: (2) valid with restrictions
When the result of Potassium dichromate (96 h, LC50) used as a reference substance, is compared with the result from another study (96 h, LC50 183 mg/l, Brachydanio rerio), it can be seen that it is in the same order of magnitude. This means that the result supports the accuracy of the result of the test substance, sodium sulfate.
This study would be considered as validity 3 because of the shortcomings. However, based on the other data, Sodium sulfate is a substance of very low toxicity and the results of this study confirm this, therefore this study is evaluated as valid with restrictions.

26-SEP-2005 (80)

Type: static
Species: Morone saxatilis (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring:
LC50: ca. 81000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Mortality):

24 hours LC50 : 650 mg/l
48 hours LC50 : 320 mg/l
72 hours LC50 : 160 mg/l

- Concentration / response curve:
- Effect concentration vs. test substance solubility:
- Other effects:

RESULTS: CONTROL
- Number/percentage of animals showing adverse effects:
- Nature of adverse effects:

RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (56)

Type: static
Species: Morone saxatilis (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring:
LC50: ca. 790000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Mortality):
24 hours LC50 : 790 mg/l
48 hours LC50 : 790 mg/l
72 hours LC50 : 790 mg/l
- Concentration / response curve:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS: CONTROL
- Number/percentage of animals showing adverse effects:
- Nature of adverse effects:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (56)

Type: static
Species: Morone saxatilis (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring:
LC50: ca. 1100000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Mortality):
24 hours LC50 : 1100 mg/l
48 hours LC50 : 1100 mg/l
72 hours LC50 : 1100 mg/l
- Concentration / response curve:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS: CONTROL
- Number/percentage of animals showing adverse effects:
- Nature of adverse effects:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (56)

Type: static
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: = 7960 -
Limit Test: no

Method: other: see freetext, based on EPA/600/4-90/027 (1991)

Year:	1997
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED: 96-hours static test in reconstituted water. STATISTICAL METHODS: logistic multiple regression METHOD OF CALCULATION: Probability regression model. measured values used for calculation whenever concentration was < 80% of initial concentration. ANALYTICAL METHODS: anion analyses by ion-chromatograpy
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: both - Effect data (Mortality): 24-hours LC50 : > 8080 mg/l 48 hours LC50 : > 7960 mg/l - Concentration / response curve: yes - Effect concentration vs. test substance solubility: no - Other effects: Not described RESULTS: CONTROL - Number/percentage of animals showing adverse effects: Not described - Nature of adverse effects: Not described
Test condition:	TEST ORGANISMS - Strain: not described - Supplier: ENSR, Fort Collins, CO, USA, in-house culture - Wild caught: no - Age/size/weight/loading: according to EPA, 1 to 7 days old - Feeding: yes, brine shrimp nauplii - Pretreatment: no - Feeding during test: yes, after 48 hours 100 microliter concentrated brine shrimp nauplii. DILUTION WATER - Source: reconstituted - Aeration: yes - Alkalinity: moderately - Hardness: not described - Salinity: not described - TOC: not described - TSS: not described - pH: 7.5 - 9.0 - Oxygen content: > 40% saturation - Conductance: not described - Holding water: tap water (purified by activated carbon) TEST SYSTEM - Test type: static - Concentrations: 4 concentrations with dilution factor 0.5 - Dosing rate: single-fold - Renewal of test solution: no - Exposure vessel type: plastic beakers 30 ml with 10 ml of water - Number of replicates, fish per replicate: 3-5, 5 - Test temperature: 25 degree C - Dissolved oxygen: > 40% saturation - pH: 7.5 - 9 - Adjustment of pH: no - Intensity of irradiation: not described - Photoperiod: not described DURATION OF THE TEST: 96 hours TEST PARAMETER: mortality SAMPLING: no

MONITORING OF TEST SUBSTANCE CONCENTRATION: yes
Reliability: (2) valid with restrictions
Test performed according to standardized EPA guideline for testing of effluents, with determination of test concentrations. Test parameters pH and oxygen measured but not all reported. No information about survival in controls. Replicate test performance.
Flag: Critical study for SIDS endpoint
26-SEP-2005 (71)

Type: static
Species: other: Morone saxatilis (striped bass, fingerlings)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 3500 -

Test substance: other TS:Na2SO4 tech. grade
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (56)

Type: static
Species: other: Morone saxatilis ,striped bass, larvea
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 250 -

Test substance: other TS:Na2SO4 tech. grade
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (56)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
LC0: = 15000 -

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (65)

Species: Gambusia affinis (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 17500 -

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (36)

Species: Lepomis gibbosus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 13500 -

Reliability: (4) not assignable

Reference not available
13-JUN-2003 (83)

Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 17500 -
Limit Test: no

Method: other: see freetext, method based on Freeman, L. "A standardized method for determining toxicity of pure compounds to fish", Sewage and Industrial wastes, 25, 7, 845 (1953)
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
96 hours static test. Test parameters were monitored, but not reported.
METHOD OF CALCULATION: not described
Median Tolerance Limit (TLm), not reported. Only a 24 hours TLm was determined.
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Mortality):
- Concentration / response curve: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described
Test condition: TEST ORGANISMS
- Strain: not described
- Supplier: Local pet shop
- Wild caught: no
- Age/size/weight/loading: not described
- Feeding: not described
- Pretreatment: not described
- Feeding during test: no
DILUTION WATER
- Source: reconstituted water
- Aeration: yes
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- TSS: not described
- pH: not described
- Oxygen content: not described
- Conductance: not described
- Holding water: reconsituted water
TEST SYSTEM
- Test type: static
- Concentrations: geometric series, not known
- Dosing rate: not described
- Renewal of test solution: no
- Exposure vessel type: not described
- Number of replicates, fish per replicate: 1, 10
- Test temperature: not described
- Dissolved oxygen: not described
- pH: not described
- Adjustment of pH: not described
- Intensity of irradiation: not described

- Photoperiod: not described
DURATION OF THE TEST: 96 hours
TEST PARAMETER: Mortality

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (34)

Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: ca. 13500 - 14500

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (36)

Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC100: = 7000 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
24 hours: LC50 705 mg/l
- Effect data (Mortality):
- Concentration / response curve:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS: CONTROL
- Number/percentage of animals showing adverse effects:
- Nature of adverse effects:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (65)

Species: other: Cyprinus carpio
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
LC0: < 2000 -

Reliability: (4) not assignable
Reference not translated

26-SEP-2005 (99)

Species: other: Notropis spilopterus
Exposure period: 120 hour(s)
Unit: mg/l Analytical monitoring:
MLc : = 100 -

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (105)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:	static
Species:	Daphnia magna (Crustacea)
Exposure period:	48 hour(s)
Unit:	mg/l Analytical monitoring: no
EC50:	= 9124 -
Limit Test:	no
Method:	other: see freetext
Year:	1995
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4
Method:	METHOD FOLLOWED: 48-hours static test in reconstituted water. STATISTICAL METHODS: not described METHOD OF CALCULATION: not described ANALYTICAL METHODS: no
Result:	RESULTS: EXPOSED - Nominal/measured concentrations: nominal - Effect data (Immobilisation): not described - Concentration / response curve: not described - Cumulative immobilisation: not described - Effect concentration vs. test substance solubility: not described - Other effects: not described
Test condition:	TEST ORGANISMS - Breeding method: in-house in reconsituted water - Age: < 24 hours - Feeding: no - Pretreatment: not described - Feeding during test: no - Control group: yes DILUTION WATER - Source: reconstituted water - Aeration: not described - Alkalinity: not described - Hardness: not described - Salinity: not described - TOC: not described - Ca/Mg ratio: not described - Na/K ratio: not described - TSS: not described - pH: not described - Oxygen content: not described - Conductance: not described - Holding water: reconstituted water TEST SYSTEM - Test type: semi-static - Concentrations: not described - Renewal of test solution: yes - Exposure vessel type: 100 ml solution - Number of replicates, individuals per replicate: 2, 10 - Test temperature: 20 degree C - Dissolved oxygen: not described - pH: not described - Adjustment of pH: not described - Intensity of irradiation: not described - Photoperiod: dark

DURATION OF THE TEST: 48 hours
TEST PARAMETER: immobility
SAMPLING: no
MONITORING OF TEST SUBSTANCE CONCENTRATION: no
Reliability: (3) invalid
documentation was insufficient for assessment
26-SEP-2005 (8)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: = 2564 -
Limit Test: no

Method: other: see freetext, based on Anderson, B.G. et al. The evaluation of aquatic invertebrates as assay organisms for the determination of the toxicity of industrial wastes. Report of the Ohio State University (1948)
Year: 1965
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
48 - 96 hours static test. Test parameters were monitored, but not reported.
METHOD OF CALCULATION: not described
Median Tolerance Limit (TLm), not reported.
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Immobilisation):
24 hours EC50 : 8384 mg/l
72 hours EC50 : 725 mg/l
96 hours EC50 : 630 mg/l
- Concentration / response curve: not described
- Cumulative immobilisation: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described
Test condition: TEST ORGANISMS
- Strain: not described
- Source/supplier: Put-In Bay, Ohio, USA
- Breeding method: In-house, not described
- Age: not defined, but designated as a) young, b) adult.
- Feeding: not described
- Pretreatment: not described
- Feeding during test: no
- Control group: not described
Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (34)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: yes
EC50: = 4580 -
Limit Test: no

Method: other: see freetext, based on EPA/600/4-90/027 (1991)

guideline
Year: 1997
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: 48-hours static test in reconstituted water.
STATISTICAL METHODS: logistic multiple regression
METHOD OF CALCULATION: Probability regression model. Measured values used for calculation whenever concentration was < 80% of initial concentration.
ANALYTICAL METHODS: anion analyses by ion-chromatograpy

Result: RESULTS: EXPOSED
- Nominal/measured concentrations: both
- Effect data (Immobilisation):
24 hours EC50 : 6290 mg/l
- Concentration / response curve: yes
- Cumulative immobilisation: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Strain: not described
- Source/supplier: ENSR, Fort Collins, CO, USA
- Breeding method: in-house in reconsituted water at 20 degree C
- Age: < 24 hours
- Feeding: yeast/cerophyl/trout chow (YCT)
- Pretreatment: no
- Feeding during test: yes, 100 microliter concentrated algae/ YCT 1:1 mixture at start test
- Control group: yes
DILUTION WATER
- Source: reconstituted hard water (EPA)
- Aeration: yes
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- Ca/Mg ratio: not described
- Na/K ratio: not described
- TSS: not described
- pH: 7.5 - 9.0
- Oxygen content: > 40% of saturation value
- Conductance: not described
- Holding water: reconstituted water (hard, EPA)
TEST SYSTEM
- Test type: static
- Concentrations: 4 concentrations in geometric series with factor 0.5
- Renewal of test solution: no
- Exposure vessel type: plastic vessels 30 ml with 10 ml dilution water.
- Number of replicates, individuals per replicate: 3-5, 5
- Test temperature: 20 degree C
- Dissolved oxygen: > 40% saturation
- pH: 7.5 - 9.0
- Adjustment of pH: no
- Intensity of irradiation: not described
- Photoperiod: 16:8 hour light-dark
DURATION OF THE TEST: 48 hours

TEST PARAMETER: immobility
SAMPLING: no
MONITORING OF TEST SUBSTANCE CONCENTRATION: yes
Reliability: (2) valid with restrictions
Test performed according to standardized EPA guideline for testing of effluents, with determination of test concentrations. Test parameters pH and oxygen measured but not all reported. No information about controls. Replicate test performance.
Flag: Critical study for SIDS endpoint
26-SEP-2005 (71)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: = 4547 -
Limit Test: no

Method: other:see freetext
Year: 1953
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: A 100 hours static test with 9 concentrations in three-fold.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: Toxicity Threshhold, defined by Anderson et al., Report by Ohio State Univ. Research Found. To Amer. Petrol. Inst., New York, N.Y. (1948). Toxicity Threshold is comparable with LC50 value.
ANALYTICAL METHODS: not described
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Immobilisation):
- Concentration / response curve: not described
- Cumulative immobilisation: not described
- Effect concentration vs. test substance solubility: not described
- Other effects: not described
Test condition: TEST ORGANISMS
- Strain: not described
- Source/supplier: West Virginia University, USA
- Breeding method: in-house
- Age: < 12 hours
- Feeding: yeast
- Pretreatment: not described
- Feeding during test: no
- Control group: yes
DILUTION WATER
- Source: reconstituted water
- Aeration: not described
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- Ca/Mg ratio: not described
- Na/K ratio: not described
- TSS: not described
- pH: not described
- Oxygen content: not described

- Conductance: not described
- Holding water: reconsituted water
TEST SYSTEM
- Test type: static
- Concentrations: 9 concentrations, not defined
- Renewal of test solution: no
- Exposure vessel type: pyrex vessels, 100 ml
- Number of replicates, individuals per replicate: 3, 10
- Test temperature: 22 - 24 degree C
- Dissolved oxygen: not described
- pH: < 7.7
- Adjustment of pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described
DURATION OF THE TEST: 100 hours
TEST PARAMETER: Immobility

Reliability: (3) invalid
Documentation insufficient for assessment
26-SEP-2005 (36)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC50: = 2564 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Immobilisation):
24 hours EC50 : 8384 mg/l
- Concentration / response curve:
- Cumulative immobilisation:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (33)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC100: = 5200 -

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (65)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Chlorella pyrenoidosa (Algae)
Exposure period: 8 day(s)
Unit: mg/l Analytical monitoring:
EC100 : = 57700 -

Method: other

Reliability: (4) not assignable
Reference not translated
26-SEP-2005 (77)

Species: other algae: Nitzschia linearis
Exposure period: 120 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: = 1900 -
Limit Test: no

Method: other: see freetext, based on Cairns J. et al. Industrial water and Wastes Journal. 9 (1), 22-28 (1964).
Year: 1968
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
a static 120 hours test in defined test medium.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: Median tolerance limit (TLm) method not defined.
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data/Element values: growth (cell counts)
- Cell density data: not described
- Growth curves: not described
- Reference substance: Potassium dichromate, TLm = 0.208 mg/l
Test condition: TEST ORGANISMS
- Strain: W.Sm.
- Source/supplier: not described
- Laboratory culture: not described
- Method of cultivation: not described
- Pretreatment: no
- Controls: yes
- Initial cell concentration: not described
DILUTION WATER
- Source: reconstituted water
- Aeration: not described
TEST SYSTEM
- Test type: static
- Concentrations: geometric series
- Renewal of test solution: no
- Exposure vessel type: 150 ml glass
- Number of replicates: not described
- Concentrations: not described
- Test temperature: 16 - 22 degree C
- pH: not described
- Intensity of irradiation: not described
- Photoperiod: not described
TEST PARAMETER: growth
Reliability: (2) valid with restrictions
In this test a different algae species is used than recommended in the OECD-guidelines. When the results of Potassium dichromate (72 h, EbC50) used as a reference substance, are compared with the results given in the EC-directive 92/69/EEC (mean 0.53 mg/l, range 0.20 - 0.75 mg/l) the sensitivity of Nitzschia linearis is not

significantly different from that of Selenastrum capricornutum or Scenedesmus subspicatus.

It is recognised that the duration of this study was greater than the recommended OECD study time but as the reference result from this study is on the lower boundary of the EC recommendation, the two results are considered comparable.

This study would be considered as validity 3 because of the shortcomings. However, based on the other data, Sodium sulfate is a substance of very low toxicity and the results of this study confirm this, therefore this study is evaluated as valid with restrictions (2).

Flag: Critical study for SIDS endpoint

26-SEP-2005 (80)

Species: other aquatic plant: Myrophilium spicatum (Eurasian watermilfoil)
Endpoint: other: root weight
Exposure period: 32 day(s)
Unit: mg/l Analytical monitoring: no
EC50: = 10228 -
EC50 shoot length :
= 4120 -
EC50 shoot weight :
= 9376 -
EC50 root length :
= 10370 -
Limit Test: no

Method: other: see freetext
Year: 1974
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED:
A 32 days test with plants cultivated in liquid/soil medium under continuous illumination.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: root weight and shoot length, quotient of effect of test substance added in soil fraction and effect of test substance added to water phase, corrected for control effect
ANALYTICAL METHODS: not described
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data/Element values: not described
- Cell density data: not described
- Growth curves: yes
Test condition: TEST ORGANISMS
- Strain: L.
- Source/supplier: Clone from Friesland, The Netherlands
- Laboratory culture: yes
- Method of cultivation: cultivated in greenhouse in woods earth/ferric silicate/tap water mixture
- Pretreatment: CuSO4 to reduce algae growth
- Controls: yes
- Initial cell concentration: not described
DILUTION WATER
- Source: Tap water
- Aeration: no

GROWTH/TEST MEDIUM CHEMISTRY
- Alkalinity: not described
- Hardness: not described
- Salinity: not described
- TOC: not described
- EDTA: not described
- TSS: not described
- pH: not described
- Dissolved oxygen: not described
TEST SYSTEM
- Test type: static
- Concentrations: not described
- Renewal of test solution: not described
- Exposure vessel type: flatt-bottom tubes 200 ml
- Number of replicates: 10
- Concentrations: not described
- Test temperature: 20 degree C
- pH: not described
- Intensity of irradiation: 300 fc
- Photoperiod: continuous
TEST PARAMETER: root weight and shoot length

Reliability: (3) invalid
Non-standardized test method, and insufficient documentation

26-SEP-2005 (92)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge
Exposure period: 37 day(s)
Unit: g/l Analytical monitoring:
NOEC: ca. 26 -

Method: other: see freetext
Year: 1986
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Test condition: TEST ORGANISMS
- Bacteria in activated sludge
- Supplier: obtained from a local municipal wastewater treatment plant.
- Pretreatment: acclimated for a period of over a month.
- Substrate: synthetic substrate
TEST SYSTEM

- Concentrations: concentrations were increased from 8 to 35 g/l over a time period of 37 days. Concentration steps were 2 - 5 g/l.
- Exposure vessel: 10 l reactor of which 8 l were aeration chamber and 2 l settling basin.
- Analyses: BOD, COD, TSS etc. analyses were done according to APHA standard methods.
- Dissolved oxygen: 6 - 8 mg/l
- Temperature: 18.5 - 22.5 degree C

Reliability: (2) valid with restrictions
Although it is not a standard test and not all test parameters were reported, the results are reliable for assessment. Study with enough details.

26-SEP-2005 (95) (96)

Type: aquatic
Species: activated sludge
Exposure period: 37 day(s)
Unit: g/l Analytical monitoring:
NOEC: ca. 26 -

Method: other: see freetext
Year: 1986
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Test condition: TEST ORGANISMS
- Motile protozoa in activated sludge
- Supplier: obtained from a local municipal wastewater treatment plant.
- Pretreatment: acclimated for a period of over a month.
- Substrate: synthetic substrate
TEST SYSTEM
- Concentrations: concentrations were increased from 8 to 35 g/l over a time period of 37 days. Concentration steps were 2 - 5 g/l.
- Exposure vessel: 10 l reactor of which 8 l were aeration chamber and 2 l settling basin.
- Analyses: BOD, COD, TSS etc. analyses were done according to APHA standard methods.
- Dissolved oxygen: 6 - 8 mg/l
- Temperature: 18.5 - 22.5 degree C
Reliability: (2) valid with restrictions
Although it is not a standard test and not all test parameters were reported, the results are reliable for assessment. Study with enough details.
26-SEP-2005 (95) (96)

Type: aquatic
Species: activated sludge
Exposure period: 37 day(s)
Unit: g/l Analytical monitoring:
NOEC: ca. 8 -

Method: other: see freetext
Year: 1986
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Test condition: TEST ORGANISMS
- Stalked ciliates in activated sludge
- Supplier: obtained from a local municipal wastewater treatment plant.
- Pretreatment: acclimated for a period of over a month.
- Substrate: synthetic substrate
TEST SYSTEM
- Concentrations: concentrations were increased from 8 to 35 g/l over a time period of 37 days. Concentration steps were 2 - 5 g/l.
- Exposure vessel: 10 l reactor of which 8 l were aeration chamber and 2 l settling basin.
- Analyses: BOD, COD, TSS etc. analyses were done according to APHA standard methods.
- Dissolved oxygen: 6 - 8 mg/l
- Temperature: 18.5 - 22.5 degree C

Reliability: (2) valid with restrictions
Although it is not a standard test and not all test parameters were reported, the results are reliable for assessment. Study with enough details.
26-SEP-2005 (95) (96)

Type: aquatic
Species: activated sludge
Exposure period: 40 day(s)
Unit: g/l Analytical monitoring:
NOEC: ca. 30 -

Method: other: see freetext
Year: 1980
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Test condition: TEST ORGANISMS
- Activated sludge
- Supplier: not described
- Pretreatment: not described
- Substrate: not described
TEST SYSTEM
- Concentrations: concentrations were increased from 10 to 40 g/l over a time period of ca. 40 days. Concentration steps were 10 g/l.
- Exposure vessel: 10 l
- Analyses: effluent analyses were done according to APHA standard methods.
- pH: 7 - 7.5
- Temperature: 20 - 23 degree C
- Dissolved oxygen: 2.3 - 3.5 mg/l
Reliability: (2) valid with restrictions
Although it is not a standard test and not all test parameters were reported, the results are reliable for assessment. Study with enough details.
26-SEP-2005 (40)

Type: aquatic
Species: Pseudomonas fluorescens (Bacteria)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = 10000 -

Method: other: Bestimmung der biologichen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L8 (1968) modifiziert

Reliability: (4) not assignable
Reference not available
13-JUN-2003 (14)

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 16 hour(s)
Unit: mg/l Analytical monitoring:
EC10: > 1000 -

Method: other: DIN 38412 Teil 8

Reliability: (4) not assignable
Reference not available

26-SEP-2005 (55)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

Species: other: Lymnaea (Pond snail)
Endpoint: Mortality
Expos. period: 96 other: hours
Unit: other: mg/l
LC50: = 1151 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Immobilisation):
24 hours LC50 : 1750 mg/l
48 hours LC50 : 1750 mg/l
72 hours LC50 : 1750 mg/l
- Concentration / response curve:
- Cumulative immobilisation:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (33)

Species: other: Lymnaea (Pond snail)
Endpoint: Mortality
Expos. period: 96 other: hours
Unit: other: mg/l
LC50: = 799 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Immobilisation):
24 hours LC50 : 1215 mg/l
48 hours LC50 : 1215 mg/l
72 hours LC50 : 1215 mg/l
- Concentration / response curve:
- Cumulative immobilisation:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (4) not assignable

Reference not available
26-SEP-2005 (33)

Species: other: Ophryotrocha labronica (Polychaete)
Endpoint: Mortality
Expos. period: 20 other: hours
Unit: other: mg/l
LC50: = 5.4 -

Reliability: (4) not assignable
Reference not available
26-SEP-2005 (85)

Species: other: Lymneae sp. (eggs)
Endpoint: Mortality
Expos. period: 96 other: hour(s)
Unit: other: mg/l
LC50: = 3553 -

Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Immobilisation):
24 hours LC50 : 5401 mg/l
48 hours LC50 : 5400 mg/l
72 hours LC50 : 5400 mg/l
- Concentration / response curve:
- Cumulative immobilisation:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (3) invalid
Documentation insufficient for assessment
26-SEP-2005 (34)

Species: other: Trycorythus sp.
Endpoint: Mortality
Expos. period: 96 other: hours
Unit: other: g/l
LC50: = .66 -

Method: other: see freetext
Year: 1996
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: 96-hours acute semi static test in river water.
STATISTICAL METHODS: one-way ANOVA
METHOD OF CALCULATION: probit analysis
ANALYTICAL METHODS: nutrient concentrations by spectrophotometer
Full chemical analyses by ICP-ES, AAS and autoanalyzer
Result: RESULTS: EXPOSED
- Nominal/measured concentrations: nominal
- Effect data (Immobilisation):
96 hours LC50 : 0.66 g/l

NB. The probit analysis could not be used since there was no normal distribution of concentration response data.
- Concentration / response curve: no
- Cumulative immobilisation: yes
- Effect concentration vs. test substance solubility: not described
- Other effects: not described

Test condition: TEST ORGANISMS
- Source/supplier: Sabie river, Kruger national park, South Africa
- Pretreatment: 25 individuals were acclimated unfed per raceway for 36 h. All dead animals were removed and numbers were equalized between the raceways, before addition of salt solutions.
- Feeding during test: no
- Control group: yes

DILUTION WATER
- Source: Sabie river water
- Salinity: not described
- TOC: not described
- Ca/Mg ratio: not described
- Na/K ratio: not described
- TSS: not described
- pH: not described

Conductance: not described
- Holding water: Sabie river water

TEST SYSTEM
- Test type: semi static
- Concentrations: 4 concentrations, 0.20, 0.66, 1.46 and 4.40 g/l.
- Renewal of test solution: yes, 20% of the water was replaced daily.
- Exposure vessel type: 12.5 l perspex experimental stream system; raceways. Four kaolinite stones were placed in the channel to serve as a substrate.
- Number of replicates, individuals per replicate: 3, not known
- Current: 0.75 or 1 m/s
- Test temperature: 9-16 degree C
- Dissolved oxygen: 65.0-105.0% saturation
- pH: 6.93-7.20
- Adjustment of pH: no
- Aeration: no
- Alkalinity: 62-101 mg/l
- Hardness: approx. 69.4 mg/l
- Intensity of irradiation: not described
- Photoperiod: 12:12 hour light-dark

DURATION OF THE TEST: 96 hours

TEST PARAMETER: immobility

Reliability: (2) valid with restrictions
No standard test, but test with a lot of detailed information. The test results did not give a normal dose respons curve.

Flag: Critical study for SIDS endpoint

26-SEP-2005 (42)

4.6.2 Toxicity to Terrestrial Plants

Species: other terrestrial plant: Capsicum annuum L.

Endpoint: other: Number and size of fruit

Expos. period: 4 month

Method: other: see freetext
Year: 2000
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A 4 months test in a greenhouse.
- Endpoints: Fruit was collected at ripening (at the red stage) and weight, total number and yield were recorded.
STATISTICAL METHOD
Data were statistically analysed by ANOVA.
Result: RESULTS
- Effect data:
Fruit number: Increased with concentration
Fruit size: decreased with concentration
Yield: decreased with concentration
Fructose, glucose and amino acids significantly decreased with higher concentrations.
The pulp thickness became less with increasing concentration.
Test condition: TEST SPECIES
- Capsicum annuum L.
- Source: not known
- pretreatment: No
- Substrate: Hoagland nutrient solution
TEST SYSTEM
- Concentrations: 2 (control), 3, 4, 6 and 8 dS/m solution (this is 0, 6.1, 12.2, 24.1 and 36.7 mM Sodium sulfate) in Hoagland nutrient solution.
- Test vessel: 120 l container
- Number of plants per replicate: 1
- Replicates: 5
- Temperature: 18-35 degree Celsius
- Relative humidity: 55-75%
- pH: 5.5-6.0
- Photoperiod: not known
- Watering: daily addition of deionized water
- Solutions were analysed weekly and readjusted to initial nutrient concentrations
Reliability: (3) invalid
No standard method. The method is described in detail but the results are not in much detailed. It is not clear at what concentration a significant decrease or increase occurs.
26-SEP-2005 (72)

Species: other terrestrial plant: Picea glauca
Endpoint: other: emergence, survival, shoot and root length, number of lateral roots, leaf necrosis, fresh weight and photosynthesis
Expos. period: 42 day(s)

Method: other: see freetext
Year: 2000
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A six weeks test in sand.
- Endpoints: Percentage emergence was noted daily. After six

weeks survival, leaf necrosis, shoot and root length, number of lateral roots, fresh weight and photosynthesis were recorded.
Photosynthesis was determined spectrophotometrically from methanol extract and calculated using MacKinney equation.
STATISTICAL METHOD
- Emergence data was analyzed using a general linear model (GLM) repeated measure technique.
- Growth data were analyzed with a glm using one-way ANOVA.
- The means were compared using Duncan's multiple range test.

Result: RESULTS
- Effect data:
Emergence: percentage germination was significantly less in 20 mM and higher
Survival: significant decrease at 50 mM and higher
Root length: significant reduction in length from 20 mM and higher
Number of lateral roots: significant decrease from 50 mM and higher
Leaf necrosis: significant necrosis in 50 mM and higher
Fresh weight: reduction in 50 mM and higher
Photosynthesis: Chlorophyll content did not change compared to the control

Test condition: TEST SPECIES
- Picea glauca
- Source: Pine Ridge Nursery, Alberta, Canada (seedlot DL 68-12-4-83)
- pretreatment: No
- Substrate: quartz-feldspar sand (particle size range 0.19-3 mm)
TEST SYSTEM
- Concentrations: 0, 10, 20, 50, 100 and 250 mM solution in deionized water.
- Test vessel: 4 l germination trays.
- Number of seeds per replicate: 40
- Replicates: 5 trays per concentration.
- Moisture content of sand: 13%
- Thermoperiod: 20/15 degree Celsius
- Photoperiod: 18 hours
- High humidity was obtained by covering the trays with transparant plastic lids
- After two weeks the lids were removed
- Watering: Every other day after removing the lids, 500 ml of deionized water was sprayed over the sand. Every seven days 50 ml of Hoagland's mineral solution was sprayed on the sand.

Reliability: (2) valid with restrictions
No standard method, but study with enough details.

26-SEP-2005 (28)

Species: other terrestrial plant: Pinus banksiana
Endpoint: other: emergence, survival, shoot and root length, number of lateral roots, leaf necrosis, fresh weight and photosynthesis
Expos. period: 42 day(s)

Method: other: see freetext
Year: 2000
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A six weeks test in sand.
- Endpoints: Percentage emergence was noted daily. After six weeks survival, leaf necrosis, shoot and root length, number of lateral roots, fresh weight and photosynthesis were recorded.
Photosynthesis was determined spectrophotometrically from methanol extract and calculated using MacKinney equation.
STATISTICAL METHOD
- Emergence data was analyzed using a general linear model (GLM) repeated measure technique.
- Growth data were analyzed with a glm using one-way ANOVA.
- The means were compared using Duncan's multiple range test.

Result: RESULTS
- Effect data:
Emergence: germination was significantly enhanced at 20 mM. At 250 mM the germination was only 7%
Survival: significant decrease at 50 mM and higher
Shoot length: significant reduction in 50 mM and higher
Root length: significant reduction in length from 10 mM and higher
Number of lateral roots: significant decrease from 10 mM and higher
Leaf necrosis: significant from 50 mM on
Fresh weight: reduction in 50 mM and higher
Photosynthesis: Chlorophyll content did not change compared to the control

Test condition: TEST SPECIES
- Pinus banksiana
- Source: Pine Ridge Nursery, Alberta, Canada (seedlot SJ 75-15-4-77)
- pretreatment: No
- Substrate: quartz-feldspar sand (particle size range 0.19-3 mm)
TEST SYSTEM
- Concentrations: 0, 10, 20, 50, 100 and 250 mM solution in deionized water.
- Test vessel: 4 l germination trays.
- Number of seeds per replicate: 40
- Replicates: 5 trays per concentration.
- Moisture content of sand: 13%
- Thermoperiod: 20/15 degree Celsius
- Photoperiod: 18 hours
- High humidity was obtained by covering the trays with transparant plastic lids
- After two weeks the lids were removed
- Watering: Every other day after removing the lids, 500 ml of deionized water was sprayed over the sand. Every seven days 50 ml of Hoagland's mineral solution was sprayed on the sand.

Reliability: (2) valid with restrictions
No standard method, but study with enough details.

26-SEP-2005 (28)

Species: other terrestrial plant: Picea mariana
Endpoint: other: emergence, survival, shoot and root length, number of lateral roots, leaf necrosis, fresh weight and photosynthesis
Expos. period: 42 day(s)

Method: other: see freetext

Year: 2000
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A six weeks test in sand.
- Endpoints: Percentage emergence was noted daily. After six weeks survival, leaf necrosis, shoot and root length, number of lateral roots, fresh weight and photosynthesis were recorded.
Photosynthesis was determined spectrophotometrically from methanol extract and calculated using MacKinney equation.
STATISTICAL METHOD

- Emergence data was analyzed using a general linear model (GLM) repeated measure technique.
- Growth data were analyzed with a glm using one-way ANOVA.
- The means were compared using Duncan's multiple range test.

Result: RESULTS
- Effect data:
Emergence: percentage germination was significantly less in 100 mM.
Survival: significant decrease at 100 mM and higher
Shoot length: significant reduction in 50 mM and higher
Root length: significant reduction in length from 20 mM and higher
Number of lateral roots: significant decrease from 50 mM and higher
Leaf necrosis: no significant necrosis
Fresh weight: reduction in 50 mM and higher
Photosynthesis: Chlorophyll content did not change compared to the control

Test condition: TEST SPECIES
- Picea mariana
- Source: Pine Ridge Nursery, Alberta, Canada (seedlot MW 61-13-5-9)
- pretreatment: No

- Substrate: quartz-feldspar sand (particle size range 0.19-3 mm)
TEST SYSTEM
- Concentrations: 0, 10, 20, 50, 100 and 250 mM solution in deionized water.
- Test vessel: 4 l germination trays.
- Number of seeds per replicate: 40
- Replicates: 5 trays per concentration.
- Moisture content of sand: 13%
- Thermoperiod: 20/15 degree Celsius
- Photoperiod: 18 hours
- High humidity was obtained by covering the trays with transparant plastic lids
- After two weeks the lids were removed
- Watering: Every other day after removing the lids, 500 ml of deionized water was sprayed over the sand. Every seven days 50 ml of Hoagland's mineral solution was sprayed on the sand.

Reliability: (2) valid with restrictions
No standard method, but study with enough details.

26-SEP-2005 (28)

Species: other terrestrial plant: Medicago sativa L.
Endpoint: other: plant growth, nodule number and weight

Method: other: see freetext
Year: 1995
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A 55 days test in a greenhouse.
- Endpoints: Plant dry weight and nodule number and dry weight.
STATISTICAL METHOD
Data were statistically analysed by ANOVA.
Result: RESULTS
- Effect data:
Plant growth: decreased with concentration, dry weight was 50% of control at 130 mOsm at the end of the test.
Nodule specific weight: did not change much at any osmotic level
Number of nodules: decreased with concentration, 71% reduction in the highest concentration.
Test condition: TEST SPECIES
- Medicago sativa L.
- Source: not known
- pretreatment: seeds were surface-steriized with 70% ethanol for 7 minutes, rinsed in sterile distilled water, and allowed to germinate on 1% water agar for 20 h.
10 germinated seeds were planted in a sterile-modified Leonard jar containing sand, and inoculated with R. meliloti. Plants were thinned out to 5 plants per jar, 14 days after planting.
- Substrate: Hoagland nutrient solution
TEST SYSTEM
- Concentrations: 0, 70, 130, 200 or 250 mOsm in N-free nutrient solution. Salt was added 72 h after planting and checked weekly
- Number of plants per replicate: 5
- Replicates: 6
- Temperature: 27/21 degree Celsius (day/night)
- Relative humidity: not known
- Photoperiod: 14 h
- Plants were watered every following day
- Watering: daily addition of deionized water
- Solutions were analysed weekly and readjusted to initial nutrient concentrations
Reliability: (3) invalid
No standard method. The method is described in detail but the results are not in much detailed. It is not clear at what concentration a significant decrease or increase occurs.
26-SEP-2005 (11)

Species: other terrestrial plant: Altriplex prostrata
Endpoint: other: survival, height, nodes, branches, leaves, dry mass and photosynthesis
Expos. period: 1 month

Method: other: see freetext
Year: 1996
GLP: no

Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED
A one month semi static test in defined test medium.
- Endpoints: Plant height, number of leaves, nodes and branches were recorded weekly. Photosynthesis was measured once before harvesting and dry mass was determined after one month.
Photosynthesis was measured using a infra-red gas analyzer.
STATISTICAL METHOD
Two-way ANOVA was used to determine differences among treatments.
The Bonferroni test was used for other comparisons.

Result: RESULTS
- Effect data:
Survival: All plants survived in every concentration
Plant height: The height decreased as osmotic potential was lowered
Number of nodes: The number decreased as osmotic potential was lowered
Number of branches: The number decreased as osmotic potential was lowered
Number of leaves: The number decreased from -1.00 MPa on
Dry mass: Mass decreased from -1.00 MPa on
Photosynthesis: Photosynthesis decreased from -1.00 MPa on

Test condition: TEST SPECIES
- Atriplex prostrata
- Source: Salt marsh in Rittman, Ohio (Wayne county)
- Size of seeds: 1.5-2.0 mm diameter
- pretreatment: Seeds were germinated in an incubator.
12h thermoperiod of 5:25 degree celcius.
12h photoperiod 20.0 micromol/m2/s, 400-700 nm.
Acclimated to greenhouse conditions for two days in individual pots. Grown for 15 days under natural light conditions. Plants were acclimated to the test solutions by placing them at lower osmotic potential every two days until the final osmotic potential was reached
- Substrate: Sand
TEST SYSTEM
- Concentrations: 0.00, -0.75, -1.00 and -1.50 MPa solution, dissolved in half strength Hoagland and Arnon's no. 2 solution. Solutions were replaced after two weeks.
- Test vessel: 9x9 cm black plastic pots.
- Replicates: 10 per concentration.

Reliability: (3) invalid
Study with a lot of details on the method, but in the results no statistics is mentioned. It is not clear were significant differences were found.

26-SEP-2005 (35)

4.6.3 Toxicity to Soil Dwelling Organisms

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

Species: other: Culex (Mosquito)
Endpoint: mortality
Expos. period: 48 hour(s)
Unit: other: mg/l
LC50: = 4325 -

Result: RESULTS: EXPOSED
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (33)

Species: other: Culex (Mosquito)
Endpoint: mortality
Expos. period: 48 hour(s)
Unit: other: mg/l
LC50: = 3004 -

Result: RESULTS: EXPOSED
Reliability: (4) not assignable
Reference not available
26-SEP-2005 (33)

Species: other: Culex sp. larvea
Endpoint: mortality
Expos. period: 48 hour(s)
Unit: other: mg/l
LC50: = 13350 -

Method: METHOD FOLLOWED: not described in detail.
METHOD OF CALCULATION:
not described
Result: RESULTS: EXPOSED
- Nominal/measured concentrations:
- Effect data (Immobilisation):
24 hours LC50 : 11430 mg/l
- Concentration / response curve:
- Cumulative immobilisation:
- Effect concentration vs. test substance solubility:
- Other effects:
RESULTS CONTROL:
RESULTS: TEST WITH REFERENCE SUBSTANCE
- Concentrations:
- Results:
Reliability: (3) invalid
Documentation insufficient for assessment
26-SEP-2005 (34)

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

Memo: TOXICITY TO FISH

Remark: Method:
Acute toxicity to Lake Emerald shiner (Notropis a. atherinoides) and spotfin shiner (Notropis spilopterus). 96 hours testing according to Powers, E.B. Biol. Monograpgs IV, No. 2 pp.1-73 (1917). 18 degree C in 2-liter vessels. Oxygen > 4 mg/l.

Results:
Minimum Lethal Concentration (NOEC) : 100.0 mg/l for both fish. 100% survival in controls.

26-SEP-2005 (106)

Memo: TOXICITY TO INVERTEBRATES

Remark: Method:
Static bioassay, 28.5 +/-1.5 degree C:
Effect parameters determined graphically. Tests with three replications + control. Dilution water: Unchlorinated bore-hole water.,pH=7, DO 7.5 mg/l, alkalinity 110 mg/l CaCO3.
Results: 96h; LC 100 - LC 50 - LC 0 (mg/l).
Branchiura sowerbyi (worm) 12000 - 7700 - 4750
Cyclops viridis (plankton) 4500 - 2000 - 1000
Lymnaea luteola (mollusc) 9500 - 8250 - 4000

15-OCT-2001 (44)

Memo: TOXICITY TO INVERTEBRATES

Remark: Method:
Static test with Daphnia magna, 48 hours in Lake Erie (USA) water. Method according to Anderson, B.G. Sewage Works J. 16(6):1156-1165 (1944).
Results:
Threshold concentration for immobilization:
5960 mg/l (16 hours)
7105 mg/l (48 hours)

15-OCT-2001 (6)

Memo: TOXICITY TO INVERTEBRATES

Remark: Marine invertebrates; salinity of sea water 30g/kg, static

	length mm	24h EC50 mg/l
Annelida:		
Lepidonotus squamatus	15	>6400
Polydora sp.		>6400
Crustacea:		
Balanus crenatus (Rock barnacle)	6	>6400
Eupagurus bernhardus (Hermit crab)	11.4	>6400
Carcinus maenas (shore or green crab)	12.6	>6400
Mollusca:		
Lepidochitona cinerea (Chiton)	6.5	>800
Acmaea testudinalis (Limpet)	2.5	>6400
Aphorrhais pes-pelicani (Pelican's foot)	43	>3200
Thais (Nucella) lapillus (Dow whelk)	15	>6400
Buccinum undatum (Large whelk)	31	>6400
Onchidoris fusca (Sea slug)	13	>6400
Mytilus edulis (Common bay mussel)	28	>6400
Anomia ephippium (False saddle oyster)	6.5	>6400
Hiatella (Saxicava) arctica (Red nose)	23	>1600
Echinodermata:		
Asterias rubens (Starfish)	59	>6400
Psammechinus miliaris (Sea urchin)	31	>6400
Urochordata:		
Ascidiella scabra (Sea squirt)		>6400

17-OCT-2001 (82)

Memo: TOXICITY TO INVERTEBRATES

Remark: Toxicity of sodium sulfate in vitro on the fish nematode Procamallanus sp. was examined. Complete mortality was observed after 48 hours with 0.5% solution, and after 20 hours in 1.0% solution.

11-JUL-2003 (61)

Memo: TOXICITY TO INVERTEBRATES

26-SEP-2005 (5)

Memo: TOXICITY TO MICROORGANISMS

Remark: Stimulation of growth (117 - 120 %) of Spruce seedlings was observed after addition of sodium sulfate (84 mg NaSO4 added to vessel of 110x230 mm with 150 mm soil layer) to soil, due to activation of soil microflora. The total test period was 107 days.

15-OCT-2001 (64)

Memo: TOXICITY TO PLANTS

Remark: 48 hours test with bulbs/seeds in a liquid test medium and with Na2SO4 in a semi-static test. Test parameter root length.

Allium cepa, bulbs (Modified Allium test) : 7756 mg/l IC50
Lepidium sativum, seeds (Lepidium test): 8533 mg/l IC50

15-OCT-2001 (8)

Memo: TOXICITY TO PLANTS

Remark: Method: greenhouse equipped with an activated charcoal air filtration system,
22 degree C day/18 degree C night, 50-55 % rel. air humidity, 12h photoperiod,
treatment 3 x/week:
0.5, 1, 3, 5 g Na2SO4 as dust / 6 moistened plants
Pinto-beans, 28d old
"Veemore" tomatoes, 35d old
Results:
Pinto-beans; Progressive decrease in growth and dry weight with increasing Na2SO4 conc. over 4w
"Veemore" tomatoes;
1w with 3 and 5 g/l or 2w with 1 g/l : growth inhibition
3w with 0.5 g/l : no inhibition

15-OCT-2001 (93)

Memo: TOXICITY TO PLANTS

Remark: Effect of Na2SO4 on the symbiotic effectiveness of the host Vigna radiata (mungo bean) and Rhizobium, 30 d:
Initiation of nodulation was delayed by one day at 0.05 %;
Total number of nodules and total nitrogen content of plant was maximum at 0.05 %;
Nodulation was caused only upto 0.3 %.
Method: Test tube method acc. to:
Vincent, J.M.: Manual for the practical study of root nodule

bacteria, Blackwell Scientific Publications, Oxford (1970)
24-OCT-2001 (10)

Memo: TOXICTY TO AQUATIC PLANTS / INVERTEBRATES

Remark: Na2SO4, dissolved in tap water, neutralized with Ca(OH)2:
==========
Hydra oligactis (Coelenterata):
disintegration in 0.5% within 20-36h
Turbellaria:
Planaria gonocephala: death and disintegration in 1% after 48 h
Stenostomum: death and disintegration in 0.5% after 24h
Mollusca:
Limnaea stagnalis
Planorbis carinata in 1.5% after 24h dead, in 1% within
Valvata piscinalis 3-14d dead
Bythinia tentaculata
Crustacea:
Daphnia hyalina 0.25% lethal
Insects:
Limnophilus (Caddisfly,larvae): in 0.5% within 15-19d dead, in 1 und 1.5% within 4d dead
Fishes:
Carassius vulgaris (Gold fish): 0.5-1.25% no effect;
1.5% within 24d dead;
2% within 7-8d dead
Tinca vulgaris (Tench) : 0.5% no effect;
1% within 21d dead;
2% within 1-2d dead
Perca fluviatilis (Perch) : 0.5% no effect;
in 2% within 2-7d dead
Alburnus bipunctatus (Bleak) : in 1% within 16-17d dead
Scardinius erythrophtalmus
(Rudd) : in 1.5% within 7d dead
Squalis leuciscus (Chub) : in 2% within 2d dead
Salmo fario and : in 1.5% after 48h dead;
Salmo gairdneri (Trout) 15-20 cm in 2% after 36h dead
Tadpoles in 2% after 3.25-9h dead;
in 1.1 % after 6h dead
Submerse plants:
Potamogeton luceus (pondweed):
in 1.5 and 2% within 26d disintegration
Ceratophyllum demersum (horn wort):
in 0.3% no damage;
in 1.5% within 40d disintegration
Myriophyllum verticillatum (milfoil):
in 1.5% within 12d dead;
in 1% within 40d disintegration
Elodea canadensis (pondweed):
in 0.1% no damage;
in 0.25% within 18d disintegration
Lemna minor (duckweed):
in 1% after 30d end of leaf reproduction;
in 0.5% no damage
Callitriche: in 0.8% permanent damage and deformation;
in 1% dead
Fontinalis : in 0.8% within 25d no damage;
in 1.5% dead and disintegrated
Chara foetida (filamentous green alga):
in 0.5 and 0.75% up to 60d increased growth;

within 72d dead
26-SEP-2005 (86)

09-NOV-2001

5.0 Toxicokinetics, Metabolism and Distribution

In Vitro/in vivo:	In vivo
Type:	Absorption
Species:	other: homo sapiens
No. of animals, males:	7
No. of animals, females:	0
Doses, males:	13.9 g (8.6 g of the anhydrous salt)
Route of administration:	oral unspecified
Exposure time:	3 hour(s)

Year:	1983
GLP:	no
Test substance:	other TS: Mg2SO4

Remark: Conclusion: Magnesium sulfate is less completely absorbed than sodium sulfate as described by Cocchetto et al, 1981

Result: prior to study, three consecutive 24-hour periods for urine volume determination (twice, one -week interval). Subjects received either above dose in four hourly increments or just water; one week later the alternative.
72 -hour urine was collected at 4-hourly intervals (8 at night) Urinary sulfate excretion corrected for baselien was about 30.2% +- 17.2 in the first 24 hours, negligible in the following 48 hours. All subjects given the sulfate had gastro-intestinal complaints and loose stools or diarrhea.

Test condition: Frequency of treatment: once
Post exposure period: 72 hours
Control group: No; subject as own control

Reliability: (2) valid with restrictions
non-standard study

26-SEP-2005 (70)

In Vitro/in vivo:	In vivo
Type:	Distribution
Species:	other: homo sapiens
No. of animals, males:	8
No. of animals, females:	0
Doses, males:	60-80 microCurie
Route of administration:	other: intravenously and oral

Year:	1976
GLP:	no
Test substance:	other TS: Na2SO4 (35S-labeled)

Result: Volunteers received above dose IV, followed by 24-hours fluid restriction and blood and urine collection to determine radio-activity and creatinine concentration
Same volunteers received same amount orally 14 days later, followed by same regimen.
Plasma equilibrium iwas reached within 90 and 105 minutes respectively.
Calculated mean extracelluar fluid space was 16.8 +- 1.1 and 15.3 +- 1.2 respectively or only 9%.
Conclusion: 35S-labeled sulfate is absorbed completely and rapidly.

Test condition: Exposure period: single dose I.Vl, single dose oral 14 days later
Frequency of treatment: once daily
Post exposure period: 24 hours
Control group: No; subject as own control

Reliability: (2) valid with restrictions
non-standard study
(12)

In Vitro/in vivo: In vivo
Type: Absorption
Species: other: homo sapiens
No. of animals, males: 5
No. of animals, females: 0
Doses, males: 18.1 g Na2SO4 decahydrate (800 g of the anhydrous salt)
Route of administration: oral unspecified

Year: 1981
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Conclusion: Sodium sulfate is better absorbed from the intestine when given in divided dose than from a single large dose, indicating saturation of the transport system.
Result: Prior to exposure three separate 24-hour periods for urine volume and baseline sulfate excretion determination (twice, one -week interval). Subjects received either above dose in a single dose or in four hourly increments; one week later the alternative dosing schedule.
72 -hour urine was collected in 24-hour portions. Urinary free sulfate excretion corrected for baseline was about 53.4 +-16.8 for the single dose and 61.8 +-7.8 for the divided dose. Single dose causeds severe diarrhoea, divided dose did not. Excretion of free sulfate is not influenced by urine flow, but excretion of organicaly bound sulfate is.in a linear fashion.
Test condition: Exposure period: single oral dose or divided over three hours
Frequency of treatment: twice with one week interval
Post exposure period: 72 hours
Control group: No; subject as own control
Reliability: (2) valid with restrictions
non-standard study
26-SEP-2005 (27)

Type: Absorption
Species: rat

26-SEP-2005
Result: Absorption of inorganic sulfate after ingestion in rats (male, Wistar (30-330 g body weight) was investigated. A

inorganic sulfate concentration was measured in the serum after 2 hours of oral administration of 5 mmol Na2SO4. A threefold increase in serum sulfate concentration was measured. Compete absorption from the gastrointestinal tract was measured using 35S labelled sulfate.
Reliability: (2) valid with restrictions
non-standard study
26-SEP-2005 (60)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50
Species:	rat
No. of Animals:	10
Vehicle:	water
Doses:	2-5 ml/100 g body weight oral
Value:	> 10000 mg/kg bw
Method:	other: not defined
Year:	1971
GLP:	no data
Test substance:	as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: not described
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described

Result: MORTALITY:
- Time of death: after 8 days
- Number of deaths at each dose: not described

CLINICAL SIGNS: no clinical signs observed
NECROPSY FINDINGS: not described
POTENTIAL TARGET ORGANS: not described
SEX-SPECIFIC DIFFERENCES: not described

Test condition: TEST ORGANISMS:
- Source: not described
- Age: not described
- Weight at study initiation: mean weight 270 gram
- Controls: not described

ADMINISTRATION:
- Doses: as described
- Doses per time period: not described
- Volume administered or concentration: 2-5 ml
- Post dose observation period: 8 days

EXAMINATIONS: not described

Reliability: (4) not assignable
Original reference not available

27-SEP-2005 (52)

Type:	LD50
Species:	mouse
Value:	= 5989 mg/kg bw
Year:	1963
GLP:	no data
Test substance:	as prescribed by 1.1 - 1.4

Reliability: (4) not assignable
Original reference in Japanese not available

27-SEP-2005 (78)

Type:	other: human drinking-water study
Species:	human
Sex:	male/female
No. of Animals:	10
Vehicle:	water
Doses:	dose ranging study: 0, 400, 600, 800, 1000 and 1200 mg/l.

Single dose study: 0 and 1200 mg/l.

Method: other
Year: 1997
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS: 10 Normal Human Subjects, 80% caucasian.
- Source: -
- Age: 24-45 years
- Weight at study initiation: -
- Controls: -
ADMINISTRATION:
- Doses: dose ranging study: 0, 400, 600, 800, 1000 and 1200 mg/l. Single dose study: 0 and 1200 mg/l.
- Doses per time period: dose ranging study: 4 subjects (2 male, 2 female) received a dialy dose in the order listed above for 6 consectutive 2 day periods. Single dose study: 6 subjects (3 male, 3 female) received a dialy dose of 0 and 1200 mg/l for 2 consecutive 6 day periods.
Colored markers were given at the beginning of each change in drinking water sulfate concentration.
- Volume administered or concentration: volume 36 ml/kg/d.
- Post dose observation period:
EXAMINATIONS: The health of the subjects was determined by studying their history, physical examination, urineanalysis, blood cell counts and serum chemistries. During the study stool mass, frequency and consistency in mouth to anus appearance of colored markers were measured.

Wilcoxon signed rank test was used to compare the effects of specific concentrations of sulfate compared to distilled water.

Result: MORTALITY: -
- Time of death: -
- Number of deaths at each dose: -
CLINICAL SIGNS: No significant change in bodyweight. All blood and urine test results were normal. At 1200 mg/l 8 subjects rated the taste of the water as neutral-slightly unpleasant, 1 subject as moderately unpleasant and 1 subject as very unpleasant.

Dose ranging study:
Increasing the sulfate concentration in drinking water every 48 hours from 0 - 1200 mg/l produced no significant trend in stool mass per hours (based on Page's L-statistic test). During the six periods the mean number of stools were 2.5, 3.0, 2.3, 3.0 2.0 and 2.8 respectively, and the mean consistency ratings were 3.5, 3.3, 3.1, 3.4, 3.0 and 2.7 respectively. There was a significant trend toward decreasing mouth to anus appearance time with increasing sulfate concentration. The mean appearance times were (hours) 27.3, 17.9, 26.0, 16.1, 19.2, 17.2 respectively. No diarrhea during daily diaries were reported during the entire study. Mild abdominal cramps were reported by one subject for two days while receiving distilled water.

Single dose study:
Compared to distilled water, water containing 1200 mg/l sulfate produced a statistically significant increase in the

mean stool mass per six-day pool, from 629 to 922 g and in mean stool mass per hour from 4.8 to 6.6 g. Each subject showed an increase in stool mass per pool and in stool mass per hour. Stool frequencey, stool consistency, and mouth to anus appearance time were not significantly different. Two of the six subjects reported abdominal cramps, no other symptoms were recorded.

When combing the results from both studies for 0 an 1200 mg/l significant decreases in stool consistency and appearance time were noted at 1200 mg/l.
NECROPSY FINDINGS: -
POTENTIAL TARGET ORGANS: -
SEX-SPECIFIC DIFFERENCES: -

Test substance: Anhydrous sodium sulfate from UPS was used.
Reliability: (2) valid with restrictions
Acceptable, well documented study.
The results of the blood and urine test an bodyweights are not shown.

27-SEP-2005 (51)

5.1.2 Acute Inhalation Toxicity

Type: LCLo
Species: rat
Strain: Sprague-Dawley

Sex: male
No. of Animals: 6
Vehicle: water
Doses: 10 mg/m3
Exposure time: 72 hour(s)
Value: > 10 mg/m³

Method: other: see freetext, not a guideline study: method according to Last and Cross, J. Lab. Clin. Med. 91:328-339 (1978)
Year: 1980
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: rats were exposed to well characterized aerosols of sodium sulfate at levels of 10 mg/m3 and particle sizes of around 1 micron. the responses to breathing these aerosols for three days were evaluated by measurements of glycoprotein, RNA and DNA contents of homogenates of the lungs and quantification of wet to dry weight ratios of the lung lobs.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described
ANALYTICAL METHODS: Ion chromatography as described by Asgupta et al., Amer. Ind.Hyg. Assn. J. (1980) in prep.
Result: MORTALITY: no death reported
CLINICAL SIGNS: RNA, DNA and protein levels in lung homogenates (control = 100)
RNA: 99, DNA: 100, protein content: 107. (mean values form 6 rats)
NECROPSY FINDINGS: Lung wet to dry ratio: (control = 4.5). 4.35 and 4.5 for exp. 1 and 2 resp.
POTENTIAL TARGET ORGANS: Lungs
SEX-SPECIFIC DIFFERENCES: not determined
Test condition: TEST ORGANISMS: rat

- Source: Charles River, Portage, MI, USA
- Age: 70-80 days
- Weight at study initiation: not described
- Number of animals: 6 rats per exposure
- Controls: yes
ADMINISTRATION:
- Type of exposure: inhalation
- Concentrations: 10 mg/m3
- Particle size: app. 1 µm
- Type or preparation of particles: Babington (1-15 mg/m3) and Retec nebulizers (> 0.1 mg/m3)
EXAMINATIONS: Lungs: RNA, DNA, protein from homogenates. Quantification of wet to dry weight ratios of right apical lung lobs.

Reliability: (2) valid with restrictions
Acceptable, well documented study.

27-SEP-2005 (62)

Type: other: effect on pulmonary function
Species: human
Vehicle: other
Doses: 1, 2 and 3 mg/m3
Exposure time: 10 minute(s)

Method: other: unspecified
Year: 1979
GLP: no
Test substance: no data

Method: TEST ORGANISMS: human
- Source: -
- Age: -
- Weight at study initiation: -
- Number of animals: 5 astmatic and 5 normal humans and 6 astmatic and 6 normal humans
- Controls: -
ADMINISTRATION:
- Type of exposure: aerosols
- Concentrations: 1, 2, 3 mg/m3 and 3 mg/m3 in the second experiment
- Particle size: 0.5 micrometer mass mediam aerodynamic diameter
- Type or preparation of particles: particles were generated by an ultrasonic nebulizer and sized by elctron micrographs and an electrical aerosol size analyzer.
EXAMINATIONS:
Respiratory resistance (Rrs) was meaured continuesly during exposure. Rrs, Forced Expiratory Volume1 and VC were measured 5, 15, 30, 45 and 60 minutes after exposure. In the second experiment lung volumes by spirometer and plethysmography, dynamic mechanisms of breathing by Rrs: specified airway conductance and flow volume curve, distribution of ventilation by single and multiple breath nitrogen washouts, random noise oscillations and diffuse capacity.

Result: MORTALITY:
- Time of death: -
- Number of deaths at each dose: -
CLINICAL SIGNS:
In the first experiment 2 of 5 astmatic people experienced a

15-20% fall in FEV1 at 1 mg/m3. This did not get worse at higher concentrations. The groups means were not altered as comapred with NaCl. In the second experiment no adverse effect on pulmonary function was found over 3 hours compared to NaCl. 2 of 6 astmatic people experienced a 15-20% fall in FEV1 at 1 mg/m3 after breathing NaCl and sodium sulfate aerosols.
NECROPSY FINDINGS: -
POTENTIAL TARGET ORGANS: -
SEX-SPECIFIC DIFFERENCES: -

Test substance: No data on sodium sulfate supplier, purity or storage.

Reliability: (4) not assignable
Not assignable. Only abstract available.

26-SEP-2005 (84)

Type: other: irritant potency (mucociliary clearance)
Species: rabbit
Strain: other: mixed breed
Sex: male
No. of Animals: 5
Doses: 1800-1950 microgram particles/m3
Exposure time: 1 hour(s)

Method: other
Year: 1984
GLP: no
Test substance: no data

Method: TEST ORGANISMS: Mixed breed rabbits.
- Source: -
- Age: -
- Weight at study initiation: 2.5-2.7 kg
- Number of animals: 5 males
- Controls: animals served as their own controls in 'sham'-control experiments. 10 of these experiments were performed exposing the animals for 1 hour to temperature and humidity conditioned air.
ADMINISTRATION:
- Type of exposure: inhalation.
- Concentrations: 1800-1950 microgram particles/m3.
- Particle size: mean mass aerodynamic diameter 0.4 micrometer.
- Type or preparation of particles: Aerosols were prpared by nebulization using a Laskin nebulizer. The aerosols were mixed with filtered room air which had been temperature and humidity conditioned.
EXAMINATIONS: The bronchial mucociliary clearance was measured by brief inhalation of radiolabelled, insoluble tracer microspheres (99mTc-tagged ferric oxide). The thoracic retention was measured externally in vivo.
These measuerments began within 2 min. After the inhalation and were repeated after 24 hours to determine a value for residual activity (R24). It is expected that the tracer is completely cleared after 24 hours. The mucociliary clearance was determined as mean residence time (MRT) of the tracer.

Result: MORTALITY: -
- Time of death: -
- Number of deaths at each dose: -
CLINICAL SIGNS: No effect on mucociliary clearence was found (one way ANOVA, two tailed).

NECROPSY FINDINGS: -
POTENTIAL TARGET ORGANS: -
SEX-SPECIFIC DIFFERENCES:-

Test substance: No details on where the sodium sulfate was obtained or on purity are given.

Reliability: (2) valid with restrictions
Limited documentation but sufficient for assessment of primary effects.

27-SEP-2005 (87)

Type: other: irritant potency
Species: guinea pig
Strain: other: random bred
Sex: no data
No. of Animals: 10
Vehicle: no data
Doses: 0.90 +/- 0.11 mg/m3
Exposure time: 1 hour(s)

Method: other
Year: 1978
GLP: no
Test substance: no data

Method: TEST ORGANISMS: guinea pigs
- Source: -
- Age: -
- Weight at study initiation: 200-300 g
- Number of animals: 10
- Controls: during a 30 min. control period before exposure to the test substance measurements were taken every 5 min. The same animals were used in the exposure.
ADMINISTRATION:
- Type of exposure: inhalation.
- Concentrations: 0.90 +/- 0.11 mg/m3
- Particle size: 0.11 micrometer
- Type or preparation of particles: aerosols were prepared witha Dautrebande D30 aerosol generator.
EXAMINATIONS:
The respiratory meachanisms of the guinea pigs were measured. Intrapleural pressure, tidal volume, and rate flow of gas in and out of the respiratory system are recorded. From these data the pulmonary flow resistance may be obtained. Pulmonary flow resistance and the compliance are in cm water/ml/s and mm/cm water, respectively.

Result: MORTALITY: -
- Time of death: -
- Number of deaths at each dose: -
CLINICAL SIGNS: Pulmonary resistance and compliance of sodium sulphate was not significantly different from the control.
NECROPSY FINDINGS: -
POTENTIAL TARGET ORGANS: -
SEX-SPECIFIC DIFFERENCES: -

Test substance: No details on where the sodium sulfate was obtained or on purity are given.

Reliability: (4) not assignable
Documentation insufficient for assessment

27-SEP-2005 (4)

5.1.3 Acute Dermal Toxicity

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Route of admin.: i.p.
Value: 3000 - 4100 mg/kg bw

Reliability: (4) not assignable
Reference not translated
26-SEP-2005 (20)

Type: LD50
Species: mouse
Route of admin.: i.p.
Value: 2400 - 3400 mg/kg bw

Reliability: (4) not assignable
Reference not translated
26-SEP-2005 (20)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: 500 mg
Exposure: Occlusive
Exposure Time: 4 hour(s)
No. of Animals: 3
Vehicle: other: polyetyleneglycol 400
Result: not irritating
EC classificat.: not irritating

Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1991
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Determination of irritant/corrosive effects were examined using rabbits, according to OECD 404.
DEVIATIONS FROM GUIDELINE: no deviations reported
GLP: yes
STATISTICAL METHODS: DRAIZE score system was used
METHOD OF CALCULATION: not described
ANALYTICAL METHODS: not applied
Result: AVERAGE SCORE
- Erythema: score = 0, after 14 days
- Edema: score = 0 after 14 days
REVERSIBILITY: not described
OTHER EFFECTS: Irrit. index : edema = 0.0; erytheme = 0.0.
Body weight, 3.7 - 4.2 kg
Test condition: TEST ANIMALS: Rabbits
- Strain: HC:NZW
- Sex: not described
- Source: Interfauna, Ltd, UK

- Age: adults
- Weight at study initiation: not described
- Number of animals: 3
- Controls: Contralateral skin area not treated
ADMINISTRATION/EXPOSURE
- Preparation of test substance: 500 mg pulverized in PEG 400
- Area of exposure: dorso-lateral areas of the trunk.
- Occlusion: Patches hypoallergenic Hansamed (Beiersdorf)
- Vehicle: PEG 400
- Concentration in vehicle: 500 mg
- Total volume applied: not described
- Postexposure period: 14 days
- Removal of test substance: washed with water
EXAMINATIONS
- Scoring system: DRAIZE scores
- Examination time points: 1, 24, 48, 72 hours, 7, 14 days.

Reliability: (1) valid without restriction
Guideline study

26-SEP-2005 (13)

5.2.2 Eye Irritation

Species:	rabbit
Concentration:	90 mg
Dose:	100 other: µl
Exposure Time:	24 hour(s)
No. of Animals:	3
Vehicle:	no data
Result:	slightly irritating
EC classificat.:	irritating

Method:	Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"
Year:	1991
GLP:	yes
Test substance:	as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Determination of irritant/corrosive effects were examined using rabbits, according to OECD 405.
DEVIATIONS FROM GUIDELINE: no deviations reported
GLP: yes
STATISTICAL METHODS: DRAIZE score system was used
METHOD OF CALCULATION: not described
ANALYTICAL METHODS: not applied

Result: AVERAGE SCORE
- Cornea: 0 no effect (7 days), irrit. index 0.0
- Iris: 0 no effect (7 days) irrit. index 0.0
- Conjuntivae (Redness): 1 (48 hours) irrit. index 1.0
- Conjuntivae (Chemosis): 0 (7 days)
- Overall irritation score: 1.3 (slightly irritating)

DESCRIPTION OF LESIONS: no

REVERSIBILITY: within 7 days

OTHER EFFECTS: -

Test condition: TEST ANIMALS: Rabbits
- Strain: HC:NZW
- Sex: not described
- Source: Interfauna, Ltd, UK

- Age: adults
- Weight at study initiation: not described
- Number of animals: 3
- Controls: other eye

ADMINISTRATION/EXPOSURE
- Preparation of test substance: Pulverized powder
- Amount of substance instilled: 90 mg
- Vehicle: not described
- Postexposure period: 21 days
- exposure : 24 hours

EXAMINATIONS
- Ophtalmoscopic examination: yes
- Scoring system: DRAIZE system
- Observation period: 21 days
- Tool used to assess score: optical instrument (hand slit lamp)

Reliability: (1) valid without restriction
Guideline study
26-SEP-2005 (13)

5.3 Sensitization

Type:	Patch-Test	
Species:	human	
Concentration 1st:	Induction	1.25 % semiocclusive
2nd:	Challenge	1.25 % semiocclusive
No. of Animals:	65	
Vehicle:	water	
Result:	not sensitizing	
Classification:	not sensitizing	

Method: other: not specified
Year: 1976
GLP: no
Test substance: other TS

Method: TEST ANIMALS: human
- Strain: -
- Sex: male/female
- Source: -
- Age: 16-70
- Weight at study initiation: -
- Number of animals: 56 male and 5 female
- Controls: -

ADMINISTRATION/EXPOSURE
- Study type: Patch test.
- Preparation of test substance for induction: A 1.25% aqueous solution was prepared. This concentration represents a 100 fold increase of the normal use level.
- Induction schedule: Subjects were exposed on their backs. The test patch unit consited of a strip of two-inch wide blenderm surgical tape with two rows of five 12.7 mm filter paper discs each. The first application lasted for 48 hours. All other inductions were for 24 hours. Reactions tohe initial site were scored 48 and 96 hours after patch removal. 8 other 24 hour inductions were done on mondays, Wednesdays and Fridays (3.5 weeks)on 3 alternate sites (unless the reaction or tape irritation was severe than

other sites were used). Reactions were recorded 3-9 hours before application and 24 hours after patch removal.
- Concentrations used for induction: 1.25% aqueous solution.

- Concentration in Freuds Complete Adjuvant (FCA): -
- Challenge schedule: On monday in week 7 subjects were challenged on a previously unpatched site. After 48 hours the patches were removed. The patches were scored 48 hours 48 following removal.
- Concentrations used for challenge: 1.25% aqueous solution.

- Rechallenge: subjects that showed signs of sentisation in the challenge phase were tested again after a 2 week rest period.
At the original concentration under occlusion, in a dilution of original strenght (1:3) under occlusion, as used in practice (subject applied the project to the flex part of the arm 3 times/day for 5 days.
- Positive control: -
EXAMINATIONS
- Grading system: patch reactions were scored by experienced technitians. According to teh following scoring system:
0 No evidence of any effect
+/- Barely perceptible. Minimal faint unifrom spotty erythema.
1 Mild. Pink unifrom erythema covering most of the contact site.
2 Moderate. Pink-red erythema visibly uniform in the whole contact site.
3 Marked. Bright red erythrema with accompanying edema, petechiae or papules.
4 Severe. Deep red erythema with vesiculation or weeping with or without edema.
- Pilot study: -

Result: RESULTS OF PILOT STUDY: -

RESULTS OF TEST
- Sensitization reaction: One subject showed a score 1 reaction during the induction period. Other subjects did not react to the application (data not shown).
- Clinical signs: Mild. Pink unifrom erythema covering most of the contact site.
- Rechallenge: Data not shown.

Test substance: Bath salt crystals allegedly containing 80.8% sodium sulfate.

Reliability: (4) not assignable
The report is incomplete and unsigned. Lab and authors are unknown and there is no quality control. Individual data are not shown.

26-SEP-2005 (22)

5.4 Repeated Dose Toxicity

Type: Sub-acute
Species: rat Sex: male
Strain: Sprague-Dawley
Route of administration: oral feed
Exposure period: 4 weeks
Frequency of treatment: diets were provided ad libitum for 4 weeks

Post exposure period: none
Doses: Experiment a 0.88 mmol/kg feed
Experiment b 8.64 mmol/kg feed day 1-8
17.28 mmol/kg feed day 9-16
34.56 mmol/kg feed day 17-24
65.12 mmol/kg feed day 25 for 4-6 days
Experiment c 138 mmol/kg feed
Control Group: yes, concurrent no treatment
NOAEL: ca. 2000 mg/kg

Method: other: not specified
Year: 1960
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS: Sprague Dawley rats
- Age: weanling, young
- Weight at study initiation:
- Number of animals: 6 rats per group
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 4 weeks
- Type of exposure: oral feed, diet avaialable ad libitum
- Post exposure period: none
- Vehicle: basal diet, cornstarch diet, 67% cornstarch, 24% 'vitamin free' casein, 5% crisco (cristalized cottonseed oil) and 4% salt mixture (3.8% magnesium sulfate, anhydrous and 0.02% maganous sulfate. No sodium sulfate.) and vitamins.
- Concentration in vehicle: see doses
- Total volume applied: the feed intake in week 4 of the rats receiving sodium sulfate is presented: 408 (371-453) g.

- Doses:
Experiment a 0.88 mmol/kg feed
Experiment b 8.64 mmol/kg feed day 1-8
17.28 mmol/kg feed day 9-16
34.56 mmol/kg feed day 17-24
65.12 mmol/kg feed day 25 for 4-6 days
Experiment c 138 mmol/kg feed
SATELLITE GROUPS AND REASONS THEY WERE ADDED: -
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: records of any diarrhea that occurred were kept. In experiment c teeth were examined.
- Mortality: -
- Body weight: at the beginning of the study, at the end of each week and just before study termination.
- Food consumption: feed intakes and feed:gain ratios were obtained for each week.
- Water consumption: In experiment c the amount of water drunk during the first 48 h of the third week was recorded.
- Ophthalmoscopic examination: -
- Haematology: In experiment c blood was colelcted from the tail after 3.5 weeks for red and white bloodcell counts and hemoglobin was determined. At termination of the study bllod was collected from the neck vain and analyzed for alkaline phosphate, inorganic phosphate and protein.
- Biochemistry: -
- Urinalysis: In experiment c the volume of urine was determined.
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: gastrointestinal organs were examined. The

small intestine and colon plus rectum were hung full length were measured. Organs were clenaed dried and weighed. I
- Microscopic: In experiment c a small snip of the stomach was removed for histological examination.
OTHER EXAMINATIONS: -
STATISTICAL METHODS:
In experments b and c the numerical results were analyzed statistically by analysis of variance, the hypothesis in every case being that the groups were equal. A multiple range test was performed when it was indicated that there was a difference among the groups at the 5% level or less. results were significantly different if P<0.05.

Result: NOAEL (NOEL), LOAEL (LOEL): At the top dose, the food contained around 2% of the respective sulfates, calculated to be around 2000 mg/kg/d.
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX:
- Time of death: -
- Number of deaths at each dose: 0
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
Data for experiment a are not presented in the article because at this low dose level no effects were seen.
- Mortality and time to death: -
- Clinical signs: Experiment c teeth: no changes compared with control group. Two slight cases of diarrhea that lasted for a day were observed in experiment b in the sodium sulfate group. One rat in experiment c showed diarrhea on 4 different days (3 conseccutive days) in the middle of the feeding period.
- Body weight gain: Experiment b and c: no changes compared with control group.
- Food/water consumption: Experiment c: no changes compared with control group.
- Ophthalmoscopic examination: -
- Clinical chemistry: -
- Haematology: Experiment c: no changes compared with control groups or other dose groups In red or white blood cell counts, hemoglobin, protein, alkaline phosphatase orminorganic phosphatase.
- Urinalysis: Experiment c urine volume: no changes compared with control groups or other dose groups.
- Organ weights: Experiment b and c: no changes compared with control group.
- Gross pathology: -
- Histopathology: -
- Other: -
STATISTICAL RESULTS: see above

Test substance: Sodium Sulfate was obatined as anhydrous powder from Merck, A.C.S.

Reliability: (2) valid with restrictions
Old study non-GLP and not according to standard guideline.

26-SEP-2005 (68)

Species: rat Sex: male
Strain: no data
Route of administration: inhalation
Exposure period: 8, 12, 44, 90, 720 hrs
Frequency of treatment: continuous (?)
Post exposure period: 1 month (size of recovery group not given)
Doses: 3, 11.06, 18.03, 40.05, 60.45 mg respectively, with concurrent exposure to 500 mg/l in drinking water
Control Group: other: one control group for each exposure group, size

not specified

Year: 1989
GLP: no

Remark: ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX:
cannot be calculated
Aerosol generation not described. Aerosol size, stability not described. exposure duration / day not given
Concentrations measured by potentiometric method
Calculated daily dose from inhalation at 3 mg/m3 is 0.66 (8 hr/day) to 2 mg/kg/day (24hr/day), compared to intake from drinking water 60 mg/kg/day.
LOAEC: 2 mg/m3
log(time-to-first appearance) plotted against log(concentration) shows 100% linear correlation for 2 of the 3 reported effect parameters. Such precision is unlikely to occur in biological systems.
Number of animals: 200; 5 exposure groups and 5 control groups, size not given. Report mentions complete recovery at 1 month post-exposure but size of recovery group not given. method for monthly isnpections of inner organs not given.
Time of death: n/a
Nr. of of deaths at each dose: none
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality and time to death: n/a
Clinical signs: not specifed

Result: At concentrations of 60, 40, 16, 11 and 3 mg/m3:
small but statistically significant effects on serum liver cholinesterase concentration (first appearing at 6, 12, 44, 90 and 720 hours respectively), prolongation of blood coagulation time (first appearing at 4, 8, 30, 64 and 510 hours respectivey) and brain irritablity as measured by "summated threshold potential (?)", (first appearing at 4, 8, 24, 45 and 288 hours respectively),
effects stated to be worse at end-of exposure (no data provided). Depression of spermatogenesis (presumably at end-of-exposure), at al concentrations.
All effects stated to be completely reversible within one month post-exposure (size of recovery groups not given).
Body weight gain:
- Food/water consumption: drinking water contained 500 mg sodium sulfate/liter. Consumptio data not given -
Ophthalmoscopic examination:
- Clinical chemistry: no abnormalities in blood histamine, brain cholinesterase, number of sulfhydryl groups,basic phosphatase activity in blood serum and content of ascorbic acid in the adrenals.
- Haematology:
No abnormalities were observed in number of erythrocytes and leucocytes, total haemoglobin, meth- and sulfhaemoglobin, presence of Heinz-Ehrlich bodies
- Urinalysis:
- Organ weights:
- Gross pathology:
- Histopathology: (? method not given) suppression of spermatogenesis
- Other:
STATISTICAL RESULTS: see above

Reliability: (3) invalid
results biologically implausible / insufficient

documentation for assessment
26-SEP-2005 (29)

Type: Chronic
Species: rat Sex: male
Strain: no data
Route of administration: inhalation
Exposure period: 3 months
Frequency of treatment: not given
Post exposure period: 1 month (size of recovery group not given)
Doses: dust concentration 1 mg/m3, with concurrent exposure to 500 mg/l in drinking water
Control Group: yes

Year: 1990
GLP: no

Remark: Dust generation, particle size, aerosol stability etc not described
exposure duration per day not given
Measured exposures in workplace atmosphere (shift average) 88 mg/m3, yet apparenty no clinical symptoms or complaints from humans
Method for "monthly ispection of inner organs" not given
Sulfate concentration in drinking water 500 mg/l;
caluculated maximum uptake from air < 0.1 (8-hr exposure) to .6 mg/kg/day (24hr/day exposure) vs. 60 mg/kg/day from drinking water

Result: small but significant changes in "summarized threshold potential" (measure of brain irritability), liver cholinesterase, blood cholinesterase, number of lymphocytes and neutrophils, body weight, relative liver weigt;
depression of spermotagenesis, histopathological changes in liver and testes, serious histopathological changes in the lungs and several cases of pneumonomia, all fully reversible after 1 month recovery.
results similar to those found in concurrent studies with sodium sulfite at 01. and 1 mg/m3 and a mixture of sulfite/sulfate at 1 mg/m3.
Test substance: Na2SO4 dust, not specified
Reliability: (3) invalid
Results biologically implausible; insufficient documentation for assessment
26-SEP-2005 (30)

Species: rat Sex:
Route of administration: oral feed
Exposure period: 6 weeks
Frequency of treatment: daily (feeding study)
Doses: 1 or 2 % in diet
Control Group: other: saline in equal concentrations

Method: other: not described
Year: 1976
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: In two experiments the direct effect of dietary intake of sodium sulfate was examined. One experiment with weanling rats, and another with adults, over

a 6 weeks exposure period.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described

Result: NOAEL (NOEL), LOAEL (LOEL): not determined
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality and time to death: not described
- Clinical signs: not described
- Body weight gain: exp1 weanling rats upto 10 g S/kg dm and exp2 adult rats upto 20 g S/kg dm (exp1/exp2)
control exp1 : 4.54 g/d
control exp2 : -1.42 g/d
exp1 : 4.49 g/d
exp2 : -1.95 g/d
- Food/water consumption:
water:
control exp1 : 28.0 ml/d
control exp2 : 36.8 ml/d
exp1 : 36.2 ml/d
exp2 : 57.4 ml/d
food:
control exp1 : 13.4 g/d
control exp2 : 13.8 g/d
exp1 : 13.5 g/d
exp2 : 15.2 g/d
STATISTICAL RESULTS: not described, Overall dietary supplementation with sodium sulfate did not significantly affect food/water intake and live-weight gain of rats.

Test condition: TEST ORGANISMS
- Age: not described
- Weight at study initiation: not described
- Number of animals: eight weaning and eight adult animals
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 6 weeks
- Type of exposure: oral
- Post exposure period: not described
- Vehicle: commercial diet
- Concentration in vehicle: 10-20 gram S/kg dm
- Total volume applied: not described
- Doses: in daily diet
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: no
- Mortality: not described
- Body weight: yes
- Food consumption: yes
- Water consumption: yes
- Ophthalmoscopic examination: no
- Haematology: no
- Biochemistry: no
- Urinalysis: no
STATISTICAL METHODS: not described

Reliability: (3) invalid
documentation was insufficient for assessment

26-SEP-2005 (104)

Type: Chronic
Species: hen Sex: female
Strain: other: White Leghorn
Route of administration: drinking water
Exposure period: 3-4 weeks
Frequency of treatment: continuous
Doses: 250-23328 mg/l

Control Group: yes
LC100 : ca. 23328 mg/l

Method: other: not a guideline study, see freetext
Year: 1974
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Commercial strain hens were supplied with sodium sulfate containing drinking water for a period of 4 weeks. Egg production, body weight, water en feed consumption and mortality were examined.
STATISTICAL METHODS: performance of treatement were compared to performance during pretreatment.
METHOD OF CALCULATION: not described
ANALYTICAL METHODS: no
Result: NOAEL (NOEL), LOAEL (LOEL): not described
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Mortality and time to death: at 16000 mg/l Na2SO4 cumulative death of 100% was observed at day 14, while death was already apparent at day 5.
- Clinical signs: not described

Conc. (mg/l Na2SO4)	egg production	water consumption	food consumtion	body weight
250	+6.5	-2.3	+13.3	+9.0
370	-16.1	-12.9	-3.7	-0.6
1000	+26.7	-2.0	+1.3	+1.3
1480	-15.6	-14.9	-1.7	+2.0
4000	+0.5	-12.0	+8.1	+1.1
5920	-24.4	+58.8	-14.2	-0.3
16000	-43.7	+146.7	-25.5	-14.7
23328	-73.8	-47.1	-77.8	*

* all animals died

- Ophthalmoscopic examination: -
- Clinical chemistry: -
- Haematology: -
- Urinalysis: -
- Organ weights: -
- Gross pathology: Necropsis of birds receiving 16000 mg/l sulphate showed extreme emaciation and visceral gouit.
- Histopathology: Microscopic examination of kidney tissues showed urate accumulation of individual glomeruli and tubules losing cellular detail.
- Other: none
STATISTICAL RESULTS: not described
Test condition: TEST ORGANISMS
- Age: not described
- Weight at study initiation: not described
- Number of animals: 2 hens per cage, 6 per block in 2 or 3 cage rows in
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 4 weeks with 4 weeks pretreatment
- Type of exposure: continuous in drinking water
- Post exposure period: no
- Vehicle: water
- Concentration in vehicle: 250, 1000, 4000 and 16000 mg/l

Na2SO4
- Total volume applied: n.a.
- Doses: not described
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: no
- Mortality: yes
- Body weight: yes
- Food consumption: yes
- Water consumption: yes
- Ophthalmoscopic examination: no
- Haematology: no
- Biochemistry: no
- Urinalysis: no
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: gout
- Microscopic: kidneys
OTHER EXAMINATIONS: egg production
STATISTICAL METHODS: all data were converted to performance percentages using the formula performance during treatment/performance during pretreatement x 100. Data were analyzed by analysis of variance when warranted.

Reliability: (2) valid with restrictions
No guideline study, but includes detailed information on used method, endpoints and statistical evaluation procedures.

07-AUG-2006 (1)

Type: Sub-acute
Species: other: Cattle Sex: male
Strain: other: Holstein
Route of administration: oral feed
Exposure period: 21 days
Frequency of treatment: ad lib
Post exposure period: not applicable
Doses: 0.8% in diet
Control Group: yes
LOAEL: ca. .8 %

Method: other: non-protocol
Year: 1991
GLP: no
Test substance: other TS

Remark: only three controls, sulfur content of diet not reported. However, effects so serious that they can safely be assumed to be absent in any control population.

Result: In a study with 9 young Holstein steers (validity 3, controls insufficiently desribed), a concentrate diet containing 0.8 % sodium sulfate (total sulfur content appoximately 0.36%) was given during 21 days. 3 controls were given the same diet without added sodium sulfate (total sulfur or sulfate content not reported). Five out of nine test animals vs. no controls developed clinically manifest poli-encephalomalacia (PEM) as well as macroscopically visible and histologically recognisable cerebral lesions (brain histology of not-affected animals not reported) . The onset of the disease correlated well with increasing concentrations of sulfide in the rumen. Thiamine concentrations in serum (another alleged cause of PEM) were not significantly affected. Similar disease due to high sulfur content of food was allegedly also reported earlier

in sheep
Test substance: Test substance: dosing based on total sulfur content of feed, brought up to required level by adding sodium sulfate
Reliability: (2) valid with restrictions
26-SEP-2005 (45)

Type: Sub-acute
Species: other: cattle Sex: male
Route of administration: oral feed
Exposure period: 5 weeks
Frequency of treatment: ad lib
Post exposure period: not applicable

Doses: 3860 ppm; 5540 ppm; 7010 ppm
Control Group: no
LOAEL: ca. 3860 ppm

Method: other: non-protocol
Year: 2002
GLP: no
Test substance: other TS

Result: three groups of 5 young heifers / group were fed diets with 3860 ppm, 5540 ppm and 7010 ppm of sulfur respectively during 5 weeks. Sulfur concentrations were reached by adding sodium sulfate to the desired level. Microscopic signs of PEM were seen in all four low-dose animals, macroscopic signs in 4/5 medium-dose and 4/5 high-dose animals. Clinical signs of PEM were seen in all animals. Onset of PEM correlated highly with sulfide concentrations in rumen. Other potential causes of PEM were excluded. (Niles, 2002.)
Test substance: Test substance: dosing based on total sulfur content of feed, brought up to required level by adding sodium sulfate
Reliability: (2) valid with restrictions
No control group. Effects so serious that they can safely be assumed to be absent in any control population.
26-SEP-2005 (73)

Type: Chronic
Species: other: chicken Sex:
Strain: other: S.C.W.L.
Route of administration: oral feed
Exposure period: 11 days
Frequency of treatment: Daily (feeding study)
Doses: 1,2,3,4 or 5 % in diet
Control Group: yes

Method: other: no guideline study, see freetext
Year: 1976
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: The response of chicks of 14 days of age to increasing levels of dietary sodium sulfate were investigated. Weight gain and feed intake were observed.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described
Result: NOAEL (NOEL), LOAEL (LOEL): not determined
- Number of deaths at each dose: No death recorded
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL: yes
- Mortality and time to death: No mortality

- Clinical signs: not described
- Body weight gain: weight gain decreased with increasing sulfate concentration.
- Food/water consumption: not reported
STATISTICAL RESULTS: not described

Test condition: TEST ORGANISMS
- Age: 14 day-old male chicks
- Weight at study initiation: weight was main test parameter

- Number of animals: randomized block design with 60 treatments arranged as a 2x5x6 factorial, with two

replications.
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 11 days
- Type of exposure: oral
- Post exposure period: not described
- Vehicle: commercial diet (basal diet wth 18% crude protein)
- Concentration in vehicle: 0 - 5 gram sulfate per 100 gram food
- Total volume applied: water ad libitum
- Doses: in daily diet 30 diets in total
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: no
- Mortality: yes
- Body weight: yes
- Food consumption: yes
- Water consumption: not described
- Ophthalmoscopic examination: no
- Haematology: no
- Biochemistry: no
- Urinalysis: no
STATISTICAL METHODS: analysis of variance for determination of weight gain and gain:feed ration according to Snedecor, G.W. Statistical Methods, Coll. Press Ames, Iowa, USA (1956).

Reliability: (3) invalid
documentation was insufficient for assessment

26-SEP-2005 (91)

Species: pig Sex: no data
Route of administration: drinking water
Exposure period: 28 days
Frequency of treatment: daily
Doses: 54-1800 mg/l
Control Group: yes, concurrent vehicle

Method: other: see freetext
Year: 1992
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: The effect of sulfate in drinking water on nursery pig performance and health was examined over 28 days with 415 weaned pigs.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described

Result: NOAEL (NOEL), LOAEL (LOEL): not determined
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX
- Time of death: 1 pig died within the first week

- Number of deaths at each dose: 1 pig at 600 mg/l
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Clinical signs: Increased prevalence of diarrhea was a trend as sulfate concentration increased.
- Body weight gain: cumulative weight in kg of body-weight/kg (sd)

Week	Control	600 mg/l	1800 mg/l
1	0.79 (0.61)	0.94 (0.78)	0.80 (0.63)
2	2.56 (1.14)	2.78 (1.90)	2.4 (1.05)
3	4.30 (1.70)	5.05 (2.67)	4.49 (1.94)
4	6.53 (2.31)	7.59 (3.37)	7.16 (2.75)

Observations in week 4 were for both 600 and 1800 mg/l statistically significantly different

Increased
- Food/water consumption: A non-significant trend in increase water intake was observed with increasing sulfate concentration.No differences in feed intake were observed between various sulfate concentrations. Feed to gain ratios for all treatments were not different.

- Clinical chemistry: isolates of E-coli were found in 14% of the pigs, from 1 pig rotavirus was isolated. No pigs were exposed to transmissible gastroenteritis virus. None of the treatments had an adverse effect on nursery pig performance.

STATISTICAL RESULTS: not described separately

Test condition: TEST ORGANISMS
- Age: 28 +/- 2 days
- Weight at study initiation: 6.8 kg mean weight
- Number of animals: 415 (male/female, males were castrated)
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 4 weeks
- Type of exposure: drinking water
- Post exposure period: not described
- Vehicle: farm well water
- Concentration in vehicle: 54, 600 and 1800 mg/l
- Doses: continuous in drinking water
- Feeding: pelleted 22% crude protein corn-soybean meal containing 20% dried whey. At the start of the third week the crude protein content was 18%.
CLINICAL OBSERVATIONS AND FREQUENCY:
- Clinical signs: Diarrhea, pathogenic E.coli and rota virus detection, enteropathogenicity in ligated intestinal loops, transmissable gastroentritus.
- Mortality: yes
- Body weight: yes, feed to gain ratio
- Food consumption: yes
- Water consumption: yes
- Ophthalmoscopic examination: no
- Haematology: yes
- Biochemistry: no
- Urinalysis: no
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: no

- Microscopic: no
OTHER EXAMINATIONS:
STATISTICAL METHODS: 7 replicates of 8 pigs/pen on water and 6 replicates of 8 pigs/pen for treatment with sulfate. Statistical evaluation compared mean water consumption, feed consumption, cumulative gain and feed-gain ratios by treatment group and week. Analysis of variance with repeated measures was used to account for the differences in treatment group over time. Initial weight was used as covariate in all analysis. Diarrhea scores were evaluated on an individual basis, using a non-parametric repeated measures design.

Reliability: (2) valid with restrictions
Acceptable, well documented publication which meets basic scientific principles.

26-SEP-2005 (108)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: S. Typhimurium TA1535, TA1537, TA100, TA98
Concentration: 312.5 to 5000 µg per plate with 4 dilutions
Cytotoxic Concentration: no cytotoxicity observed
Metabolic activation: with and without
Result: negative

Method: other: Salmonella/Microsome test, Ames et al, Mutation Res. 31, 347-364 (1975)
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Ames test as described by Ames et al (1975). Test was performed in duplicate with varying concentration range.
DEVIATIONS FROM GUIDELINE: no guideline study
GLP: yes
STATISTICAL METHODS: not applicable
METHOD OF CALCULATION: not applicable
ANALYTICAL METHODS: not described

Result: EFFECTS:
- With metabolic activation: both tests, no effects
- Without metabolic activation: both tests, no effects
FREQUENCY OF EFFECTS: n.a.
PRECIPITATION CONCENTRATION: not described
MITOTIC INDEX: not described
CYTOTOXIC CONCENTRATION: no toxicity observed up to 5000 mg/l
TEST-SPECIFIC CONFOUNDING FACTORS: not described
STATISTICAL RESULTS: n.a.

Test condition: SYSTEM OF TESTING
- Species/cell type: Salmonella typhimurium LT2 mutants: TA 1535, TA 100, TA 1537, TA 98
- Deficiences/Proficiences: Histidine
- Metabolic activation system: LT2 system
- No. of metaphases analyzed: not described
ADMINISTRATION:
- Dosing: 4 concentrations, 312.5-625-1250-2500-5000 mg/l and 8-40-200-1000-5000 mg/l
- Number of replicates: 4 per test

- Application: plate
- Positive and negative control groups and treatment: pos. control: sodium azide, nitrofurantoin, 4-nitro-1,2-phenylene diamine and 2-aminoanthracene; negative control
- Pre-incubation time: not described
CRITERIA FOR EVALUATING RESULTS: Based on Maron and Ames (1983).

Reliability: (1) valid without restriction
Comparable to guideline study

26-SEP-2005 (13)

Type: Cytogenetic assay
System of testing: human blood lymphocytes
Concentration: 5*10e-5 to 5*10e-3 M
Cytotoxic Concentration: no data
Metabolic activation: no data
Result: negative

Method: other: not specified
Year: 1992
GLP: no
Test substance: no data

Method: SYSTEM OF TESTING
- Species/cell type: human lymphocytes
- Deficiences/Proficiences: -
- Metabolic activation system: -
- No. of metaphases analyzed: -
ADMINISTRATION:
- Dosing: -
- Number of replicates: -
- Application: -
- Positive and negative control groups and treatment: -
- Pre-incubation time: -
DESCRIPTION OF FOLLOW UP REPEAT STUDY: -
CRITERIA FOR EVALUATING RESULTS: -

Result: GENOTOXIC EFFECTS: -
- With metabolic activation: -
- Without metabolic activation: -
FREQUENCY OF EFFECTS: -
PRECIPITATION CONCENTRATION: -
MITOTIC INDEX: -
CYTOTOXIC CONCENTRATION: -
- With metabolic activation: -
- Without metabolic activation: -
TEST-SPECIFIC CONFOUNDING FACTORS: -
STATISTICAL RESULTS:
The frequency of chromosomal abberations, sister chromatid exchanges, and micronuclei was not increased in human blood lymphocytes in this experiment. Also there were no changes in mitotic index or lymphocyte cell cycle.

Test substance: No data on the test substance sodium sulfate.

Reliability: (4) not assignable
Not assignable. Results are given but this is just a statement. No expsrimental data are given. The study is non-GLP and non-guideline.

26-SEP-2005 (66)

5.6 Genetic Toxicity 'in Vivo'

5.7 Carcinogenicity

Species: rat Sex: male
Strain: Sprague-Dawley
Route of administration: oral feed
Exposure period: up to 27 or 44 weeks
Frequency of treatment: daily (feeding study)
Doses: 0.84 % in diet
Result: negative
Control Group: yes

Method: other: no standardized method used
Year: 1975
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Male rats were fed diets containing Na2SO4. The study was part of a toxicity study on Azo Dyes. The sodium sulfate were included as control series.
METHOD OF CALCULATION:
not described

Result: MORTALITY: no mortality was observed (10 surviving rats in both series) in both test series after 27 and 44 weeks of exposure as compared to control (10 surviving rats).
CLINICAL SIGNS: No tumors were detected. No evidence of hyperplastic and/or dysplatic change after 16 weeks. No cholangiofibrosis or mild cirrhosis in the liver after 16 weeks were observed as compared to control.

BODY WEIGHT CHANGES: No significant differences in overall body weight gain or in liver weight were observed.

_group	Eff.no. of rats	starting weight g +/- SD mean	no. of rats surviving	Terminal body wght g +/- SD mean	Terminal liver wght g +/- SD mean
Control					
a	5	230.8-18.6	2	358.5	10.11
b	5	193.4 33.6	5	358.4-16.0	10.2-0.49
Na2SO4					
a	5	252.0-30.2	3	414.7-39.5	14.3-1.42
b	5	194.2-35.7	5	332.0-53.7	10.03-0.99

FOOD AND WATER CONSUMPTION CHANGES: no changes observed

Test condition: TEST ORGANISMS
- Age: not described
- Weight at study initiation: mean weight of animals 211.6 gram
- Number of animals: total 90 , 5 in a cage
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: Study was divided in two series. One series lasted 27 weeks, and the other 44 weeks
- Type of exposure: feeding study, daily feeding

- Post exposure period: no
FOR ORAL STUDIES:
- Vehicle: maize oil
- Concentration in vehicle: 8.4 gram/kg
- Total volume applied: 30 ml
- Doses: 0.84 % in diet
CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: yes
- Food consumption: Basal diet consited of pellets with 15-16% protein, 6-8% fat and 8-9 % fibre (Victoria Wheat growers Corp. Ltd, Melbourne, Aus.). The consumption rate was 10 g/rat per day at the start up to 17 g/rat per day at the end of the study.
- Water consumption: free acces to tap water
- Clinical signs: not described
- Mortality: yes
- Macroscopic examination: yes
- Ophthalmoscopic examination: not described
- Haematology: yes, haemoglobin estimations were performed.
- Clinical chemistry: not described
- Urinalysis: not described
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic: spleen, liver
- Microscopic: not described
OTHER EXAMINATIONS: lung sections were examined after staining with haematoxylin, eosin and the PAS method.
STATISTICAL METHODS: The probability of observing liver tumors of 1 cm or more in diameter, and evidence of metastatic spread or multiple tumors at death was calculated by an actuarial method, as described by Pilgrim and Dowd, Cancer Res. 23, 45 (1963). Differences between numbers rats bearing tumours of at least 1 cm diameter, were compared using Fisher's exact test.

Reliability: (3) invalid
No guideline study, 5 male animals only

26-SEP-2005 (16)

Species: mouse Sex: male/female
Strain: Swiss

Route of administration: s.c.
Exposure period: 26 weeks
Frequency of treatment: weekly
Doses: 31 µg in 0.01 ml sodium chloride (0.9%) per g body weight / week
Result: negative
Control Group: other: Na2SO4 served as control for 4-HMBD / historical controls

Method: other: see freetext
Year: 1987
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: Test was control test of investigation of carcinogenity of 4-(hydroxymethyl)benzenediazonium ion in mice. Mice were treated for 26 weeks, and observed for 150 weeks, to test substance and control (Na2SO4)
METHOD OF CALCULATION:
not described
Result: MORTALITY AND TIME TO DEATH: see attachement, table I

CLINICAL SIGNS: see attachment, table II
BODY WEIGHT GAIN: not described
FOOD/WATER CONSUMPTION: not described
GROSS PATHOLOGY: see attachment, table II
HISTOPATHOLOGY: see attachementm, table II
OTHER: see attachment, table II
TIME TO TUMOURS: see attachment, table II
STATISTICAL RESULTS: not described

Test condition: TEST ORGANISMS
- Age: 6 weeks (50:50 male/female)
- Weight at study initiation: not described
- Number of animals: 50 male and 50 female
ADMINISTRATION / EXPOSURE
- Duration of test/exposure: 26 weeks
- Type of exposure: subcutaneously injections weekly
- Post exposure period: not described
FOR ORAL STUDIES:
- Vehicle: 0.9 %v sodium chloride
- Concentration in vehicle: 31 µg per 0.01 ml vehicle per g body weight
- Total volume applied: not described
- Doses: weekly
CLINICAL OBSERVATIONS AND FREQUENCY
- Body weight: yes
- Food consumption: no
- Water consumption: no
- Clinical signs: yes
- Mortality: yes
- Macroscopic examination: yes
- Ophthalmoscopic examination: no
- Haematology: no
- Clinical chemistry: no
- Urinalysis: no
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Macroscopic Histological study: skin, subcutis, liver, spleen, kidneys, bladder, thyroid, heart, pancreas, testes, ovaries, uterus, nasal turbinals, lungs
- Microscopic: Yes, after staining with hematoxylin and eosin
OTHER EXAMINATIONS: All other pathological changes
STATISTICAL METHODS: not described

Attached doc.: RS2-Toth.doc
Reliability: (3) invalid
26-SEP-2005 (97)

5.8.1 Toxicity to Fertility

Type:	other: two parities using the same mice
Species:	mouse
Sex:	female
Strain:	ICR
Route of administration:	drinking water
Exposure Period:	1 week prior to breeding until study termination
Frequency of treatment:	drinking water was avaialble ad libitum
Premating Exposure Period	
male:	no exposure
female:	1 week
Duration of test:	1 week prior to breeding until study termination
No. of generation studies:	1
Doses:	0, 0.924, 1.848, 3.696, 7.392 g/liter

Control Group: other: One control group received deionized distilled water and one received deionized distilled water with 2,392 ppm Na
NOAEL Parental: >= 7392 mg/l
NOAEL F1 Offspring: >= 7392 mg/l
other: NOAEL F1 Offspring 2 : >= 7392 mg/l
Result: No effects on litter size and weaning weight were seen. Reproductive performance is not affected in this study.

Method: other: not specified
Year: 1988
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS: ICR mouse
ADMINISTRATION / EXPOSURE
- Type of exposure: drinking water
- Duration of test/exposure: 1 week before study until study termination.
- Treatment: drinking water was available ad libitum
- Control group and treatment: One control group received deionized distilled water and one received deionized distilled water with 2,392 ppm Na
- Vehicle: deionized water
- Concentration in vehicle: 0, 0.924, 1.848, 3.696, 7.392 g/liter
- Total volume applied: -
- Doses: drinking water with 0, 0.924, 1.848, 3.696, 7.392 g/liter sodium sulfate ad libitum.
- Concentrations: -
- Particle size: -
- Type or preparation of particles:-
MATING PROCEDURES:
After one week a male mouse that had received tap water only was randomely bred withe ach female mouse. The female was checked every day for a vaginal plug. When a vaginal plug was observed the male was removed.
STANDARDIZATION OF LITTERS:
The litter were standardized to 8 pups per litter. The dams with fewer tahn 8 pups received pups from other dams in the same dose group. If these were not available they were assigned pups from a lower dose group.
PARAMETERS ASSESSED DURING STUDY P AND F1(1) AND F1(2):
- Clinical observations:
water consumption was measured daily during the 2nd and 3rd week of gestationa and 1st and 2nd week of lacation. (the measureemnts during week 1 of gestation were discarted due to leakage from drinking bottles, the measurements performed during week 3 of lacation were also discarted because the pups started drinking water).
Bodyweights of the dams were recorded at parturition and litter sizes were determined.
At 21 days pp the dams and litters were weighed.
- Estrous cycle: -
- Sperm examination: -
- Others: -
OFFSPRING: -
ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
- Organ weights P and F1: -

- Histopathology P and F1: -
- Histopathology F1 not selected for mating, F2: -
OTHER EXAMINATIONS: -
STATISTICAL METHODS:
The description of the statistical analysis remains unclear: The least square mean analysis of variance technique was used to analyze the data. One contrast was used to compare the different groups. Sulfate treatment effects were partitioned into linear, quadratic and cubic components using orthogonal contrasts. Student's t-test were used to determine the difference in water consumption between weeks in both gestation and lactation.

Result: NOAEL (NOEL): 7392 mg/l = 5000 ppm
ACTUAL DOSE RECEIVED BY DOSE LEVEL BY SEX:
TOXIC RESPONSE/EFFECTS BY DOSE LEVEL:
- Parental data and F1:
- Body weight: gestational and lactational body weight gian was not influenced by level of sulfate consumed.
- Food/water consumption: a decrease in water consumption was seen. It is suggested that the amials became acclimated to the high sulfate levels because the water consumtion levels ere higher during the 2nd week of lactation comared to the 1st week during the 2nd parity.
- Description, severity, time of onset and duration of clinical signs: -
- Fertility index: -
- Precoital interval: -
- Duration of gestation: -
- Gestation index: -
- Changes in lactation: -
- Changes in estrus cycles: -
- Effects on sperm: -
- Hematological findings incidence and severity:-
- Clinical biochemistry findings incidence and severity: -
- Mortality: 0
- Gross pathology incidence and severity: -
- Number of implantations: -
- Number of corpora lutea: -
- Ovarian primordial follicle counts: -
- Organ weight changes: -
- Histopathology incidence and severity: -
- Offspring toxicity F1 and F2: -
- Litter size and weights: litter size was not affected by treatment.
- Sex and sex ratios: -
- Viability index: none of the pups died.
- Post natal survival until weaning: none of the pups died.
- Effects on offspring: -
- Postnatal growth, growth rate: -
- Vaginal opening (F) or preputial separation (M): -
- Other observations; -
STATISTICAL RESULTS: -

Test substance: Sodium sulfate, reagent grade.

Reliability: (4) not assignable
Non-GLP and non-guideline study. Not sufficiently detailed. The set up of the study differs from the standard. Mice were exposed from 1 week before the study until study termination. The same female mice gave birth to the first and the second litter. The litter was weaned at 21 days pp and the mice were mated again.The males were not exposed. Possibly only the mice with two subsequent litters were

involved in the analysis.
27-SEP-2005 (7)

5.8.2 Developmental Toxicity/Teratogenicity

Species: mouse Sex: female
Strain: other: ICR/SIM
Route of administration: other: oral (gavage)
Exposure period: 4 days (gestation day 8-12)
Frequency of treatment: once daily
Duration of test: up to day 22 of pregnancy
Doses: 2800 mg/kg/day
Control Group: other: yes (N=28, vehicle alone H2O)

Method: other: no guideline study
Year: 1986
GLP: no

Result: As part of a validation of a developmental screen, pregnant mice were exposed to 55 compounds, composed of known teratogens, known non-teratogens or equivocal substances.
Exposure: single daily dose by gavage; dose level at or near induction of maternal toxicity.
Vehicle alone (H20): 15 control groups of 28-30 mice.
Vehicle alone (Corn oil): 13 control groups of 28-30 mice.

Endpoints: maternal weight gain, delivery rate, litter size, % live birhts, pup weight day 1 and day 3, neonatal survival rate, macrospoci visceral and skeletal abnormalities
Statistical analysis:
maternal weight :two-tailed analysis of variance
live and dead litter size: one-tailed analysis of variance
neonatal survival rate: Fisher one-tailed exact probability.
neonatal weight: two-tailed analysis of variance with litter size as co-variant
Overal results: reported "Seidenberg JM , Becker RA: A summary of the results of 55 chemiclas screened for developmental toxicity im mice. Teratogenesis, Carcinogenesis, Mutagenesis 7:17-28 (1987)
Results for sodium sulfate:
Compared to controls, slight increase in neonatal body weigh at day 1 pp.(1.80+0.14 vs 1.72 + 0.13 grams).
Normal maternal weight gain, normal delivery rate, normal litter size, normal nr. of live births, normal weight of pups on day 3, no macroscopic visceral or sceletal abnormalities
Test substance: Na2SO4, not specified
Reliability: (2) valid with restrictions
non-standard screening test.
26-SEP-2005 (90)

Species: mouse Sex: female
Strain: other: ICS/SIM
Route of administration: other: oral (gavage)
Exposure period: 4 days (gestation day 8-12)
Frequency of treatment: once daily
Duration of test: up to day 22 of pregnancy
Doses: Na2SO4: 2800 mg/kg
Control Group: other: yes (N=28, vehicle alone H2O)

Method: other: no guideline study

Year: 1987
GLP: no

Remark: Reviewer disagrees, slight increase in body weight of neonates on day 1 p.p. only is not an adverse effect and is biologically totally irrelevant.
Result: Summary of results of a screening study fully described in: Seidenberg JM, Anderson DG, ecker RA: validation of an in vivo developmental screen in the mouse. Teratogenesis, Carcinogenesis and Mutagenesis, 6:361-374 (1986) See RS
Overal results:
24 of 26 substances previously reported as positive in teratogenicity / embryotoxicity tests scored positive in this screen.
93% of substances previously reported as negative scored negative in this screen.
equivocal substances 4of 5 positive in this screen
no data: 3 out of 9 considered positive, among them sodium sulfate.
Results for sodium sulfate:
Compared to controls, slight increase in neonatal body weigh at day 1 pp.(1.80+ -0.14 vs 1.72 + -0.13 grams).
Normal maternal weight gain, normal delivery rate, normal litter size, normal nr. of live births, normal weight of pups on day 3, no macroscopic visceral or sceletal abnormalities; Considered by authors as a positive outcome of screening
test.
Test substance: Na2SO4, not specified
Reliability: (2) valid with restrictions
non-standard screening test.; scoring criteria too strict.
27-SEP-2005 (89)

Species: mouse Sex: female
Strain: other: CF-1
Route of administration: s.c.
Frequency of treatment: single injection at day 8 or 9 of gestation
Duration of test: not described
Doses: 60 mg/kg bw
Control Group: yes
Result: increased maternal weight gain, no soft tissue abnormalities, increase of skeletal abnormalities (delayed ossification)

Method: other: no standardized method used
Year: 1973
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: METHOD FOLLOWED: The teratogenic effects of sodium sulfate injected s.c. in albino mice was investigated. The study examined mice after administration at day 8 and 9 of gestation.
STATISTICAL METHODS: not described
METHOD OF CALCULATION: not described
Result: NOAEL (NOEL), LOAEL (LOEL): not determined
MATERNAL TOXIC EFFECTS BY DOSE LEVEL:
- Mortality and day of death: not described
- Number aborting: not described
- Number of resorptions: See attachement
- Duration of Pregnancy: not described

- Body weight: see attachement
- Food/water consumption: not described
- Description, severity, time of onset and duration of clinical signs: Soft tissue abnormalities were not significantly different from the control group. Skeletal abnormalities , described as delayed ossification, especially in phalanges, sternebrae and skull, were statistically different form control group .
- Hematological findings incidence and severity: not described

- Clinical biochemistry findings incidence and severity: not described
- Gross pathology incidence and severity:
- Organ weight changes:
- Histopathology incidence and severity:

FETAL DATA:
- Litter size and weights: 6, no weight determined
- Number viable: 51 fetuses
-·Sex ratio: not determined
- Postnatal growth: not described
- Postnatal survival: not described
- Grossly visible abnormalities: no abnormalities
- External abnormalities: see attachement, no abnormalities
- Soft tissue abnormalities: see attachement, no abnormalities
- Skeletal abnormalities: see attachement, no abnormalities

STATISTICAL RESULTS: not described

Test condition: TEST ORGANISMS:
Albino mice (CF-1) (25-30 gram), obtained from Carworth Farms, Inc. New York, USA.
ADMINISTRATION / EXPOSURE
- Type of exposure: injection subcutaneous
- Duration of test/exposure: as described by Iuliucci, J.D., Gautieri, R.F., J. Pharm. Sci, 60:420 (1971).
- Treatment: at day 8 or 9 of gestation
- Control group and treatment: yes, untreated (saline)
- Vehicle: distilled water
- Concentration in vehicle: 10 mg/ml
- Total volume applied: not described
- Doses: one injection
- Concentrations: 60 mg/kg body weight

PARAMETERS ASSESSED DURING STUDY:
- Body weight gain: yes, ratio between start and end of study
- Food consumption: no
- Clinical observations: yes, soft tissue abnormalities, skeletal abnormalities and resorption uterine horns
- Examination of uterine content: no
- Examination of fetuses: yes
- Litter : yes

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC):
OTHER EXAMINATIONS: Exencephaly, Axial skeletal fusions and cryptorchid testes.
STATISTICAL METHODS: as described by Iuliucci, J.D., Gautieri, R.F., J. Pharm. Sci, 60:420 (1971).

Attached doc.: RS1-Arcuri&Gautieri.doc

Reliability: (2) valid with restrictions
Not a guideline study. Experiment described in detail. Not

all parameters determined. Endpoints are not all clearly described.

27-SEP-2005 (9)

5.8.3 Toxicity to Reproduction, Other Studies

5.9 Specific Investigations

5.10 Exposure Experience

Type of experience: Human - Epidemiology

Method: Method: Cross-sectional study, internal sub-cohort study
Subjects: 119 male workers from natural sodium sulfate mines.
Age range: 17 to 58
exposure duration: 0.6-31 years
(no control group, study outcomes compared with "normal values", source not given).
Exposure: Na2SO4 dust ,range 5 mg/m3 to 150 mg/m3
(sampling method, strategy, number, frequency and timespan of sampling not given).

Result: General medical screening, lung function tests, blood pressure, skin condition, gastro-intestinal functioning, serum sodium, calcium, potassium chloride and sulfate content were all within normal ranges (i.e presumably as found in the general population).

Mean urinary excretion of inorganic sulfate exceeded 2.2 gr/liter in all workers and thirty percent of the workers excreted more than 3 gr of inorganic sulfate per day, indicating massive uptake from recent exposure. The only subjective symptom indicated by the workers was nasal irritation and runny noses on exposure to dust.

Internal sub-cohort study:
Short exposure duration subcohort:
subjects: More than 10 years of exposure (n=77)
age 28.0 +-10,
exposure duration 3.1 + 2.8 years
Long exposure duration subcohort:
Subjects: more than 10 years exposure (n=42)
age 454.5 + 8.8,
exposure duration 19.9 + 3.6 years
Results:
No differences other than explained by age difference.

Reliability: (2) valid with restrictions
Absence of control group, incomplete description of exposure
and possibility for healthy worker effect severely restrict extrapolation

01-DEC-2004 (59)

Type of experience: Livestock - Exposure through Feeding

Remark: Method:
31 sows and 27 gilts were each allotted to three treatments to study the effect of water quality during gestation and lactation. Sulfate was added to the water at concentrations

in three treatments (1) 320 - 620 mg/l (2) 1820 - 2840 mg/l (3) 3320 - 5080 mg/l. Water was offered ad libitum. from 30 days post-breeding through 28 days lactation.
Results:
There was no significant difference in gestation or lactation, number or weight of pigs at birth or at weaning. Water consumption did not differ during gestation, but increased as salt levels increased. Water consumption was 13.6, 14.2 and 16.8 liter/day for lactating females in treatment 1, 2 and 3.
These results suggests that sulfates up to and including 3320 mg/l, in water have no significant effect on reproduction in the gilt or sow.

Reliability: (3) invalid

Documentation insufficient for assessment

07-NOV-2001 (79)

Type of experience: other: Human - controlled study

Remark: METHOD:
The objective of the study was to provide additional information regarding whether sensitive populations (infants
and transients) may be adversely affected by sudden exposure
to drinking water containing high levels of sulfate.

One hundred and five study participants were divided among the dose groups as follows: 24
received 0 mg/L sulfate; 10 received 250 mg/L sulfate; 10 received 500 mg/L sulfate; 33 received 800
mg/L sulfate; and 28 received 1200 mg/L sulfate. The number of bowel movements recorded each day by study participants were analyzed. There were no statistically significant differences in the bowel movements among the groups on days 3, 4, 5, or 6. There were also no statistically significant differences in the bowel movements reported when comparing days 1 and 2 (the days when there was no sulfate in the water) with days 3, 4, and 5 within each dose group. To examine the data for a trend toward increased frequency of reports of diarrhea with increased dose of sulfate, a logistic regression model were the dose as an ordinal variable was included for osmotic diarrhea was included. There was no statistically significant increase in reports of diarrhea with increasing dose (one-sided p = 0.099).

RESULTS:

One hundred five study participants were divided among the dose groups as follows: 24 received 0 mg/L sulfate; 10 received 250 mg/L sulfate; 10 received 500 mg/L sulfate; 33 received 800 mg/L sulfate; and 28 received 1200 mg/L sulfate. The demographic information for the study population was as follows: the mean age of participants was 42 years; the majority (62%) was female;
the races included in the study population were white (80%), black (13%), and Asian/Pacific Islander (7%). Ninety-five percent of the participants were non-Hispanic.

In the experimental trials with adult volunteers, no significant dose-response association between acute exposure to sodium sulfate in water (up to 1200 mg/L) and reports of diarrhea were found.
However, a weak (not statistically significant) increase in reports of diarrhea at the highest dose level when it was compared to the combined lower doses was observed.

Remark: concentration in drinking water known, but not actual dose.

Reliability: (4) not assignable
Documentation insufficient for assessment: Abstract only.

27-SEP-2005 (76)

Type of experience: Human

Remark: Inhalation of sodium sulfate dust causes irritation of the mucuous membranes, and prolonged skin contact has a drying effect.

Reliability: (3) invalid
Documentation insufficient for assessment.

27-SEP-2005 (101)

Type of experience: Livestock - Exposure through Feeding

Remark: Association between sulfate in drinking water and diarrhea in swine was investigated. Sulfate concentrations ranged from 5.99 to 1629 mg/l recorded at 54 farms in Ohio USA. Associations between sulfate concentrations and prevalence of diarrhea could not be established.

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (107)

Type of experience: Human - Epidemiology

Remark: Evaluation of infant diarrhea associated with elevated levels of sulfate in drinking water.

Method:
274 households were investigated in South-Dakota USA.
Sulfate concentrations in drinking water was determined.
Data on infant diarrhea were collected using questionnaires.
Logistic regression was used to estimate the risk for diarrhea.

Results:
69% of the households drank municipal water and 54% used it in the infants diet. 39 infants developed diarrhea. Of the 170 households that submitted water samples, 141 were using the water in the infants diet. The median sulfate concentration of the water was 264 mg/l. 25 infants developed diarrhea.
Average infant daily sulfate intake was not significantly associated with an increase diarrhea rate. There was no significant association between sulfate intake and the incidence of diarrhea for the range of sulfate studies. There was no effect of a dose-response or threshold effect.

Reliability: (4) not assignable

Only secondary literature available

09-NOV-2001 (39)

Type of experience: Livestock - Exposure through Feeding

Remark: Artificially reared neonatal piglets were used to study the effect of inorganic sodium sulfate on bowel function in human infants.

Method:
Two experiments were conducted to evaluate the effect of high levels of inorganic sulfate intake on the growth, feed intake and feaces consistency.
40 pigs with an average age of 5d were individually caged abd reared with an automatic feeding device. Ten pigs per dietary treatment were fed one of four diets containing the following levels of inorganic sodium sulfate (mg/l diet): 0, 1200, 1600, 2000 for exp 1 (18 days study), and 0, 800, 2000, 22000 for exp. 2 (16 days study).

Results:
The levels of sulfate did not affect (P>0.05) the growth of piglets, or their food intake. 1200 mg/l sulfate had no effect on feaces consistency, while 1800 mg/l sulfate did (non-pathogenic diarrhea). Added sulfate did not affect (P> 0.05) relative kidney weight. The results suggest that the level of added dietary inorganic sulfate at which 50% of piglets develop nonpathogenic diarrhea is between 1600 and 1800 mg/l.

Reliability: (2) valid with restrictions
Acceptable, well documented study.

22-JUN-2005 (43)

Type of experience: Direct observation, poisoning incidents

Remark: Two outbreaks of poisoning (eosinophilic meningoencephalitis) in pigs due to treatment with sodium sulfate. Experimental reproduction indicated a similar syndrome.

Method:
8 12 weeks old pigs were each given by drneching gun 50 gram of sodium sulfate, dissolved in a minimum amount of water daily for 3 consecutive days. Controls were treated with water.
Results:
2 of the treated pigs were found dead on day 4, and 3 were in prostrate and in extremis. The latter 3 animals were killed for examination. The three were all inco-ordination, blind and had epileptiform convulsions. Histopathological examination revelaed lesions of the central nervous system, vacuolation, nueronal degeneration, cortical laminar malacia. Large numbers of eosinophils and some macrophages were present in the meninges and in the perivascular spaces in the cortical white matter.

Reliability: (3) invalid

Documentation insufficient for assessment

22-JUN-2005 (32)

Type of experience: Human - Exposure through Food

Remark: Three illustrative cases of diarrhea in infants in Canada following ingestion of well waters with a sulfate content above 600 mg/l. Other causes such as infections or other presence of chemicals were excluded. The estimated daily dose would have been around 70- 100 mg/kg/day.
It is recommended that water with more than 400 mg/l sulphate be regarded as unsuitable for infant feeding.

Remark: clinically, cause and effect relationship clearly established. Extrapolation to general population not possible in the absence of data on the population at risk and incidence

Reliability: (4) not assignable

27-SEP-2005 (25)

5.11 Additional Remarks

Type: Toxicokinetics

Remark: Review:

Sulfate is a normal constituent of the blood and is a normal metabolite of sulfur-containing amino acids, and excess sulfate is excreted in the urine. Daily sulfate excretion is reported to be 0.20 to 0.25 mmol/kg bw/day and higher in children.

In male adult Wistar rats, approximately 73% of dietary calcium or magnesium sulfate salts was absorbed, although absorption was partly dependent on other dietary elements.

Reliability: (4) not assignable

29-SEP-2005 (50)

Type: other: Oral toxicity to pigs

Remark: Sodium sulfate (Glauber's salt) toxicity was observed in pigs after drenching eight-week old pigs with 50 g sodium sulfate for three days, and restricting their water supply. The animals showed nervous signs, twitching, tremors and convulsions. The most noticeable lesion at post mortem was widespread vacuolation and necrosis of the cerebral cortex. The sodium concentration of the cerebrospinal fluid was significantly higher than normal.

Reliability: (3) invalid
Documentation insufficient for assessment

26-SEP-2005 (26)

(1) Adams, A.W., Cunningham, F.E., Munger, L.L. (1975). Some effects on layers of sodium sulfate and magnesium sulfate in their drinking water. Poultry Sci. 54(3):707-714.

(2) Allgemeine Verwaltungsvorschrift (1990). Uber die nahere bestimmung wassergefahrdender stoffe und ihre einstufung entsprechend ihrer gefahrlichkeit-VwV wassergefahrende stoffe (VwVwS) 9.3.1990.

(3) Ambient water Quality Guidelines for sulphate (2000). Ministry of Environment, Lands and Parks Province of British Columbia, Water Quality Section Water Management Branch Victoria, BC, Canada.

(4) Amdur M.O., Bayles, J., Ugro, V., Underhill, D.W. (1978). Comparative irritant potency of sulphate salts. Environ. Res. 16(1-3):1-8.

(5) Anderson, B.G. (1944). The toxicity thresholds of various substances found in industrial wastes as determined by the use of daphnia magna. Sewage Works J. 16(6):1156-1165.

(6) Anderson, B.G. (1946). Industrial wastes - The toxicity thresholds of various sodium salts determined by the use of daphnia magna. Sewage Works J. 18(1):82-87.

(7) Andres, C.J. Cline, T.R. (1989). Influence of Sulfate in Drinking Water on Mouse Reproduction during two Parities. Journal of Animal. Sciences. 67:1313-1317.

(8) Arambasic, M.B., Bjelic, S., Subakov, G. (1995). Acute toxicity of heavy metals (copper, lead, zinc), phenol and sodium on Allium cepa l., Lepidium sativum l. and Daphnia magnaSt.: comparitive investigations and the practical applications. Water Res. 29(2):497-503.

(9) Arcuri, P. and Gautieri, F. J. (1973). Morphine-induced fetal malformations. 3. Possible mechanisms of action. Pharmaceut. Sci. 62(10): 1626-1634.

(10) Awasthi, S.P.(1989). Effect of different salts on the nodulation of Vigna radiata (L.) Wilczeck. J. Phytol. Res. 2(1): 109-112.

(11) Banet, G., Wininger, S., Badani, H., Ben-Dor, B., Friedman andY., Kapulnik, Y. (1996). Toxic and osmitic effects of salinity on growth and nodulation of Medicago sativa. Symbiosis. 21:209-222.

(12) Bauer, J.H. (1976) Oral administration of radioactive sulfate to measure extracellular fluid space in man. J. Appl. Physiol. 40(4):648-650.

(13) Bayer A.G. (1988). Salmonella/Microsome test to evaluate for point mutagenic effects. Unpublished report. Study no. T9027163, Report no. 16839, Wuppertal, Germany.

(14) Bayer AG data

(15) BC Ministry of Environment, Lands and Parks, and Environment Canada, (1996)ac. State of water Quality of Liard river at Fort Liard, 1984-1995, Canada-British Columbia water Quality Monitoring agreement.

(16) Blunck, J.M. and Crowther, C.E. (1975). Enhancement of azo dye carcinogenesis by dietary sodium sulphate. Europ. J. Cancer. 11(1): 23-31.

(17) British Chrome & Chemicals, Cleveland, producers data.

(18) Bundesminister des Innern (1990): Gemeinsames Ministerialblatt Nr.41 Jahrgang 8 (1990).

(19) Bundesminister des Innern (1996). Gemeinsames Ministerialblatt Nr.16, 47, Jahrgang 345, Kenn-nr. 286 (29-04-1996).

(20) Bycov, L.A. et al. (1977). Neftepererab. Neftekhim. (Moscow) ISS 4:40-41.

(21) Cairns, J.C.J., and Scheier, A. (1959). The relationship of Bluegill sunfish body size to tolerance for some common chemicals. Proc. 13th Ind. Waste. Conf., Purdue Univ. Eng. Bull 96:243-252.

(22) CFTA (1976). Allergic contact sensitization test (Test No. <intentionally blanked-out>.003-76) on Bubble Bath 60082-C containing 80.8% Sodium Sulfate. Unpublished report. Study no. <intentionally blanked-out>.003-76, Report no. Not stated.

(23) Chapmann and Hall (1992). Dictionary of Inorganic Compounds. Vol.3.

(24) Chemiekaarten (2000). pp. 921, C-0979, The Netherlands.

(25) Chien, L., Robertson, H., Gerrard, J. (1968). Infantile gastroenteritis due to water with high sulfate content. Can. Med. Assoc. J. 99:102-104.

(26) Clarke, M., Harvey, D.G., Humphreys, D.J. (1981). Sodium sulphate. Veterinary Toxicology. 2nd ed. London:Bailliere Tindall, p.42.

(27) Cocchetto, D.M. and Levy, G. (1981). Absorption of orally administered sodium sulfate in humans. J. Pharm. Sci. 70(3):331-333.

(28) Croser, C., Renault, S., Franklin, J and Zwiazek, J. (2001). The effect of salinity on the emergence and seedling growth of Picea mariana, Picea glauca and Pinus bankciana. Environmentla pollution. 115:9-16.

(29) Denisov, Y.N. and Tkachev, P.G. (1989). Hygienic characteristics of small doses of sodium sulfate after its inhalation. Gigiena i sanitaria. 4:69-71.

(30) Denisov, Y.N. and Tkachev, P.G. (1990). Health aspects of

sodium salts of sulfurous and sulfuric acids as environmental pollutants. Gigiena i sanitariia. 9:11-13.

(31) Diem, K. (ed.) (1972). Documenta Geigy scientific tables. 6th edition. J.R. Geigy S.A., Basle, Switzerland. 533 pp.

(32) Dow, C., Lawson, G.H.K., Todd, J.R. (1963). Sodium sulphate toxicity in pigs. Vet. Rec. 75:1052-1055.

(33) Dowden, B.F. (1961). Cumulative toxicities of some inorganic salts to Daphnia maena as determined by median tolerance limits. Proc. La. Acad. Sci. 23:77-85.

(34) Dowden, B.F. and Bennett H.J. (1965). Toxicity of selected chemicals to certain animals. J. Water Pollut. Control Fed. 37(9):1308-1316.

(35) Egan, T.P. and Ungar, I.A. (1998). Effect of different salts of sodium and potassium on the growth of Atriplex prostrata (Chenopodiaceae). Journal of plant nutrition. 21(10):2193-2205.

(36) Environment Canada (1985). Tech Info for Problem Spills: Sodium sulfate.

(37) Environment Canada. (1984). Detailed surface water quality data, Northwest Territories 1980-1981, Alberta 1980-1981, Saskatchewan 1980-1981. Manitoba 1980-1981. Unpublished results provided by Inland Waters Directorate, Ottawa. Cited from Health Canada, 1996.

(38) EPI Suite (2000). U.S. Environmental Protection Agency.

(39) Esteban, E., Rubin, C., McGeehin, M., Flanders, D., Baker, M.J., Sinks, T.H. (1997). Evaluation of human health effects associated with elevated levels of sulfate in drinking water: a cohort investigation in South Dakota. manuscript submitted. Int. J. Occup. Med. Environ. Health. 3:171-176.

(40) Gilli, G. and Comune, P.M. (1980). Effetti della salinità su sistemi biologici. Inquinamento 22(100):31-35.

(41) Gilman, A.G., Goodman, L.S., Gilman, A. (eds). (1980). Goodman and Gilman's The Pharmalogical Basis of Therapeutics. 6th ed. New York: Macmillan Publishing Co. Inc. p.1005.

(42) Goetsch, P.A. and Palmer, C.G. (1997). Salinity tolerance of selected macroinvertebrates of the Sabie river, Kruger national park, South Africa. Arch. Environ. Contam. Toxicol. 32:32-41.

(43) Gomez, G.G., Sandler, R.S., Seal, E., Jr. (1995). High levels of inorganic sulfate cause diarrhea in neonatal piglets. J. Nutr. 125:2325-2322.

(44) Gosh, T.K., Konar, S.K. (1980). Toxicity of chemicals and wastewaters of paper and pulp mills to worms plankton and

molluscs. Indian J. Environ. Hlth. 22(4):278-285.

(45) Gould, D.H., McAllister, M.M., Savage, J.C., Hamar, D.W. (1991). High sulfide, concentrations in rumen fluid associated with nutritionally induced polioencephalomalacia in calves. Am. J. Vet. Res.51(7):1164-1169.

(46) Greben, H.A., Maree, J.P., Mnqanqeni, S., (2000). Comparison between sucrose, ethanol and methanol as carbon and energy source for biological sulphate reduction. Water Science and Technol. 41(12):247-253.

(47) Handbook of chemistry and Physics (1997-1998). 78th ed. CRC press, pp. 4-87.

(48) Handbook of Chemistry and Physics (2003-2004). 84th ed. CRC press.

(49) Hawley, G.G. (1981). The Condensed Chemical Dictionary, 10th ed. New York, Van Nostrand Reinhold Co. USA.

(50) Health Canada, November 1987 (updated September 1994), Sulphate. Avialable: http://www.hc-sc.gc.ca/. [Accessed 09-22-2005]

(51) Heizer, W.D., Sandler, R.S., Seal, E., Jr., Murray, S.C., Busby, M.G., Schliebe, B.G., Pusek, S.N. (1997). Intestinal effects of sulfate on drinking water on normal human subjects. Dig. Dis. Sci. 42(5):1055-1061.

(52) Henkel, KGgA, unpublished data, Archive-No. TBD 710056.

(53) Henry, J.G. and Prasad, D., (2000). Anaerobic treatment of landfill leachate by sulphate reduction. Water Science and Tecnol. 41(3):239-246.

(54) Hitchcock, D.R., (1975). Biogenic contribution to atmospheric sulfate levels. Water's interface with energy, air and solids: proceedings of the second national conference on complete water-reuse, Chicago, Illinois, May 4-8, 1975. pp 291-310.

(55) Hoechst, A.G. (1989). Unveroffentl. Unters. (V-88-0938).

(56) Hughes, J.S. (1973) Acute Toxicity of Thirty Chemicals to Striped Bass (Morone saxatilis). La.Dep.Wildl.Fish.318-343-2417:15p.

(57) ICRP (1984). International Commission on Radiological Protection: Report No. 23: Report of the Task Group on Reference Man. Pergamon Press, Oxford, UK.

(58) Katz, M. (1977). The Canadian Sulphur Problem. In: Sulphur and its inorganic derivatives in the Canadian Environment. NRCC No. 15015, Associate Committee on Scientific Criteria for Environmental Quality, National Research Council of Canada. Ottawa. 21pp.

(59) Kelada, F. and Euinton, L.E. (1978). Health effects of long term exposure to sodium sulfate dust. J. Occup. Med. 20(12):812-814.

(60) Krijgsheld, K.R., Frankena, H., Scholtens, E., Zweens, J. and Mulder, G.J. (1979). Absorption, serum levels and urinary excretion of inorganic sulfate after oral administration of sodium sulfate in the conscious rat. Biochim. Biophys. Acta, 586(3):492-500.

(61) Lal, S.S. and Mithal, R.P. (1979) On the control of some nematode parasites of fishes. Bioresearch 3(1):15-17.

(62) Last, J.A. Purnendu, K.D., Ethinson, J.R. (1980). Inhalation Toxicology of Sodium Sulfite Aerosol in Rats. Toxicol. Appl. Pharmacol. 55:229-234.

(63) Laury, N.A. (1927). Hydrochloric acid and sodium sulfate. American Chemical Society. Monograph series 36. Chemical catalog Co, USA.

(64) Lettl, A. (1981). Effects of some sulpher compounds on soil microflora of Spruce rizosphere. Folia Microbio. 26(3):243-252.

(65) Mckee, J.E. and Wolf, H.W. (1963). Water Quality criteria, The Resources Agency of California, State Water Quality Control Board, Publ. No.3-A, USA.

(66) Meng, Z.Q. and Zhang, L.Z. (1992). Cytogenetic damage induced in human lymphocytes by sodium bisulfite. Mutation Research. 298:63-69.

(67) Merck 12ed (1996). pp. 1483, Merck&Co, NJ, USA.

(68) Moinuddin, J.F., Wing-Tsit Lee, H., (1960) Alimentary, blood and the other changes due to feeding MnSO4, MgSO4 and Na2SO4. American Journal of Physiology. 199(1): 77-83.

(69) Moore, F.W. (1952). Physiological effects of the consumption of saline drinking water. A progress report to the 16th meeting of the subcommittee on Sanitary Engineering and Environment. Appendix B. January 1952. Washington D.C., National Acadamy of Sciences.

(70) Morris, M.E. and Levy, G. (1983). Absorption of sulfate from orally adminsitered magnesium sulfate in man. J. Toxicol-clinical toxicol 20(2)107-114.

(71) Mount, D.R., Gulley, D.D., Hockett, J.R., Garrison, T.D., Evans, J.M. (1997) Statistical models to predict the toxicity of major ions to Ceriodaphnia dubia, Daphnia magna and Pimephales promelas (Fathead minnows). Environ. Toxicol. Chem. 16(10):2009-2019.

(72) Navarro, J.M., Garrido, C., Carvajal, M and Martinez, V. (2002). Yield and fruit quality of pepper plants under sulphate and chloride salinity. Journal of Horticulture and biotechnology. 77(1):52-57.

(73) Niles G.A. , Morgan S., Edwards W.C. , Lalman D. (2002). Effects of Dietary Sulfur Concentrations on Incidence and Pathology of Polioencephalomalicia in Beef Calves. Vet. Human Toxicol. 44(2):70-72.

(74) Notification of the Ministry of Industry, No. 232, B.E. 2521 (1978), issued under the Industrial products Standards Act. B.E. 2511 (1968), published in the Royal Gazette, Vol. 95, Part 68, (1978).

(75) Occupational exposure limits (1993). Health & Safety executive publ. ISBN 0-11-882080-X Par39&40 pg.6. EH40/93.

(76) Office of Drinking Water and Ground Water (1999). US-EPA, National centre for Environmental Health, Centres for Disease Control and Prevention (CDC). "Health effects from exposure to high levels of sulfate in drinking water study", CDC protocol 1779, EPA 815-R-99-001.

(77) Oganesyan, D.A., Mikaelyan K.A., Barseghyan M.N. (1977) Soobscenija Akademija Nauk Armjankoj SSR, Institut Agrochimiceskich Problem [Effect of high quantities of magnesium, potassium and sodium on the growth and biochemical indices of chlorella.] Gidroponiki Hagordoimner 16:26-31.

(78) Okahara. (1963). Food Hygiene Journal (Shokuhin Eiseigaku Zassi) 4:15.

(79) Paterson, D.W., Whalstrom, R.C., Libal, G.W., Olson, O.E. (1979). Effects of sulfate in water on reproduction in swine and young pig performance. J.Anim. Sci. 49(S1):105.

(80) Patrick, R.J., Cairns, J., Scheier, A. (1968). The relative sensitivity of diatoms, snails, and fish to twenty common constituents of industrial wastes. Prog. Fish-Cult. 30(3):137-140.

(81) Prased, D.Y. (1980). Toxicity of kraft pulp mill waste constituents on fresh water gambusia affinis. Indian Pulp & Paper 35(2):9-12.

(82) Robinson, D.J.S. and E.J. Perkins. (1977). The Toxicity of Some Wood Pulp Effluent Constituents. Cumbria Sea Fish. Comm., Sci. Rep. No. 74/1, The Courts, Carlisle, England:22 p.

(83) Roth, Wassergefährende stoffe: 20. Erg. Lfg. 6/93

(84) Sackner, M.A., Ford, D. Kim, C. (1979). Effect of brief exposure to high concentrations of sodium chloride and sodium sulfate aerosols with mass median aerodynamic diameter of 0.5 µm on pulmonary function of normal and asthmatic adults. American Review of Respiratory Disease. 119(4):.233.

(85) Saliba, L.J. and Ahsanullah, M. (1973). Acclimation and Tolerance of Artemia salina and Ophryotrocha labronica to Copper Sulphate. M. Mar.Biol. 23(4):297-302.

(86) Scheuring, L. and Stetter, H. (1950/1951). Versuche über die Wirkung van Natriumsulfat auf Wasserorganismen. Vom Wasser 18:78-100.

(87) Schlessinger, R.B. (1984). Comparative irritant potency of inhalated sulfate aerosols-Effects on bronchial mucociliary

clearance. Environ. Res. 34(2):268-279.

(88) Schwartz, D.L. (1984). Water quality, VSE 81c. Penn. state Univ., Waggoner, R., Good R.. Water Quality and Poultry Pedormance, In Proceedings AVMA Annual/Conference.

(89) Seidenberg, J.M. and Becker, R.A. (1987). A summary of the results of 55 chemicals screened for developmental toxicity in mice. Teratogenesis, Carcinogenesis, mutagenesis. 7:17-28.

(90) Seidenberg, J.M., Anderson, D.G., Becker, R.A. (1986). Validation of an in vivo developmental toxicity screen in the mouse. Teratogenesis, Carcinogenesis and Mutagenesis. 6:361-374.

(91) Sibblad, I.R. and Cave, N.A. (1976). The responses of chicks to ammonium, calcium, magnseium, potassium and sodium sulphates and to ammonium and potassium carbonates. Poult. Sci. 55:2209-2213.

(92) Stanley, R.A. (1974) Toxicity of heavy metals and salts to Eurasian watermilfoil (Miriophyllum spicatum l.). Arch. Environ. Contam. Toxicol. 2(4):331-341.

(93) Temple, P.J. and Richards, R.A. (1978) Effects of atmospheric deposition of sodium sulfate on bean and tomato plants. Bull. Environ. Contam. Toxicol. 19(3):257-263.

(94) The Economics of Sodium Sulphate (1992). 7th Ed, Roskill Information Services Ltd., London, UK.

(95) Tokuz, R.Y. (1986). The effect of high salinity on activated sludge effluent quality. Curr. Pract. Environ. Sci. Eng. 2:143-154.

(96) Tokuz, R.Y. and Eckenfelder, W.W. (1979). The effect of inorganic salts on the activated sludge process performance. Water Res. 13(1):99-104.

(97) Toth, B. (1987). Cancer Induction by the sulfate form of 4-(Hydroxymethyl)-benzenediazonium ion of Agaricus bisporus. In Vivo 1:39-42.

(98) Trama, F.B. (1954). The acute toxicity of some common salts of sodium potassium and calcium to the common Bluegill. (Lepomis Macrochirus Rafinesque). Proc. Acad. Nat. Sci. Philadelphia 106:185-205.

(99) Tuoboyski, L. (1960). Rocz. Nauk. Roln. 75B(3):401-445.

(100) U.S. Geological Survey (2000). Mineral Commodity Summaries. February 2000.

(101) Ullmann (1979). Vol. 17, 211-229.

(102) Ullmann's Encyclopedia of Industrial Chemistry (2004). 7th ed. John Wiley & Sons, Inc.

(103) United States Environment Program. Global Environmental Monitoring System. Freshwater Quality Program (GEMS)."Salts

and Salinization of Surface Waters". Available: http://www.gemswater.org/atlas-gwq/salts-e.html. [Accessed 09-22-2005]

(104) Upton, P.K. and L'Estrange, J.L. (1976). Effects of high intakes of dietary sodium sulphate and sodium chloride on voluntary food intake of rats. Proc. Nutr. Soc. 20A-21A.

(105) Van Horn, W.M. (1943). Possible stream pollutional aspects of mill antiseptics. Paper Trade Journal 117(24):33-35.

(106) Van Horn, W.M. (1949). The effect of kraft pulp mill wastes on some aquatic organisms. Trans. Am. Fish. Soc. 79:55-63.

(107) Veenhuizen, M.F. (1993). Association between water sulfate and diarrhea in swine on Ohio farms. JAVMA. 8:1255-1260.

(108) Veenhuizen, M.F., Shurson, G.C., Kohler, E.M. (1992). Effect of concentration and source of sulfate on nursery pig performance and health. JAVMA. 201(8):1203-1208.

(109) Wallen, I.E., Greer, W.C., Lasater, R. (1957). Toxicity to Gambusia affinis of certain pure chemicals in turbid waters. Sewage Ind. Wastes 29(6):695-711.