FOREWORD INTRODUCTION

SODIUM DITHIONITE

CAS N°: 7775-14-6

SIDS Initial Assessment Report

For

SIAM 19

Berlin, Germany, 19-22 October 2004

1. Chemical Name:	Sodium dithionite
2. CAS Number:	7775-14-6
3. Sponsor Country:	Germany Contact Point: BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit) Contact person: Prof. Dr. Ulrich Schlottmann Postfach 12 06 29 D- 53048 Bonn
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners:	BASF AG = lead company
• Name of industry sponsor /consortium	BASF AG, Germany Contact person: Dr. Hubert Lendle GUP/CL – Z 570 D-67056 Ludwigshafen
• Process used	The BUA Peer Review Process : see next page
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme?	by ICCA-Initiative
7. Review Process Prior to the SIAM:	last literature search (update): 14 February 2003 (Human Health): databases medline, toxline; search profile CAS-No. and special search terms 5 February 2004 (Ecotoxicology): databases CA, biosis; search profile CAS-No. and special search terms OECD/ICCA
8. Quality check process:	As basis for the SIDS-Dossier the IUCLID was used. All data have been checked and validated by BUA. A final evaluation of the human health part has been performed by the Federal Institute for Risk Assessment (BfR) and of the ecotoxicological part by the Federal Environment Agency (UBA).
9. Date of Submission:	Deadline for circulation: 23 July 2004
10. Date of last Update:	
11. Comments:	

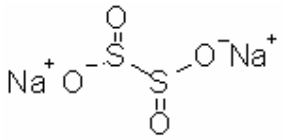
OECD/ICCA - The BUA* Peer Review Process

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

– a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
– Review of data and assessment of the quality of data
– Review of data evaluation
– Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
– Review of key study description according to robust summary requirements; completeness and correctness is checked against original reports/publications (if original reports are missing: reliability (4), i.e. reliability not assignable)
– Review of validity of structure-activity relationships
– Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)
– In case of data gaps, review of testing plan or rationale for not testing

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	7775-14-6
Chemical Name	Sodium dithionite
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Sodium dithionite is not stable under physiological conditions, with the rate of decomposition increasing with increasing acidity. Upon contact with moisture, it is oxidized to hydrogen sulfite (HSO_3^-), sulfite (SO_3^{2-}) and hydrogen sulfate (HSO_4^-), and under strongly acidic conditions it may liberate sulfur dioxide. Under anaerobic conditions (such as in the lower gastrointestinal tract), hydrogen sulfite (HSO_3^-) and thiosulfate ($S_2O_3^{2-}$) may be formed. Hydrogen sulfite (HSO_3^-) can be absorbed after ingestion. It is efficiently metabolized, and the major part rapidly excreted as sulfate into the urine.

The acute oral LD_{50} of sodium dithionite in rats was about 2500 mg/kg bw, with atony, gastro-intestinal irritation, diarrhea and dyspnea as the main clinical and pathological signs at doses near to or exceeding the LD_{50}. There were no acute dermal and no valid acute inhalation studies available.

Sodium dithionite was slightly irritating to the skin, and strongly irritating to the eyes of rabbits. Under acidic conditions, sodium dithionite may liberate sulfur dioxide, which is known to induce respiratory irritation in humans. There was no animal data available regarding sensitization. In humans, allergic dermatitis from exposure to sulfites is rare and, consequently, sodium dithionite is not considered to possess a significant skin sensitization potential. Although there were no specific reports with regard to sodium dithionite available, the potential for allergoid reactions ("sulfite-asthma") should be assumed in sensitive individuals following oral or inhalation exposure.

Sodium dithionite was not tested for its toxicity after repeated dosing. Due to its rapid degradation under *in vivo* conditions, the toxicity data on its decomposition products were used for the evaluation of this endpoint. The conversion products, including sulfite (SO_3^{2-}), hydrogen sulfite (HSO_3^-), sulfate (SO_4^{2-}) and thiosulfate ($S_2O_3^{2-}$), are considered as substances of very low order systemic toxicity. It should be noted that sulfites, in general, reduce the thiamine content in food. For disodium disulfite, oral NOAELs (30 and 104 weeks) of 942 mg/kg bw/day and 217 mg/kg bw/day were obtained for systemic toxicity and local gastrointestinal toxicity in rats, respectively. These results appear to be sufficiently representative also for the assessment of sodium dithionite. Repeated dose studies in animals using the dermal or respiratory routes were not available.

Sodium dithionite was not mutagenic in standard bacterial tests with and without metabolic activation (OECD TG 471, 472). No experimental data was available on the potential of sodium dithionite to induce chromosomal aberrations *in vitro*. An increase in the frequency of micronuclei in bone marrow cells of mice was found after intraperitoneal injection of high doses (2 x 500 or 2 x 750 mg/kg bw) of a mixture of sodium hydrogen sulfite (HSO_3^-) and sodium sulfite, the degradation products of sodium dithionite under physiological conditions.

No experimental data were available on the carcinogenic potential of sodium dithionite. In 1992, IARC concluded that degradation products of dithionite, i.e. sulfur dioxide, sulfites, hydrogen sulfites and metabisulfites "are not classifiable as to their carcinogenicity to humans (Group 3)".

Sodium dithionite has not been tested for its effects on reproduction and development. Based on its physico-chemical behavior and its rapid conversion in the body, it is not expected that the intact molecule reaches the reproductive organs, or has any direct effect on reproduction and development. Data relating to the degradation products of sodium dithionite do also not indicate any adverse effects. At high dietary doses, which can cause

maternal malnutrition and destruction of thiamine, fetal growth retardation was however observed. In a rat dietary study with sodium sulfite (similar to OECD TG 414), the NOAEL for developmental toxicity was at 5 % (about 1450 mg/kg bw/day; highest tested dose). At this dose clear signs of maternal toxicity were observed (LOAEL, maternal toxicity: 5 % in diet = about 1450 mg/kg bw/day). The NOAEL for maternal toxicity was at 2.5 % in feed (about 850 mg/kg bw/day).

Environment

Sodium dithionite dihydrate is very sensitive towards atmospheric oxygen in the finely crystalline state and oxidizes under heat development: the heat of oxidation can lead to ignition, e.g. upon contact with moisture. The anhydrous salt decomposes exothermically in air on prolonged heating above 90 °C (decomposition/oxidation products: sodium sulfate (Na_2SO_4) and sulfur dioxide (SO_2)). Above ca. 150 °C, in exclusion of air, vigorous decomposition occurs, yielding mainly sodium sulfite (Na_2SO_3), sodium thiosulfate ($Na_2S_2O_3$), sulfur dioxide (SO_2) and a small amount of sulfur. Because of decomposition on heating, boiling point and melting point are not relevant. The vapour pressure is negligible and the Henry constant is near to zero due to the ionic character of the inorganic salt. Biodegradation or elimination tests are not appropriate for the inorganic substance. Hydrolysis occurs within hours at pH 7 and room temperature. There is no indication of a bioaccumulation potential.

Main hydrolysis products are thiosulfate ($S_2O_3^{2-}$) and sulfite (SO_3^{2-}). Small amounts of sulfur and sulfide (S^{2-}) have been detected during oxygen-free hydrolysis. Oxygen dissolved in water is consumed by dissolved sodium dithionite. Final oxidation products are sulfate (SO_4^{2-}) and sulfite (SO_3^{2-}).

Because of the high water solubility at 20 °C of 182 g/l (value related to formula $Na_2S_2O_4$) and 219 g/l (related to formula $Na_2S_2O_4 * 2\ H_2O$) respectively, for hydrated sodium dithionite, aquatic environment is the target compartment. Sodium dithionite is expected not to be stable in soil because of its rapid decomposition in water and the reaction with oxygen.

From acute toxicity test to fish (*Leuciscus idus*), 96-hr LC_{50} was 62.3 mg/l. For algae (*Scenedesmus subspicatus*), 72-hr ErC_{50} was 206 mg/l and 72-hr NOErC was 62.5 mg/l(corresponding values for biomass are 135 and 62.5 mg/l respectively; nominal concentration). For *Daphnia magna*, the acute toxicity value of 48-hr EC_{50} was 98.3 mg/l, and the chronic value of 21-day NOEC was > 10 mg/l. Due to oxygen concentrations < 1 mg/l at test start in high test concentrations in the fish and acute daphnia test, it cannot be excluded that the effect values found in these studies are at least partly caused by oxygen deficiency. A PNEC of 0.1 mg/l for the aquatic organisms was calculated from the chronic value (NOEC for daphnia > 10 mg/l) using an assessment factor of 100.

Exposure

For workers, the main potential routes of exposures to sodium dithionite are the respiratory and dermal route, for consumers the dermal route through the use of household products.

In 2001, the estimates for sodium dithionite production for the world market amounted to approx. 550 000 tonnes/year. These are distributed as follows: 60 000 - 120 000 tonnes in Germany, 40 000 – 80 000 tonnes in the rest of Europe, 100 000 - 150 000 tonnes in NAFTA and 200 000 – 300 000 tonnes in Asia. The production volume is used in dispersive manner, primarily in industrial applications to approx. 90 %. The use pattern is 50 % textile bleaching, 35 % pulp and paper bleaching, 5 % kaolin bleaching, 10 % other applications (e.g. household colour remover). According to Swiss, Danish and Swedish Products Registers sodium dithionite is contained in a large number of products. Some of them are available to consumers. Release of the substance, its reaction and hydrolysis products into the environment (especially waste water) is likely to occur during the production and processing of sodium dithionite and from the use of the substance itself, as well as from the formulation and use of products containing the substance.

During production and internal processing at one company in the Sponsor country, approx. 115 kg sodium dithionite (dust) were emitted into the air in 2000, where it is expected to be oxidized to sulfate (SO_4^{2-}). No information on the emission into waste water or surface water are available for this site. Emission data from other production and processing sites or literature was not available.

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

Human Health: The chemical is a candidate for further work. Sodium dithionite possesses properties indicating a hazard to human health (sulfite asthma, irritant effects on the eye, chromosomal aberrations *in vivo* were observed following intraperitoneal injection of the degradation products). There is only limited information on the exposure of workers in manufacturing and down-stream industries, and consumers may be exposed through household products (detergents, stain removers). It is therefore recommended to conduct an exposure assessment, and, if then indicated, a risk assessment.

Environment: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for the environment. These hazards do not warrant further work as they are related to acute toxicity which may become evident only at very high exposure levels. They should nevertheless be noted by chemical safety professionals and users.

SIDS Initial Assessment Report

1 IDENTITY

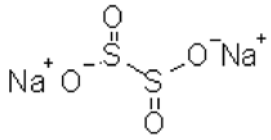
1.1 Identification of the Substance

CAS Number: 7775-14-6

IUPAC Name: Dithionous acid, disodium salt (8CI, 9CI)

Molecular Formula: $Na_2S_2O_4$

Structural Formula:



Molecular Weight: 174.114 g/mol

Synonyms: Disodium hydrosulfite
Dithionous acid, disodium salt (8CI, 9CI)
Sodium dithionite
Sodium hydrosulfite
Sodium hyposulfite
Sodium-sulfoxilate

1.2 Purity/Impurities/Additives

Purity:	> 88 % w/w
Impurities:	Disodium disulfite (1 – 5 % w/w)
	Sodium sulfite (1 – 5 % w/w)
	Sodium thiosulfate (0 – 2 % w/w)

Remark: Data refer to product HYDROSULPHITE P CONC. BASF (BASF AG, 2004a)

According to McKenna et al. (1991) products from commercial suppliers in the USA had a purity < 84 % (w/w). No additional data are available from these production sites.

1.3 Physico-Chemical properties

All information refers to anhydrous sodium dithionite if not stated otherwise.

Table 1 Summary of physico-chemical properties (anhydrous sodium dithionite as far as not stated otherwise)

Property	Value	References / Comments
Physical state	solid	white powder
Melting point	Decomposition > 90 °C	Ullmann, 2000
Boiling point	not applicable	
Relative density	2.38 (20 °C)	Ullmann 1994
Vapour pressure	not applicable	non-volatile inorganic solid
Water solubility hydrated sodium dithionite	approx. 182 g/l (20 °C) related to formula $Na_2S_2O_4$ approx. 219 g/l (20 °C) related to formula $Na_2S_2O_4$	Patel and Rao, 1952
Partition coefficient n-octanol/water (log value)	< –4.7	BASF AG, 1988a
Henry's law constant	not applicable	due to ionic solution in water, very high water solubility and decomposition in water (see below)

Because of decomposition on heating, boiling point, and melting point are not relevant. The vapour pressure is negligible due to the ionic character of the inorganic salt.

Sodium dithionite has strongly reducing properties and decomposes/disproportionates rapidly in aqueous media (especially under acidic conditions and under oxygen consumption) to sulfite, SO_2 and sodium thiosulfate ($Na_2S_2O_3$) as major decomposition products (BASF AG, 1988a).

According to Hofmann and Rüdorff (1969) and Holleman and Wiberg (1995) (see also BASF AG, 1988a), this process can roughly be described by the following equations:

$$2\ Na_2S_2O_4 + H_2O \rightarrow Na_2S_2O_3 + 2\ NaHSO_3 \quad \text{(anaerobic conditions)} \qquad (1)$$

$$Na_2S_2O_4 + O_2 + H_2O \rightarrow NaHSO_4 + NaHSO_3 \quad \text{(aerobic conditions)} \qquad (2)$$

Under aerobic conditions and with low concentrations, reaction (2) is favoured.

The formation of hydrogen sulfite (HSO_3^-) and hydrogen sulfate (HSO_4^-) lowers the pH of the media and accelerates the process of decomposition strongly. Therefore, to keep solutions of dithionite stable for several days, they need to be cooled, kept in an alkaline state by excess of NaOH and oxygen has to be excluded.

According to the literature overview of Münchow (1992) the following principal decomposition patterns can be described for dithionite in relation to pH ranges at temperatures between 0°C and 32°C for 0.0025 molar solutions:

- strongly alkaline medium: $3\ Na_2S_2O_4 + 6\ NaOH \rightarrow 5\ Na_2SO_3 + Na_2S + H_2O$
- weakly alkaline to weakly acidic medium: $2\ Na_2S_2O_4 + H_2O \rightarrow 2\ NaHSO_3 + Na_2S_2O_3$
- acidic medium: $2\ H_2S_2O_4 \rightarrow 3\ SO_2 + S + 2\ H_2O$
- strongly acidic medium: $3\ H_2S_2O_4 \rightarrow 5\ SO_2 + H_2S + 2\ H_2O$

Higher temperatures appear to further accelerate these reactions. At pH 9 – 11 there was 1 % decomposition within 1 hour and at pH 7 there was a 2 % decomposition within 1 hour. This mirrors a slow induction phase and is later followed by rapid acceleration due to autocatalytic processes. Below pH 6, there is a much shorter induction time and below pH 4.8 there is no induction time at all. Minimal concentrations of H_2S and S^{2-} anions abolish the induction time, too, and trigger the fast decomposition.

Sulfite and hydrogen sulfite anions are both in a pH-dependent equilibrium with gaseous SO_2:

$$SO_2 + H_2O \rightleftharpoons H^+ + HSO_3^- \quad HSO_3^- + OH^- \rightleftharpoons H_2O + SO_3^{2-} \qquad (3)$$

A related chemical, disodium disulfite (= sodium metabisulfite; $Na_2S_2O_5$) readily hydrolyses to (hydrogen)sulfite (and thus SO_2), too:

$$Na_2S_2O_5 + H_2O \rightarrow 2\ NaHSO_3 \qquad (4)$$ (Holleman and Wiberg, 1995)

Disodium disulfite has already been evaluated in the OECD HPV program (OECD, 2001).

In the presence of oxygen, the sulfite anion may be further oxidized to sulfate:

$$2\ Na_2SO_3 + O_2 \rightarrow 2\ Na_2SO_4 \qquad (5)$$

Sodium dithionite dihydrate is very sensitive towards atmospheric oxygen in the finely crystalline state and oxidizes under heat development: the heat of oxidation can lead to ignition, e.g. upon contact with moisture (Gärtner, 1939). The anhydrous salt decomposes exothermically in air on prolonged heating above 90 °C (decomposition/oxidation products: sodium sulfate and sulfur dioxide). Above ca. 150 °C, in exclusion of air, vigorous decomposition occurs, yielding mainly sodium sulfite, sodium thiosulfate, sulfur dioxide and a small amount of sulfur (Ullmann, 2000).

Because of these chemical properties, sodium dithionite is labeled in the European Union with R7 (May cause fire) and R31 (Contact with acids liberates toxic gases) (ANNEX I, 67/548/EC) (BASF AG, 2002).

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

All processes for the production of dithionite start with the reduction of sulfurous acid, which can either be present in the free form (SO_2) or as hydrogen sulfite (HSO_3^-). The production processes with zinc dust, sodium amalgam, sodium formate, sodium borohydride and electrochemical or cathodic reduction as reducing agent are important industrially (Ullmann, 2000).

In 2001, the estimates for sodium dithionite production for the world market amounted to approximately 550 000 tonnes/year. These are distributed as follows (BASF AG, 2004a):

Germany:	60 000 - 120 000 t/a
Europe (without Germany):	40 000 - 80 000 t/a
USA (Nafta):	100 000 - 150 000 t/a
Asia	200 000 - 300 000 t/a
World:	approx. 550 000 t/a

The chemical is widely used.

The production volume is used to 90 % in industrial applications. All uses of sodium dithionite are based on its reducing properties. In the textile industry, sodium dithionite is primarily used as reducing agent for vat dyes and sulfur containing dyes, and for the removal of pigments on textiles. It is also used as a bleaching agent in reductive bleaching processes, for instance, in the bleaching of mechanical paper pulp, and the bleaching of cotton and wool (Westbroek et al., 1999), as well as sugar (GESTIS, 2002). It is also a bleaching agent for soap, straws, and sugar (SRI, as cited in HSDB, 2003).

The use pattern is 50 % textile bleaching, 35 % pulp and paper bleaching, 5 % kaolin bleaching, 10 % other applications (e.g. household stain remover). Additional applications are cited in the European Product registers. According to the Swiss Product Register (2002), there are 113 products marketed containing sodium dithionite. Among them are 21 consumer products with concentrations of up to 100 %. Product types are unspecified additives; adhesive, lute, priming material; cleaning/ washing agents and additives; water treatment; photographic chemicals; galvanic additive; spot remover.

In the Danish Product Register (2003), there are 24 products listed, 16 of them with a content of 50 – 100 %. The product types are reducing agents, bleaching agents, coloring agents and cleaning/washing agents. The chemical is used in the manufacture and finishing of textiles, fibres, fabrics, tanning and dressing of leather, industrial cleaning, laundries and dry cleaners.

The Swedish Product Register (2002) lists 34 products, 5 of these available to consumers (main use bleaching agent with content 10 – 100 %). The most common/frequent industry categories are textile industry, tanneries, industry for pulp, paper and paper products, and trade.

In the Norwegian Product Register (2003), 11 products containing a total quantity of 637 tons are registered.

Release into the environment is likely to occur during the production and processing of sodium dithionite and from the use of the substance itself, as well as from the formulation and use of products containing the substance.

During production and internal processing at BASF AG, Ludwigshafen (Germany), approx. 115 kg sodium dithionite (dust) were emitted into the air in 2000 (German Emission Register, year of reference: 2000), where it is expected to be oxidized to sulfate.

No information on the emission into waste water or surface water is available for this site.

Emission data from other production and processing sites was not available.

2.2 Environmental Exposure and Fate

According to its instability towards water and atmospheric oxygen, sodium dithionite is not expected to be found in the environment after emission during production, processing and use.

2.2.1 Sources of Environmental Exposure

During industrial use as reductive substance, sodium dithionite is oxidized to sulfate, going to wastewater/hydrosphere.

During use as consumer product (color remover) it is oxidized to sulfate. Remaining product is rapidly hydrolyzed and oxidized in wastewater and wastewater treatment plants.

2.2.2 Photodegradation

Photodegradation of sodium dithionite in water is not relevant because it dissociates quickly and decomposes in water.

2.2.3 Stability in Water

The test material is chemically unstable under usual test conditions and is transformed into sodium sulfite and thiosulfate without the influence of air and to sodium sulfite and sodium sulfate by oxidation with air (see chapter 1.3 for a detailed desription). Hydrolyses is slowed down at low temperature. Sodium dithionite dissolves in water and forms sodium hydrogen sulfite, sodium hydrogen sulfate and sodium thiosulfate (BASF AG, 1988a). Depending on the pH-value, sulfur dioxide, sodium hydrogen sulfite, sodium sulfite and sodium sulfide are present in aqueous solution. Although the substance can release sulfur dioxide under acid conditions, this is not likely to occur under normal natural environmental conditions.

2.2.4 Transport between Environmental Compartments

Due to the inherent properties of the compounds involved, the main compartment of dithionite and its conversion products is the hydrosphere. The application of the fugacity model for sodium dithionite is not relevant due to ionic solution and its instability in the water phase.

2.2.5 Biodegradation

As an inorganic compound sodium dithionite does not undergo biodegradation.

2.2.6 Bioaccumulation

Due to its inherent physico-chemical properties as outline above, bioaccumulation is not expected.

2.2.7 Other Information on Environmental Fate

The product may lead to chemical consumption of oxygen in biological sewage treatment plants or in natural water. Inhibition of degradation activities in sewage treatment plants is not to be expected from the introduction of low concentrations (BASF AG, 1988b).

Because of hydrolysis and oxidation, sodium dithionite decomposes rapidly in soil.

2.3 Human Exposure

2.3.1 Occupational Exposure

Workers can be exposed to dust of sodium dithionite during manufacturing, processing, and use of sodium dithionite containing products, with the respiratory and dermal routes being the main routes of exposure.

The manufacture of dithionite at BASF AG takes place within a closed system under controlled conditions. Packaging takes place in an automated filling unit fitted with LEV (local exhaust ventilation). This also applies to the manufacture of products containing sodium dithionite or using it in their production. In all cases, the regulations and safety procedures for working with chemicals are adhered to. Employees' personal protective equipment consists of work clothes, safety shoes, helmet and safety glasses. Dust masks and protective gloves are available to be used if required.

Eating, drinking and smoking are prohibited in the workplace. All employees receive regular safety training.

Exposure measurements (n = 26) at workplace were performed at the production site of BASF AG, Ludwigshafen (Germany) between 1990 and 2001. The measured total dust concentrations were in the range between < 0.25 mg/m³ and 1.6 mg/m³. Although the actual amounts of dithionite were not determined in these samples, it can be assumed that the sodium dithionite concentrations were considerably below 1.6 mg/m³.

There is no information on workplace exposure levels at processing units, or in the down-stream user industry. Sodium dithionite and the products based on it are mainly used in the paper and textile industries. Paper production is mainly confined to a few large corporate groups, whilst in the textile industry this product category has a relatively large number of users, including many smaller ones. In the paper industry, sodium dithionite and the products based on it are used in both solution and powder form. In each case, apportioning of the product is an automated process. In the textile industry mainly product packed in drums is being used, and occasionally packing into smaller units is being done manually.

2.3.2 Consumer Exposure

Approximately 0.1 % of the total sodium dithionite production is used for products with household applications (mainly as bleaching agent in laundry and stain remover products). Exposure of consumers may therefore mainly occur through dermal contact. However, no data were available on the extent of consumer exposure.

The related compounds sodium sulfite, sodium hydrogen sulfite, and sodium metabisulfite are currently allowed in the EU as food additives (preservatives). In 1998, the FAO/WHO joint expert committee on food additives set a group ADI of 0 - 0.7 mg/kg bw, expressed as sulfur dioxide, for calcium hydrogen sulfite, calcium metabisulfite, calcium sulfite, potassium hydrogen sulfite, potassium metabisulfite, potassium sulfite, sodium hydrogen sulfite, sodium metabisulfite, sodium sulfite, sodium, thiosulfate, and sulfur dioxide (JECFA, 1999).

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

Reliable toxicity data on sodium dithionite were available for acute toxicity, skin and eye irritation, sensitization and for its potential to induce gene mutations. The substance has not been tested for its repeated- dose toxicity, its ability to induce chromosomal aberrations, and for its reproductive and developmental effects.

As sodium dithionite is chemically unstable in the presence of water and oxygen, in particular under acidic conditions, rapid conversion of sodium dithionite into various related sulfite species is expected to occur under physiological conditions. Therefore, it is justified to take account of toxicological data of sodium sulfite [CAS No.7757-83-7], sodium hydrogen sulfite [CAS No. 7631-90-5], and disodium disulfite (= sodium metabisulfite; $Na_2S_2O_5$) [CAS No. 7681-57-4] in the human health assessment of dithionite with a view of bridging the data gaps relating to sodium dithionite. In this context, sodium sulfite and sodium hydrogen sulfite are considered to be the predominant chemicals that are systemically available to the body.

Table 2 Chemicals used to evaluate human health endpoints

Endpoint	Chemical(s) used to evaluate endpoint
Acute toxicity (LD_{50})	**Sodium dithionite**
Skin irritation	**Sodium dithionite**
Eye irriation	**Sodium dithionite**
Sensitization	**Sodium dithionite**, sulfites
Repeated dose toxicity	Sodium hydrogen sulfite, sodium sulfite, sodium thiosulfate, sulfur dioxide, disodium disulfite)
Gene mutations *in vitro*	**Sodium dithionite**, sodium hydrogen sulfite, disodium disulfite
Chromosomal aberrations *in vitro*	No studies available
Genotoxicity *in vivo*	Sodium hydrogen sulfite, sodium sulfite, disodium disulfite
Carcinogenicity	Sulfur dioxide, sulfites, hydrogen sulfites and metabisulfites
Toxicity to fertility	Sodium hydrogen sulfite and disodium disulfite
Developmental toxicity	Sodium sulfite, disodium disulfite

3.1.1 Toxicokinetics, Metabolism and Distribution

Sodium dithionite has not been tested in toxicokinetic or metabolism studies.

As previously described in this document, sodium dithionite is not stable under physiological conditions, with the rate of decomposition increasing with increasing acidity. Upon contact with moisture, it oxidizes to hydrogen sulfite and hydrogen sulfate:

$$Na_2S_2O_4 + O_2 + H_2O \rightarrow NaHSO_4 + NaHSO_3$$

and, under strongly acidic conditions, may liberate SO_2 (Warner, Diachenko and Bailey, 2000):

$$SO_2 + H_2O \leftrightarrow SO_2(H_2O) = H_2SO_3 \leftrightarrow H^+ + HSO_3^- \leftrightarrow 2\ H^+ + SO_3^{2-}$$

$$pK_1 \sim 2 \qquad pK_2 \sim 7$$

If present in high concentrations and under anaerobic conditions (such as in the lower gastrointestinal tract), hydrogen sulfite and thiosulfate may also be formed:

$$2\ Na_2S_2O_4 + H_2O \rightarrow\ 2\ NaHSO_3 + Na_2S_2O_3$$

Studies in Animals with Hydrogen Sulfite, Sulfite and Thiosulfate

In vivo Studies

The main decomposition product of sodium dithionite, i.e. hydrogen sulfite, can be absorbed from the rat gastrointestinal tract. It is oxidized *in vivo* to sulfate, principally by hepatic sulfite oxidase (cytochrom-c oxidoreductase), with lesser amounts metabolized by the kidneys, intestines, heart, and lungs. About 70 to 95 % of the radioactivity associated with a 50 mg/kg bw oral hydrogen

sulfite dose appeared in rodent and monkey urine within 3 days as sulfate. Only a small fraction (8 - 10%) of the absorbed hydrogen sulfite was eliminated intact (ACGIH, 1991; Gunnison, Bresnahan and Chiang, 1977).

Physiologically, sulfite oxidase is involved in the methionine and cysteine metabolism. The endogenous sulfite body burden resulting from amino acid degradation is in the range of 0.3 - 0.4 mmol/kg bw/day, which is reported to be about 15- to 130-fold higher than the estimated value for exogenous sulfite exposure (Institute of Food Technologists and Committee on Public Information, 1976).

Thiosulfate is eliminated mainly unchanged by renal excretion, but a certain amount is enzymatically oxidized in the liver to sulfate. This latter fraction increases as the dose of thiosulfate decreases (JECFA, 1983).

In anaesthetised rats with pre- and post-hepatic cannulation for blood withdrawal, blood levels of free sulfite in portal blood increased within minutes after intraduodenal administration of 100 mg Na_2SO_3/kg (approx. 65 mg sulfite). The pre-hepatic plasma peak after 10 to 20 min represented about 1 mg/ml sulfite (12.5 to 13.5 µmol/ml). No free sulfite was detected in the general circulation (post-hepatic). It was concluded that sulfite was efficiently eliminated from blood (Wever, 1985).

Conclusion

Sodium dithionite is not stable under physiological conditions, with the rate of decomposition increasing with increasing acidity. Upon contact with moisture, it is oxidized to hydrogen sulfite (HSO_3^-), sulfite (SO_3^{2-}) and hydrogen sulfate (HSO_4^-), and under strongly acidic conditions it may liberate sulfur dioxide. Under anaerobic conditions (such as in the lower gastrointestinal tract), hydrogen sulfite (HSO_3^-) and thiosulfate ($S_2O_3^{2-}$) may be formed. Hydrogen sulfite (HSO_3^-) can be absorbed after ingestion. It is efficiently metabolized, and the major part rapidly excreted as sulfate into the urine.

3.1.2 Acute Toxicity

Studies in Animals

Inhalation

There were no valid inhalation studies available.

Dermal

There were no studies available.

Oral

For sodium dithionite (tested as suspension in aqueous carboxymethylcellulose), an oral LD_{50} of about 2500 mg/kg bw was determined for rats (BASF AG, 1973). No clinical signs were noted at doses up to and including 1600 mg/kg bw. At higher doses (≥ 2000 mg/kg bw), clinical signs included atony, dyspnea and diarrhea. Gross pathology revealed acute hyperemic congestion, cardiac dilatation, gastrointestinal irritation and dilatation, associated with bloody ulceration in animals administered doses of 2500 mg/kg bw or higher.

Studies in Humans

No data were available.

Conclusion

The acute oral LD_{50} of sodium dithionite in rats was about 2500 mg/kg bw, with atony, gastro-intestinal irritation, diarrhea and dyspnea as the main clinical and pathological signs at doses near to or exceeding the LD_{50}. There were no acute dermal and no valid acute inhalation studies available.

3.1.3 Irritation

Skin Irritation

Studies in Animals

An 80 % aqueous suspension of sodium dithionite tested in two rabbits under occlusive conditions for 20 hours produced mild skin erythema. The mild erythema seen at 24 hours post-treatment did not persist to 8 days (BASF AG, 1973). With an exposure time of 20 hours (instead of 4 hours), and occlusive conditions (instead of semi-occlusive), the test conditions were more stringent than those required in the current OECD TG 404.

Studies in Humans

No data were available.

Eye Irritation

Studies in Animals

Sodium dithionite was tested for its effects on the eye of rabbits in a study performed in accordance with OECD TG 405 (BASF AG, 2003). 97 mg of the finely powdered test substance (purity 88 %) were instilled in the conjunctival sac of three rabbits, and washed out with physiological saline after one hour of exposure. In all animals, moderate to severe erythema and slight edema were found after 1 hour and persisted until 72 and 48 hours, respectively. Mean scores for erythema were 3.0 (24 h), 3.0 (48 h), and 2.3 (72 h), and for edema 1.3 (24 h), 0.67 (48 h), and 0.33 (72 h). No changes were noted in the cornea and iris. All effects were completely reversible by day 7 after exposure except for 1 animal which still showed slight conjunctival redness.

In an earlier study (BASF AG, 1973), a bulk volume of about 0.05 ml of sodium dithionite (tested as dry solid material not further specified) caused strong eye irritation in two rabbits. The effects were still persistent as mild conjunctival edema and slight corneal opacity at 8 days post-exposure (end of the study). There was evidence of some necrosis of the eyelids and scar formation, but these findings were not further specified.

Studies in Humans

No data were available.

Respiratory Irritation

Under acidic conditions, sodium dithionite may liberate sulfur dioxide (SO_2). Sulfur dioxide is known to induce respiratory irritation in humans (Greim, 1998).

Conclusion

Sodium dithionite was slightly irritating to the skin, and strongly irritating to the eyes of rabbits.
Under acidic conditions, sodium dithionite may liberate sulfur dioxide (SO_2), which is known to induce respiratory irritation in humans.

3.1.4 Sensitization

Studies in Animals

Skin

There were no animal data available for sodium dithionite.

Respiratory Tract

There were no animal data available for sodium dithionite.

Studies in Humans

Skin

Allergic dermatitis at the workplace appears to be rare. In one isolated case, a female dry cleaner is reported to have developed hand dermatitis presumably due to regular preparation of sodium sulfite solutions. Patch testing gave a positive response on application of a 0.5 % and 1 % solution of sodium dithionite. In a consecutive control group of 18 dermatitis patients, the respective treatment failed to produce positive reactions (Rudzki, 1980).

Respiratory Tract

Under acidic conditions, sodium dithionite may liberate sulfur dioxide (SO_2). Sulfur dioxide is known to induce respiratory irritation and in disposed humans also bronchospasms (Klaassen, 2001). The hypersensitivity reaction is also known as "sulfite-asthma" and linked to SO_2 exposure or the use of SO_2 or bisulfite as antioxidants in foodstuffs (Marquardt and Schäfer, 1994). About 10 % of asthmatic humans are reportedly sulfite- or SO_2-sensitive (Lewis, 1998).

Other

In humans, allergoid (pseudoallergic) reactions (asthma, urticaria, headache, intestinal irritation) have been reported following the exposure of sensitive persons to sulfites or sulfur dioxide via the oral or respiratory routes (Henschler, 1974; Greim, 1998; Klaassen, 2001).

Conclusion

There was no animal data available regarding sensitization. In humans, allergic dermatitis from exposure to sulfites is rare and, consequently, sodium dithionite is not considered to possess a significant skin sensitization potential. Although there were no specific reports with regard to sodium dithionite available, the potential for allergoid reactions ("sulfite-asthma") should be assumed in sensitive individuals following oral or inhalation exposure.

3.1.5 Repeated Dose Toxicity

No experimental data on sodium dithionite were available. Due to its instability under physiological conditions, data on the degradation products (hydrogen sulfite, sodium sulfite, thiosulfate, sulfur dioxide) and of disodium disulfite (= sodium metabisulfite; $Na_2S_2O_5$) can be used for the evaluation of the effects of sodium dithionite after repeated exposure, as these substances or their degradation products will be the predominant chemical species after systemic exposure.

Studies in Animals

Oral

- Disodium disulfite

Disodium disulfite was fed to groups of 20 rats/sex/dose with the diet for 30 and 104 weeks at dose levels of 0; 0.125; 0.25; 0.5; 1.0; and 2.0 % in the diet, corresponding to about 0; 50; 100; 217; 450 and 942 mg/kg bw/day). The predominant effect was the induction of stomach lesions due to the local irritant effect, characterized by forestomach and glandular stomach hyperplasia and inflammation at about 450 mg/kg bw/day and higher (NOAEL 217 mg/kg bw/day). The NOAEL for systemic toxicity was 942 mg/kg bw/day, the highest tested dose level (Til, Feron, and de Groot, 1972, peer-reviewed by OECD, 2001).

- Sodium hydrogen sulfite and sodium sulfite

Early long-term feeding studies with sodium sulfite had shown NOAELs at dietary levels of 0.05 % $NaHSO_3$ (which is equivalent to 15 mg SO_2/kg bw/day) (Fitzhugh, Knudsen and Nelson, 1946) and at 34 – 56 mg SO_2/kg bw/day when $NaHSO_3$ was administered via drinking water (reviewed by Til, Feron, and de Groot, 1972).

Sulfites, in general, reduce the thiamine content in food. Til and Feron (1992) reviewed the degrading effects of sulfites to stored diets for rats and also showed a marked reduction of extractable lipids from the diet, especially of unsaturated components such as linoleic acid and the appearance of a rancid flavor. The depletion of essential dietary components via the reductive power of sulfiting agents was shown to result in growth retardation and lower food efficiency. Such effects did not occur when sulfites were administered in drinking water (Hui et al, 1989; JECFA, 1999).

The thiamine depletion observed in the stored feed appears to be related to the reductive power of disulfite/(hydrogen)sulfite in the diet. However, there are observations that high levels of sulfite administered by gavage or parenterally may also induce or aggravate thiamine deficiency in rats, possibly via effects on bacteria which may take part in thiamine production. In feeding studies this effect is confined to high concentrations and may be compensated by thiamine addition as low as 50 ppm even at 2 % sulfite concentrations in the diet (reviewed by Til, Feron and de Groot, 1972).

Studies in Humans

Sodium thiosulfate is used in humans to lessen some of the side effects of cisplatin (a cancer medicine). It is also used in the emergency treatment of cyanide poisoning. Sodium thiosulfate is assumed to be intrinsically non-toxic (IPCS/CEC, 1993).

In humans, no increased vulnerability towards 400 mg SO_2 per person and day for 25 days was observed on a thiamine-deficient diet (reviewed by Til, Feron and de Groot, 1972). Chronic thiamine depletion leads to the Beri-Beri syndrome in humans.

The FAO/WHO joint expert committee on food additives derived a long-term NOAEL of 72 mg/kg bw/day for sulfites expressed as SO_2 equivalent and has set a group ADI of 0 - 0.7 mg SO_2/kg bw/day for calcium hydrogen sulfite, calcium metabisulfite, calcium sulfite, potassium hydrogen sulfite, potassium metabisulfite, potassium sulfite, sodium hydrogen sulfite, sodium metabisulfite, sodium sulfite, sodium, thiosulfate, and sulfur dioxide (JECFA, 1999).

Conclusion

Sodium dithionite was not tested for its toxicity after repeated dosing. Due to its rapid degradation under *in vivo* conditions, the toxicity data on its decomposition products were used for the evaluation of this endpoint. The conversion products including sulfite (SO_3^{2-}), hydrogen sulfite (HSO_3^-), sulfate (SO_4^{2-}), and thiosulfate ($S_2O_3^{2-}$), are considered as substances of very low order

systemic toxicity. It should be noted that sulfites, in general, reduce the thiamine content in food. For disodium disulfite ($Na_2S_2O_5$), oral NOAELs (30 and 104 weeks) of 942 mg/kg bw/day and 217 mg/kg bw/day were obtained for systemic toxicity and local gastrointestinal toxicity in rats, respectively. These results appear to be sufficiently representative also for the assessment of sodium dithionite. Repeated dose studies in animals using the dermal or respiratory routes were not available.

3.1.6 Mutagenicity

In vitro Studies

The potential of sodium dithionite to induce gene mutations was investigated in two Ames tests. No studies were available on its potential to induce chromosomal aberrations *in vitro*.

Bacterial mutagenicity studies (Ames tests) were conducted with sodium dithionite in *Salmonella typhimurium* and *Escherichia coli* WP2 according to standard procedures and in accordance with OECD TGs 471 and 472, with and without metabolic activation. In one of the two available studies the pre-incubation method was used, and the testing was performed on *Salmonella typhimurium* strains TA1535, TA100, TA98, TA1537, TA1538 and on *Escherichia coli* WP2 (Shimizu et al., 1985). In the other study, *Salmonella typhimurium* strains TA1535, TA100, TA1537, and TA98 were used for both the direct plate incorporation and the pre-incubation methods (BASF AG, 1989a). Both studies showed consistently negative results up to and including the top dose of 5 mg/plate.

Sodium hydrogen sulfite [CAS No. 7631-90-5] and disodium disulfite [CAS No. 7681-57-4] produced mutations in bacteria *in vitro* at low pH (pH 5.0 – 6.0) but not at pH 7.0 and 8.0 (Shapiro, 1977; Gunnison, 1981; Pagano and Zeiger, 1987). Mutagenicity of sodium hydrogen sulfite in tester strain TA97 was significant at 27 °C, but disappeared at 37 °C. The results suggest a radical mechanism, in which temperature, pH and oxygen availability determine the rate of autoxidation via the formation of a sulfur trioxide radical, $SO_3^{-\bullet}$. This may occur spontaneously or through the action of the peroxidase/H_2O_2 system (Pagano, Zeiger and Stark, 1990).

No *in vitro* studies on clastogenic activity were available.

In vivo Studies

No experimental data were available on sodium dithionite.

A 1:3 mixture of sodium hydrogen sulfite [CAS No. 7631-90-5] and sodium sulfite [CAS No. 7757-83-7] in saline was recently shown to be positive in a bone-marrow mouse micronucleus assay after intraperitoneal injection of 20, 100, 500 or 750 mg/kg bw. The treatment was repeated after 24 hours. The clastogenic effect (2- to 4-fold above baseline), appeared between 12 and 48 h after exposure, and was no longer apparent after 72 h (Meng, Sang and Zhang, 2002).

In a further micronucleus assay, performed under GLP-conditions, sodium hydrogen sulfite (75, 150, and 300 mg/kg bw in citrate buffer, pH 5.0, intraperitoneal) failed to show evidence of a clastogenic potential in male and female mice after sampling of bone-marrow erythrocytes at 24 and 48 h (Honarvar, 2000, peer-reviewed by the SCCNFP, 2003). The single doses applied in this test were distinctly lower than those applied twice by Meng, Sang and Zhang (2002) and were in a range which showed an ambiguously to marginally positive effect in the study by Meng, Sang, and Zhang (2002). Therefore, the negative result observed by Honarvar (2000) is not in contrast to that obtained by Meng, Sang, and Zhang (2002) because of the possibly underlying dose effects.

In an *in-vivo/in-vitro* UDS bioassay, performed under GLP-conditions, oral doses of 625 and 1250 mg sodium hydrogen sulfite/kg bw revealed no UDS induction in the hepatocytes of treated

rats 2 and 16 h after treatment as compared to the current vehicle controls (Schulz, 2000, peer-reviewed by the SCCNFP, 2003).

Disodium disulfite was investigated in a cytogenetic assay in rats after gavage administration (30, 700, 1200 mg/kg bw; single treatment with sacrifice after 6, 24 or 48 hours) or 5-fold treatment for 5 days (sacrifice after 6 hours). No clastogenic effect on bone-marrow chromosomes was observed (NTIS, 1972; Maxwell and Newell, 1974). Likewise, an evaluation for mutagenicity in a dominant lethal assay (0, 125, 417, 1250 mg/kg bw/day with the diet for 10 weeks) showed no substance-related effect attributable to disodium disulfite given in the diet (NTIS, 1979). The negative results with disodium disulfite for clastogenic effects are particulary noteworthy in view of the positive effects found with the mixture of sodium hydrogen sulfite and sodium sulfite after intraperitoneal injection of high doses, as sodium hydrogen sulfite and sodium sulfite are decomposition products of disodium disulfite. The discrepancy may be explained by the different routes of administration in these studies with positive results at high intraperitoneal doses, but negative results after oral exposure.

Conclusion

Sodium dithionite was not mutagenic in standard bacterial tests with and without metabolic activation (OECD TG 471, 472). No experimental data is available on the potential of sodium dithionite to induce chromosomal aberrations *in vitro*. An increase in the frequency of micronuclei in bone marrow cells of mice was found after intraperitoneal injection of high doses (2 x 500 or 2 x 750 mg/kg bw) of a mixture of sodium hydrogen sulfite and sodium sulfite, the degradation products of sodium dithionite under physiological conditions.

3.1.7 Carcinogenicity

No experimental data were available on sodium dithionite, sodium sulfites or sodium hydrogen sulfites.

No evidence for carcinogenicity was found in a 2-year dietary study with disodium disulfite, in which six groups of rats (20 rats/sex/dose) were maintained on a diet containing 0, 0.125, 0.25, 0.5, 1.0 or 2.0 % of disodium disulfite (corresponding to about 0; 50; 100; 217; 450 and 942 mg/kg bw/day). The basal diet was supplemented with 50 ppm thiamine, due to the destruction of thiamine by sulfite. Elevated numbers of thyroid and pituitary tumours in test animals were observed in males relative to controls due to a lower than normal incidence of these lesions in the male control group. All other neoplasms occurred in a random manner (Til, Feron, and de Groot, peer-reviewed by OECD, 2001).

According to IARC (1992), there is inadequate evidence for the carcinogenicity in humans of sulfur dioxide, sulfites, hydrogen sulfites and metabisulfites. There is *limited evidence* for the carcinogenicity in experimental animals of sulfur dioxide (IARC, 1992). The overall evaluation by IARC (1992) is that “Sulfur dioxide, sulfites, hydrogen sulfites and metabisulfites are not classifiable as to their carcinogenicity to humans (Group 3).”

Conclusion

No experimental data were available on the carcinogenic potential of sodium dithionite. In 1992, IARC concluded that degradation products of dithionite, i.e. sulfur dioxide, sulfites, hydrogen sulfites and metabisulfites “are not classifiable as to their carcinogenicity to humans (Group 3)”.

3.1.8 Toxicity for Reproduction

Effects on Fertility

No experimental data were available on sodium dithionite. Based on its physico-chemical behavior and its rapid degradation in the body, it is not expected that the intact molecule reaches the reproductive organs, or has any direct effect on fertility. Data relating to sodium hydrogen sulfite and disodium disulfite do not indicate adverse effects (see below).

Sodium hydrogen sulfite

The effect of sodium hydrogen sulfite on differentiating spermatogonia has been investigated in adult mice, given either a single intraperitoneal injection (500, 600, 700, 800, 900 and 1000 mg/kg bw) or repeated intraperitoneal injections (200 and 400 mg/kg bw) of sodium hydrogen sulfite. In the latter case the doses were administered 20, 30 and 40 times during 28, 42 and 56 days, respectively. No mortality was observed up to and including 700 mg/kg dose within 24 hours. At the 1000 mg/kg dose, 80 % of the mice died within 24 hours post-treatment. Cytotoxicity data showed that the high doses of sodium hydrogen sulfite, at any of the dosage levels tested after acute or repeated administration did not alter the population of various types of spermatogonia (Bhattacharjee, Shetty and Sundaram, 1980, peer-reviewed by JECFA,1983). The study has limitations in validity. On the other hand, the high dose levels employed for all dose groups in the absence of observable effects do not indicate adverse effects on fertility.

Disodium disulfite

No toxicity to reproduction was observed in rats in a three-generation study over a period of 2 years. The basal diet was supplemented with 50 ppm thiamine, due to the destruction of thiamine by sulfite (NOAEL oral, feed: about 942 mg/kg bw/day, the highest dose tested) (Til, Feron, and de Groot, 1972, peer-reviewed by OECD, 2001).

Developmental Toxicity

No experimental data were available on sodium dithionite. Based on its physico-chemical behavior and its rapid degradation in the body, it is not expected that the intact molecule reaches the developing organism. Data relating to the degradation products of sodium dithionite or disodium disulfite do not indicate adverse effects on the developing organism.

Sodium sulfite

Groups of 10 - 12 pregnant Wistar rats received sodium sulfite (Na_2SO_3 x 7 H_20) with the diet at doses of 0; 0.32; 0.63; 1.25; 2.5 and 5 % in the diet (corresponding to 0; 200; 400; 900; 1750; and 2900 mg/kg bw/day of Na_2SO_3 x 7 H_20 or about 0; 100; 200; 450; 850; and 1450 mg/kg bw/day of sodium sulfite (without crystal water)) from day 8 to 20 of gestation. The top dose corresponded to about 1000 mg/kg bw/day sulfite (excluding sodium and bound water). Additional groups of 4 - 5 animals exposed to 0, 0.32 and or 5 % were allowed to litter, and growth and viabilities of the neonates were assessed. Maternal food intake and body weight gains were reduced during pregnancy in the top dose. The lower doses produced some mild fetal growth retardation with decreased fetal body weights in all treated groups ($p < 0.05$), except for the female 2.5 % group, which probably explains the slight increase of developmental variations in these groups, and which, according to the study authors, might be related to maternal malnutrition and/or disturbance in metabolism by liberated sulfur dioxide, for instance, inhibition of acetylcholine esterase and destruction of thiamine. No external, visceral or skeletal malformations were recorded. The NOAEL for developmental toxicity was at 5 % (about 1450 mg/kg bw/day; highest tested dose). At this dose clear signs of maternal toxicity were observed (LOAEL, maternal toxicity: 5 % in diet = about 1450 mg/kg bw/day). The NOAEL for maternal toxicity was at 2.5 % in feed (about 850 mg/kg bw/day) (Itami et al., 1989).

Disodium disulfite

No developmental effects were found in rats and rabbits at the highest tested dose levels (NOAEL 110 and 123 mg/kg bw/day, respectively) (OECD, 2001).

Conclusion

Sodium dithionite has not been tested for its effects on reproduction and development. Based on its physico-chemical behavior and its rapid conversion in the body, it is not expected that the intact molecule reaches the reproductive organs or has any direct effect on reproduction and development. Data relating to the degradation products of sodium dithionite generally do not indicate an adverse effects. At high dietary doses, which can cause maternal malnutrition and destruction of thiamine, fetal growth retardation was however observed. In a rat dietary study with sodium sulfite (similar to OECD TG 414), the NOAEL for developmental toxicity was at 5 % (about 1450 mg/kg bw/day; highest tested dose). At this dose clear signs of maternal toxicity were observed (LOAEL, maternal toxicity: 5 % in diet = about 1450 mg/kg bw/day). The NOAEL for maternal toxicity was at 2.5 % in feed (about 850 mg/kg bw/day).

3.2 Initial Assessment for Human Health

Sodium dithionite is not stable under physiological conditions, with the rate of decomposition increasing with increasing acidity. Upon contact with moisture, it is oxidized to hydrogen sulfite (HSO_3^-), sulfite (SO_3^{2-}) and hydrogen sulfate (HSO_4^-), and under strongly acidic conditions it may liberate sulfur dioxide. Under anaerobic conditions (such as in the lower gastrointestinal tract), hydrogen sulfite (HSO_3^-) and thiosulfate ($S_2O_3^{2-}$) may be formed. Hydrogen sulfite (HSO_3^-) can be absorbed after ingestion. It is efficiently metabolized, and the major part rapidly excreted as sulfate into the urine.

The acute oral LD_{50} of sodium dithionite in rats was about 2500 mg/kg bw, with atony, gastro-intestinal irritation, diarrhea and dyspnea as the main clinical and pathological signs at doses near to or exceeding the LD_{50}. There were no acute dermal and no valid acute inhalation studies available.

Sodium dithionite was slightly irritating to the skin and strongly irritating to the eyes of rabbits.

Under acidic conditions, sodium dithionite may liberate sulfur dioxide (SO_2), which is known to induce respiratory irritation in humans.

There was no animal data available regarding sensitization. In humans, allergic dermatitis from exposure to sulfites is rare and, consequently, sodium dithionite is not considered to possess a significant skin sensitization potential. Although there were no specific reports with regard to sodium dithionite available, the potential for allergoid reactions (“sulfite-asthma”) should be assumed in sensitive individuals following oral or inhalation exposure.

Sodium dithionite was not tested for its toxicity after repeated dosing. Due to its rapid degradation under *in vivo* conditions, the toxicity data on its decomposition products were used for the evaluation of this endpoint. The conversion products, including sulfite (SO_3^{2-}), hydrogen sulfite (HSO_3^-), sulfate (SO_4^{2-}), and thiosulfate ($S_2O_3^{2-}$), are considered as substances of very low order systemic toxicity. It should be noted that sulfites, in general, reduce the thiamine content in food. For disodium disulfite ($Na_2S_2O_5$), oral NOAELs (30 and 104 weeks) of 942 mg/kg bw/day and 217 mg/kg bw/day were obtained for systemic toxicity and local gastrointestinal toxicity in rats, respectively. These results appear to be sufficiently representative also for the assessment of sodium dithionite. Repeated dose studies in animals using the dermal or respiratory routes were not available.

Sodium dithionite was not mutagenic in standard bacterial tests with and without metabolic activation (OECD TG 471, 472). No experimental data was available on the potential of sodium dithionite to induce chromosomal aberrations *in vitro*. An increase in the frequency of micronuclei in bone marrow cells of mice was found after intraperitoneal injection of high doses (2 x 500 or 2 x 750 mg/kg bw) of a mixture of sodium hydrogen sulfite and sodium sulfite, the degradation products of sodium dithionite under physiological conditions.

No experimental data were available on the carcinogenic potential of sodium dithionite. In 1992, IARC concluded that degradation products of dithionite, i.e. sulfur dioxide, sulfites, hydrogen sulfites and metabisulfites "are not classifiable as to their carcinogenicity to humans (Group 3)".

Sodium dithionite has not been tested for its effects on reproduction and development. Based on its physico-chemical behavior and its rapid conversion in the body, it is not expected that the intact molecule reaches the reproductive organs or has any direct effect on reproduction and development. Data relating to the degradation products of sodium dithionite do also not indicate any adverse effects. At high dietary doses, which can cause maternal malnutrition and destruction of thiamine, fetal growth retardation was however observed. In a rat dietary study with sodium sulfite (similar to OECD TG 414), the NOAEL for developmental toxicity was at 5 % (about 1450 mg/kg bw/day; highest tested dose). At this dose clear signs of maternal toxicity were observed (LOAEL, maternal toxicity: 5 % in diet = about 1450 mg/kg bw/day). The NOAEL for maternal toxicity was at 2.5 % in feed (about 850 mg/kg bw/day).

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

The following reliable aquatic effect concentrations are available:

Acute Toxicity Test Results

Fish

In a study with *Leuciscus idus*, following the German Industrial Standard DIN 38 412, Part 15, six concentrations from 21.5 - 147 mg/l (nominal), plus a control and pH adjusted 147 mg/l and 500 mg/l group, were tested. An LC_{50} (96 h) of 63.2 mg/l (nominal) was calculated. All fish in the pH adjusted 147 mg/l and 500 mg/l concentration groups died within one hour. Less than 1 mg/l oxygen was measured in those test solutions at test start. In a pre-test in which the fish were placed into the aquaria 1 h after preparation of the test solution the initial oxygen consumption was compensated by the continuous aeration and the concentration of 100 mg/l did not cause any mortality or symptoms. Therefore, the toxic effect may be, in part, due to oxygen deficiency (BASF AG, 1982; Priesmann, 2003).

Daphnia

A test following Directive 79/831/EEC, C2, with Daphnia magna with 10 nominal concentrations, plus a control ranging from 0.976 – 500 mg/l, resulted in an EC_{50} (48 h, immobilisation) of 98.3 mg/l (BASF AG, 1989b). As oxygen values in the 250 mg/l and 500 mg/l test solutions were below 1 mg/l at the beginning of the test, it cannot be excluded that the toxicity was in part due to oxygen deficiency effects.

Algae

Acute toxicity to Scenedesmus subspicatus was determined in a study, following the German Industrial Standard DIN 38 412 Part 9, with 7 nominal concentrations ranging from 7.81 –500 mg/l, plus a control. The ErC50 (72 h) for growth rate was 206 mg/l (nominal concentration) and the

NOEC 62.5 mg/l (nominal concentration); corresponding values for the endpoint biomass were 135 mg/l and 62.5 mg/l respectively. (BASF AG, 1989c; BASF AG, 2004b).

Chronic Toxicity Test Results

The following chronic toxicity test with aquatic organisms is available:
Water flea *(Daphnia magna)*: NOEC (21 d) > 10 mg/l (BASF AG, 1994).
Three concentrations (1, 5, and 10 mg/l) were tested.

Toxicity to Microorganisms

Acute toxicity to *Pseudomonas putida* was determined in a study, following the German Industrial Standard DIN 38 412 Part 8, with 7 nominal concentrations ranging from 15.6 – 1000 mg/l, plus a control. An EC_{50} (17 h) of 106.5 mg/l (nominal concentration) was calculated (BASF AG, 1988b).

4.2 Terrestrial Effects

There are no data available with terrestrial organisms. However, sodium dithionite is expected to be unstable in soil because of its rapid decomposition in water with a half life of less than 1 day at room temperature (BASF AG, 1988a). Therefore given the low potential for exposure in the terrestrial compartment, significant toxicity to terrestrial organisms is unlikely.

4.3 Other Environmental Effects

No data available

4.4 Initial Assessment for the Environment

Sodium dithionite dihydrate is very sensitive towards atmospheric oxygen in the finely crystalline state and oxidizes under heat development: the heat of oxidation can lead to ignition, e.g. upon contact with moisture. The anhydrous salt decomposes exothermically in air on prolonged heating above 90 °C (decomposition/oxidation products: sodium sulfate (Na_2SO_4) and sulfur dioxide (SO_2)). Above ca. 150 °C, in exclusion of air, vigorous decomposition occurs, yielding mainly sodium sulfite (Na_2SO_3), sodium thiosulfate ($Na_2S_2O_3$), sulfur dioxide (SO_2) and a small amount of sulfur. Because of decomposition on heating, boiling point and melting point are not relevant. The vapour pressure is negligible and the Henry constant is near to zero due to the ionic character of the inorganic salt. Biodegradation or elimination tests are not appropriate for the inorganic substance. Hydrolysis occurs within hours at pH 7 and room temperature. There is no indication of a bioaccumulation potential.

Main hydrolysis products are thiosulfate ($S_2O_3^{2-}$) and sulfite (SO_3^{2-}). Small amounts of sulfur and sulfide (S^{2-}) have been detected during oxygen-free hydrolysis. Oxygen dissolved in water is consumed by dissolved sodium dithionite. Final oxidation products are sulfate (SO_4^{2-}) and sulfite (SO_3^{2-}).

Because of the high water solubility at 20 °C of 182 g/l (value related to formula $Na_2S_2O_4$) and 219 g/l (related to formula $Na_2S_2O_4 * 2\ H_2O$) respectively, for hydrated sodium dithionite aquatic environment is the target compartment. Sodium dithionite is expected not to be stable in soil because of its rapid decomposition in water and the reaction with oxygen.

From acute toxicity test to fish (*Leuciscus idus*), 96-hr LC_{50} was 62.3 mg/l. For algae (*Scenedesmus subspicatus*), 72-hr ErC_{50} was 206 mg/l and 72-hr NOErC was 62.5 mg/l (corresponding values for biomass are 135 and 62.5 mg/l respectively; nominal concentration). For *Daphnia magna*, the acute toxicity value of 48-hr EC_{50} was 98.3 mg/l, and the chronic value of 21-day NOEC was > 10 mg/l.

Due to oxygen concentrations < 1 mg/l at test start in high test concentrations in the fish and acute daphnia test, it cannot be excluded that the effect values found in these studies are at least partly caused by oxygen deficiency. A PNEC of 0.1 mg/l for the aquatic organisms was calculated from the chronic value (NOEC for daphnia > 10 mg/l) using an assessment factor of 100.

5 RECOMMENDATIONS

Environment

The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for the environment. Although these hazards do not warrant further work (as they are related to acute toxicity which may become evident only at very high exposure level), they should nevertheless be noted by chemical safety professionals and users.

Human Health

The chemical is a candidate for further work. Sodium dithionite possesses properties indicating a hazard to human health (sulfite asthma, irritant effects on the eye, chromosomal aberrations *in vivo* were observed following intraperitoneal injection of the degradation products). There is only limited information on the exposure of workers in manufacturing and down-stream industries, and consumers may be exposed through household products (detergents, stain removers). It is therefore recommended to conduct an exposure assessment, and, if then indicated, a risk assessment.

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I U C L I D

D a t a S e t

Existing Chemical	ID: 7775-14-6
CAS No.	7775-14-6
EINECS Name	sodium dithionite
EC No.	231-890-0
Index number	016-028-00-1
Molecular Weight	174.11 g/mol
Molecular Formula	Na2 S2 O4

Producer Related Part

Company:	BASF AG
Creation date:	12-NOV-1992

Substance Related Part

Company:	BASF AG
Creation date:	12-NOV-1992

Memo:	master
Printing date:	21-APR-2006
Revision date:	20-JUL-2004
Date of last Update:	**21-APR-2006**
Number of Pages:	**117**
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, SIDS

1.0.1 Applicant and Company Information

Type: lead organisation
Name: BASF AG
Contact Person: Dr. Rolf Sarafin **Date:**
GUP/CR - Z570
Street: Carl-Bosch-Strasse
Town: 67056 Ludwigshafen
Country: Germany
Phone: +49 621 60 44712
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Homepage: www.basf.com

Flag: non confidential, Critical study for SIDS endpoint
09-FEB-2006

Type: cooperating company
Name: Clariant Ltd.
Country: Switzerland

Flag: non confidential, Critical study for SIDS endpoint

Type: cooperating company
Name: IDROSOL s.r.l.
Country: Italy

Flag: non confidential, Critical study for SIDS endpoint

Type: cooperating company
Name: Mitsubishi Gas Corp.
Country: Japan

Flag: non confidential, Critical study for SIDS endpoint

Type: cooperating company
Name: Prayon Rupel
Country: Belgium

Flag: non confidential, Critical study for SIDS endpoint

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 dithionite
Mol. Formula: Na2 O4 S2
Mol. Weight: 174.11 g/mol

Remark: Anhydrous sodium dithionite.
Flag: non confidential, Critical study for SIDS endpoint
09-FEB-2006

1.1.1 General Substance Information

Substance type: inorganic
Physical status: solid
Purity: >= 88 - % w/w
Colour: white
Odour: pungent

Flag: non confidential, Critical study for SIDS endpoint (1)

Remark: Sodium dithionite [7775-14-6] , Na2S2O4 , is the only industrially important salt of dithionous acid (H2S2O4), which has not been isolated. The importance of sodium dithionite lies in its powerful reducing capacity, which allows, for example, vat dyes to be reduced at room temperature. It is also used as a bleaching agent, mainly in the textile, paper and clay industries.

Sodium dithionite is known as the dihydrate Na2S2O4 · 2 H2O, Mr 210.146, and as the anhydrous salt, Mr 174.114. The dihydrate crystallizes in thin, yellowish shiny, soft prisms of density 1.58 g/cm3. The anhydrous salt forms monoclinic white crystals of density 2.38 g/cm3.

Sodium dithionite dihydrate is very sensitive toward atmospheric oxygen in the finely crystalline state. The heat of oxidation can lead to ignition.

The anhydrous salt decomposes exothermically in air on prolonged heating above 90 °C. The main decomposition/oxidation products are sodium sulfate and sulfur dioxide. Above ca. 150 °C, with exclusion of air, sodium dithionite decomposes in a vigorous reaction, giving mainly sodium sulfite, sodium thiosulfate, sulfur dioxide, and a small amount of sulfur. In the absence of air, moisture only causes a small degree of decomposition. Sodium dithionite in powder form can decompose in air on contact with a small amount of water with such intense heat formation that it burns with a flame.
Aqueous dithionite solutions decompose slowly in the cold and rapidly in the warm.

In weakly acidic solution dithionite decomposes rapidly, especially under warm conditions. In alkaline solution the reaction is slower. Main decomposition products are thiosulfate and disulfite or hydrogensulfite (1). To a small amount (2-4%) sulfide and consecutively sulfur occurs (2):

(1) 2 Na2S2O4 -(H2O)-> Na2S2O3 + Na2S2O5 (NaHSO3 respectively)
(2) Na2S2O4 + Na2S2O3 -(H2O)-> Na2S + 3 NaHSO3

The decomposition in alkaline solution is accelerated by thiosulfates and polysulfides. On addition of strong acids the dithionite solution first becomes yellow-red, and after a short time complete decomposition occurs with precipitation of sulfur. The dithionite can be recovered if the solution is

rapidly neutralized before the sulfur precipitates. Weak alkalis (pH 8 - 13) stabilize dithionite solutions, which can then be kept for weeks below 10 °C with the exclusion of air. In the presence of air the dissolved dithionite is converted rapidly into sulfate and sulfite at room temperature, with or without stabilizer.
Commercial sodium dithionite generally has a purity of ca. 88 %. It contains ca. 3 % of each of the following: sodium disulfite, sodium sulfite, sodium sulfate, and sodium carbonate. The latter stabilizes the Na2S2O4. The total heavy metal content is generally < 20 ppm. The product from the zinc-dust process has a zinc content of up to 300 ppm.

Flag: non confidential, Critical study for SIDS endpoint (2) (3) (4) (5)

Purity: <= 84 - % w/w

Result: analyses of sodium dithionite from four commercial (U.S.A.) suppliers: none of the samples was better than 84% pure.

Flag: non confidential, Critical study for SIDS endpoint (6)

1.1.2 Spectra

1.2 Synonyms and Tradenames

Disodium dithionite

Flag: non confidential, Critical study for SIDS endpoint

Disodium hydrosulfite

Flag: non confidential, Critical study for SIDS endpoint

Dithionous acid, disodium salt (8CI, 9CI)

Flag: non confidential, Critical study for SIDS endpoint

Natriumdithionit

Flag: non confidential, Critical study for SIDS endpoint

Sodium dithionite

Flag: non confidential, Critical study for SIDS endpoint

Sodium dithionite (Na2(S2O4))

Flag: non confidential, Critical study for SIDS endpoint

Sodium dithionite (Na2S2O4)

Flag: non confidential, Critical study for SIDS endpoint

Sodium hydrosulfite

Flag: non confidential, Critical study for SIDS endpoint

Sodium hydrosulfite (Na2S2O4)

Flag: non confidential, Critical study for SIDS endpoint

Sodium hyposulfite

Flag: non confidential, Critical study for SIDS endpoint

1.3 Impurities

CAS-No: 7681-57-4
EC-No: 231-673-0
EINECS-Name: disodium disulphite
Mol. Formula: Na2 S2 O5
Contents: ca. 3 - % w/w

09-MAR-2006 (5)

CAS-No: 7757-83-7
EC-No: 231-821-4
EINECS-Name: sodium sulphite
Mol. Formula: Na2 S O3
Contents: ca. 3 - % w/w

09-MAR-2006 (5)

CAS-No: 7757-82-6
EC-No: 231-820-9
EINECS-Name: sodium sulphate
Mol. Formula: Na2 O4 S
Contents: ca. 3 - % w/w

09-MAR-2006 (5)

CAS-No: 7757-83-7
EC-No: 231-821-4
EINECS-Name: sodium sulphite
Mol. Formula: Na2 S O3
Contents: 1 - 5 % w/w

Remark: refers to the product:
HYDROSULPHITE P CONC. BASF (contains approx. 88% sodium dithionite)
Flag: non confidential, Critical study for SIDS endpoint
(7)

CAS-No: 7681-57-4
EC-No: 231-673-0
EINECS-Name: disodium disulphite
Mol. Formula: Na2 S2 O5
Contents: 1 - 5 % w/w

Remark: refers to the product:
HYDROSULPHITE P CONC. BASF (contains approx. 88% sodium dithionite)
Flag: non confidential, Critical study for SIDS endpoint
(7)

CAS-No: 7772-98-7
EC-No: 231-867-5
EINECS-Name: sodium thiosulphate
Mol. Formula: Na2 S2 O3
Contents: 0 - 2 % w/w

Remark: refers to the product:
HYDROSULPHITE P CONC. BASF (contains approx. 88% sodium dithionite)
Flag: non confidential, Critical study for SIDS endpoint
(7)

1.4 Additives

CAS-No: 497-19-8
EC-No: 207-838-8
EINECS-Name: sodium carbonate
Mol. Formula: C O3 Na2
Contents: ca. 3 - % w/w
Funct. of add.: Stabilizer

09-MAR-2006 (5)

CAS-No: 497-19-8
EC-No: 207-838-8
EINECS-Name: sodium carbonate
Mol. Formula: C O3 Na2
Contents: 1 - 3 % w/w
Funct. of add.: Stabilizer

Remark: Hazard symbol(s): Xi
R-phrase(s): 36
INDEX-No.: 011-005-00-2
refers to the product:
HYDROSULPHITE P CONC. BASF (contains approx. 88% sodium dithionite)
Flag: non confidential, Critical study for SIDS endpoint
(1)

1.5 Total Quantity

Remark: Production quantity for 2001:

Germany : 60,000 - 120,000 t/a
Europe (excl. Germany): 40,000 - 80,000 t/a
NAFTA : 100,000 - 150,000 t/a
Asia : 200,000 - 300,000 t/a

World : approx. 550,000 t/a
Flag: Critical study for SIDS endpoint
09-FEB-2006 (7)

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: (Xn) harmful

Specific limits: no
R-Phrases: (7) May cause fire
(22) Harmful if swallowed
(31) Contact with acids liberates toxic gas
S-Phrases: (2) Keep out of reach of children
(7/8) Keep container tightly closed and dry
(26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
(28) After contact with skin, wash immediately with plenty of water
(43) In case of fire, use large quantities of water

Remark: INDEX-No. 016-028-00-1
Flag: non confidential, Critical study for SIDS endpoint (1) (8)

Labelling: provisionally by manufacturer/importer
S-Phrases: (3) Keep in a cool place

Remark: additional to the labelling as in Directive 67/548/EEC
Flag: non confidential, Critical study for SIDS endpoint (1)

1.6.2 Classification

Classified: as in Directive 67/548/EEC
Class of danger: harmful
R-Phrases: (22) Harmful if swallowed

Remark: INDEX-No. 016-028-00-1
Flag: non confidential, Critical study for SIDS endpoint (8)

Classified: as in Directive 67/548/EEC
R-Phrases: (7) May cause fire

Remark: INDEX-No. 016-028-00-1
Flag: non confidential, Critical study for SIDS endpoint (8)

Classified: as in Directive 67/548/EEC
R-Phrases: (31) Contact with acids liberates toxic gas

Remark: INDEX-No. 016-028-00-1
Flag: non confidential, Critical study for SIDS endpoint (8)

1.6.3 Packaging

1.7 Use Pattern

Type: type
Category: Wide dispersive use

Flag: non confidential, Critical study for SIDS endpoint

Type: industrial

Category: Basic industry: basic chemicals

Flag: non confidential, Critical study for SIDS endpoint

Type: industrial
Category: Leather processing industry

Flag: non confidential, Critical study for SIDS endpoint

Type: industrial
Category: Paper, pulp and board industry

Flag: non confidential, Critical study for SIDS endpoint

Type: industrial
Category: Textile processing industry

Flag: non confidential, Critical study for SIDS endpoint

Type: use
Category: Bleaching agents

Flag: non confidential, Critical study for SIDS endpoint
(1)

Type: use
Category: Cleaning/washing agents and disinfectants

Flag: non confidential, Critical study for SIDS endpoint

Type: use
Category: Reducing agents

Flag: non confidential, Critical study for SIDS endpoint
(1)

Remark: Usage of the world production:

approx. 50% for textile bleaching
approx. 35% for pulp & paper bleaching
approx. 5% for clay bleaching
approx. 10% for other applications

nearly 100% of the total world use is "industrial use".
Flag: non confidential, Critical study for SIDS endpoint
09-MAR-2006

Remark: All uses of sodium dithionite are based on its reducing properties. It is used predominantly in the textile industry as a dyeing and printing auxiliary and as a bleaching agent in the textile and paper industries.
In dyeing and printing, sodium dithionite is used to convert insoluble vat dyes to the soluble leuco form. High-purity sodium dithionite (e.g., Blankit) is used to bleach wool, cotton, silk, bristle, straw, horsehair, coconut fiber, raffia, soaps, glues, clay, sand, bauxite, and in some countries for bleaching sugar, syrup, fruit, edible oils, edible fats, and gelatine.
For special applications in the paper or textile industries

complexing agents such as trilons or phosphates, or also optical brighteners are added to dithionite-containing products.
The reducing action of sodium dithionite is also used in preparative and analytical chemistry. It can reduce azo, diazo, nitro, nitroso, and carbonyl groups.
09-MAR-2006 (5)

Type: use
Category: Bleaching agents

Result: Bleaching agents usual in the trade contains sodium dithionite and possibly soda
Reliability: (2) valid with restrictions
expert judgement
Flag: non confidential, Critical study for SIDS endpoint
(9)

Type: use
Category: Bleaching agents

Remark: Dithioinite is also found in household decolorants present in formulations containing typically >30% sodium dithionite, and some additives such as soda, tensides and in some formulations perfume.
Flag: non confidential, Critical study for SIDS endpoint

Type: use
Category: other:

Remark: According to the Swiss Product Register (2002), there are 113 products marketed containing sodium dithionite. Among them are 21 consumer products with concentrations of up to 100 %. Product types are unspecified additives; adhesive, lute, priming material; cleaning/washing agents and additives; water treatment; photographic chemicals; galvanic additive; spot remover.
In the Danish Product Register (2003), there are 24 products listed, 16 of them with a content of 50 - 100 %. The product types are reducing agents, bleaching agents, coloring agents and cleaning/washing agents. The chemical is used in the manufacture and finishing of textiles, fibres, fabrics, tanning and dressing of leather, industrial cleaning, laundries and dry cleaners.
The Swedish Product Register (2002) lists 34 products, 5 of these available to consumers (main use bleaching agent with content 10 - 100 %). The most common/frequent industry categories are textile industry, tanneries, industry for pulp, paper and paper products, and trade.
In the Norwegian Product Register (2003), 11 products containing a total quantity of 637 tons are registered.
20-APR-2006 (10) (11) (12) (13)

1.7.1 Detailed Use Pattern

1.7.2 Methods of Manufacture

Orig. of Subst.: Synthesis
Type: Production

Remark: All processes for the production of dithionite start with the reduction of sulfurous acid, which can either be present in the free form or as hydrogensulfite. The production processes with zinc dust, sodium amalgam, sodium formate, sodium borohydride, and electric current as the reducing agent are important industrially.

Zinc-Dust Process
Some important producers still use the zinc-dust process, which was developed by BASF. The basic reactions are:

$Zn + 2\ SO_2 \rightarrow ZnS_2O_4$
$ZnS_2O_4 + 2\ NaOH \rightarrow Zn(OH)_2 + Na_2S_2O_4$

An aqueous slurry of zinc dust is treated in a stirred reactor with cooling at ca. 40 °C with liquid or gaseous sulfur dioxide to give zinc dithionite. After completion of the reaction the solution is passed through a filter press to remove unreacted zinc dust and impurities from the zinc. The zinc is then precipitated from the zinc dithionite by adding sodium carbonate or sodium hydroxide in stirred vessels. The zinc carbonate or hydroxide is removed in filter presses. Anhydrous sodium dithionite is precipitated from the clarified sodium dithionite solution by concentration under vacuum and addition of sodium chloride at > 60 °C. It is filtered, washed with methanol, and dried at 90 - 100 °C.

Amalgam Process
In the amalgam process, sodium hydrogensulfite is reduced to sodium dithionite in aqueous solution in a cooled, stirred vessel using the sodium amalgam of a chloralkali electrolysis cell.

Formate Process
Sodium formate, dissolved in 80 % aqueous methanol, is charged to a stirred vessel. At a pressure of 2 - 3 bar sulfur dioxide and sodium hydroxide are introduced into this solution such that a pH of 4 - 5 is maintained. The reaction can be described by the following equation:
$HCOONa + 2\ SO_2 + NaOH \rightarrow Na_2S_2O_4 + CO_2 + H_2O$
Under the above conditions anhydrous sodium dithionite precipitates as fine crystals. It is filtered, washed with methanol, and dried.

Sodium Borohydride Process
Sodium borohydride is stable in strong aqueous alkali and can be used in this form for the production of sodium dithionite by adding SO_2 and sodium hydroxide:
$NaBH_4 + 8\ NaOH + 8\ SO_2 \rightarrow 4\ Na_2S_2O_4 + NaBO_2 + 6\ H_2O$

Electrolytic Process
The electrolytic process, developed by BASF and by Olin (USA).

The zinc dust process accounts for ca. 35 % of the capacity, the formate process 40 %, the amalgam process 15 %, and the sodium borohydride process 10 %.

Flag: non confidential, Critical study for SIDS endpoint

(5)

1.8 Regulatory Measures

1.8.1 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value: other: no MAK value available

Flag: non confidential, Critical study for SIDS endpoint

(14)

Type of limit: other:

Remark: The sodium dithionite related compounds sodium sulfite, sodium hydrogen sulfite, and sodium metabisulfite are currently allowed in the EU as food additives (preservatives). In 1998, the FAO/WHO joint expert committee on food additives set a group ADI of 0 - 0.7 mg/kg bw, expressed as sulfur dioxide, for calcium hydrogen sulfite, calcium metabisulfite, calcium sulfite, potassium hydrogen sulfite, potassium metabisulfite, potassium sulfite, sodium hydrogen sulfite, sodium metabisulfite, sodium sulfite, sodium, thiosulfate, and sulfur dioxide.
Flag: non confidential, Critical study for SIDS endpoint
20-APR-2006

(15)

1.8.2 Acceptable Residues Levels

1.8.3 Water Pollution

Classified by: other: VwVwS (Germany), Annex 2
Labelled by: other: VwVwS (Germany), Annex 2
Class of danger: 1 (weakly water polluting)

Remark: ID-number: 1170
Flag: non confidential, Critical study for SIDS endpoint

(16)

1.8.4 Major Accident Hazards

1.8.5 Air Pollution

1.8.6 Listings e.g. Chemical Inventories

Type: TSCA

Flag: non confidential, Critical study for SIDS endpoint

(17)

Type: DSL

Flag: non confidential, Critical study for SIDS endpoint

(17)

Type: AICS

Flag: non confidential, Critical study for SIDS endpoint (17)

Type: other: SWISS
Additional Info: SWISS No. G-5445

Flag: non confidential, Critical study for SIDS endpoint (17)

Type: PICCS

Flag: non confidential, Critical study for SIDS endpoint (17)

Type: EINECS
Additional Info: EINECS No. 231-890-0

Flag: non confidential, Critical study for SIDS endpoint (17)

Type: ENCS
Additional Info: ENCS No. 1-504

Flag: non confidential, Critical study for SIDS endpoint (17)

Type: ECL
Additional Info: ECL Serial No. KE-31508

Flag: non confidential, Critical study for SIDS endpoint (17)

1.9.1 Degradation/Transformation Products

CAS-No: 7446-09-5
EC-No: 231-195-2
EINECS-Name: sulphur dioxide

Flag: non confidential, Critical study for SIDS endpoint (1) (5)

CAS-No: 7757-82-6
EC-No: 231-820-9
EINECS-Name: sodium sulphate

Flag: non confidential, Critical study for SIDS endpoint (5)

Type: degradation product in water

Remark: Sodium dithionite (anhydrous/dihydrate) has strongly reducing properties and decomposes/disproportionates rapidly in aqueous media (especially under acidic conditions and under oxygen consumption) to sulfites [CAS No. 7757-83-7; 7631-90-5]], SO2 7446-09-5] and sodium thiosulfate (Na2SO3S) [7772-98-7] as major decomposition products.

The test material is chemically unstable under usual test conditions and is transformed into sodium sulfite and thiosulfate without the influence of air and to sodium sulfite and sodium sulfate by oxyidation with air. Sodium dithionite dissolves in water and forms sodium bisulfite, sodium hydrogenium sulfate and sodium thiosulfate [BASF AG, 1988].

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, sufficiently documented for assessment

Flag: Critical study for SIDS endpoint

28-JUL-2005 (18)

Type: degradation product

Remark: Cleghorn and Davies (J. Chem. Soc. A 1:137 (1970)) investigated the decomposition using an infrared technique combined with nonisothermal thermo-gravimetric analysis (TGA) over a temperature range of 25-400 °C. They observed an exothermic reaction which occurred at 190 °C.
The gas released was predominantly SO2 [CAS 7446-09-5] and the solid products were identified as mostly sodium thiosulfate [CAS 7772-98-7] with some sodium sulfite [CAS 7751-83-7] and sodium dithionate [CAS 7631-94-9]. The most likely decomposition reaction is:

$$5Na_2S_2O_4 \rightarrow 3Na_2S_2O_3 + Na_2SO_3 + Na_2S_2O_6 + SO_2$$

Reliability: (4) not assignable
Secondary literature

(19)

Type: degradation product in water

Remark: The degradation and transformation process can roughly be described by the following equations:

$2\ Na_2S_2O_4 + H_2O \rightarrow Na_2S_2O_3 + 2\ NaHSO_3$ (anaerobic conditions)
$Na_2S_2O_4 + O_2 + H_2O$ (r) $NaHSO_4 + NaHSO_3$ (aerobic conditions)

Under aerobic conditions and with low concentrations, reaction (2) is favoured.
The formation of hydrogen sulfite and hydrogen sulfate lowers the pH of the media and accelerates the process of decomposition strongly.

Reliability: (1) valid without restriction

Flag: Critical study for SIDS endpoint

(20) (21)

Type: degradation product in water

Remark: According to the literature overview of Münchow (1992), the following principal decomposition patterns can be described for dithionite in relation to pH ranges at temperatures between 0°C and 32°C for 0.0025 molar solutions:

- strongly alkaline: $3\ Na_2S_2O_4 + 6\ NaOH \rightarrow 5\ Na_2SO_3 + Na_2S + H_2O$
- weakly alkaline to weakly acidic: $2\ Na_2S_2O_4 + H_2O \rightarrow 2\ NaHSO_3 + Na_2S_2O_3$
- acidic medium: $2\ H_2S_2O_4 \rightarrow 3\ SO_2 + S + 2\ H_2O$
- strongly acidic: $3\ H_2S_2O_4 \rightarrow 5\ SO_2 + H_2S + 2\ H_2O$

Higher temperatures appear to further accelerate these reactions. At pH 9 - 11 there was 1% decomposition within 1 hour and at pH 7 there was a 2% decomposition within 1 hour. This mirrors a slow induction phase and is later followed by rapid acceleration due to autocatalytic processes. Below pH 6, there is a much shorter induction time and below pH 4.8 there is no induction time at all.

Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint

(22)

1.9.2 Components

1.10 Source of Exposure

1.11 Additional Remarks

Memo: workplace exposure levels

Remark: Exposure measurements (n = 26) at workplace were performed at the production site of BASF AG, Ludwigshafen (Germany) between 1990 and 2001. The measured total dust concentrations were in the range between < 0.25 mg/m³ and 1.6 mg/m³. Although the actual amounts of dithionite were not determined in these samples, it can be assumed that the sodium dithionite concentrations were considerably below 1.6 mg/m³.
Flag: non confidential, Critical study for SIDS endpoint
21-APR-2006 (23)

1.12 Last Literature Search

Chapters covered: 1
Date of Search: 27-JAN-2003

Flag: non confidential, Critical study for SIDS endpoint

Chapters covered: 8
Date of Search: 27-JAN-2003

Flag: non confidential, Critical study for SIDS endpoint

Type of Search: Internal and External
Chapters covered: 5
Date of Search: 20-JAN-2003

Remark: update 2003, no new data found

Type of Search: Internal and External
Chapters covered: 5.10
Date of Search: 14-NOV-2002

1.13 Reviews

Memo: IARC 1992

Remark: According to IARC (1992), there is inadequate evidence for the carcinogenicity in humans of sulfur dioxide, sulfites, hydrogen sulfites and metahydrogen sulfites. There is limited evidence for the carcinogenicity in experimental animals of sulfur dioxide.
The overall evaluation is that "Sulfur dioxide, sulfites, hydrogen sulfites and metabihydrogen sulfites are not classifiable as to their carcinogenicity to humans (Group 3)."

Flag: Critical study for SIDS endpoint

(24)

2.1 Melting Point

Value: = 54.4 degree C

Test substance: Presumably pure (anhydrous) sodium dithionite
Reliability: (4) not assignable
secondary quotation
(25)

Value: = 52 degree C
Decomposition: yes at degree C

Test substance: no details
Reliability: (4) not assignable
secondary quotation
(26)

Value: = 52 degree C
Decomposition: yes at degree C

Test substance: presumably anhydrous sodium dithionite
Reliability: (4) not assignable
secondary quotation
(27)

Decomposition: yes at 52 degree C

Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Test substance: no details
Reliability: (4) not assignable
manufacturer/producer data without proof

Value: > 100 degree C
Decomposition: yes at degree C

Remark: Thermal decomposition above the indicated temperature is possible.
Test substance: anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof
(1)

Value: ca. 100 degree C
Decomposition: yes at degree C
Sublimation: no

Source: Guaber SPA Funo di Argelato (BO)
BASF AG Ludwigshafen
Test substance: no details
Reliability: (4) not assignable
manufacturer/producer data without proof

Decomposition: yes at > 267 degree C

Remark: Product loses all its water of crystallisation at 110 °C and decomposes. Decomposition products are sodium sulfate and sulfoxide / dihydrate > 267 °C.
Reliability: (4) not assignable
secondary quotation
(26)

Value: = 52 degree C
Decomposition: yes at degree C

Test substance: Sodium dithionite dihydrate
Reliability: (2) valid with restrictions
Data from handbook or collection of data
(28)

Decomposition: yes at > 90 degree C
Sublimation: no

Remark: reason for flagging this information: reliable data on this endpoint, this information is from peer-reviewed handbooks
Result: The anhydrous salt decomposes exothermically in air on prolonged heating above 90 °C (decomposition/oxidation products: sodium sulfate and sulfur dioxide). Above ca. 150 °C, (exclusion of air) vigorous decomposition, giving mainly sodium sulfite, sodium thiosulfate, sulfur dioxide, and a small amount of sulfur. In the absence of air, moisture only causes a small degree of decomposition. Sodium dithionite in powder form can decompose in air on contact with a small amount of water with such intense heat formation that it burns with a flame.
Aqueous dithionite solutions decompose slowly in the cold and rapidly in the warm

Main decomposition products are thiosulfate and hydrogensulfite. To a small amount (2-4%) sulfide and consecutively sulfur occurs.
2 $Na_2S_2O_4$ -(H_2O)-> $Na_2S_2O_3$ + $Na_2S_2O_5$ ($NaHSO_3$ respectively)
NaS_2O_4 + $Na_2S_2O_3$ -(H_2O)-> Na_2S + 3 $NaHSO_3$
Test substance: anhydrous sodium dithionite
Reliability: (2) valid with restrictions
Data from handbook or collection of data
Flag: Critical study for SIDS endpoint
(2) (3) (4) (29) (5)

Decomposition: yes at degree C
Sublimation: no

Result: Anhydrous sodium dithionite is combustible and can decompose exothermically if subjected to moisture. Sulfur dioxide is given off violently if the dry salt is heated above 190 °C. At room temperature, in the absence of oxygen, alkaline (pH 9-12) aqueous solutions of dithionite decompose slowly over a matter of days. Increased temperature dramatically increases the decomposition rate. A representation of the decomposition chemistry is as follows:

2 S2O4(2-) + H2O ---> 2 HSO3(-) + S2O3(2-)

The decomposition of dithionite in aqueous solution is accelerated by thiosulfate, polysulfide, and acids. The addition of mineral acid to a dithionite solution produces first a red color which turns yellow on standing; subsequently, sulfur precipitates and evolution of sulfur dioxide takes place.

Reliability: (2) valid with restrictions
Data from handbook or collection of data
(30)

Decomposition: yes at 135 degree C
Sublimation: no

Method: other: measured
Year: 1939
GLP: no
Test substance: no data

Remark: Addition of 10% of water to the solid anhydrous material caused a vigorous exotherm and spontaneous ignition.
Test substance: Sodium dithionite anhydrous
Reliability: (2) valid with restrictions
study meets basic scientific principles
(31)

Decomposition: yes at 190 degree C

Method: other: measured

Remark: dust layer ignition temperature
Test substance: presumably anhydrous sodium dithionite
Reliability: (2) valid with restrictions
study meets basic scientific principles
(32)

2.2 Boiling Point

Value:
Decomposition: yes

Remark: regarding the intrinsic property "decomposition" see also chapter 2.1 Melting Point (decompostion: Yes at >90 degree C)
Result: n.a.
Test substance: anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof
(33)

Value:
Decomposition: yes

Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof

2.3 Density

Type: density
Value: = 2.4 g/cm³ at 20 degree C

Remark: data refer to the anhydrous salt
Reliability: (4) not assignable
manufacturer/producer data without proof
(1)

Type: density
Value: = 2.189

Remark: In the reference there are no informations about the units of that value.
Reliability: (4) not assignable
secondary quotation
(26)

Type: relative density
Value: = 2.38 at 20 degree C

Test substance: presumably anhydrous sodium dithionite
Reliability: (4) not assignable
secondary quotation
(27)

Type: relative density
Value: ca. 1250 kg/m3 at 20 degree C

Remark: There are no units defined for relative density.
Source: Guaber SPA Funo di Argelato (BO)
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof

Type: bulk density
Value: ca. 1150 - 1400 kg/m3

Remark: bulk density of the product varies for different production processes. This value is valid for the amalgam process.
Test substance: presumably anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof
(34)

Type: bulk density
Value: ca. 750 - 900 kg/m3 at 20 degree C

Method: other
GLP: no

Remark: Produced by formiat process
Test substance: presumably sodium dithionite dihydrate

Reliability: (4) not assignable
manufacturer/producer data without proof

Type: bulk density
Value: ca. 1100 - 1400 kg/m3 at 20 degree C

Method: other
GLP: no

Remark: Produced by zinc dust or amalgam process
Test substance: presumably anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof

Type: density
Value: = 12.636 at 25 degree C

Remark: solid density
although the value ist published by an competent scientific institution this value differs considerably from the other reported values for density
Test substance: pure sodium dithionite
presumably anhydrous sodium dithionite
Reliability: (4) not assignable
secondary quotation
(25)

Type: density
Value: = 1.58 g/cm³

Test substance: sodium dithionite dihydrate
Reliability: (2) valid with restrictions
Data from handbook or collection of data
28-JUL-2005 (29)

Type: density
Value: = 2.38 g/cm³

Remark: reason for flagging this information: important data on this endpoint, handbook has a good reputation
reason for flagging this infromation: important data on this endpoint, handbbok has bood reputation. The anhydrous salt forms monoclinic white crystals of denistiy 2.38 g/cm3
Test substance: anhydous sodium dithionite
Reliability: (2) valid with restrictions
Data from handbook or collection of data
Flag: Critical study for SIDS endpoint
28-JUL-2005 (29)

Type: bulk density
Value: ca. 1300 kg/m3

Reliability: (4) not assignable
manufacturer/producer data without proof
28-JUL-2005 (1)

2.3.1 Granulometry

2.4 Vapour Pressure

Result: not applicable:
the vapour pressure is negligible due to the ionic character of the inorganic salt
Reliability: (4) not assignable
manufacturer/producer data without proof
(33)

2.5 Partition Coefficient

Partition Coeff.: octanol-water
log Pow: < -4.7 at 20 degree C

Method: other (calculated)

Remark: - is out of relevance due to instability in water (t1/2 < 1d at 25°C)

- calculation based on the following data:
  - temperature: 20 °C
  - water-solubility: 250 g/L
  - 1-octanol-solubility: <5*10-3 g/L
  - Pow = c(octanol) / c(water) <2*10-5
    log Pow = <-4.7

reason for flagging this information: important information on this endpoint
Test substance: anhydrous sodium dithionite, purity 88 %
Reliability: (4) not assignable
value for solubility in n-octanol is used without reference

Only data available on this endpoint
Flag: Critical study for SIDS endpoint
(35)

2.6.1 Solubility in different media

Solubility in: Water
Value: = 186.7 g/l at 20.5 degree C

Method: other: visual observation, stirring time: 10 - 15 minutes
Stable: no

Result: 18.67 g/100g solution ~ 186.7 g/l
Test substance: CAS 7775-14-6 (anhydrous sodium dithionite), purity 88%
Reliability: (2) valid with restrictions
study meets national industrial standard
(36)

Solubility in: Water
Value: > 150 g/l at 20 degree C
pH value: 8 - 10.5
Conc.: 50 g/l at 20 degree C

Stable: no

Remark: slow decomposition
Test substance: anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof
(1)

Solubility in: Water
Value: = 241 g/l at 20 degree C

Test substance: presumably anhydrous sodium dithionite
Reliability: (4) not assignable
secondary quotation
(27)

Solubility in: Water
Value: ca. 220 g/l at 20 degree C

Result: ca. 22 g $Na_2S_2O_4$ * $2H_2O$/100 g water at 20 °C ~ ca. 220 g/l
Test substance: Sodium dithionite dihydrate
Reliability: (2) valid with restrictions
information is from peer reviewed handbook
(29)

Solubility in: Water
Value: = 220 g/l at 20 degree C

Result: ca. 22 g/100 g water at 20 °C ~ ca. 220 g/l
Test substance: presumably anhydrous sodium dithionite
Reliability: (2) valid with restrictions
information is from peer reviewed handbook
(30)

Solubility in: Water
Value: = 254 g/l at 20 degree C

Result: 25.4 g /100 cc at 20 °C ~ ca. 254 g/l
Test substance: Sodium dithionite dihydrate
Reliability: (2) valid with restrictions
Data from handbook or collection of data
(28)

Solubility in: Water
Value: = 181.6 g/l at 20 degree C
Temp. Eff.: = 11.06 g $Na_2S_2O_4$/100 ml solution (~ 110.6 g/l) at -2.8 °C
= 11,86 g $Na_2S_2O_4$/100 ml solution (~ 118.6 g/l) at 0.0 °C
= 15.55 g $Na_2S_2O_4$/100 ml solution (~ 155.5 g/l) at 10.0 °C
= 18.61 g $Na_2S_2O_4$/100 ml solution (~ 186.1 g/l) at 20.0 °C

Method: other: measured in an inert atmosphere
Year: 1952
GLP: no
Stable: no

Remark: reason for flagging this information: experimentially derived data, the examination of solubility of sodium dithionite was one of the main purposes of the literature
Test substance: hydrated Sodium Hydrosulphite, purity >= 99.6 %
Reliability: (2) valid with restrictions
study meets basic scientific principles
Flag: Critical study for SIDS endpoint
(37)

Solubility in: Water
Value: = 218 g/l at 20 degree C

Method: other: measured
Year: 1911
GLP: no

Result: 21.8 g $Na_2S_2O_4$/100 g H_2O ~ 218 g/l
Test substance: hydrated Sodium Hydrosulphite, pure
Reliability: (2) valid with restrictions
study meets basic scientific principles
(38)

Solubility in: Water
Value: = 276.5 g/l at 20 degree C

GLP: no

Result: water solubility = 1.57 mol/l at 20 °C (original value)
Reliability: (2) valid with restrictions
Data from handbook or collection of data
(39)

Solubility in: Water
Value: ca. 270 g/l at 20 degree C

Result: Solubility of Sodium dithionite anhydrous: ca. 27 g $Na_2S_2O_4$/100 g water at 20 °C ~ ca. 270 g/l
Test substance: Sodium dithionite anhydrous
Reliability: (2) valid with restrictions
information is from peer reviewed handbook
29-JUL-2005 (29)

2.6.2 Surface Tension

2.7 Flash Point

Value: > 100 degree C

Method: other: DIN 51 758

Remark: reason for flagging this information: important information on this endpoint
Test substance: Sodium dithionite anhydrous salt
Reliability: (4) not assignable
manufacturer/producer data without proof
Flag: Critical study for SIDS endpoint

(33)

Value: ca. 100 degree C
Type: open cup

Method: other
GLP: no

Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof

Value: = 125 degree C

Source: IUCLID Data Set. European Commission 11-FEB-2000
BASF AG Ludwigshafen
Reliability: (4) not assignable

Remark: non inflammable
Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Reliability: (4) not assignable

2.8 Auto Flammability

Value: > 100 degree C

Remark: Ignition temperature
reason for flagging this information: important data on this endpoint
Self-ignition in contact with water (small amounts)
Test substance: Sodium dithionite anhydrous salt
Reliability: (4) not assignable
manufacturer/producer data without proof
Flag: Critical study for SIDS endpoint

(33)

Value: > 100 degree C

Source: Guaber SPA Funo di Argelato (BO)
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof

Value:

Remark: non-inflammable
Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof

Value:

Method: other: measured
GLP: no

Result: Exptl. results are presented which show how differences of approach to the detn. of the ignition temp. of a dust layer can lead to widely differing exptl. values. For the material used, Na dithionite, expts. starting at a high temp. and working down lead to an apparent ignition temp. of nearly 400 °C, compared to a value of about 190 ° when expts. start at a low temp. and work up. The cause of this behavior is a 2-stage decompn. characteristic of Na dithionite.
Test substance: presumably anhydrous sodium dithionite
Reliability: (2) valid with restrictions
study meets basic scientific principles

(32)

Value:

Method: other
GLP: no

Result: Cleghorn and Davies (J. Chem. Soc. A 1:137 (1970)) investigated the decomposition using an infrared technique combined with nonisothermal thermo-gravimetric analysis (TGA) over a temperature range of 25-400 °C. They observed an exothermic reaction which occurred at 190 °C. The gas released was predominantly SO2 and the solid products were identified as mostly sodium thiosulfate with some sodium sulfite and sodium dithionate. The most likely decomposition reaction is: $5Na_2S_2O_4 \rightarrow 3Na_2S_2O_3 + Na_2SO_3 + Na_2S_2O_6 + SO_2$
Test substance: presumably anhydrous sodium dithionite
Reliability: (4) not assignable
secondary quotion

(19)

Value:

GLP: no

Result: Combustible solid but not explosive. Burns slowly, about like sulfur. Heats spontaneously in contact with moisture and air, and may ignite nearby combustible materials.
Test substance: presumably anhydrous sodium dithionite
Reliability: (2) valid with restrictions
Data from handbook or collection of data

(40)

2.9 Flammability

Result: non flammable

Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Test substance: presumably anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof

Result: other: Risk of spontaneous ignition

Reliability: (4) not assignable
manufacturer/producer data without proof
(1)

2.10 Explosive Properties

Result: not explosive

Test substance: presumably anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof
(1)

2.11 Oxidizing Properties

2.12 Dissociation Constant

Method: other
GLP: no

Result: Dithionite dissociates slightly in aqueous solution at 25 °C (Keq approx. 1*10-9 M, kdis approx. 2 s-1, or higher forming two equivalents of sulfoxyl radical anion (SO2-).

Aqueous solutions of dithionite samples from four commercial (U.S.A.) suppliers, even if prepared anaerobically, give acidic solutions.
Reliability: (4) not assignable
secondary quotion
(6)

2.13 Viscosity

Result: n.a.
Reliability: (4) not assignable
manufacturer/producer data without proof
(33)

2.14 Additional Remarks

Memo: Decomposition

Remark: can decompose at above 80 °C
Test substance: anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof
(41)

Memo: Stability and reactivity

Remark: -Conditions to avoid: Avoid temperatures above 80 °C. Avoid humidity.
-Substances to avoid: acids, oxidizing agent
-Hazardous reactions: Self inflammation possible by spray waters or water in small quantities. On contact with water, gaseous decomposition products are formed, which cause build-up of pressure in tightly closed containers.
-Hazardous decomposition products: Sulphur dioxide

Test substance: anhydrous sodium dithionite

Reliability: (4) not assignable
manufacturer/producer data without proof

(1)

Remark: Sodium dithionite decomposes from 52 °C upwards. The anhydrous salt decomposes only after heating at 90 °C for a longer time. Under hermetic seal moisture causes only low decomposition, but little amounts of water in presence of air may cause self-ignition. Under circumstances the dry Dihydrate is spontaneous inflammable.
Strong exothermic reaction, heat development with oxidising agents, with little water, with moist air. With little amounts of water generation of hazardous gases and vapours, with moist air danger of self-ignition or generation of inflammable gases or vapours

Reliability: (4) not assignable
secondary quotation

(27)

3.1.1 Photodegradation

Remark: inorganic salt, not applicable

3.1.2 Stability in Water

Type: abiotic

Method: Directive 84/449/EEC, C.10 "Abiotic degradation: hydrolysis as a function of pH"
Year: 1984
GLP: no

Remark: -Preliminary test at pH 8.5 (50 deg Celsius) shows, that already after 1.5 h half of sodium dithionite is hydrolyzed. Therefore a half life time < 1 day for the hydrolytic degradation of sodium dithionite at 25°C can be derived.
-The pH drops during the decomposition into the acid range. Decomposition products are mainly sodium bisulfite, sodium hydrogensulfate and sodium thiosulfate.
reason for flagging this information: experimentially derived data
Test description is not detailed. Preliminary test is done with only one pH at 8.5. pH 9, 7 and 4 is claimed by Directive 84/449/EEC for preliminary hydrolysis test. Nevertheless test seems valid because test method is named, and preliminary hydrolysis test at pH 8.5 is sufficient near to pH 9. Hydrolysis is faster at lower pH.
Test substance: anhydrous sodium dithionite
Reliability: (2) valid with restrictions
study meets basic scientific principles
Flag: Critical study for SIDS endpoint
29-JUL-2005 (35)

Method: other

Remark: -Inorganic reducing agent. In solution it reacts with air/oxygen
Test substance: anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof
29-JUL-2005 (41)

Type: abiotic

Method: other
GLP: no

Remark: Decomposition by hydrolysis, oxidation in presence of air (oxygen)
Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof

Type: abiotic

Degradation: ca. 50 % after 25 minute(s)
Deg. products: yes

Method: other: Polarographic study of the kinetics of dithionite decomposition in aqueous solution
Year: 2001
GLP: no

Remark: reason for flagging this information: experimentially derived data
Result: The decomposition depends strongly on the pH and is rapid at pH < 5.5. At pH values close to 7 the main decomposition reaction for dithionite predominantly results in sulfite and thiosulfate as major decomposition products. Sulfide and elemental sulfur are formed as minor decomposition products (3-6 mol% after 4 hours).
Test condition: Decomposition of a 6.5 x 10-3 M dithionite aqueous solution vs. time
Test substance: Sodium dithionite (85%) obtained from Fluka
Reliability: (2) valid with restrictions
study meets basic scientific principles
Flag: Critical study for SIDS endpoint

(42)

Type: abiotic

Remark: Decomposition products of hydrolysis in oxygen-free water are mainly thiosulfate and hydrogensulfite. To a minor extent always sulfur and sulfid is formed.
Reliability: (2) valid with restrictions
Data from handbook or collection of data

(2) (4)

Type: abiotic

Year: 1992
GLP: no data

Remark: According to the literature overview of Münchow (1992), the following principal decomposition patterns can be described for dithionite in relation to pH ranges at temperatures between 0°C and 32°C for 0.0025 molar solutions:

·strongly alkaline: $3\ Na_2S_2O_4 + 6\ NaOH \rightarrow 5\ Na_2SO_3 + Na_2S + H_2O$
·weakly alkaline to weakly acidic: $2\ Na_2S_2O_4 + H_2O \rightarrow 2\ NaHSO_3 + Na_2S_2O_3$
·acidic medium: $2\ H_2S_2O_4 \rightarrow 3\ SO_2 + S + 2\ H_2O$
·strongly acidic: $3\ H_2S_2O_4 \rightarrow 5\ SO_2 + H_2S + 2\ H_2O$

Higher temperatures appear to further accelerate these reactions. At pH 9 - 11 there was 1% decomposition within 1 hour and at pH 7 there was a 2% decomposition within 1 hour. This mirrors a slow induction phase and is later followed by rapid acceleration due to autocatalytic processes. Below pH 6, there is a much shorter induction time and below pH 4.8 there is no induction time at all.

Test substance: anhydrous sodium dithionite

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, sufficiently documented for assessment
Flag: Critical study for SIDS endpoint
29-JUL-2005 (22)

3.1.3 Stability in Soil

Method: other

Remark: expert judgement: as disodium dithionite is not stable in water, it decomposes in wet soil. It's sensitive toward oxygen as it may occur in dry soil.
reason for flagging this information: important information on this endpoint
Test substance: anhydrous sodium dithionite
Reliability: (2) valid with restrictions
evaluation based on experimentially derived data (BASF AG, Report BRU 88.224, 1988) and comprehensible information from Safety Data Sheet (Hydrosulphite conc.BASF, 2001)
Flag: Critical study for SIDS endpoint
29-JUL-2005 (43) (44)

3.2.1 Monitoring Data (Environment)

Type of measurement: other

Remark: According to its sensitiveness towards water and atmospheric oxygen, it's not expected to find the substance in the environment.
reason for flagging this information: important information on this endpoint
Test substance: anhydrous sodium dithionite
Reliability: (2) valid with restrictions
evaluation based on experimentially derived data (BASF AG, Report BRU 88.224, 1988) and comprehensible information from Safety Data Sheet (Hydrosulphite conc.BASF, 2001)
Flag: Critical study for SIDS endpoint
29-JUL-2005 (35) (41)

3.2.2 Field Studies

3.3.1 Transport between Environmental Compartments

Type: adsorption
Media: water - soil
Method: other: calculated with PCKOCWIN v1.63

Remark: -the Koc should be treated as rough estimation, because the calculation model used is based on validation sets of polar organics, but not of inorganic salts
-the metal (sodium) has been removed to allow estimation
data refers to the anhydrous salt
Result: log Koc = 0.2287 (Koc = 1.693)
Reliability: (3) invalid

The database of PCKOCWIN v1.63 does not allow calulating a valid Koc value for Disodium dithionite. Among the substances used for confirmation of structure activity relationship, there is no comparable sulphur compound.

29-JUL-2005 (45)

Type: adsorption
Media: water - soil

Remark: A very small Koc value is expected due to the polarity of the inorganic salt/dianion. Sodium dithionite does only exist for hours in aqueous solution because of it's hydrolysis property. reason for flagging this information: important information on this endpoint
Reliability: (2) valid with restrictions
evaluation based on experimentially derived data (BASF AG, Report BRU 88.224, 1988)
Flag: Critical study for SIDS endpoint

(35)

3.3.2 Distribution

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Remark: reason for flagging this information: important information on this endpoint
testing for the endpoint biodegradability is not appropriate, because the substance is an inorganic compound
Reliability: (4) not assignable
expert judgement
Flag: Critical study for SIDS endpoint

(46)

3.6 BOD5, COD or BOD5/COD Ratio

Method:

C O D

Method: other
Year:
COD: ca. 210 mg/g substance
Method:
Test substance: anhydrous sodium dithionite
Reliability: (4) not assignable
manufacturer/producer data without proof

29-JUL-2005 (1)

Method:

C O D

Method: other
Year:
GLP: no data
COD: ca. 210 mg/g substance
Method:
Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof

Method:

C O D

Method: other
Year:
GLP: no data
COD: ca. 210 mg/g substance
Method:
Source: Guaber SPA Funo di Argelato (BO)
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof
Method: other: Winkler-procedure
GLP: no
Concentration: 1000 mg/l related to COD (Chemical Oxygen Demand)
Year:
Method:
Result: -BOD5 = 22% of the theoretical COD at 20°C
Test substance: anhydrous sodium dithionite
Reliability: (4) not assignable
secondary quotion
29-JUL-2005 (47) (48)

3.7 Bioaccumulation

3.8 Additional Remarks

Memo: emmision via air

Remark: During production and internal processing at BASF AG, Ludwigshafen (Germany), approx. 115 kg sodium dithionite (dust) were emitted into the air in 2000, where it is expected to be oxidized to sulfate.
Flag: non confidential, Critical study for SIDS endpoint
20-APR-2006 (49)

Remark: Oxygen consumption in waters or in biological sewage plants
Source: L. Brueggemann KG Heilbronn
IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Reliability: (4) not assignable
manufacturer/producer data without proof
20-APR-2006

Remark: when appropriate feeding in adopted sewage plants is applied

no inhibition of the degradation activity of sewage has to be expected

Reliability: (4) not assignable
manufacturer/producer data without proof
(41)

Remark: inorganic reducing agent, in water it reacts with air / oxygen

Reliability: (4) not assignable
manufacturer/producer data without proof
(41)

4.1 Acute/Prolonged Toxicity to Fish

Type: field observation
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:**
NOEC: = 10 - 100

Remark: no experimental details are reported
Source: Guaber SPA Funo di Argelato (BO)
BASF AG Ludwigshafen
Reliability: (4) not assignable
original reference not available

Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48
Unit: mg/l **Analytical monitoring:**
LC50: = 10 - 100

Source: IUCLID Data Set. ECB- Existing Chemicals 23-OCT-95
BASF AG Ludwigshafen
Reliability: (4) not assignable
original reference not available

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC0: = 46.4
LC50: 63.2

Method: other: DIN 38412, Part 15 (Draft January 1979)
Year: 1979
GLP: no
Test substance: other TS: Hydrosulfite conc. BASF, Hydrosulfite P conc, purity: 88 % (anhydrous salt)

Remark: Analysis according to: Finney DJ, Probit Analysis, Cambr. Univ. Press, 3.edition, 1971
Closely followed the German national standard DIN 38 412, Part 15 (draft 1979):
- Animal species: Leuciscus idus L., golden variety (golden orfe)
- Test water: reconstituted freshwater was prepared from fully demineralized tap water according to DIN 38 412, Part 11 (1981) which was resalted by the addition of 294.0 mg/L CaCl2.2H2O, 123.3 mg/L MgSO4.7H2O, 64.8 mg/L NaHCO3 and 5.8 mg/L KCl; test water had a total hardness of 2.5 mmol/L, an acid capacity of 0.8 mmol/L, ratio Ca/Mg ions = 4:1, ratio Na/K ions = 10:1 and a pH of 7.8+-0.2
- Water volume: 10 L
- Aeration: continuous aeration (air free of oil)
- No. of animals per test concentration: 10
- Loading (g fish / L test water): 1.18
- Test vessels: non-sealed all-glass aquarium (30*22*24 cm)
- Temperature: 20°C
- Duration of adaptation to test water and test temperature: 3 days
- Body length: 5.4 cm (range: 5.0 - 5.8 cm)

- Body weight: 1.18 g (range: 0.85 - 1.5 g)
- Positive control of animals conducted with chloracetamide: LC50 (96 h): ca. 38 mg/L (this lethal concentration corresponds to the normal sensitivity)
- Test concentration: 21.5, 31.6, 46.4, 68.1, 100.0, 147.0;
- pH neutralized test solutions: 147, 500 mg/L (pH-adjustment with NaOH-solution, 20 %)
- Preparation of test substance: the product was added to the test water in the form of an aqueous solution (1 % w/v). The test substance was completely dissolved.
- The effect of oxygen consumption was balanced by the continuous aeration of the test solution, therefore the fish were put into the aquarium immediately after addition of the test substance.

- pH values at the start of the experiment and after 96 h:

concentration (mg/L)	pH (0h)	pH (96h)
21.5	6.5	7.8
31.6	6.3	7.8
46.4	6.1	7.7
68.1	5.8	7.6
100.0	5.6	
147.0	5.8	
control	7.5	7.9
147.0 (*)	7.0	
500.0 (*)	7.1	

(*) test solution after pH-adjustment

- Oxygen values at the start of the experiment and after 96 h:

concentration (mg/L)	oxygen (0 h)	(24 h)	(96 h)
21.5	5.80	7.6	7.7
31.6	4.80	7.7	7.7
46.4	2.60	7.8	7.5
68.1	0.57	7.9	7.9
100.0	0.26	8.1	
147.0	0.09	7.6	
control	8.00	7.4	7.7
147.0 (*)	0.12	8.1	
500.0 (*)	0.08	8.2	

(*) test solution after pH-adjustment

- Test water without test substance were used as control
- Median lethal concentrations (LC50) were estimated using Probit Analysis
reason for flagging this information: most reliable data available on this endpoint, experimentially derived data

Result:
- effect values (related to nominal concentrations):
  LCO (96 h) = 46.4 mg/L
  LC50 (96 h) = 62,3 mg/L (>46.4 - <68 mg/L)
- Symptoms: gasping (after 1 h)
- No observed effect concentration (NOEC): <21.5 mg/L
- Maximum concentration causing no mortality: 46.4 mg/L
- Minimum concentration causing 100 % mortality: 100.0 mg/L

- Total number of living fish at the beginning and after 1 h and 96 h:

concentration (mg/L)	No. of living fish

	(0 h)	(1 h)	(96 h)
21.5	10	10	10
31.6	10	10	10
46.4	10	10	10
68.1	10	2	2
100.0	10	0	0
147.0	10	0	0
control	10	10	10
147.0 (*)	10	0	0
500.0 (*)	10	0	0

(*) after pH-adjustment

- In the parallel test with neutralized concentrations of 147.0 mg/L and 500.0 mg/L all fish died within 1 hour due to oxygen deficiency

- In a pre-test in which the fish were placed into the aquaria 1 h after preparation of the test solution the initial oxygen consumption was compensated by the continuous aeration and the the conc. of 100 mg/L did not cause any mortalities or symptoms

Reliability: (2) valid with restrictions
test procedure according to national standard with acceptable restrictions (eg. low initial oxygen concentration at higher test concentrations)

Flag: Critical study for SIDS endpoint

29-JUL-2005 (50) (51)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC0: = 62.5
EC50: = 98.31
EC100: = 250

Method: other: Directive 79/831/EEC, Annex V, Part C
Year: 1984
GLP: no
Test substance: other TS: Hydrosulfite F conc. BASF, purity: 88 % (anhydrous salt)

Method: Procedures to determine EC-values after 48 h:
- EC50: Spearman-Kaerber
- EC0: highest concentration tested at which <= 10 % of the animals were immobile
- EC100: lowest concentration tested at which 100 % of the animals were immobile;

Analysis according to: Sachs L, Angewandte Statistik, Springer Verlag, Berlin, Heidelberg, New York, 4th edition, 1974

Remark: reason for flagging this information: only data available on this endpoint, experimentially derived data
Test conditions:
- Test water: reconstituted water using deionized water was prepared and then aerated (oil-free air) and stored for 24h

hours to allow stabilization. The specifications at the start were: total hardness: 2.88 mmol/L, ratio Ca:Mg: 4:1, ratio Na:K: 10:1, conductivity: 690 µS/cm, pH: 8.0, alkalinitiy up to pH 4.3: 0.97 mmol/L
- Solubility in water: >500 mg/L at 21 °C (293 K)
- Illumination: diffuse light
- Temperature: 20-22 °C (292-294 K)
- Test volume: 10 ml
- Test vessels: test tubes (glass) with flat bottom
- Replicates: 4 per concentration
- Volume/animal: 2 ml
- Number of animals/vessel: 5
- Total number of animals/conc.: 20
- Age of animals: 2-24 h
- Observation times: visually after 0, 3, 6, 24 and 48 h
- Observation parameters: swimming ability, pH, oxygen
- Test concentrations: 0.976, 1.95, 3.9, 7.81, 15.6, 31.2, 62.5, 125.0, 250.0, 500.0 mg/L (nominal)

Result: - Number of mobile test animals after exposure (48 h) to various test concentrations:

concentration (mg/L)	mobile daphnids
0.976	20
1.95	20
3.9	20
7.81	20
15.6	20
31.2	20
62.5	19
125.0	4
250.0	0
500.0	0
control	20

- Effect values after 48 h:
  EC50 = 98.31 mg/L
  95 % confidence limits: 59.61 - 162.12 mg/L

- Effect values after 24 h:
  EC0 = 62.5 mg/L
  EC50 = 116.88 mg/L
  95 % confidence limits: 79.64 - 171.54 mg/L
  EC100 = 250.0 mg/L

- pH at start:

concentration (mg/L)	pH
0.976	7.97
1.95	7.93
3.9	7.88
7.81	7.77
15.6	7.62
31.2	7.33
62.5	7.02
125.0	6.61
250.0	5.97
500.0	5.58
control	8.01

- pH after 48 h:

concentration (mg/L)	pH
0.976	7.99

1.95	7.99
3.9	7.99
7.81	7.99
15.6	7.97
31.2	7.94
62.5	7.85
125.0	7.27
250.0	5.29
500.0	3.65
control	8.01

- Oxygen (O2, mg/L) at start:

concentration (mg/L)	oxygen
0.976	9.40
1.95	9.33
3.9	9.18
7.81	9.04
15.6	8.86
31.2	8.43
62.5	7.42
125.0	5.10
250.0	0.56
500.0	0.40
control	9.22

- Oxygen (O2, mg/L) after 48 h:

concentration (mg/L)	oxygen
0.976	8.51
1.95	8.42
3.9	8.32
7.81	8.28
15.6	8.23
31.2	8.21
62.5	7.96
125.0	7.66
250.0	8.05
500.0	1.44
control	8.33

- Mortality at 250.0 mg/L and 500.0 mg/L may be due to oxygen deficiency in the test assays

Reliability: (2) valid with restrictions
comparable to guideline study with acceptable restrictions (eg. low initial oxygen concentration at higher test concentrations)

Flag: Critical study for SIDS endpoint

29-JUL-2005 (52)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: = 62.5
LOEC: = 125
EC10: 81.7
EC50: = 206.2
EC90 : = 421.8

Method: other: following German Industrial Standard DIN 38412, Part 9
Year: 1984
GLP: no
Test substance: other TS:Hydrosulfite F conc. BASF, purity: 88 % (anhydrous salt)

Remark: reason for flagging this information: only data available on this endpoint, experimentially derived data
Test was performed according to the German standard DIN 38412, Part 9:

Pre-culture:
- Species: Scenedesmus subspicatus, SAG 86.81
- Medium: OECD-medium
- Temperature: 20 °C
- Test vessels: 250 ml-Erlenmeyer flasks
- Test volume: 100 ml
- Illumination: permanent artificial light
- Light intensity: approx. 120 µE/(m2*s)
- a 72 h-old pre-culture was used in the test

Test conditions:
- Algae in test vessels at start: 10000 cells/mL
- Temperature: 21°C
- Test vessels: 20 ml tubes plugged with gas permeable silicon-sponge caps
- Test volume: 10 ml
- Stock solution: 1000 mg/L, pH 3,5 (O2-content of a 500 mg/L test solution immediately after preparation: 1.4 mg/L)
- Test concentrations: 7.81, 15.69, 31.85, 62.5, 125.0, 250.0 and 500.0 mg/L (nominal)
- Replicates: 5 per concentration and control, blank per concentration: (w/o cells): 2
- Control: untreated test medium
- Tubes were incubated in an incubation chamber for 96 h at 23 °C
- Tubes were shaken once a day to hold cells in suspension
- Illumination: permanent artificial light
- Light intensity: approx. 120 µE/(m2*s)
- Samples were taken at regular intervals (0, 24, 48, 72 and 96 h)

- Measurements: photometric determination (chlorophyll-a fluorescence at 685 nm as a size for biomass (pulsed excitation with light flashes havinentration-response relationship a wavelength of 435 nm)), pH
- The effect values are related to the nominal concentrations
- Effect values (endpoints: growth rate and biomass) were recalculated according to OECD 201 guideline using linear regression analysis considering fluorescence values mentioned in the original report

Result: Recalculated effect values:

- Endpoint: growth rate:
  ErC10 (72 h): 81.7 mg/L
  ErC50 (72 h): 206.2 mg/L
  ErC90 (72 h): 421.8 mg/L
  NOErC (72 h): 62.5 mg/L
  LOErC (72 h): 125.0 mg/L

- Endpoint: biomass:
  EbC10 (72 h): 82.9 mg/L
  EbC50 (72 h): 135.0 mg/L
  EbC90 (72 h): 339.0 mg/L
  NOEbC (72 h): 62.5 mg/L
  LOEbC (72 h): 125.0 mg/L

Original effect values given in the report:

(effect values relate to the inhibition of the fluorescence in vessels containing differnt concentrations of the test substance compared to a control without the chemical)
- Effect values after 72 h:
EC20 (72 h) = 86.0 mg/L
EC50 (72 h) = 115.1 mg/L
EC90 (72 h) = 273.3 mg/L

- Effect values after 96 h:
EC20 (96 h) = 56.5 mg/L
EC50 (96 h) = 87.3 mg/L
EC90 (96 h) = 187.1 mg/L

pH values:

- pH values at test start (w/o algae) and after 96 h (inoculated assays):

concentration (mg/L)	pH (0 h)	pH (96 h)
7.81	7.56	9.9
15.6	7.33	9.9
31.25	7.07	9.7
62.5	6.88	8.9
125.0	6.5	7.1
250.0	6.15	6.5
500.0	5.5	5.6
control	8.05	9.5

Reliability: (2) valid with restrictions
test procedure according to National Standard with acceptable restrictions (eg. exposure concentrations in the test and the stability of the test substance were not confirmed by analysis)
Flag: Critical study for SIDS endpoint
29-JUL-2005 (53) (54)

Species: other algae: Spirulina labyrinthiformis (blue green alga)
Exposure period: 2 hour(s)
Unit: mg/l **Analytical monitoring:**
EC : = 1.74

Method: other: Static test (Photosynthesis effect)

Remark: reason for flagging this data: important information on this endpoint
Result: sodium dithionite was somewhat inhibitory on photoincorporation of 14C-HCO3- at 10 µM (ca. 1.74 mg/l; only concentration tested). It lowered the incorporation rate to about 66 % of the untreated light control
Test condition: - species:
sulfide-adapted blue-green algae Spirulina labyrinthiformis,

isolated from waters of hot springs with 1-2 mg/l sulfide. The sulfide adapted Spirulina photosynthesized at maximum rates at 45 °C and at approximately 300 to 700 µE/m2*sec of visible radiation. Sulfide (0.6-1.2 µM) severely poisoned photosynthesis of nonadapted populations, but those continuously exposed to over 30 µM tolerated at least 1 mM without inhibition.

- important test conditions:
temperature: 40 °C- 46 °C
pH: 7.0-7.6
time: 1- to 1.5 h
vials: dram (ca. 11 ml) capacity screw-cap glass vials; vials were shaken at 20 min intervals

- medium:
the chemical conditions of the experiment varied, but native water from the spring of the inoculum was used. Medium was supplemented with different kind of compounds to test for their effect on photoincorporation of 14C-HCO3-

Reliability: (3) invalid
Does not meet important criteria of today standard methods (e.g. the effect of only one test concentration was determined)

Flag: Critical study for SIDS endpoint

(55)

4.4 Toxicity to Microorganisms e.g. Bacteria

Species: other bacteria: Bacteria
Unit: mg/l **Analytical monitoring:**
EC10: > 20

Method: other: DEV-L3

Remark: no inhibition of the dehydrogenase activity up to 20 mg/l
Reliability: (4) not assignable
original reference not available

Species: Saccharomyces cerevisiae (Fungi)
Exposure period: 4 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC75 : = 2000

Test condition: the yeast was incubated in basal yeast medium for 6 to 7 h at 30 °C on a laboratory shaker. After centrifugation and washing, the cells were suspended in fresh sterile media and were grown with shaking to a concentration of 1.0*1E7 cells/ml (9.5 h to 10.5 h), at which time aliquots of the culture were transferred into smaller flasks containing the chemical to be tested. After being shaken for 4 h, aliquots of the culture were removed for mass and count determinations.

Culture mass was determined by measurement of turbidity or of dry weights (24 h at 105 °C). In all cases in which enlarged cells were observed, culutre dry weight determinations were made. Cell counts were made with a hemacytometer.
The cultures were grown in Erlenmeyer flasks, the volumes of

which were 5 times those of the total culture volumes. All the cultures were diluted 10 per cent at the beginning of the test by the addition of the chemical.

Reliability: (3) invalid
Does not meet important criteria of today standard methods (e.g. only one test concentration reported)
(56)

Species: other bacteria: Clostridium hemolyticum
Exposure period: 8 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC : 1.5

Remark: Clostridium hemolyticum is a strictly anaerob bacteria.
Test condition: - bacteria were incubated at 37°C for 8 h, pH 7, under strictly anaerob conditions
- test concentrations: 0.00015, 0.0003, 0.00045, 0.0015, 0.003, 0.0045 %
- analytical method: cell density (turbidity) was measured at 560 nm
- statistics: Student´s test, Chi2-test

Reliability: (3) invalid
Does not meet important criteria of today standard methods
(57)

Type: other: species: bacteriophage phi X174
Exposure period: 2 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC0: = 99.2

Remark: Endpoint: Inactivation of phage particles
Result: - Bacteriophage phi X174 was inactivated by mitomycin C reduced with sodium hydrosulfite in the presence of cupric ions (Cu2++).

- 99 % of the phage particles lost their plaque-forming abilities when incubated with 1.5*10-4 M mitomycin C, 5.7*10-4 M sodium hydrosulfite and 1.0*10-4 M CuCl2 for 120 min at 37 °C in 0.05 M Tris-HCl buffer (pH 8.1).

- Sodium borohydride and thiol-reducing agents such as L-cysteine, 2-mercaptoethanol or dithiothreitol could not serve as a substitute for sodium hydrosulfite.

- Strand-scission was observed when phi X174 single-stranded DNA was directly reacted with mitomycin C reduced with sodium hydrosulfite in the presence of CuCl2.

Test condition: Purified phage phi X174 was diluted in 0.05 M Tris-HCl buffer (pH 8.1) to 2*1E8 plaque-forming units (p.f.u.)/ml. The concentrated CuCl2*2H2O solution (Cu++ solution) and the sodium hydrosulfite (Na2S2O4) solution were freshly prepared with cold redistilled water, and the concentrated mitocmycin C solution with cold 0.05 M Tris-HCl buffer (pH 8.1) prior to each experiment. An amount of 0.1 ml of each Cu++, sodium hydrosulfite, and mitomycin C solutions and 0.1 ml of the phage suspension were mixed, and the total volume of reaction mixture was adjusted to 1 ml with 0.05 M Tris-HCl buffer (pH 8.1). Zero time of incubation corresponded to the time of

addtion of the phage suspension to the reaction mixture as the last component. The reaction was carried out for 120 min at 37 °C with gentle shaking. The reaction was stopped by dilution with ice-cold 0.05 M Tris-HCl buffer (pH 8.1) below the level of effective concentration of mitomycin C and the survival of phage was assayed by the double agar layer technique. Escherichia coli CN was used as the indicator bacteria for phi X174.

Test substance: presumably anhydrous sodium dithionite

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

29-JUL-2005 (58)

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 17 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC10: = 61.6
EC50: = 106.5
EC90 : = 219.8

Method: other: German Industrial Standard DIN 38412, Part 8
GLP: no
Test substance: other TS:Hydrosulfite F conc. BASF, purity: 88 % (anhydrous salt)

Remark: Pre-culture:
- Species: Pseudomonas putida, DSM 50026
- Incubated at 24 °C (297 K +- 1 K), 150 rpm for 7+-1 h
- Medium: AK-medium according to DIN 38412, Part 8 (draft)
- Test vessel: 300 ml-Erlenmeyer flasks, 1 baffle
- Liquid volume: 100 ml

Test conditions:
- Test vessel: Penicillium glass vessel
- Liquid volume: 10 ml
- Inoculum: 1 ml pre-culture (adjusted to 10 TE/F)
- Test medium: Ak-medium according to DIN 38412, Part 8 (draft)
- Test concentrations (nominal): 15.63, 31.25, 62.5, 125, 250, 500 and 1000 mg/L
- Replicates: inoculated: 4 per concentration and control; non-inoculated: 1 per concentration and control
- Incubated at 20°C (292 K), 150 rpm for 17 h
- Measurements: photometric determination at 436 nm and pH at test start and after 17 h
reason for flagging this information: most reliable data available on this endpoint, experimentially derived data

Result: - EC-values (17 h) are based on the nominal concentrations

- pH at the start (0 h; w/o cells) and after 17 h (w cells):

concentration (mg/L)	pH (0 h)	pH (17 h)
15.63	7.0	6.4
31.25	6.9	6.7
62.5	6.8	6.9
125.0	6.6	6.8
250.0	6.4	6.4
500.0	6.1	6.0
1000.0	5.7	5.4

control 7.0 5.1

- Oxygen (mg/L) at the start (0 h; w cells) and after 17 h (w cells):

concentration (mg/L)	O2 (0 h)	O2 (17 h)
15.63	8.2	0.7
1000.0	8.6	8.8

Reliability: (1) valid without restriction
guideline study.

Most reliable study available on this endpoint
Flag: Critical study for SIDS endpoint
29-JUL-2005 (59)

Species: activated sludge

Remark: The product may lead to chemical consumption of oxygen in biological sewage treatment plants or in natural water. Inhibition of degradation activities in sewage treatmant plants is not to be expected from the introduction of low concentrations
Reliability: (4) not assignable
expert judgement
(46)

Species: other bacteria: Eschericha coli (strain B)
Exposure period: 2 hour(s)
Unit: **Analytical monitoring:** no

Result: no adverse effects were observed
Test condition: cells from agar slants were suspended in sterile salts-glucose medium enriched with 1 mg/ml each of yeast extract and peptone., grown for 6 to 8 h at 37 °C, resuspended in sterile enriched medium (1 to 3 cells/ml), and grown with shaking for 16 h. These cells were then suspended in sterile salts-glucose medium (1.0*1E8 cells /ml) and allowed to grow with shaking to 4.5*1E8 cells/ml (ca. 1,5 h). Aliquots were then transferred into smaller flaks containing the chemical to be tested and grown for an additional 1,5 h.
Analytical methods: culture-dry weight and cell-count determinations (Petroff-Hauser counter).
The cultures were grown in Erlenmeyer flasks, the volumes of which were 5 times those of the total culture volumes. All the cultures were diluted 10 per cent at the beginning of the test by the addition of the chemical.

Reliability: (3) invalid
Does not meet important criteria of today standard methods
(56)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Endpoint: other: reproduction and mortality
Exposure period: 21 day(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: > 10
LC0 : > 10

Method: other: Semistatic test according to draft 4 of the EC-guideline XI/681/86
Year: 1986
GLP: yes
Test substance: other TS: Hydrosulfite conc. BASF, purity: 88 % (anhydrous salt) (secondary components: Na2SO3, Na2SO4, Na2S2O5, Na2CO3

Remark: The test was performed according to EG-guideline XI/681/86 (draft 4):

- Test vessel: glass beakers with caps, nominal volume 100 ml
- Test volume: 50 ml
- Test medium: synthetic Medium M4 on the basis of an ultrapure, deionized water. The test water has the following properties: total hardness: 2.20-3.20 mmol/l, alkalinity up to pH 4.3: 0.80-1.00 mmol/l, molar ratio Ca:Mg: approx. 4:1, pH: 7.5-8.5, conductivity: 550-650 uS/cm. The medium was aerated until saturated with oxygen, and was left to stand for 24 h for stabilization
- Test concentrations (nominal): 10, 5 and 1 mg/l
- Stock solutions: 100 mg/l nominal, freshly prepared at the beginning of the test and before changing the test solution
- pH-adjustment: no
- Solvents/emulsifiers: no
- Number of parallels/conc.: 10
- Number of parallels/control.: 10
- Control: test water without the substance
- Age of animals at the start of the test: 2- 24 h
- Age of the stock animals: 2-4 weeks
- Number of animals/vessel: 1
- Loading (animal/ml): 1/50
- Total number of animals/conc.: 10
- Renewal of the test solution: every 2-3 days
- Removal of the young from test beakers and counting: at each renewal of the test solution
- Test parameters: reproduction and survivial
- Check of the study and recording (mortality, hatching of the young): daily
- Feeding: daily, according to a feeding schedule (green algae (Scenedesmus subspicatus, cultured in a synthetic medium))
- Temperature: 20 °C +-2 °C
- Light: day/night rhythm: 16:8
- Light intensity: approximately 5-6 uE/(m2*s) at a wavelenght between 400 and 700 nm
- Measurements: swimming ability (at the beginning and afterwards daily), pH, oxygen, temperature

- Minimum and maximum values of the chemical and physical characteristics of the test solutions:

parameter	minimum	maximum
pH	7.5	8.2
oxygen (mg/L)	7.8	15.5
temperature (°C)	19.1	21.2

- Statistics for the evaluation of th NOEC: Duncan's multiple range test

- Because sodium dithionite (purity: 88 %) decomposes in water, the observed effects cannot be ascribed to sodium dithionite alone. The predominant effect of sodium dithionite (purity: 88 %) is oxygen consumption due to its reducing properties
reason for flagging this study: only experimentially derived data available on this endpoint

Result: - NOEC value for reproduction after 21 d exposure:
NOEC > 10 mg/L

- LC0 (21 d) value for mortality after 21 d exposure:
LC0 (21 d) > 10 mg/L

- In the control and at 10 mg/L the first young were observed on day 9

- The LC0 (mortality) and the NOEC value for repoduction after 21 d exposure is based on nominal concentrations, because of the decomposition of sodium dithionite in water

- The quality criteria of the control (mortality of parent animals <= 20%, average of >= 60 juveniles per surviving control adult, coefficient of variation of the mean number of surviving juveniles <= 25%) were achieved.

- Summary of the effect of the test substance on the reproduction of Daphnia magna. The values gien are the mean, cumulative values for parent animals which survived the exposure for 21 days:

Conc. (mg/L)	survival of parent animals (%)	live young per live parent an. (n)	dead young per live parent animal (n)
0	100	108.3	0
1	100	99.3	0
5	100	116.3	0
10	100	116.9	0

Conc. (mg/L)	aborted eggs per live parent animal (n)
0	0
1	0
5	0
10	0

- Mean total number of live young per parent animal, which survived the exposure for 21 days, at various concentrations of the test substance:

conc. (mg/L)	live young per parent animal

(n; mean value)
0 108.3
1 99.3
5 116.3
10 116.9

- Survival of parent animals at various concentrations of the test substance during the test. The values given are the total number of live parent animals at the corresponding concentration and day of the test:

conc. (mg/L)	time (d) 0	2	5	7	9	12	14	16	19	21
0	10	10	10	10	10	10	10	10	10	10
1	10	10	10	10	10	10	10	10	10	10
5	10	10	10	10	10	10	10	10	10	10
10	10	10	10	10	10	10	10	10	10	10

- Oxygen content (mg/L) ot the test solutions at the start of the test or in the 2- or3-days old test solution:

conc. (mg/L)	range of oxygen between day 0 and 21 (mg/L)
0	8.2 - 15.5
1	8.0 - 11.2
5	7.9 - 11.9
10	8.0 - 12.3

- pH of the test solutions at the start of the test or in the 2- or 3-days old test solution:

conc. (mg/L)	range of pH between day 0 and 21
0	7.6 - 8.0
1	7.6 - 8.1
5	7.7 - 8.1
10	7.5 - 8.2

Reliability: (1) valid without restriction guideline study

Flag: Critical study for SIDS endpoint

29-JUL-2005 (60)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

4.6.2 Toxicity to Terrestrial Plants

4.6.3 Toxicity to Soil Dwelling Organisms

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

5.0 Toxicokinetics, Metabolism and Distribution

In Vitro/in vivo: In vivo
Type: Toxicokinetics
Species: rat
No. of animals, males: 3
No. of animals, females: 3
Doses, males: single dose of 100 mg sodium sulfite/kg bw, corresponding to 50 mg mg sulfur dioxide/kg bw
Doses, females: single dose of 100 mg sodium sulfite/kg bw, corresponding to 50 mg mg sulfur dioxide/kg bw
Vehicle: physiol. saline
Route of administration: other: intraduodenal (in 2 ml)
Exposure time: minute(s)

GLP: no
Test substance: other TS: Sodium sulfite [CAS 77

Method: Kinetic study with anaesthetised Sprague-Dawley rats with pre- and post-hepatic cannulation for blood withdrawal.
Result: Blood levels of free sulfite in portal blood increased within minutes after intraduodenal administration of 100 mg Na2SO3/kg. The pre-hepatic plasma peak after 10 to 20 min represented about 1 mg sulfite/ml (increase: approx. 12.5 to 13.5 µmol/ml plasma in male and female animals).

No free sulfite was detected in the general circulation (post-hepatic) [average of 3 rats each].

An increase in S-sulfonates was measured in pre- and post-hepatic blood plasma which rapidly reached and maintained a level about 20-25% of maximum sulfite concentration. The concentration of S-sulfonates was higher before liver passage.It is concluded that sulfite was rapidly absorbed after intraduodenal application and quickly metabolized by either oxidation or formation of S-sulfonates.

Test substance: other TS: Sodium sulphite [CAS 7757-83-7], analytical grade, no information about whether the heptahydrate or anhydrous substance was used.
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, sufficiently documented
Flag: Critical study for SIDS endpoint
21-FEB-2006 (61)

In Vitro/in vivo: In vivo
Type: Excretion
Species: other: rat, monkey

GLP: no
Test substance: other TS: sodium bisulfite

Remark: Sodium dithionite [CAS No. 7775-14-6] is not stable under physiological conditions, with the rate of decomposition increasing with increasing acidity. Upon contact with moisture, it oxidizes to bisulfite [CAS No. 7631-90-5] and bisulfate [CAS No. 10034-88-5]:

Na2S2O4 + O2 + H2O --> NaHSO4 + NaHSO3

and, under strongly acidic conditions, may liberate SO2 [CAS No. 7446-09-5] [Warner et al., 2000]:

SO2 +H2O<-->SO2(H2O) = H2SO3<-->H+ +HSO3-1<-->2 H+ +SO3-2
pK1 ~ 2 pK2 ~ 7

If present in high concentrations and under anaerobic conditions (such as in the lower gastrointestinal tract), bisulfite [CAS No. 7631-90-5] and thiosulfate [CAS No. 7772-98-7] may also be formed:

2 Na2S2O4 + H2O --> 2 NaHSO3 + Na2S2O3

Bisulfite [CAS No. 7631-90-5] can be absorbed from the rat gastrointestinal tract. It is oxidized in vivo to sulfate, principally by hepatic sulfite oxidase (sulfite cytochrom-c oxidoreductase), with lesser amounts metabolized by the kidneys, intestines, heart, and lungs.

Physiologically, sulfite oxidase is involved in the methionine and cystein metabolism. The endogenous sulfite body burden resulting from amino acid degradation is in the range of 0.3-04 mmol/kg bw/day, which is about 15-130fold higher than the estimated value for exogenous sulfite exposure [(Institute of Food Technologists and Committee on Public Information, 1976]).

Result: Comparative investigations of sulfite metabolism in rats, rabbits and rhesus monkeys are summarised. The relative excretion rates for rats, rabbits and rhesus monkeys were 1:0.34:0.2. Large i.p. doses of sulfite can be oxidized to sulfate within minutes [Gunnison et al., 1977].

About 70 to 95% of the radioactivity associated with a 50 mg/kg bw oral bisulfite dose appeared in rodent and monkey urine within 3 days as sulfate. Only a small fraction (8-10%) of the absorbed bisulfite was eliminated intact [ACGIH, 1991; Gunnison et al., 1977].

Test substance: NaHSO3 [CAS 7631-90-5]
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, sufficiently documented

Flag: Critical study for SIDS endpoint
21-FEB-2006 (62) (63) (64) (65)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: other: Gassner
Sex: male/female
No. of Animals: 10

Vehicle: other: suspension in 0.5 % CMC
Doses: 200, 1600, 2000, 2500, 3200 and 6400 mg/kg
Value: ca. 2500 mg/kg bw

Method: other: BASF-Test, acc. to OECD 401
Year: 1973
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Result: MORTALITY:
200 mg/kg bw: no deaths
1600 mg/kg bw: no deaths
2000 mg/kg bw: no deaths
2500 mg/kg bw: 3 males and 2 females died within the first 24 hours
3200 mg/kg bw: 4 males and 5 females died within the first 24 hours
6400 mg/kg bw: 5 males and 5 females died in the first hour.

CLINICAL SIGNS:
6400 mg/kg bw: intermittent respiration, squatting posture and atony immediately after application.
3200 mg/kg bw: intermittent respiration, squatting posture and atony immediately after application. No clinical signs and findings in the surviving animal from the first post observation day onward.
2500 mg/kg bw: intermittent respiration, squatting posture and atony immediately after application. No clinical signs and findings in the surviving animals from the forth post observation day onward.
2000 mg/kg bw: intermittent respiration, squatting posture and atony immediately after application. No clinical signs and findings in the surviving animals from the forth post observation day onward.
1600 and 200 mg/kg bw: no clinical signs and findings.

GROSS PATHOLOGY:
6400 and 3200 mg/kg bw: Congestive hyperemia, heart: dilation, stomach: dilatation, partly bloody ulcers and liquid content, intestine: hematinized, diarrheic content 2500 mg/kg bw: Congestive hyperemia, heart: dilatation, stomach: dilatation, liquid content, red discoloration of the glandular stomach, intestine: partly diffuse discoloration, diarrheic content 2000, 1600 and 200 mg/kg bw: Organs without particular findings.

Test condition: TEST ORGANISM: rat, 170 - 203 g
ADMININSTRATION: TS was applied by gavage as an aqueous suspension with 2, 16, 20 % (2000 and 2500 mg/kg) and 30 % (3200 and 6400 mg/kg) of the TS in 0.5-% carboxymethyl cellulose (10 ml volume/kg each), with no vehicle controls included.
EXAMINATIONS: 7 day observation period after dosing
STATISTICAL METHOD: graphical probit analysis

Test substance: Purity approx. 88% (not further specified).
Reliability: (1) valid without restriction
Comparable to guideline study
Flag: Critical study for SIDS endpoint

5.1.2 Acute Inhalation Toxicity

Type: other: IRT (Inhalation risk test)
Species: rat
Strain: no data
Sex: no data
No. of Animals: 12
Exposure time: 8 hour(s)

Method: other: BASF-Test
Year: 1973
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: This test provides toxicity information at or near the concentration of vapor saturation, i.e a fixed concentration that usually is not analysed. This test is suitable to estimate inhalation toxicity risks of volatile substances after spills in confined spaces with low ventilation.
Result: No mortality and no clinical signs observed, no macroscopically pathological findings noted.
Test substance: Purity approx. 88 %
Test condition: ADMINISTRATION OF TEST SUBSTANCE:
Animals were exposed to a TS-saturated atmosphere generated by passing air through a 5-cm layer of the test material at 20 °C.
EXPOSURE PERIOD: 8 hours
EXAMINATION: Animals were observed for signs of toxicity for a period of 8 hours.
POST-EXPOSURE OBSERVATION PERIOD: not reported.

Reliability: (3) invalid
3b: Unsuitable test system, in general not applicable to poorly volatile, solid test substances.

(66)

5.1.3 Acute Dermal Toxicity

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Strain: no data
Sex: no data
Vehicle: CMC
Doses: no data
Route of admin.: i.p.
Value: ca. 900 mg/kg bw

Method: other: BASF-Test
Year: 1973
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Result: CLINICAL SIGNS: dyspnea, atony, seizures, apathy, and lateral position.

GROSS PATHOLOGY: General hyperemic congestion observed.

Test condition: ADMINISTRATION: TS was given intraperitioneally as an 2 - 30% aqueous preparation with carboxymethylcellulose. Dosing volume not reported.

Test substance: Purity approx. 88% (not further specified).

Reliability: (2) valid with restrictions
Acceptable screening study in compliance with current standards

(66)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: 80 % active substance
Exposure: Occlusive
Exposure Time: 20 hour(s)
No. of Animals: 2
Vehicle: other: 80 % aqueous preparation (88 % x0.8 = approx. 70 % dithionite)
Result: slightly irritating

Method: other: BASF-Test
Year: 1973
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Result: Exposure times from one to 15 min were without any irritation (Score 0).
20-h exposure produced mild erythema after 24 h post-treatment (Score 0 or 1); after 8 d, Score 0, weak scaling was noted.
No edema were observed at any time.

Test condition: TEST ANIMALS: Rabbit White Vienna, male and/or female

EXPOSURE and OBSERVATION procedure:
Two White Vienna rabbits were treated for 1, 5 and 15 minutes and 2 other animals for 20 hours using occlusive conditions. An application site of 2.5 cm X 2.5 cm was covered with powdered and moistened test substance. In addition, skin tissue from the ear was tested by wrapping the ear. The results from the ear are not taken into account for evaluation, as they do not represent testing of the dorsal/lateral flank of the back.

After the application time, the skin was washed with water or aqueous solution of a mild detergent.

The animals were observed for 8 days and skin changes were observed on working days.

The report and the raw data describe findings after 24 hours and at the end of the observation period. Thus, for final evaluation, the findings after 48 and 72 hours cannot be taken into account.

GRADING SYSTEM:
The data reported were converted from the BASF grading system into the presently used numerical grading system as given in the following table:

BASF grading for redness and edema	Numerical grading acc. to the OECD Draize scheme
Ø-(+) (no symptom-questionable)	0
+ (slight)	1
++ (marked)	2
+++ (severe)	>=3

N + (superficial necrosis) = sign of severe irritation.
N ++ or N+++ = full thickness necrosis.

Test substance: Purity approx. 88 %, not further specified
Conclusion: According to current evaluation criteria the findings trigger no classification as skin irritant.

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, sufficiently documented for assessment
Flag: Critical study for SIDS endpoint
21-FEB-2006 (66)

5.2.2 Eye Irritation

Species: rabbit
Concentration: undiluted
Dose: .05 ml
Exposure Time: 24 hour(s)
Comment: not rinsed
No. of Animals: 2
Vehicle: none
Result: highly irritating
EC classificat.: risk of serious damage to eyes

Method: other: BASF-Test
Year: 1973
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Result: 1 h until 24 h post-treatment: Slight erythemas (Score 1) and moderate edemas (Score 1 and 2) at the conjunctivae as well as mild corneal opacity, but associated with bleeding and secretion.

After 48 h, slight erythemas and edemas (Score 1) at the conjunctivae as well as mild corneal opacity and mild iritis (Score 1).

After 8 days: Mild erythema, edema, opacity and iritis still prevailed, but associated with slight scar formation; purulent inflammation developed, eye lids showing necrotic lesions.

Test condition: TEST ANIMAL: Rabbit White Vienna

APPLICATION OF TEST SUBSTANCE: The TS was applied as solid material (bulk volume approx. 50 µl).

OBSERVATIONS: visual inspection at 24, 48 hours, and 8 days after application.

GRADING SYSTEM:
The data reported were converted from the BASF grading system into the presently used numerical grading system as given in the following table:

BASF grading for redness and edema	Numerical grading acc. to the OECD Draize scheme
Ø-(+) (no symptom-questionable*)	0
+ (slight)	1
++ (marked)	2
+++ (severe)	>=3

* of borderline nature
Iritis + or ++ = Iritis grade 1 or 2
corneal opacity + = 1;+-++ = 2; ++ = 3; +++ = >3

Test substance: Purity approx. 88 %
Conclusion: The treatment led to slight corneal opacity, slight or marked iritis, slight conjunctival redness and to slight or marked conjunctival edema. All findings were not reversible within the 8-day observation period.

According to current evaluation criteria the findings trigger a classification as severe eye irritant.

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, sufficiently documented for assessment
Flag: Critical study for SIDS endpoint
21-FEB-2006 (66)

Species: rabbit
Concentration: % active substance
Dose: 97 other: mg
Exposure Time: 1 hour(s)
Comment: rinsed after (see exposure time)
No. of Animals: 3
Vehicle: none
Result: irritating

Method: Directive 92/69/EEC, B.5
Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: Moderate to severe erythemas after 1 through 72 h occurred in all animals, slight oedemas were noted in all animals from 1 through 48 h with decreasing trend.

The mean scores of conjunctival effects over all animals were:

erythema 3.0 (24 h), 3.0 (48 h), and 2.3 (72 h)
oedema 1.3 (24 h), 0.67 (48 h), and 0.33 (72 h).

The erythema score of >2.5 over time indicates irritation.

No changes of the cornea and iris were observed.

All effects were completely reversible by 7 d, but only in one rabbit there was still evidence of slight redness of the conjunctiva of the treated eye.

Test condition: The test substance was applied as fine powder and rinsed after one hour.
Reliability: (1) valid without restriction
1a: GLP guideline study
Flag: Critical study for SIDS endpoint
20-FEB-2006 (67)

5.3 Sensitization

5.4 Repeated Dose Toxicity

Type: Chronic
Species: rat **Sex:** male/female
Strain: Wistar
Route of administration: oral feed
Exposure period: 104 weeks (F0 and F1 generation) and 30 weeks (F2 generation)
Frequency of treatment: daily
Doses: 0.125, 0.25, 0.5, 1.0, 2.0% (ca. 50, 100, 220, 450 and 940 mg/kg bw)

Method: other: Multigeneration study (see also entry 5.8)
Year: 1972
GLP: no
Test substance: other TS: disodium disulfite

Remark: Disodium disulfite was fed to rats with the diet for 30 and 104 weeks. The predominant effect was the induction of stomach lesions due to the local irritant effect, characterized by forestomach and glandular stomach hyperplasia and inflammation at about 450 mg/kg bw/day and higher (NOAEL 217 mg/kg bw/day).

The NOAEL for systemic toxicity was 942 mg/kg bw/day, the highest tested dose level.

Test substance: Na2S2O5 [CAS No. 7681-57-4]
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
(68) (69)

Type: Sub-chronic
Species: rat **Sex:** female
Strain: Wistar
Route of administration: drinking water
Exposure period: 8 weeks
Frequency of treatment: daily
Post exposure period: none

Doses: 7, 70 or 350/175 mg SO2 equivalents/kg bw (ca. 10, 100 and 500 mg/kg Na2S2O5)
Control Group: yes, concurrent vehicle
LOAEL: = 175 mg/kg bw
NOAEL(SO2 equ.) : = 70 mg/kg bw

Method: other: see method freetext
Year: 1989
GLP: no data
Test substance: other TS: disodium disulfite

Method: SCOPE:
The subchronic toxicity of free inorganic sulfite (as sodium metabisulfite) and acetaldehyde hydroxysulfonate, a major bound form of sulfite in beer and wine, was evaluated after their addition to the drinking-water of normal and sulfite oxidase-deficient rats.

Groups of 8 normal or sulphite-oxidase deficient rats were compared. Rats were made sulfite-oxidase deficient by concurrent treatment with 200 ppm tungsten in drinking water.

The following parameters were investigated: body weights, clinical signs, histopathology of 6 different organs, plasma protein concentration, blood total haemoglobin concentration, thiamine deficiency in liver tissue, activity of hepatic sulfite oxidase, sulfite concentration in plasma and urine.

Result: Tungstate treatment effectively obliterated hepatic sulphite oxidase activity. The overall health of the animals was not affected by treatment, except that sulphite oxidase-deficient rats receiving either of the sulphite treatments had dried blood around their noses 4-5 wk after start of treatment, whereas sulphite oxidase-deficient controls showed no adverse effects. This effect was attributed to respiratory distress related to the lung oedema noted at necropsy.

The rats were not deficient in thiamine.

Body weights of high-dose group, sulphite oxidase-deficient rats were significantly depressed; no other effect on body weight was seen. All groups of rats receiving disodium disulfite consumed more feed when based on body weight, although no dose-response relationship was apparent.

In sulphite oxidase-deficient rats statistically significant and dose-related decrease in water consumption was noted.

Blood haemoglobin and plasma protein levels were similar in all groups.

Urine sulphite was found only at low concentrations or was undetectable in rats with normal sulphite oxidase activity, indicating efficient metabolism of sulphite by this enzyme.

Sulphite was detected in the urine of sulphite oxidase-deficient rats even before sulphite treatment wasinitiated, and increased with continued test substance administration; however, a clear dose or time-related effect was not established, which may have been partly due to the

reduced water intake.

Likewise, plasma sulphite concentrations were low and variable. This effect was attributed to the ability of the sulphite ion to react with many biological compounds to form S-sulphonates, possibly by sulphitolysis of disulphide bonds in proteins and free cysteine.

Gross necropsy revealed white patches in lung tissue in sulphite-oxidase deficient rats receiving sulfite treatment. Histopathological findings were lesions in the fore-andglandular stomach of both normal and sulphite oxidase-deficient rats receiving the highest dose (350/175 mg/kgbw/d) showed. The most severe lesions were observed in the sulphite oxidase-deficient rats, including moderate hyperkeratosis of forestomach epithelium and alterations in the fundic portion of the stomach.

CONCLUSION: The NOAEL was 70 mg SO2 eq./kg bw/d (ca. 100 mg [Na2S2O5]/kgbw/d for the normal and sulfite oxidase-deficient rats, based on the forestomach and glandular stomach lesions in the high dose animals.

Test substance: Na2S2O5 [CAS No. 7681-57-4]
Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given. Limitation: single sex.
Flag: Critical study for SIDS endpoint
21-FEB-2006 (70) (71)

5.5 Genetic Toxicity 'in Vitro'

Type: other: see Review Genotoxicity under 5.11

Test substance: other TS: Sulfites

Type: Ames test
System of testing: Salmonella typhimurium TA1535, TA100, TA1537, TA98 (direct plate-incorporation and preincubation assay)
Concentration: 0; 20; 100; 500; 2500; 5000 ug/plate
Cytotoxic Concentration: no bacteriotoxic effect
Metabolic activation: with and without
Result: negative

Method: other: acc. to OECD Guide-line 471
Year: 1983
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: Standard plate test according to Ames et al. Proc. Nat. Acad. Sci. USA, 70, 2281 - 2285 (1973) and Ames et al. Mut. Res., 31, 347 - 364 (1975).

Preincubation test according to Yahagi et al. Mut. Res. 48, 121 - 130 (1977) and Matsushima et al. In: Norpoth und Garner, Short-term test system for detecting carcinogens, Springer Verlag Berlin, Heidelberg, New York (1980).
Result: TS was negative in these tests, and the highest ineffective

dose tested in any S. typhimiurium strain was 5 mg/plate.
Positive controls were functional.

Test condition: METABOLIC ACTIVATION SYSTEM: rat liver S-9 mix from Sprague-Dawley male rats pretreated with 500 mg Aroclor 1254 5 days before sacrifice.
NUMBER OF REPLICATES: Three plates per dose and control were performed, all for the acitivated and the non-activated system.

VEHICLE: The TS was dissolved in distilled water.

POSITIVE CONTROLS: N-methyl-N´-nitro-N-nitrosoguanidine for TA100 and TA1535, 4-nitro-o-phenylendiamine for TA 98, 9-aminoacridine chloride for TA1537, 2-aminoanthracene was used for all strains with metabolic activation system.

DATA EVALUATION: a substance had to be characterized as positive if there was a doubling of the spontaneous mutation rate (control), a dose-response relationship and reproducibility of the results.

STATISTICAL METHOD: not reported.

Test substance: Sodium dithionite ("hydrosulfite"), purity 89.5 %
Reliability: (1) valid without restriction
Comparable to guideline study
Flag: Critical study for SIDS endpoint
20-FEB-2006 (72)

Type: Ames test
System of testing: Salmonella typhimurium TA1535, TA100, TA98, TA1537, TA1538, Escherichia coli WP2 uvrA (preincubation method)
Concentration: 0; 5; 10; 50; 100; 500; 1000; 5000 ug/plate
Cytotoxic Concentration: No bacteriotoxic effect
Metabolic activation: with and without
Result: negative

Method: other: OECD Guide-line 471 and 472 (acc. to Ames et al., 1975)
Year: 1985
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Comparative study including more than 40 chemicals.
Result: TS was negative in these tests, and the highest ineffective dose tested in any S. typhimurium strain was 5 mg/plate.
Positive controls were functional.

Test condition: TS was tested in the Salmonella/S-9 mix preincubation assay and in the E.coli/S-9 mix preincubation assay using the method described by Sugimura et al..
METABOLIC ACTIVATION SYSTEM: rat liver S-9 mix from Sprague-Dawley male rats pretreated with 500 mg PCB(KC500)/kg bw 5d before sacrifice.
NUMBER OF REPLICATES: in duplicate.
VEHICLE: The TS was dissolved in distilled water.

POSITIVE CONTROLS: Depending on the tester strain different

positive controls (2-(2-furyl)-3-(5-nitro-2-furyl)acrylamid, N-ethyl-N´-nitro-N-ntrosoguanidine, 9-aminoacridine, 4-nitroquinoline-1-oxide, benzo(a)pyrene, 2-aminoantracene, 2-nitrofluorene) were used.

DATA EVALUATION: not reported

Test substance: Sodium dithionite, purity 89.1% (from Wako Pure Chemical Ind.)
Reliability: (1) valid without restriction
Comparable to guideline study.
Flag: Critical study for SIDS endpoint
21-FEB-2006 (73)

Type: Bacterial reverse mutation assay
System of testing: S. typhimurium TA 97 (standard plate incorporation assay)
Concentration: 0.01 - 0.16 M/plate
Metabolic activation: without
Result: positive

Method: other: see Method freetext
Year: 1990
GLP: no data
Test substance: other TS: Sodium metabisulfite

Method: Mechanistic study to elucidate mechanisms underlying mutagenesis of bisulfite, acc. to Ames under special experimental conditions:
The dependence of mutagenicity on the degree of autooxidation was measured. Auto-oxidation was measured as oxygen consumption using a Clark electrode. The concentration used is not clearly defined and is given in the table as 0.01 to 0.16 M/plate.

Result: Mutagenesis in tester strain TA97 of sodium hydrogen sulfite was significant at 27 °C, but became suppressed at 37 °C.

An inverse relationship between bisulphite auto-oxidation and its ability to cause mutations in Salmonella was found. As auto-oxidation decreased, as evidenced by the increasing length of time it took to deplete 50% of the oxygen in the oxygen monitoring system, the mutagenicity increased.

Test substance: Na2S2O5 [CAS No. 7681-57-4], [Sigma Chemical Company]; no further data.
Conclusion: The results suggest a radical mechanism by which temperature and pH determine the rate of bisulfite autoxidation via the formation of the intermediate sulfur-centered sulfur trioxide radical, SO3-·. This may occur spontaneously or through the action of the peroxidase/H2O2 system.

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, sufficiently documented for assessment
Flag: Critical study for SIDS endpoint
(74)

Type: Bacterial gene mutation assay
System of testing: Micrococcus pyogenes var., aureus strain FDA209

Concentration: 0.01 %
Cytotoxic Concentration: minimum killing concentration
Metabolic activation: without
Result: negative

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

Method: Comparative study including various chemicals: The ability to grow in the presence of antibiotics (here: penicillin and streptomycin resistance) was used as genetic markers for mutagenic activity.
Test substance: Sodium hydrosulfite, not further specified
Reliability: (3) invalid
No standard method, early study

(75)

Type: Bacterial gene mutation assay
System of testing: Bacterium prodigiosum
Concentration: 0.05 %
Cytotoxic Concentration: subtoxic limit concentration
Metabolic activation: without
Result: negative

Method: other
Year: 1960
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: The TS exerted an inhibitory effect on the spontaneous mutation frequency in Bacterium prodigiosum from light to dark colonies.
Test substance: Sodium hydrosulfite, not further specified
Reliability: (4) not assignable
No standard method, early study

(76)

Type: Ames test
System of testing: Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538, E.coli WP2uvrA
Concentration: 100-10000 ug/plate
Cytotoxic Concentration: no bacteriotoxic effect
Metabolic activation: with and without
Result: negative

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

Test substance: Sodium hydrosulfite, purity chemical grade (Wako Pure Chemical Ind.)
Reliability: (4) not assignable
Handbook data from a national institution:
tabular documentation of results. Secondary literature

(77)

Type: Mammalian cell gene mutation assay
System of testing: CHO-AS52 cell culture

Concentration: no data
Result: positive

Method: other: no data
Year: 1999
GLP: no data
Test substance: other TS

Test substance: Bisulfite (not further specified)
Reliability: (4) not assignable
4b: Secondary literature
(78) (79)

Type: other: Escherichia coli reverse mutation assay / virus reverse mutation

Remark: Reverse mutations in E. coli, lambda phages and T4rII were detectable only at high sulphite concentrations (> 0.2 mol/l) and at pH 5. At pH 7 or 8, no mutations were detectable (Shapiro, 1977; Gunnison, 1981).
Hydrogen sulfite solutions at high concentrations and at pHs between 5 and 6 deaminated cytosine in DNA to uracil (Shapiro, 1977).
Test substance: other TS: Sodium hydrogen sulfite [CAS No. 7631-90-5] and disodium disulfite [CAS No. 7681-57-4]
Reliability: (2) valid with restrictions
Limited documentation
Flag: Critical study for SIDS endpoint
21-FEB-2006 (80) (81)

5.6 Genetic Toxicity 'in Vivo'

Type: other: see Review Genotoxicity under 5.11

Test substance: other TS: Sulfites

Flag: Critical study for SIDS endpoint

Type: Micronucleus assay
Species: mouse **Sex:** male/female
Strain: NMRI
Route of admin.: i.p.
Exposure period: 24 and 48 p.a.
Doses: 24 h sampling interval: 75, 150, and 300 mg/kg (15 ml/kg in citrate buffer, pH 5.0); 48-h sampling interval: 300 mg/kg
Result: negative

Method: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year: 2000
GLP: yes
Test substance: other TS: sodium bisulfite

Result: The treated mice exhibited normochromatic/polychromatic erythrocytes ratios which were higher than in negative controls, demonstrating the bioavailability of the test substance in the bone marrow. The bioavailability was also obvious on clinical effects seen in the treated animals especially in the high dose group and was supported

specifically by performing the intraperitoneal application. The number of micronucleated PCE was similar to those seen in controls.

Test results (Henkel, 2004)

Test group	PECs with nuclei [%]
vehicle (24 h)	0.055
75 mg/kg (24h)	0.040
150 mg/kg (24h)	0.075
300 mg/kg (24h)	0.075
300 mg/kg (48h)	0.025
cyclophosphamide	2.975

It was concluded that sodium bisulfite (hydrogensulfite) failed to show any evidence of mutagenic potential in this in vivo test for chromosomal alterations when administered intraperitoneally at pH 5.0.

Test condition: The average body weight of the test animals (eight to ten weeks old) was about 34 g (females) and 41 g (males), respectively. Five mice were used per dose and sex. Additional 20 animals (two per dose and sex) had been used for the range finding.

Sodium bisulfite (hydrogensulfite), formulated in citrate/NaOH buffer at pH 5.0 was administered in a total dose of 75, 150 and 300 mg/kg bw by intraperitoneal injection (15 ml/kg) to ensure bioavailability at target cells. Bone marrow of femora was prepared 24 and 48 hours after application. For each animal at least 2000 polychromatic erythrocytes (PCE) obtained from femoral bone marrow were examined. The frequency of micronuclei was calculated for each animal and dose group.

Cyclophosphamide (CPA) (40 mg/kg bw) and the vehicle (citrate/NaOH buffer), respectively served as positive and negative controls.

Test substance: NaHSO3 [CAS 7631-90-5]
Reliability: (2) valid with restrictions
Original reference not available; however, GLP guideline study and peer-reviewed by SCCNFP (2000)
Flag: Critical study for SIDS endpoint
21-FEB-2006 (82) (83) (84)

Type: Micronucleus assay
Species: mouse **Sex:** male/female
Strain: other: Kunming
Route of admin.: i.p.
Exposure period: 24 h after the first injection the treatment was repeated, with exception of the positive control (CP); the animals were killed 24 h after the second treatment
Doses: 20, 100, 500, 750 mg/kg in saline (a mixture of sodium sulfite and bisulfite, 3:1, M/M)
Result: positive

Method: other
Year: 2002

GLP: no data
Test substance: other TS: a mixture of sodium sulfite and bisulfite (3:1, M/M)

Method: In general: 6 week old mice (20-25 g) were treated with the test substance; 10 mice per group; negative control: saline; positive control: 50 mg CP/kg (CP = cyclophosphamide).

Bone marrow was removed from the femur - slide smears were prepared; 1000 PCE were examined.

1. test regime: 24 h after the first injection the treatment was repeated, with exception of the positive control (CP); the animals were killed 24 h after the second treatment, micronucleus slides were prepared and evaluated.

2. test regime to determine the relationship between MN formation and time after exposure: 7 groups of 10 mice received twice the ip dose of 500 mg/kg, animals were killed 12, 24, 36, 48, 60, and 72 h after the second injection.

3. test regime to evaluate the potential to inhibit or enhance MN formation induced by mutagens CP or mitomycin C(MMC) in the mouse PCE cells:
a) six groups of ten mice: negative control; 50 mg CP/kg; 50 mg CP/kg add 500 mg test mixture/kg; 100 mg CP/kg; 100 mg CP/kg add 500 mg test mixture/kg; 500 mg test mixture/kg).
b) Seven groups of ten mice: negative control; DMSO control group (4 ml/kg); 0.5 mg MMC/kg; 0.5 mg MMC/kg add 500 mg test mixture/kg; 1 mg MMC/kg; 1 mg MMC/kg add 500 mg test mixture/kg; 500 mg test mixture/kg.

Remark: As compared with the dosing regime of Honarvar (2000) (see previous entry), the effective doses were significantly higher (replicate dosing inclusive). Therefore, the results of both studies do not contradict each other. Furthermore, the biological significance of the lower doses of up to 100 mg/kg (2 x) appears to be low with respect to the baseline level produced by the DMSO control. But for a reasonable evaluation, the historical spontaneous rates are lacking.

Result: A. DOSE RESPONSE relationship:
For the bone marrow cells of both male and female mice: the frequencies of MNPCE was increased significantly ($p < 0.01$) in all treatment groups when compared to control (background levels: 0.23 +-0.05 % and 0.22 +-0.05 % in male and female mice, respectively).

Note: The DMSO solvent control (4 ml/kg) used in the MMC-test series produced a background of 0.46 +-0.07 % and 0.42 +-0.06 %, respectively (Tab. 3).

The pos. control (CP) resulted in 5.02 +-0.28 % and 5.01 +-0.42%, resp.).

The following test results were obtained (no significant difference between male and female animals) [Tab. 1]:

dose	yield MN

2 x 20 mg/kg	approx. 0.5 % MNPCE
2 x100 mg/kg	approx. 0.68 % MNPCE
2 x500 mg/kg	approx. 1.05 % MNPCE
2 x750 mg/kg	approx. 0.9 % MNPCE

B. TIME RESPONSE relationship:
The frequencies of MNPCE induced by the test mixture changed with time after the treatments. A significant increase was caused 12 h after exposure, the increase was the highest 24h after treatment, the %MNPCE at 36, 48, 60 h after the treatment were very similar. However, the %MNPCE at 72 h was similar to the background level.

The authors suggested that the MN might be lost at the cell division or even deceased.

The following test results were obtained (no significant difference between male and female animals) [Tab. 2]:

	time	Yield MN
saline	24 h	approx. 0.22 % MNPCE
sulfites (2 x500 mg/kg)	12 h	approx. 0.63 % MNPCE
	24 h	approx. 1.0 % MNPCE
	36 h	approx. 0.54 % MNPCE
	48 h	approx. 0.52 % MNPCE
	60 h	approx. 0.54 % MNPCE
	72 h	approx. 0.36 % MNPCE

3. COMBINED APPLICATION
The last treatment regime showed that there is an enhanced effect of the test mixture on MN formation induced by MMC, but inhibited mutagenesis of CP in the mouse bone-marrow cells.

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, sufficiently documented for assessment
Flag: Critical study for SIDS endpoint

(85)

Type: Unscheduled DNA synthesis
Species: rat **Sex:** male
Strain: Wistar
Route of admin.: gavage
Exposure period: 2 and 16 h
Doses: 625 and 1250 mg/kg (10 ml citrate buffer, pH5.0)
Result: negative

Method: OECD Guide-line 486
Year: 2000
GLP: yes
Test substance: other TS: sodium bisulfite

Result: The rats showed no substantially affected hepatocytes after treatment. No dose level of the test item revealed UDS induction in the hepatocytes of the treated animals as

compared to the current vehicle controls. The net gain values obtained after treatment with the test item were consistently negative. In addition, no substantial shift to higher values was obtained in the percentage distribution of nuclear grain counts.

From the results obtained in this study, it was concluded that sodium bisulfite (sodium hydrogensulfite) failed to show any evidence of mutagenic potential in this in vivo test for unscheduled DNA synthesis when administered orally at pH 5.0.

Test condition: The mean initial body weight of the test animals (six to ten weeks old) was about 190 g. Four rats were used per dose and eight animals (two per dose) had been used in the range finding experiment.

Two and 16 hours after treatment the animals were sacrificed by liver perfusion. Primary hepatocytes were exposed to 3HTdR (3H-thymidine-dR) for four hours to show its incorporation if UDS occurs. Hepatocytes from three animals per group were assessed for UDS.

N,N'-dimethylhydrazine dihydrochloride (DMH) (40 mg/kg bw) and 2-acetylaminofluorene (2-AAF) (100 mg/kg) served as positive controls.

Reliability: (2) valid with restrictions
Original reference not available; however, GLP guideline study and peer-reviewed by SCCNFP (2000)
Flag: Critical study for SIDS endpoint
20-FEB-2006 (84) (86)

Type: Cytogenetic assay
Species: rat **Sex:** male/female
Strain: other: no data
Route of admin.: gavage
Doses: 50 - 5000 mg/kg (single dose)
Result: negative

Method: other: bone marrow
Year: 1973
GLP: no
Test substance: other TS: Sodium thiosulfate

Test substance: Na2S2O3 [CAS No. 7772-98-7]
Reliability: (4) not assignable
4b: Secondary literature
Flag: Critical study for SIDS endpoint
(87) (88)

Type: Cytogenetic assay
Species: mouse **Sex:** male/female
Strain: other: no data
Route of admin.: gavage
Exposure period: no data
Doses: 50 - 5000 mg/kg (single dose)
Result: negative

Method: other: bone marrow
Year: 1973

GLP: no
Test substance: other TS: Sodium thiosulfate

Test substance: Na2S2O3 [CAS No. 7772-98-7]
Reliability: (4) not assignable
4b: Secondary literature
Flag: Critical study for SIDS endpoint
(87) (88)

Type: Cytogenetic assay
Species: rat **Sex:**
Strain: other: albino
Route of admin.: gavage
Exposure period: Animals were treated either one time and then sacrificed 6, 24 or 48 h later, or they were treated once/day for 5 d, and then were sacrificed 6 h after the last treatment.
Doses: 30, 700, 1200 mg/kg bw
Result: negative

Method: other: see Methods freetext
Year: 1974
GLP: no
Test substance: other TS: Disodium disulfite

Method: The positive control was triethylene melamine injected i.p. at a dose of 0.5 mg/kg. 5 animals/dose/time point were used, except in the negative control which used 3 animals. 50 bone marrow cells per animal were evaluated for breaks and rearrangements.

Result: No adverse effect on bone marrow chromosomes was observed as a result of disodium disulfite treatment. The mitotic index was reduced in the high dose groups after all single administration time points, indicating that the TS reached the bone marrow to a sufficient level. Gaps were not taken into account, however, given the lack of a disodium disulfite-induced increase in aberrations, this can be tolerated.

Test substance: Na2S2O5 [CAS No. 7681-57-4]
Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given.

Flag: Critical study for SIDS endpoint
20-FEB-2006 (89) (90)

Type: Dominant lethal assay
Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of admin.: oral feed
Exposure period: 10 weeks
Doses: 0, 125, 417, 1250 mg/kg daily
Result: negative

Year: 1979
GLP: no
Test substance: other TS: disodium disulfite

Method: The positive control was triethylene melamine given in the

drinking water at a dose of 0.6 mg/l. The diet was supplemented with 50 mg/kg in corn oil. The controls (+ and -) were fed a diet with the corn oil alone. After the 10-wk treatment, 40 male rats from the vehicle control group and20 from each TS and positive control group were individually housed and paired with 2 virgin females for 7 days. Each female was sacrificed 15-19 d after the 1st day of cohabitation. To investigate the dominant lethal effect the following parameters were investigated: total implants, total dead implants, total live implants, an pre-implantation loss. Total corpora lutea were also recorded.

Result: The evaluation for mutagenicity showed no consistent effect that could be attributed to treatment.

Test substance: Na2S2O5 [CAS No. 7681-57-4], [Baker Chem. Co,]; no further data

Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given.

Flag: Critical study for SIDS endpoint

(91)

5.7 Carcinogenicity

Species: rat **Sex:** male/female
Strain: Wistar
Route of administration: oral feed
Exposure period: 104 weeks
Frequency of treatment: continuous
Post exposure period: none
Doses: 0.125, 0.25, 0.5, 1.0, 2.0% (ca. 50, 100, 220, 450 and 940 mg/kg bw)
Result: negative
Control Group: yes, concurrent no treatment

Method: other: see method freetext
Year: 1972
GLP: no
Test substance: other TS: disodium disulfite

Method: Six experimental groups were maintained on a diet containing 0, 0.125, 0.25, 0.5, 1.0 and 2.0 % of disodium disulphite.

The basal diet was supplemented with 50 ppm thiamine, due to the destruction of thiamine by sulphite. Sulfite was added to the diet by mechanical mixing of disodium disulfite. The diet was freshly prepared every 2 weeks. To diminish the loss of sulphite and thiamine, the diets were kept frozen at -18 degrees C. Rats were provided fresh daily portions.

All rats (F0-generation) were mated at wk 21 of treatment within their dose group. Half of them were mated again at wk 34. 10 males and 10 females were selected at weaning from the 1st litters of each group to become the F1a-generation. The F0-generation rats, as well as selected F1a-generation rats were maintained on their diets for a period of 104 wk. Rats of the F1a-gen. were mated at wk 12 and 30 to produce the F2a-

and F2b- generations.
10 males and 15 females from the F2a litters were mated to produce a F3a- and F3b-generation by pairing them on wk 14 and 22. The resulting litters were discarded after weaning, and the parents were kept on their diets for about 30 wk. The number of animals used for histological examinations after 1 year was 4-5 from the F0 animals; after 104 weeks of treatment was 19-24/dose/sex from the F0-gen. and the F1-gen. together; and after 30 wk of treatment, 10-15/dose/sex were used from the F2-generation.

An extensive set of tissues from each rat of the F0-, F1a- and F2a-gen. were examined microscopically. Several special stains were also employed.

Organs examined at necropsy (macroscopic and microscopic): Interim observation on organ weight and pathological changes. Microscopic: heart, kidneys, liver, spleen, brain, testes, ovaries, pituitary, thyroid, parathyroids, adrenals, thymus, lungs, trachea, salivary glands, gastro-intestinal tract, pancreas, urinary bladder, skeletal muscle, spinal cord, femoral nerve, skin, bone marrow(sternum), axillary and mesenteric lymph nodes, exorbital lachrymal gland, aorta, mammary glands, uterus, prostate, seminal vesicle and coagulating gland.

Result: 24 to 25 animals were examined per sex and dose group.
The total numbers of tumour-bearing animals ranged from 12 - 22 per group with the control groups including 17 male and 20 female animals with tumours.

A. GENERAL TUMOUR PATHOLOGY

Overall, the highest rates of organ-specific tumours were found in the lung, thyroid, pituitary gland, adrenal gland and the mammary gland.

The number of lympho-reticular pulmonary tumours in males decreased with increasing levels of sulphite. The incidence of thyroid and pituitary tumours in control males was exceptionally low, whereas those noted in the various test groups represented numbers normally found in the strain of rats used. All other neoplasms occurred in a random manner: Tumour incidences (skin, liver, kidney, heart, brain, spinal cord, urinary bladder, hind-leg bone, mandible) were 0/25 or 1/25. (Til et al. 1972).

B. TUMOUR INCIDENCES MALES (from Til et al. 1972, Tab. 7)

Incidence and types of tumours in F0- and F1-generation rats fed sulfite for 2 years

	Males					
Dietary level[%]	0	0.125	0.25	0.5	1	2
No. of rats	24	24	25	25	25	25
No. of rats with tumours	17	22	21	18	17	18

Lung						
Malig. lymph.	10 / 10	/ 8	/ 6	/ 6	/ 3	
Sarcoma	0 / 1	/ 0	/ 0	/ 0	/ 0	
Osteosarcoma	0 / 0	/ 0	/ 0	/ 0	/ 0	
Thyroid						
Light-cell tum.						
Adenoma	1 / 8	/ 6	/ 4	/ 8	/ 5	
Carcinoma	0 / 0	/ 2	/ 0	/ 1	/ 1	
Papillary aden.	0 / 0	/ 0	/ 1	/ 0	/ 1	
Follicular aden.	0 / 0	/ 0	/ 1	/ 1	/ 0	
Solid carcinoma	0 / 0	/ 0	/ 0	/ 0	/ 0	
Pituitary						
Adenoma	0 / 5	/ 5	/ 1	/ 4	/ 4	
Carcinoma	0 / 2	/ 1	/ 2	/ 2	/ 2	
Adrenal						
Phaeochrom.						
benign	6 / 4	/ 8	/ 5	/ 1	/ 7	
malignant	1 / 2	/ 1	/ 4	/ 1	/ 0	
Cortical aden.	0 / 1	/ 0	/ 0	/ 0	/ 0	
Cortical carc.	0 / 0	/ 0	/ 0	/ 0	/ 0	
Mammary gland						
Fibroadenoma	0 / 0	/ 0	/ 1	/ 0	/ 0	
Adenoma	0 / 1	/ 0	/ 0	/ 0	/ 0	
Carcinoma	0 / 0	/ 0	/ 0	/ 0	/ 0	

C. TUMOUR INCIDENCES FEMALES (from Til et al. 1972, Tab. 7)

Incidence and types of tumours in F0- and F1-generation rats fed sulfite for 2 years

	Females					
Dietary level[%]	0 / 0.125	/ 0.25	/ 0.5	/ 1	/ 2	
No. of rats	25 / 25	/ 25	/ 25	/ 25	/ 25	
No. of rats with tumours	20 / 12	/ 16	/ 15	/ 17	/ 14	
Lung						
Malig. lymph.	2 / 5	/ 4	/ 5	/ 2	/ 4	
Sarcoma	0 / 0	/ 0	/ 0	/ 0	/ 0	
Osteosarcoma	0 / 1	/ 0	/ 0	/ 0	/ 0	
Thyroid						
Light-cell tum.						
Adenoma	4 / 5	/ 5	/ 4	/ 3	/ 7	
Carcinoma	0 / 0	/ 0	/ 0	/ 0	/ 0	
Papillary aden.	0 / 0	/ 0	/ 1	/ 0	/ 0	
Follicular aden.	0 / 0	/ 0	/ 0	/ 0	/ 0	
Solid carcinoma	1 / 0	/ 0	/ 0	/ 0	/ 0	
Pituitary						

Adenoma	8 /	2 /	4 /	3 /	4 /	0
Carcinoma	0 /	1 /	1 /	1 /	0 /	0
Adrenal						
Phaeochrom.						
benign	1 /	0 /	4 /	1 /	2 /	2
malignant	0 /	0 /	0 /	0 /	0 /	0
Cortical aden.	0 /	0 /	0 /	0 /	0 /	0
Cortical carc.	0 /	0 /	0 /	0 /	0 /	0
Mammary gland						
Fibroadenoma	3 /	0 /	1 /	4 /	5 /	2
Adenoma	0 /	0 /	1 /	0 /	1 /	0
Carcinoma	2 /	0 /	1 /	2 /	0 /	0

Test substance: CAS No. 7681-57-4; disodium disulfite; purity: 95-99% [Amsterdamsche Chinine Fabriek, Holland]
Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given.
Flag: Critical study for SIDS endpoint
21-FEB-2006 (68) (92)

5.8.1 Toxicity to Fertility

Type: Fertility
Species: mouse
Sex: male
Route of administration: i.p.
Exposure Period: a) single dose b) 28, 42, and 56 days
Frequency of treatment: a) single dose b) 20, 30, and 40x
Doses: a) 500, 600, 700, 800, 900 and 1000 mg/kg bw; b) 200 and 400 mg/(kg*d)
Result: No morphological adverse effect at any stage of spermatogenesis

Method: other: Spermatogenesis
Year: 1980
GLP: no data
Test substance: other TS: Sodium bisulfite

Method: The effect of sodium bisulfite on differentiating spermatogonia has been investigated in adult mice, given either a single intraperitoneal injection (500, 600, 700, 800, 900 and 1000 mg/kg bw) or repeated intraperitoneal injections (200 and 400 mg/kg bw) of sodium bisulfite.

Remark: No mortality was observed up to 700 mg/kg dose within 24 hours. At the 1000 mg/kg dose, 80% of the mice died within 24 hours post-treatment. Cytotoxicity data showed that sodium bisulfite, at any of the dosage levels tested after acute or repeated administration, did not alter the population of various types of spermatogonia.

Test substance: NaHSO3 [CAS No. 7631-90-5]

Reliability: (2) valid with restrictions
Secondary literature, but peer-reviewed by JECFA 1983
Flag: Critical study for SIDS endpoint

20-FEB-2006 (93) (94)

Type: other: Multigeneration study
Species: rat
Sex: male/female
Strain: Wistar
Route of administration: oral feed
Exposure Period: 104 weeks (F0 and F1 generation) and 30 weeks (F2 generation)
Frequency of treatment: daily
Premating Exposure Period
male: 21 weeks
female: 21 weeks
Duration of test: until the weaning of the F3 animals
No. of generation studies: 3
Doses: 0.125, 0.25, 0.5, 1.0, 2.0% (ca. 50, 100, 220, 450 and 940 mg/kg bw)
Control Group: yes, concurrent no treatment
NOAEL Parental: ca. 940 mg/kg bw
NOAEL F1 Offspring: ca. 940 mg/kg bw
NOAEL F2 Offspring: ca. 940 mg/kg bw

Method: other: see method freetext
Year: 1972
GLP: no
Test substance: other TS: disodium disulfite

Method: Six experimental groups were maintained on a diet containing 0, 0.125, 0.25, 0.5, 1.0 and 2.0 % of disodium disulphite.

The basal diet was supplemented with 50 ppm thiamine, due to the destruction of thiamine by sulphite. Sulphite was added to the diet by mechanical mixing of disodium disulfite. The diet was freshly prepared every 2 weeks. To diminish the loss of sulphite and thiamine, the diets were kept frozen at -18 degrees C. Rats were provided fresh daily portions.
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20 animals/dose/sex were used.
All rats (F0-generation) were mated at wk 21 of treatment within their dose group. Half of them were mated again at wk 34.
10 males and 10 females were selected at weaning from the 1st litters of each group to become the F1a-generation (this is a deviation from current guidelines).
The F0-generation rats, as well as selected F1a-generation rats were maintained on their diets for a period of 104 wk. Rats of the F1a-gen. were mated at wk 12 and 30 to produce the F2a and F2b generations. 10 males and 15 females from the F2a litters were mated to produce a F3a- and F3b-generation by pairing them on wk 14 and 22. These litters were discarded after weaning, and the parents were kept on their diets for about 30 wk.

In all generations, changes in body wt were recorded weeklyfor the 1st 12 wk, and once every 4 wk thereafter. Food consumption was measured weekly. Group matings were used throughout and lasted for a period of 2 wk.
At day 20 after the beginning of the mating period, the females were individually housed until after the litters had

been weaned. Records were made of the number of pups in each litter, and of the total wt of the litter at days 1, 8 and 21.

On the first day, the litters containing more than 8 pups were reduced to that number to equalise the stress of lactation on the dams.

Result: Body weight was not reduced in any treatment group in the F0-generation. There was a marginal reduction in body weightin both sexes of the 2% group in the F1- and F2-generations. Results in successive generations showed no substantial treatment-related effects in terms of fertility, the number of animals/litter or the birth weight or mortality of the young. During lactation the body weight of the young in the 2% group was generally lower than the controls and the lower-dosed groups. In the F1a- and F1b-generation offspring (F2a and F2b pups) dietary levels of 1 and 2% disodium disulfite were associated with decreased body weight on days 8 and 21. This effect was primarily transient for the F2a pups, since animals of the 1-% group recovered their body weight after weaning and the 2-% group nearly recovered their body weight as compared to the control.
The F2b pups were discarded after weaning. This reduced body weight was probably not a true substance-related effect since it could be due to a higher initial body weight in thecontrol groups. Furthermore, these body weight changes were within or were not dramatically different from the control values of the F1 pubs.
A reduction in the number of F2a-generation offspring(F3a pups) was observed in the 0.5, 1.0 and 2.0% dose groups, but it was not dose-dependent and did not occur in the F2b-generation offspring (F3b pups). No pronounced effects were observed on reproductive performance in any generation and no effects on gonads were seen histologically.

Thus, the NOAEL for reproductive toxicity was the highest dose tested. NOAEL, rat, fertility, oral feed: 2.0% (ca. 940 mg/kg bw).

There were no organs of systemic toxicity in the parental animals in any generation (F0, F1, and F2). Only sporadic weight changes were seen in the offspring (F1, F2, and F3); NOAEL, rat, F0, F1, F2, F3, oral feed: 2.0% (ca. 910 mg/kg bw).

Test substance: CAS No. 7681-57-4; disodium disulfite; purity: 95-99% [Amsterdamsche Chinine Fabriek, Holland]

Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given.

Flag: Critical study for SIDS endpoint

21-FEB-2006 (68) (92)

5.8.2 Developmental Toxicity/Teratogenicity

Species: rat **Sex:**
Strain: Wistar
Route of administration: gavage
Exposure period: 6 - 15 gd

Frequency of treatment: daily
Duration of test: day 20 of gestation
Doses: 1, 5, 24, 110 mg/kg/(bw*d)
Control Group: yes
NOAEL Maternal Toxity: = 110 mg/kg bw
NOAEL Teratogenicity: = 110 mg/kg bw

Method: other: see method freetext
Year: 1972
GLP: no
Test substance: other TS: disodium disulfite

Method: 24 animals were mated/dose, resulting in 21-24 pregnant rats. The control group was sham-treated rats. Body wts were recorded on days 0, 6, 11, 15 and 20 of gestation, and were observed daily for appearance, behaviour and foodconsumption. On day 20, the dams were subjected to Caesarean section and the number of implantation sites, resorptions and live and dead fetuses were recorded. All fetuses were examined grossly for the presence of abnormalities. One third of the fetuses of each litter underwent detailed viscera examinations (under magnification). The remaining two thirds were processed for staining with Alizarin Red-S dye and examined for skeletal defects.

Result: The administration of the TS to pregnant rats had no clear effect on nidation, or on maternal or foetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls.

Test substance: CAS No. 7681-57-4; disodium disulfite; purity: no data [FDA 71-22], white crystalline
Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given.

Flag: Critical study for SIDS endpoint
21-FEB-2006 (95) (68)

Species: mouse **Sex:** female
Strain: CD-1
Route of administration: gavage
Exposure period: 6-15 gd
Frequency of treatment: daily
Duration of test: until d 17 of gestation
Doses: 2, 7, 34 and 160 mg/kg bw/d
Control Group: yes, concurrent no treatment
NOAEL Maternal Toxity: = 160 mg/kg bw
NOAEL Teratogenicity: = 160 mg/kg bw

Test substance: other TS: disodium disulfite

Method: The test groups consisted of 20-21 pregnant females/dose.
Result: There was no maternal toxicity (bw. and rate of survival) observed. The number of corpora lutea, the implantations, the resorptions and the number dead at birth did not show a treatment-related effect. The number and type of variations and malformations observed in the test groups did not differ from the spontaneous changes in the control group.

Test substance: CAS No. 7681-57-4; disodium disulfite; purity: no data
Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given
21-FEB-2006 (95)

Species: rabbit **Sex:**
Strain: Dutch
Route of administration: gavage
Exposure period: days 6-18 of gestation
Frequency of treatment: daily
Duration of test: until day 29 of gestation
Doses: 1.23, 5.71, 26.5, 123 mg/(kg bw*d)
Control Group: yes
NOAEL Maternal Toxity: = 123 mg/kg bw
NOAEL Teratogenicity: = 123 mg/kg bw

Method: other: see method freetext
Year: 1974
GLP: no
Test substance: other TS: disodium disulfite

Method: On day 0, each female was given an injection of 0.4 ml of human chorionic gonadotropin (400 IU), and 3 h later they were artificially inseminated with 0.3 ml of diluted semen from aproven donor using ca. 20 million motile sperm.
15-20 animals were used per dose resulting in 12-14 pregnant rabbits/dose. A positive control group treated with 2.5 mg/kg 6-amino nicotinamide on day 9 was also included that consisted of 10 pregnant animals. The negative control group was sham treated.
Body weights were recorded on days 0, 6, 12, 18 and 29 of gestation, and were observed daily for appearance, behaviour and food consumption.

On day 29, the females were subjected to Caesarean section and the number corpora lutea, implantation sites, resorptions and live and dead foetuses were recorded. The body weight of the live pups was recorded. Live foetuses were placed in an incubatorfor 24 h to monitor neonatal survival. All surviving pups were sacrificed and then examined for visceral abnormalitiesby dissection. All fetuses were processed for staining with Alizarin Red-S dye and examined for skeletal defects.

Result: The administration of the TS to pregnant rabbits had no clear effect on nidation, or on maternal or foetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in the sham-treated controls.

Test substance: CAS No. 7681-57-4; disodium disulfite; purity: no data [FDA 71-22], white crystalline
Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given.
Flag: Critical study for SIDS endpoint
21-FEB-2006 (96) (68)

Species: hamster **Sex:** female
Route of administration: gavage
Exposure period: 6-10 gd
Frequency of treatment: daily
Duration of test: until d 14 of gestation
Doses: 1, 6, 26, 120 mg/kg
Control Group: yes, concurrent no treatment
NOAEL Maternal Toxity: = 120 mg/kg bw
NOAEL Teratogenicity: = 120 mg/kg bw

Method: other: see method freetext
Year: 1974
GLP: no
Test substance: other TS: disodium disulfite

Method: Groups of 20-21 pregnant hamsters were administered the test substance at dose levels of 1, 6, 26 or 120 mg/kg bw/d by gavage once daily during gestation days 6-10. Hamsters were killed on d 14 of gestation.

Result: There was no maternal toxicity (bw. and rate of survival) observed. The number of corpora lutea, the implantations, the resorptions and the number dead at birth did not show a treatment-related effect. The number and type of variations and malformations observed in the test groups did not differ from the spontaneous changes in the control group.

Test substance: CAS No. 7681-57-4; disodium disulfite; purity: no data
Reliability: (2) valid with restrictions
Comparable to guideline study. Essential details for an assessment are given.
21-FEB-2006 (96)

Species: rat **Sex:** female
Strain: Wistar
Route of administration: oral feed
Exposure period: 8 - 20 d of gestation
Frequency of treatment: daily
Duration of test: either until gestation day 20 (10 to 12 dams) or at weaning 21 day post partum (4-5 dams of control, 0.32-%, 5-% group with newborns)
Doses: 0.32; 0.63; 1.25; 2.5, and 5 %
Control Group: yes, concurrent no treatment
NOAEL Maternal Toxity: = 2.5 %
NOAEL Teratogenicity: = 5 %
: = 5 %
other: NOAEL Neonatal toxicity : = 5 %
Result: LOAEL maternal toxicity: 5 %
LO(A)EL slight fetal growth retardation: 0.32 %
LO(A)EL decreased maternal food intake: 0.32%

not teratogenic / not embryo- and fetotoxic

Method: other: mostly according to OECD Guide-line 414 including postnatal development
Year: 1989
GLP: no
Test substance: other TS: Sodium sulfite x 7H2O [CAS No. 7757-83-7]

Method: TEST DESIGN/EXPERIMENTAL
Groups of 10-12 pregnant Wistar rats were fed diets containing 0, 0.32, 0.63, 1.25, 2.5 or 5% sodium sulphite heptahydrate. The animals had ad libitum access to the feed on days 8-20 of gestation.

Satellite groups of 4 pregnant rats received 0, 0.32 or 5% in the diet on the same days.

Body weights, food consumption, and clinical signs of toxicity were recorded daily.

On day 20 of gestation, rats in the main group were killed and the uteri opened and examined for external abnormalities.

Half of the foetuses were subjected to visceral examination, and the other half was prepared for skeletal examination.

Dams in the satellite group were allowed to deliver and rear their litters to weaning.

Remark: Reasons for inclusion of data on sulfite as relevant agent:

In the presence of moisture (see also 3.1.2 Stability in Water), sodium dithionite [CAS No. 7775-14-6] rapidly decomposes to sulfur dioxide by transferring two electrons per molecule to a suitable recipient molecule, in particular favoured in acid media. Partial disproportion may occur by forming SO2 along with unstable sulfoxylic acid (H2SO2). SO2 forms sulfurous acid (H2SO3) in water. Sulfoxylic acid and H2SO3 ultimately react to sulfuric acid (H2SO4) in the presence of oxygen.

Result: PRENATAL - MATERNAL EFFECTS:
5%-level: clear signs of maternal toxicity were observed as distinctly reduced food consumption of the dams during the treatment period (day 8-20 p.c.: -27.3%), markedly lower mean body weight gain of the dams in comparison to the controls on day 9-20 p.c.: -25.5%).
0.63%-level: reduced food consumption on day 8-20 p.c.: -16.0%;
0.32%-level: reduced food consumption on day 8-20 p.c.: -13.7% with no apparent dose-response relationship.

REPRODUCTIVE DATA:
There were no significant differences between the control and sodium sulfite-treated groups in the number of implants, live fetuses and intrauterine death (resorptions and dead fetuses) and the sex ratio of fetuses.

EMBRYO/FOETOTOXICITY:
The total number of implantations was higher in the dams at the three highest doses than in the controls or in rats at the lower doses (statistically non-significant), but was accompanied by increased incidence of intra-uterine deaths (resorptions and dead fetuses) at 2.5 and 5%.

There were no significant differences between the control and sodium sulfite-treated groups in the number of implants, live fetuses and intrauterine death (resorptions and dead fetuses), litter size, and the sex ratio of fetuses.

The lower doses produced some mild fetal growth retardation: decreased fetal body weights were noted in all treated groups ($p<0.05$) with the exception of the female 2.5% group.

No external, skeletal, or visceral anomalies were observed in fetuses of any group. Several types of skeletal and internal variations such als lumbar rib, hypoplastic rib, renal pelvis and lateral ventricle dilatation were noted in the sodium sulfite-treated groups except for the 1.25% group. But the incidences were not dose-dependent and not statistically different from controls and considered as not significantly affected by treatment.

The degree of delayed ossification was slightly, but not significantly increased in the dose group receiving 0.32% or more.

POSTNATAL (control, 0.32 and 5% dose group):

MATERNAL EFFECTS:
The maternal body weight gain three weeks after delivery was not significantly effected by sodium sulfite-treatment during days 8-20 of pregnancy.

NEONATE EFFECTS:
The live-birth indices and survival rate of offspring between the groups during 4 weeks after birth (100, 88, 98% and 98%, 98%, 100% for control, 0.32, 5% group, respectively) was not different. Body weights of male and female offspring 3 weeks after birth indicated no evidence of growth retardation or any other signs of toxicity between groups.

The given NOAELs refer to $Na_2SO_3 \times 7H_2O$ as applied; without crystal water the NOAELs are approx. 850 (2.5%-level) and 1450 mg/(kg*d) (5%-level), respectively (see Test Conditions).

Test condition: TEST SUBSTANCE / Daily INTAKE:
For the dose, it has to be considered that half of the test compound consisted of 7 mol crystal water (= 126/252), and the effective dose for sulfite / SO_2 (not including sodium: SO_2 = 64/252 = approx. 1/4 of the TS) has to be adjusted (see below).

Reported actual intakes given in the original report and in JECFA and IARC reviews are flawed (one dose missing, incorrect allocation). Therefore, dose intakes were recalculated, based on the available mean group data on body weight, body weight gain and feed consumption given in the report (Table 1):

0.32; 0.63; 1.25; 2.5; and 5 %
= approx. 200, 400, 900, 1750, and 2900 mg/(kg bw*d) sodium sulfite $\times 7H_2O$
= approx. 100, 200, 450, 850, and 1450 mg/(kg bw*d) sodium sulfite (without crystal water)
= approx. 50, 100, 225, 440, 725 mg/(kg bw*d) SO_2 equivalents.

TEST ORGANISMS:
Virgin female and male Wistar rats supplied by KEARI Co.STD (Osaka, Japan); weight at study begin (day 0): 237 g.

MATING PROCEDURE:
Female rats were caged with male rats overnight. The day on which a vaginal plug and sperm were found was taken as "day 0" of pregnancy.

ADMINISTRATION/EXPOSURE:
The test substance was administered to pregnant females by feeding a basal diet containing TS from day 8 to 20 of pregnancy. Net amounts of sodium sulfite uptake were calculated from the food consumption.

PARAMETERS ASSESSED DURING STUDY:
Daily body weight, food consumption and clinical signs of toxicity were recorded.

PARAMETERS EXAMINED AT NECROSCOPY:
On day 20 of pregnancy, ten or twelve of the pregnant rats in each group were sacrified by cervical dislocation. The opened uterus was examined or the presence and position of resortpion, fetuses (dead or alive), and implantations sites. Each live fetus was weighed, sexed and examined for external abnormalities.
One half of the number of fetuses in each litter, randomly selected, was used for internal examination, the remaining number for skeletal examination.
An additional four or five dams in 5%, 0.32% and control group were allowed to give birth.
At birth the number of live and dead newborns were recorded. Pups were sexed, weighed, examined for external malformation.

STATISTICAL EVALUATION:
Student's t-test for body weight gain, food consumption, number of implantations, live fetuses, live newborns per litter, weights of fetuses and offspring.
Wilcoxon's rank sum test, chi-squares test Yates'correction or Fisher's exact probability test for incidence of postimplantation loss, skeletal and internal variations, delayed ossification, the live birth index, the survival rate of offspring and sex ratio of live fetuses. Significant levels set at $p < 0.05$.

Test substance: Sodium sulfite x 7H2O ("guaranteed grade") [CAS No. 7757-83-7] from Katayama Chemicals Industries Co. (Tokyo, Japan)

Reliability: (2) valid with restrictions
Comparable to guideline study, but lower number (10 to 12 instead of 20) of dams used and later start of exposure (day 8 instead day 5), thus not including the full implantation phase, no uterus weight reported.

Flag: Critical study for SIDS endpoint

23-FEB-2006 (24) (97) (71)

5.8.3 Toxicity to Reproduction, Other Studies

5.9 Specific Investigations

5.10 Exposure Experience

Remark: Probable oral lethal dose (human) 0.5-5 g/kg body weight. Because of rapid oxidation to sulfates, sulfites are well tolerated until large dises are reached; then violent colic and diarrhea, circulatory disturbances, central nervous depression, and death are described.
Reliability: (4) not assignable
4.2; only secundary literature
(98)

Remark: Incubation of normal human erythrocytes with sodium dithionite resulted in the formation of heinz bodise. Addition of superoxide dismutase to the incubation medium increased the formation of Heinz bodies by sodium dithionite.
Reliability: (4) not assignable
4.2; only abstract available
(99)

Remark: Case report of a dry cleaning worker developing hand dermatitis. Patch test was positive to 0.5 and 1 % solution.
With 0.1 % solution the reaction was doubtful. Eighteen consecutive control patients with dermatitis were negative to the 1 % solution; 10 of 12 tested with 2 % solution were patch test negative; of the two others one was doubtful.
Reliability: (2) valid with restrictions
2.2; basic data given, restrictions
(100)

Remark: Sulphites such as sodium pyrosulphite and sodium dithionite,
applied topically to the skin of cement workers, appear to be effective in prevention of dermatitis. 9 previously proven chrome sensitive individuals were patch tested with aqueous potassium dichromate 0.5 % mixed with sodium dithionite in the proportion of 3 g/l. Not one patient developed a positive reaction to the chromate mixed with sodium dithionite. Though all reacted to 0.5 % chromate in water without sodium dithionite.

Reliability: (2) valid with restrictions
2.2; basic data given, restrictions
(101)

Type of experience: other: Human: hypersensitivity

Remark: Under acidic conditions, sodium dithionite may liberate sulfur dioxide (SO_2). Sulfur dioxide is known to induce respiratory irritation and in disposed humans also bronchospasms [Klaassen, 2001, p. 1070/71].

The hypersensitivity reaction is also known as "sulfite-asthma" and linked to SO2 exposure or the use of SO2 or bisulfite as antioxidants in foodstuffs [Marquardt and Schäfer, 1994].

About 10% of asthmatic humans are reportedly sulfite- or SO2-sensitive [Lewis, 1998, p. 990].

In humans, allergoid (pseudoallergic) reactions (asthma, urticaria, headache, intestinal irritation) have been reported following the exposure of sensitive persons to sulfites or sulfur dioxide via the oral or respiratory routes [DFG, 1998; 1974].

Reliability: (2) valid with restrictions
Data from hand- or textbooks

Flag: Critical study for SIDS endpoint

(102) (103) (104) (105)

5.11 Additional Remarks

Type: other: Long-term toxicity, carcinogenicity, reproduction toxicity

Remark: Due to thiamine deficiency observed in several long-term toxicity studies with sulphites, it was not possible to establish clear causal relationships between observed effects and sulphite exposure via the feed (see for a review: Til and Feron, 1992).
This explains the conflicting results obtained in studies of Fitzhugh et al. (1946) on the one side and in studies by Locket & Natoff (1960) and Til et al. (1976a, b) on the other side.
Reduced growth development in F1 and F2 generations were observed in a 2-yr rat multigeneration study at and above 2% DIPOTASSIUM DISULPHITE [CAS No. 16731-55-8] (Til et al, 1972a). Female fertility, litter size and pup birth weights and pup mortality was not influenced by treatment. Occult faecal blood was found at 1% and higher disulfite levels.
At and above 2%, relative kidney weights were increased in F2 females, but no functional or histopathological changes were detected. Hyperplastic changes in forestomach and glandular stomach were observed in all animals given 1% or higher concentrations.
No indication of a carcinogenic effect was observed.

Long-term studies reported by other authors (Lockett & Natoff, 1960; Cluzan et al., 1965; Lanteaume et al., 1965) with up to 2 mmol sulphite/kg bw/d administration for at least a 1-year period gave no evidence of maternal or foetal toxicity in the rat or mouse (WHO, 1983; 1986).

In a long-term study with pigs, DISODIUM DISULPHITE [CAS No. 7681-57-4] was administered for up to 48-wks via the feed (Til et al., 1972b). Mortality and haematology were not influenced by treatment. Body weight development and feed consumption were clearly reduced at 1.72 % sulphite, which obviously resulted from reduced palatability (revealed in a pair-feeding

study). No evidence for the presence of occult blood in the faeces was found. After 48-wk exposure to 0.83 % or higher sulphite levels, the relative weights of the following organs were increased: heart, liver, kidney and spleen, while after 15 wk, these changes were confined to the 1.72 % group. In the pair-feeding study, only the relative liver and kidney weights were increased in the 1.72 % group. At and above 0.83 %, inflammatory and hyperplastic changes of the stomach mucosa were observed.

A mouse carcinogenicity study with DIPOTASSIUM DISULPHITE [CAS No. 16731-55-8] treatment of up to 2 % via the drinking water gave no evidence for a carcinogenic effect (Tanaka et al., 1979).

The tumour-promoting activity concluded by Takahashi (1986) appears questionable: Although a statistically significant increase in the adenomacarcinoma incidence was observed, the total tumour incidence and the incidence of hyperplastic changes was not increased over control levels.

Testing of SODIUM HYDROGEN SULPHITE [CAS No. 7631-90-5] and DISODIUM DISULPHITE [CAS No. 7681-57-4] in mouse, hamster, rat and rabbit studies (Food and Drug Research Laboratories, 1972, 1974) and of DIPOTASSIUM DISULPHITE [CAS No. 16731-55-8] in the rat and mouse (Food and Drug Research Laboratories, 1975) as well as provided no evidence for a teratogenic hazard potential. The incidence and quality of observed variations and malformations were not different from those of the control groups. Developmental toxicity studies in sulphite-oxidase deficient rats exposed to up to 50 mM DISODIUM DISULPHITE [CAS No. 16731-55-8] in drinking water also did not provide evidence for teratogenicity or foetotoxicity (Dulak et al., 1984).

Test substance: other TS:
CAS-No. 16731-55-8; dipotassium disulfite
CAS-No. 7681-57-4; disodium disulfite
CAS-No. 7631-90-5; sodium hydrogen sulfite

Flag: Critical study for SIDS endpoint

21-FEB-2006 (106) (107) (108) (109) (94) (110) (111) (95) (96) (112) (113) (114) (92) (115) (116) (117)

Type: other: Acceptable Daily Intake (JECFA, 1986, 1999)

Remark: An acceptable daily intake (ADI) of 0.7 mg/kg bw, or 50 mg for a 70 kg person, has been set by the FAO/WHO Expert Committee on Food Additives (JECFA).

A group ADI was established expressed as sulphur dioxide, for calcium hydrogen sulphite, calcium metabisulfite, potassium hydrogen sulphite, potassium metabisulfite, potassium sulfite, sodium hydrogen sulphite, sodium metabisulphite, sodium sulphite, sodium thiosulfate, and sulfur dioxide.

The ADI was based on long-term studies in rats, including a three-generation study of reproductive toxicity, with a NOEL of 0.25% sodium metabisulphite [CAS No. 7681-57-4] in the

diet (supplemented with thiamine, as treatment of foods with sulphites reduces their thiamine content), equivalent to 70 mg/kg bw/d of sulphur dioxide equivalents [Til et al., 1972] [see also: Til and Feron, 1992]. At higher doses (>= 1%), local irritation of the stomach was observed, with inflammatory changes and hyperplasia, and occult blood was detected in the faeces at even higher doses. The histopathological changes were limited to the stomach; the incidence of neoplasms was not increased at any site or at any dose. A safety factor of 100 was used.

Test substance: other TS: Disodium disulfite [CAS No. 7681-57-4]

Flag: Critical study for SIDS endpoint

20-FEB-2006 (118) (71) (114) (92)

Type: other: Review genotoxicity

Remark: A. IN-VITRO GENOTOXICITY

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The mutagenic potential of sulphite agents is pH- and temperature-dependent.
Reverse mutations in E. coli, lambda phages and T4rII were detectable only at high sulphite concentrations (> 0.2 mol/l) and at pH 5. At pH 7 or 8, no mutations were detectable (Shapiro, 1977; Gunnison, 1981). It was noted that reverse mutations coincided with "hot spot" C:G-base pairs (Mukai et al., 1970).

Mutagenesis in tester strain TA97 of sodium hydrogen sulfite was significant at 27 °C, but became suppressed at 37 °C. An inverse relationship between bisulphite auto-oxidation and its ability to cause mutations in Salmonella was found. As auto-oxidation decreased, as evidenced by the increasing length of time it took to deplete 50% of the oxygen in the oxygen monitoring system, the mutagenicity increased (Pagano et al., 1990).

The results suggest a radical mechanism by which temperature, pH and oxygen availability determine the rate of bisulfite autoxidation via the formation of the intermediate sulfur-centered sulfur trioxide radical, SO3-·. This may occur spontaneously or through the action of the peroxidase/H2O2 system (Pagano et al., 1990).

Two bacterial mutagenicity tests were conducted with sodium dithionite in the common tester strain family of Salmonella typhimurium according to standard procedures [Ames et al. 1975; acc. to OECD 471) with and without metabolic activation, one test series also employing the preincubation technique and including E. coli WP2 [Shimizu et al., 1985], another series employing the direct plate incorporation and preincubation method. Both experiments have shown consistently negative results up to the top dose of 5 mg/plate [BASF, 1983a].

Negative results have also been obtained in similar testing with disodium disulfite [CAS No. 7681-57-4] [BASF, 1989d]; a weak mutagenic response was observed in the S. typhimurium strains carrying the hisG46 and hisD6610 mutations at pH 5 and 6 (0.32 m) [Pagano and Zeiger, 1987].

In another early Ames test, disodium disulfite gave positive results in strains TA100, TA98, TA1535 and TA1537 after metabolic activation and in the host-mediated assay.

In the Spot-Test, however, only negative test results were obtained (Rao & Aiyar, 1975).

Hydrogensulphite induced mutations in Saccharomyces at pH 3.6 but not at pH 5.5 (Shapiro, 1983).

Chromosomal effects (increases in SCE or chromosomal damage have been induced by sulfites, hydrogen sulfites or disulfites in mammalian cell cultures (see BIBRA, 1996).

Only weak positive test results were obtained in in-vitro SCE studies with CHO cells (MacRae & Stich), while the test was negative in V79 cells (Mallon & Rossman, 1981). No increase in gene mutations in mammalian cells were produced by hydrogen sulphite (BIBRA, 1996).

Although chromosome aberrations in oocytes of the Camm mouse, cow and sheep were observed in vitro, no indication of germ cell mutagenicity was found under in-vivo conditions in Camm mice (Jagiello et al., 1975).

It was demonstrated that the co-mutagenic action of sulphite and UV-induced mutations in E. coli resulted from sulphite-dependent inhibition of DNA repair (Mallon & Rossman, 1981). By contrast, the mutagenic potential of coffee is inactivated in the presence of sulphites; the underlying mechanism is unknown (Suwa et al., 1982).

Inhibition of DNA synthesis (determination of (3H)-thymidine incorporation) was found in chicken embryo fibroblasts, HeLa cells, mouse hepatocytes and human lymphocytes (Chin et al., 1977; Timson, 1973).

B. IN-VIVO GENOTOXICITY

Negative results were obtained in Drosophila (Valencia et al., 1973).
In both the Dominant-Lethal test with male and female germ cells of the mouse, and in mouse oocytes, test results were negative after injection of upto 4,8 mmol sulfite/kg (Generoso et al, 1978; Jagiello et al, 1975).

Negative test results were also established in the micronucleus test and in investigations of SCEs and chromosome aberrations in sulphite-oxidase deficient mice and hamsters (Renner & Wever, 1983).

Repeated i.p. injection in mice of up to 400 mg sodium hydrogen sulphite/kg (CAS No. 7631-90-5] (= 250 mg SO2/kg bw) for 56 days (maximally 40 injections) had no effect on the shape of spermatogonia (Bhattacharjee et al. 1980).

No increases in the rate of chromosomal aberrations were produced in bone marrow cells by single and repeated gavage doses of up to 1200 mg sodium disulphite [CAS No. 7681-57-4] [NTIS, 1972; Maxwell et al. 1974, BIBRA 1996].

A 1:3 mixture of sodium hydrogen sulfite [CAS No. 7631-90-5] and sodium sulfite [CAS No. 7757-83-7] in saline was recently shown to be positive in a bone-marrow mouse micronucleus assay after intraperitoneal injection of 20, 100, 500 or 750 mg/kg bw. The treatment was repeated after 24 hours. The clastogenic effect, some 2 to 4 fold above baseline, appeared between 12 and 48 h, and was no longer apparent after 72 h (Meng et al., 2002).

In a further micronucleus assay, sodium hydrogen sulfite (75, 150, and 300 mg/kg in citrate buffer, pH 5.0, intraperitoneal) failed to show evidence of a clastogenic potential in male and female mice after sampling of bone-marrow erythrocytes at 24 and 48 h [Honarvar, 2000]. The single doses applied in this test were distinctly lower than those applied twice by Meng et al. (2002) and were in a range which showed an ambiguously to marginally positive effect in that study.
Therefore, the negative result observed by Honarvar (2000) is not in contrast to that obtained by Meng et al. (2002) because of possibly underlying dose effects.

In an in-vivo/in-vitro UDS bioassay, oral doses of 625 and 1250 mg sodium hydrogen sulfite/kg bw revealed no UDS induction in the hepatocytes of treated rats 2 and 16 h after treatment as compared to the current vehicle controls [Schulz, 2000].

There was no evidence of chromosomal damage in a bone-marrow assay in rats and mice following single oral doses of 50 to 5000 mg/kg of sodium thiosulfate [CAS No. 7772-98-7] (Litton Bionetics 1973).

Conclusion: CONCLUSION
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Genotoxic effects may be predominantly induced at high concentrations/doses of sulphites. The weight of evidence suggests that they are of clastogenic rather than of mutagenic nature.

In-vitro investigations into underlying mechanisms suggest a radical mechanism by which temperature, pH and oxygen availability determine the rate of bisulfite autoxidation via the formation of the intermediate sulfur-centered sulfur trioxide radical, SO3-·. This may occur spontaneously or through the action of the peroxidase/H2O2 system (Pagano et al. 1990).

Flag: Critical study for SIDS endpoint

21-FEB-2006 (119) (120) (93) (121) (122) (123) (80) (83) (124) (94) (87) (125) (126) (89) (127) (128) (129) (74) (130) (131) (132) (86) (81) (133) (73) (134) (135) (136) (117)

Type: Cytotoxicity

Remark: In a screening test, chemicals were tested for their cytotoxic activity on Saccharomyces cerevisiae cultures when in the logarithmic growth phase. The TS (2mg/ml) was

inhibitory on both, cell growth and cell division.

21-FEB-2006 (137)

Type: other: HET-CAM in vitro corrosion test

Remark: Non-corrosive

(138)

Type: other: Thiosulfate

Remark: Thiosulfate may be formed during metabolism and conversion of sodium dithionite.

This chemical is used in humans to lessen some of the side effects of cisplatin (a cancer medicine). It is also used in the emergency treatment of cyanide poisoning. Sodium thiosulfate is assumed to be intrinsically non-toxic

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Reliability: (4) not assignable
Secondary literature

Flag: Critical study for SIDS endpoint

(139)

Type: other: update June 2000 no new relevant data

6.1 Analytical Methods

Remark: The sodium dithionite content can most readily be determined iodometrically. It is dissolved in a neutral formaldehyde solution in a standard flask. The dithionite, which is sensitive to oxidation, reacts immediately on dissolving to give the more stable sodium hydroxymethanesulfinate, which can be titrated.

$$Na_2S_2O_4 + 2\ CH_2O + H_2O \rightarrow HOCH_2SO_2Na + HOCH_2SO_3Na$$
$$HOCH_2SO_2Na + 2\ I_2 + 2\ H_2O \rightarrow NaHSO_4 + 4\ HI + CH_2O$$

However, this method of analysis does not differentiate between dithionite and any thiosulfate which may be present. Since no acid is formed in the iodometric oxidation of thiosulfate, but is formed in the dithionite titration, the proportion of dithionite can be determined by subsequent titration of the solution with alkali.

Flag: non confidential, Critical study for SIDS endpoint

(5)

6.2 Detection and Identification

7.1 Methods Handling and Storing

Fire/Exp. Prot.: The product is self combustible but not explosive.

Remark: HANDLING

Ensure thorough ventilation of stores and work areas.
Breathing must be protected when Iarge quantities are decanted without Iocal exhaust ventilation. Do not open warm or swollen product containers. Remove persons to safety and alert fire brigade.
PERSONAL PROTECTIVE EQUIPMENT

Respiratory protection:
Breathing protection if dusts are formed. Particle filter EN 143 Type P1, low efficiency, (solid particles of inert substances). Breathing protection if gases/vapours are formed. Gas filter EN 141 Type E for acid inorganic gases/vapours (e.g. SO2, HCI). Self-contained breathing apparatus.

Hand protection:
Chemical resistant protective gloves (EN 374)
Suitable materials also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374): polyvinylchloride (PVC) - 0.7 mm coating thickness
butyI rubber (butyl) - 0.7 mm coating thickness
nitrile rubber (NBR) - 0.4 mm coating thickness
Supplementary note: The specifications are based on own tests, Iiterature data and information of glove manufacturers or are derived from similar substances by analogy. Due to many conditions (e.g. temperature) it must be considered, that the practical usage of a chemical-protective glove in practice may be much shorter than the permeation time determined in accordance to EN 374.
Manufacturer's directions for use shouId be observed because of great diversity of types.

Eye protection:
Tightly fitting safety goggles (splash goggles) (EN 166)

General safety and hygiene measures:
Avoid contact with the skin, eyes and clothing. Do not breathe dust. Wearing of closed work clothing is recommended. Handle in accordance with good industrial hygiene and safety practice. When using, do not eat, drink or smoke.
STORAGE

Segregate from acids. Segregate from oxidants.
Further information on storage conditions: Protect against moisture. Containers should be stored tightly sealed in a dry place. Keep away from heat.

Storage stability:
Large quantities of the product shouId not be kept in stockrooms with sprinkler instalIations due to a possible self inflammation by small quantities of water.
TRANSPORT INFORMATION

Land transport

ADR : Class 4.2
Packaging group II
UN-number 1384
Designation of goods SODIUM DITHIONITE (SODIUM HYDROSULPHITE).

RID : Class 4.2
Packaging group II
UN-number 1384
Designation of goods SODIUM DITHIONITE (SODIUM HYDROSULPHITE).

Inland waterway transport

ADNR : CIass 4.2
Item/Letter 13b)
Packaging group II
UN-number 1384
Designation of goods SODIUM DITHIONITE (SODIUM HYDROSULPHITE).

Sea transport

IMDG/GGVSee : CIass 4.2
Packaging group II
UN-number 1384
Marine pollutant NO
Exact technical name SODIUM DITHIONITE (SODIUM HYDROSULPHITE).

Air transport

ICAO/IATA : CIass 4.2
Packaging group II
UN-number 1384
Exact technical name SODIUM DITHIONITE (SODIUM HYDROSULPHITE).

Further information:
Specific national features of transport regulations must be observed. They are to be found in the shipping documents.

Flag: non confidential, Critical study for SIDS endpoint (1)

Remark: Above a certain dithionite concentration, mixtures in powder form decompose if subjected to prolonged exposure to high temperatures or come into contact with water. In the case of very finely divided products this decomposition can already occur at 80 °C. Product that is decomposing must be covered immediately with dry sand or powder extinguisher, or dissolved by shovelling into large quantities of water. If sodium dithionite packed in iron drums ignites, the SO2 gas produced must be allowed to escape by opening the container or drilling holes in the wall. The contents of the container are destroyed by throwing them into large quantities of water. The aqueous solution thus formed must be treated as it contains reducing agent and must be slowly introduced into an appropriate wastewater-treatment plant. Gloves and respiratory protection must be worn while extinguishing fires.
Commercial sodium dithionite (e.g., Hydrosulfit and various

product mixtures, which contain Hydrosulfit) are spontaneously combustible hazardous goods (Class 4.2, UN no. 1384), and are therefore subject to the corresponding transport regulations. Because of the danger of spontaneous ignition sodium dithionite and its mixtures must be stored dry and in a cool place. Storage or transport together with sodium nitrite, sodium nitrate, and ammonium nitrate is forbidden. Transport containers must always be kept closed. Product should only be removed in a dry area using dry equipment.

Flag: non confidential, Critical study for SIDS endpoint

(5)

7.2 Fire Guidance

Hazards: Self inflammation possible by spray waters or water in small quantities.
Contact with acids liberates toxic gases.

Prot. Equipment: Wear a self-contained breathing apparatus.

Ext. Medium: Water in copious quantities, dry extinguishing media, carbon dioxide, foam

Unsuit. Ex. Med.: water spray, water fog

Add. Information: Contaminated extinguishing water must be disposed of in accordance with official regulations.

Products arising: Sulphur dioxide can be released in case of fire.

Flag: non confidential, Critical study for SIDS endpoint

(1)

Remark: Sodium dithionite dihydrate is very sensitive toward atmospheric oxygen in the finely crystalline state. The heat of oxidation can lead to ignition. The anhydrous salt decomposes exothermically in air on prolonged heating above 90 °C.
Sodium dithionite in powder form can decompose in air on contact with a small amount of water with such intense heat formation that it burns with a flame.

Flag: non confidential, Critical study for SIDS endpoint

(5)

7.3 Emergency Measures

Type: other: general advive

Remark: Remove contaminated clothing.

Flag: non confidential, Critical study for SIDS endpoint

(1)

Type: injury to persons (skin)

Remark: Wash thoroughly with soap and water.

Flag: non confidential, Critical study for SIDS endpoint

(1)

Type: injury to persons (eye)

Remark: Immediately wash affected eyes for at least 15 minutes under running water with eyelids held open, consult an eye specialist.

Flag: non confidential, Critical study for SIDS endpoint
(1)

Type: injury to persons (oral)

Remark: Rinse mouth immediately and then drink plenty of water, seek medical attention.

Flag: non confidential, Critical study for SIDS endpoint
(1)

Type: injury to persons (inhalation)

Remark: After inhalation of decomposition products, remove the affected person to a source of fresh air and keep calm. Provide medical aid.

Flag: non confidential, Critical study for SIDS endpoint
(1)

Type: accidental spillage

Remark: Personal precautions:
Avoid contact with the skin, eyes and clothing. Use breathing apparatus if exposed to vapours/dust/aerosol.

Environmental precautions:
Do not discharge into drains/surface waters/groundwater. Do not discharge into the subsoil/soil.
Retain and dispose of contaminated wash water.

Methods for cleaning up or taking up:
For small amounts: Pick up in dry form. Dispose of absorbed material in accordance with regulations.
For large amounts: Pick up in dry form. Dispose of absorbed material in accordance with regulations.

Flag: non confidential, Critical study for SIDS endpoint
(1)

Type: other: Note to physician

Remark: Treatment: Treat according to symptoms (decontamination, vital functions), no known specific antidote.

Flag: non confidential, Critical study for SIDS endpoint
(1)

7.4 Possib. of Rendering Subst. Harmless

7.5 Waste Management

Memo: other: Must be dumped or incinerated in accordance with local regulations.

Flag: non confidential, Critical study for SIDS endpoint
(1)

7.6 Side-effects Detection

7.7 Substance Registered as Dangerous for Ground Water

7.8 Reactivity Towards Container Material

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